Kementerian Kesihatan Malaysia

HANDBOOK OF CHILDREN PALLIATIVE CARE MALAYSIA

2nd Edition

WALKING TOGETHER THROUGH LIFE-LIMITING ILLNESS

A COMPREHENSIVE GUIDE FOR HEALTHCARE PROVIDERS

HANDBOOK OF CHILDREN'S PALLIATIVE CARE MALAYSIA

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Association for Paediatric Palliative Medicine (APPM)

Formulary: 6th Edition 2024

Foreword by YB Minister of Health, Malaysia
2nd Edition of the Handbook of Children's Palliative Care Malaysia

The publication of the 2nd edition Handbook of Children's Palliative Care marked the continuous commitment of the our paediatric palliative care team in the delivery of comprehensive, compassionate care for children with life-limiting conditions across Malaysia. I would like to congratulate the editors and all who have contributed to the development of this handbook.

The Ministry of Health holds fast to the provision of excellent holistic and comprehensive care for patients, including children, with life-limiting illnesses, which is the core of the National Palliative Care Strategy 2019-2030.

In-line with World Health Organisation (WHO) recommendation - that all children has a right to access good palliative care, this handbook plays an important role to guide our healthcare providers nationwide with a structured, practical framework which is locally contextualised and evidence-based to integrate palliative principles into everyday paediatric care.

For our clinicians and healthcare teams, this book is more than a reference—it is a call to action. A call to integrate paediatric palliative care into our routine clinical practice; to advocate for systems that support continuity of care, including community and home-based services; and to uphold the dignity of every child and family in our care.

Thank you and keep up the good work for our children's benefit.

YB Datuk Seri Dr. Dzulkefly Ahmad
YB Minister of Health, Malaysia

Foreword by Director General of Health, Malaysia 2nd Edition of the Handbook of Children's Palliative Care Malaysia

I am pleased to present the second edition of the Handbook of Children's Palliative Care Malaysia, a testament to Malaysia's growing commitment to the care of children living with life-limiting conditions.

Since the first edition, we have made significant strides—notably the successful running of 15 National Training Programme of Paediatric Palliative Care Provider workshop (NTP), training over 270 level-2 paediatric palliative care providers nationwide based on the content of the handbook. This led to the initiation of paediatrician-led PPC services in a 24 Ministry of Health (MOH) hospitals. This achievement is a testament to our commitment to strengthening the healthcare workforce and expanding access to high-quality children's palliative services across all levels of care.

This updated edition incorporates new evidence, field experiences, and refined best practices to better support clinicians, service planners, and policy leaders. It reinforces the role of paediatric palliative care as a core component of universal health coverage, integrated from diagnosis through to bereavement support.

I congratulate and thank all contributors for their dedication. May this guidance continue to inspire and inform the development of services that honour the dignity, comfort, and holistic needs of every child and family in our care.

Datuk Dr Mahathar bin Abd Wahab
Director-General of Health
Ministry of Health Malaysia

PREFACE

Palliative care for children is an approach to improve the quality of life of children with life-limiting illnesses and their family, by preventing and relieving suffering. Healthcare services for children would be incomplete without provision of paediatric palliative care (PPC) services. Unfortunately, there is still a great unmet need for PPC in Malaysia.

PPC is relevant to various life-limiting diseases in children including perinatal conditions, chromosomal abnormalities, congenital malformations and deformations, malignancies and neurological disorders. An estimated 80,000 Malaysian children will require PPC at some point of their life, based on a prevalence analysis of conditions which warrant PPC support. Of these, nearly a third will require specialist PPC support. However, PPC services in Malaysia are still far from adequate to meet these needs.

While palliative care services for adults have been developing steadily in Malaysia since the 1990s, PPC is still lagging far behind. Many regions, especially rural areas, still do not have access to PPC services. PPC services in Malaysia have been championed by individual paediatricians in hospitals since 2008. To date, most PPC services are provided by individual paediatricians in public hospitals and by non-governmental organisations (NGOs) in the community. Sadly, after a decade, PPC provision has yet to achieve nationwide coverage, even in urban areas.

Different levels of PPC can be provided by different healthcare professionals, including general paediatricians, family physicians, general practitioners, and paediatric nurses. All healthcare professionals who work with children should receive basic training to provide level I PPC. Meanwhile, specialist doctors who frequently care for children with serious life-threatening conditions, such as oncologists, cardiologists, intensivists and neonatologists, should receive intermediate-level training for level II PPC. PPC training for these healthcare professionals would benefit from a practical and concise manual for PPC to guide them in their day-to-day practice.

This handbook was written with the combined experience and expertise of more than thirty contributors, consisting of paediatric palliative paediatricians, senior paediatricians, family medicine specialists, nurses, and allied health workers. These contributors were involved in providing palliative care for their patients and family in their respective settings, utilising available but limited resources. Work on this handbook, which began in April 2019, has been carefully reviewed and adapted to our local culture and healthcare settings.

This handbook is an essential tool for the implementation of the National Palliative Care Policy and Strategic Plan 2019-2030. We hope that this handbook will aid Malaysia to achieve the three main goals for PPC in the National Policy which are:

1. To expand PPC services in all major hospitals by incorporating PPC into comprehensive paediatric care.

2. To achieve seamless and holistic transition of PPC from hospital to community and home.
3. To systematically establish community-based PPC services.

We would like to take this opportunity to thank all the people involved in this handbook writing, as well as Dr Hishamshah bin Mohd Ibrahim (ex-National Advisor for Paediatrics) and the Medical Development Division, Ministry of Health, Malaysia, for their invaluable support.

We look forward to seeing Paediatric Palliative Care develop further to meet the needs of Malaysian children.

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LIST OF ABBREVIATIONS

AADC	Aromatic l-amino acid decarboxylase
ACP	Advanced care plan
ACT	Association of Children's Palliative Care
ADLs	Activity of Daily Living
AED	Anti- epileptic Drug
AML	Acute Myeloid Leukemia
CAUTI	Catheter-associated urinary tract infection
CF	Compassion fatigue
CFU	Colony-forming unit
CN	Cranial nerve
CSCI	Continuous Subcutaneous Infusion
CTZ	Chemoreceptor Trigger Zone
DIVC	Disseminated Intravascular Coagulation
FFP	Fresh frozen plasma
FMS	Family medicine specialist
GABA	Gamma aminobutyric acid
GERD	Gastro-oesophageal reflux disease
GI	Gastrointestinal
GLUT 1	Glucose Transporter Type 1
GMFCS	Gross Motor Function Classification System
ICP	Intra-cranial pressure
ID	Intellectual Disability
JKM	Jabatan Kebajikan Masyarakat
JPA	Jabatan Perkhidmatan Awam
LTOT	Long-term oxygen therapy
MACAS	Malaysian Children Aid Society
MAKNA	Majlis Kanser Nasional
MAPPAC	Malaysian Association of Paediatric Palliative Care
MAS	Modified Ashworth Scale
MDT	Multidisciplinary team
MSAS	Memorial System Assessment Scale
NGO	Non -government organization
NICU	Neonatal Intensive Care Unit

NIV	Non-invasive ventilation
NMDA receptor	N-Methyl-D Aspartate receptor
NRD	National Registration Department
OKU	Orang kurang upaya / persons with disabilities
OT	Occupational therapist
OT	Operating theatre
PaPaS	Paediatric Palliative Screening
PCC	Percutaneous cervical cordotomy
PICU	Paediatric Intensive Care Unit
PLAN	Paediatric Longitudinal Assessment of Needs
PPC	Paediatric Palliative Care
ProQOL	Professional Quality of Life (c)
PT	Physiotherapy
RCPCH	Royal College of Paediatrics and Child Health
ROM	Range of movement
SCP	Symptom Care Plan
SLT	Speech and language therapy
SOP	Standard operating procedure
SPUB	Sistem Pendispensan Ubat Bersepadu / Integrated Drug Dispensing System
STS	Secondary traumatic stress
TBP	Tabung Bantuan Perubatan / Medical Aid Fund
TCE	Trans-catheter chemo-embolisation
UTI	Urinary tract infection
WHO	World Health Organisation

Module 1

Introduction to Paediatric Palliative Care

- Who can provide paediatric palliative care?
- Categories and disease trajectory of life-threatening and life limiting condition (ACT/RCPCH categories)
- Referral to level II and above paediatric palliative care
- Introducing Paediatric Palliative Care to family
- Multidisciplinary team (MDT) in PPC
- Phase of Illness for Paediatric Palliative Care
- Paediatric Longitudinal Assessment of Needs (PLAN) Guidelines
- Revised PaPaS scale

Module 1: Introduction to Paediatric Palliative Care

World Health Organisation (WHO) definition of palliative care for children [1]

Palliative care for children represents a special, albeit closely related field to adult palliative care. The World Health Organization (WHO) defines palliative care appropriate for children as:

"The active total care of a child's body, mind and spirit in the prevention and relief of suffering associated with life-threatening illness and involves giving support to the family."

The principles of palliation apply to all chronic paediatric disorders. It begins when the illness is diagnosed and continues regardless of whether the child receives treatment directed at the disease. Health providers must evaluate and alleviate the child's physical, psychological, social and spiritual distress.

Effective palliative care requires a broad multidisciplinary approach that includes the family and utilizes available community resources; it can be successfully implemented even if resources are limited.

It can be provided in tertiary care facilities, in community health centres and at home.

The 5 W of Paediatric Palliative Care
Whole Person Care
Whole Family Care
Whole Process of the illness
Whole Team Care
Whole Community Care

This whole concept of care can be summarised with the 5W of Paediatric Palliative Care.

Why is palliative care in children different from adult palliative care? [2]

Adult Palliative Care	Paediatric Palliative Care
1. **Goal**: Both aim to relieve pain and other symptoms associated with serious illnesses. 2. **Team Approach**: Both involve a multidisciplinary team, including doctors, nurses, social workers, and other healthcare professionals. 3. **Timing**: Palliative care can be provided alongside curative treatments at any stage of the illness. 3. **Support**: Both provide emotional, psychological, and spiritual support to patients and their families.	
Conditions: Commonly deals with illnesses like cancer and end stage organ disease e.g. cardiac, renal, respiratory and some neurodegenerative diseases. Not as many rare diseases.	**Conditions**: While some conditions overlap with those in adult palliative care, many chronic non-communicable diseases in children are congenital and may have genetic causes. The natural history, prognosis, and life expectancy of these conditions can be unclear, especially for rarer diseases. *Possibility of changing from palliative care initiative to rehabilitation care in patients with illness that improved over time.*
Decision-Making: Adults typically make their own medical decisions, often with input from family members.	**Decision-Making**: Children's status as minors means decision-making is usually in the hands of parents/legal guardians. The level of maturity required for making decisions evolves as the child grows, with considerations of the child's wishes and rights. Decisions are often made based on discussions among parents, family members, and healthcare professionals about what is in the best interest of the child and the family.
Duration: Most conditions have a shorter prognosis, usually between weeks to months.	**Duration**: The survival time scale can be highly variable. Therefore, care can be delivered over a longer period, sometimes for months or years.
Developmental Milestones: Usually not a factor for consideration	**Developmental Milestones**: Palliative care needs change as the child grows, depending on developmental milestones. These needs involve age-appropriate information, recreation/play, education, and coping mechanisms.

Special consideration in Paediatric Palliative Care

- Familial Inheritance: Some conditions may be familial, affecting other siblings as well.
- Parental Role: Parents are the main decision-makers and caregivers.
- Education and Play: Education and play are integral parts of care.
- Ongoing Development: Care must consider the ongoing physical, emotional, and cognitive development of the child.

Palliative care needs of children in Malaysia

To date, Malaysia does not have a registry of children who suffer from 'life-limiting conditions'. The World Health Organization estimates that 63 out of every 100,000 children aged less than 15 years will require palliative care annually.[1]

From a global cross-sectional analysis of prevalence, it is estimated that about 80,000 (0.29%) Malaysian children would need some form of palliative care and 28.5 per 10 000 population aged 0 to 18 years require specialised palliative care.[3] Specialised palliative care provides full time palliative services which includes complex symptom management, communication regarding goals of care, coordinating multidisciplinary team meetings, terminal and end-of-life care, transition care, parental support for grief and bereavement.

Paediatric palliative care is relevant for children from the perinatal period until the age of 18 years. In 2023, the two commonest causes of death for the under-five age group are conditions originating in the perinatal period (34.2%) and congenital malformations, namely deformations and chromosomal abnormalities (25.3%). This highlights the need for perinatal palliative care services in our country. (Source: Dept of Statistics Malaysia, Oct 2023)

Paediatric palliative care is relevant for children from the perinatal period until the age of 18 years. In 2016, the two commonest causes of death for the under five age group are conditions originating in the perinatal period and congenital malformations, namely deformations (35.0%) and chromosomal abnormalities (27.2%).[4] This highlights the need for perinatal palliative care services in our country.

Beyond the neonatal period, the commonest categories of children that have palliative care needs are those with neurological disorders and neoplasms.[5]

All these children need a holistic approach to meet their needs in all aspects (physical, psychosocial, spiritual and emotional). Bereaved parents of children with life-limiting illnesses in Malaysia perceived inadequate symptom control for their children but there was also poor communication and lack of anticipatory guidance in care.[6]

Many Malaysian healthcare providers lack knowledge and understanding of palliative care, with 79% citing the lack of accessible palliative care services as the biggest barrier for referral.[7] Thus, health care providers need to be trained to manage this special group of children.

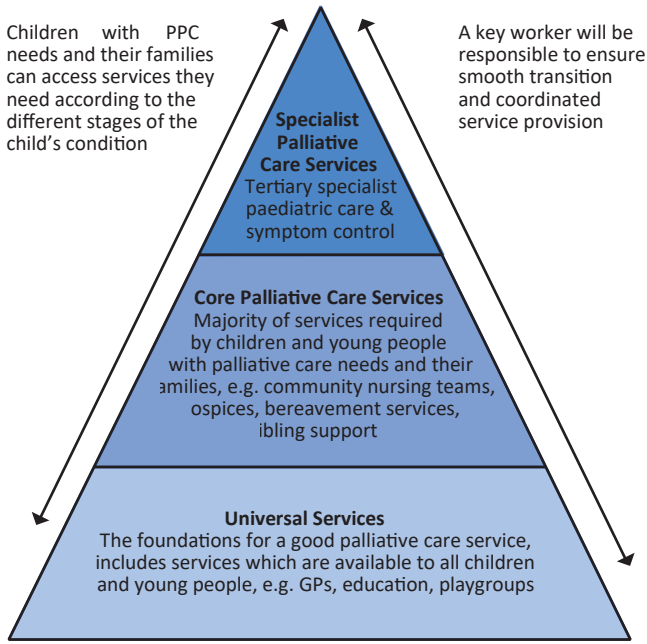
Who can provide paediatric palliative care (PPC)?

Palliative care should be part of comprehensive paediatric care.

Level	Provision of PPC
I	Basic PPC services can be provided by paediatricians, general practitioners, family medicine specialists and paediatric nurses with basic training in PPC principles.
II	Specialist doctors who frequently care for children with serious or life-threatening conditions, such as oncologists, cardiologists, intensivists, neonatologists, and general paediatricians. They should receive intermediate level training in PPC.
III	PPC specialist and PPC teams. They should be involved if a child or young person has unresolved distressing symptoms especially when they approach the end of life.

Levels of paediatric palliative care[8]

Who are the children who need palliative care?[9]



Children who need palliative care are children with the following conditions:

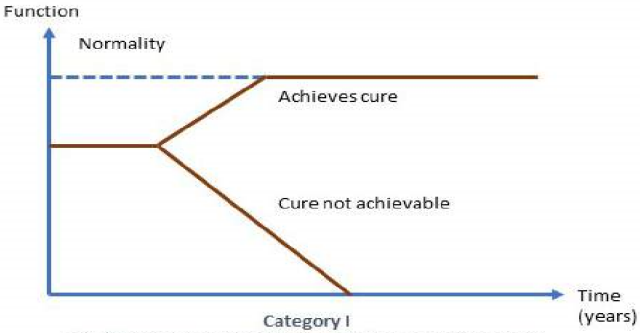
- **Life-threatening conditions:** Illnesses or conditions with a high risk of dying for children or young adults, and for which medical treatment may cure but may also fail, resulting in death.
- **Life-limiting conditions:** Illnesses or conditions for which there is no cure, and which are extremely likely to result in death at some point in time during childhood or young adulthood.

Categories and disease trajectory of life-threatening and life-limiting condition (ACT/RCPCH categories)[10]

Category	Definition	Palliative care needs
1	Life-threatening conditions for which curative treatment may be feasible but can fail. Access to palliative care services may be necessary when treatment fails or during an acute crisis, irrespective of the duration of threat to life. On reaching longterm remission or following successful curative treatment there is no longer a need for palliative care services.	Intensive symptom management and psychosocial support beginning from diagnosis
	Example: Cancer, irreversible organ failures of heart, liver, kidney.	
2	Conditions when premature death is inevitable. There may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal activities.	Requires longer term palliative care support, beginning with rehabilitation and caregiver support, and leading to symptom management and end-of-life care as the disease progresses.
	Example: Cystic fibrosis, Duchenne muscular dystrophy.	
3	Progressive conditions without curative treatment options. Treatment is exclusively palliative and may commonly extend over many years.	Symptoms will change over time. Goals of care are more focused on symptom management rather than rehabilitation.
	Example: Batten disease, mucopolysaccharidoses.	
4	Irreversible but non-progressive conditions causing severe disability, leading to susceptibility to health complications and likelihood of premature death.	Caregiver training, especially home care, is essential in the beginning phase. Provision of caregiver support, nursing care and respite care is the main need for this category.
	Example: Severe cerebral palsy (GMFCS level VI or level V), multiple disabilities such as following brain or spinal cord injury, complex health care needs, high risk of an unpredictable life-threatening event or episode.	

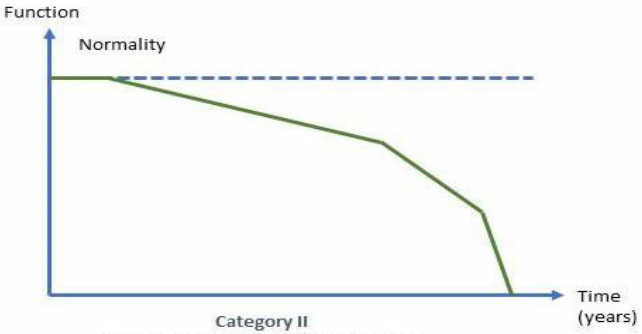
*GMFCS = Gross motor function classification system

Disease trajectories based on ACT/RCPCH categories



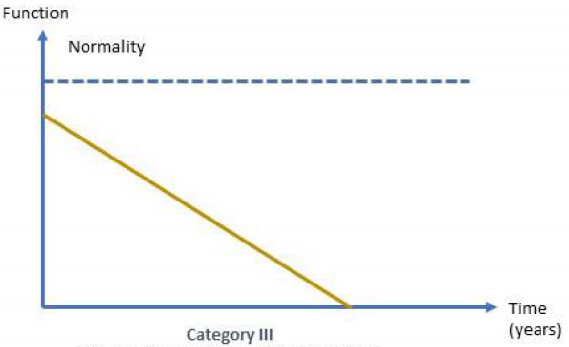
Category I

Life-threatening conditions for which curative treatment may be feasible but can fail. Access to palliative care services may be necessary when treatment fails or during an acute crisis, irrespective of the duration of threat to life. On reaching long-term remission or following successful curative treatment there is no longer a need for palliative care services.

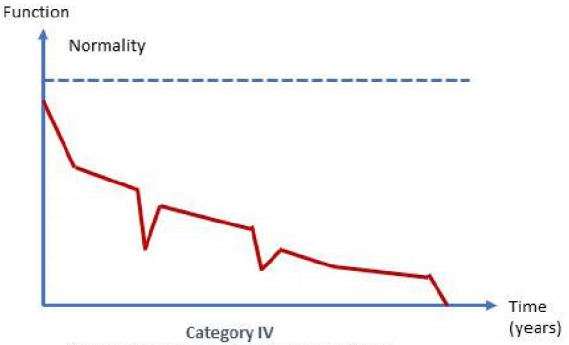


Category II

Conditions when premature death is inevitable. There may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal activities.



Category III
Progressive conditions without curative treatment options. Treatment is exclusively palliative and may commonly extend over many years.



Category IV
Irreversible but non-progressive conditions causing severe disability, leading to susceptibility to health complications and likelihood of premature death..

The scope of paediatric palliative care

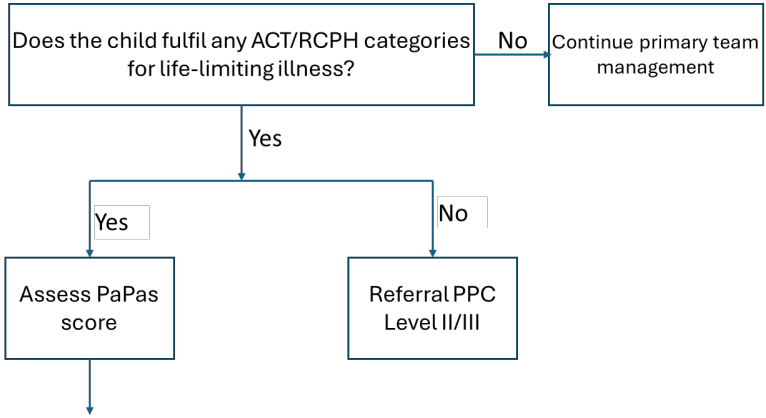
Paediatric palliative care encompasses:

- Supportive care and symptom management during curative treatment or life-prolonging treatment
- Symptom management and optimisation of quality of life when curative treatment is unavailable or is not an option
- End-of-life care
- Grief and bereavement support

Paediatric palliative care may go hand-in-hand alongside curative treatment and rehabilitation, with varying levels of involvement at different stages of illnesses.

Referral to level II and above paediatric palliative care

Referral to PPC should start at diagnosis, with the level of care tailored to the patient and family's needs. The algorithm helps decide if a referral to the PPC team is necessary. See Appendix for the PaPaS score.



PaPas Score	Action	Provider	Level of PPC	Priority of Care
0-9	Evaluation	Primary team	Level I-II	Curative treatment
10-14	Explain goals of PPC	Primary team	Level I-II	Life- prolonging treatment with supportive symptom management
15-24	Prepare start of PPC	Primary team with PPC Consultation	Level II-III	Life- prolonging treatment with supportive symptom management
25 and above	Start PPC	Primary team with PPC Consultation	Level II-III	Symptom management, psychosocial care and possible end-of- life care

Introducing Paediatric Palliative Care (PPC) to family

The following are useful phrases when communicating with family members to introduce the role of paediatric palliative care:

- As an extra layer of support, besides the primary team.
- To lessen a child's symptoms that are bothering him/her.
- To provide family support (physical, psychosocial and spiritual).

"I see that this can be a difficult time for your family.
We are here to support you and your child in every way possible."

"Palliative care is about improving the quality of life for your child
and your family, focusing on comfort and support."

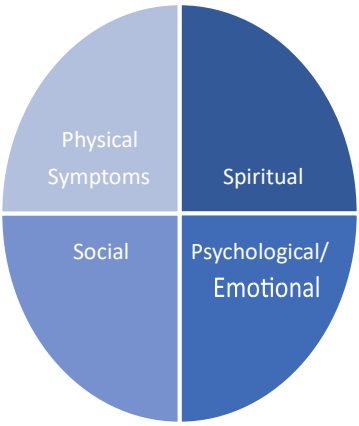
"Children's palliative care involves managing symptoms
and providing emotional, social, and spiritual support."

"Our goal is to help your child live as well as possible,
for as long as possible."

It is also useful to integrate paediatric palliative care into current services, such as clinics, inpatient management, home visits and policies.

Seamless provision of PPC services will reduce family apprehension towards the perception of PPC as loss of hope. Instead it should promote hope for better quality of life and prevent the perception of abandonment.

Whole person assessment
Domains of assessment

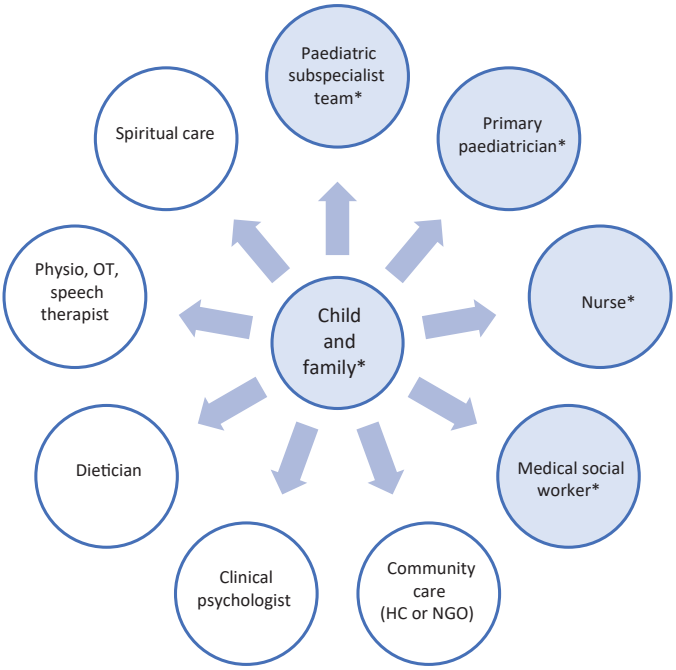


It is important to ensure that holistic assessment (bio-psychosocial-spiritual) of the child's care needs are done as care planning and reviewed regularly as the child's condition progresses.

a) General holistic assessment
b) Comprehensive assessment using validated tools e.g. Memorial Symptom Assessment Scale (MSAS) – there are versions for children of different ages.
c) Specific symptom assessment tools, e.g. pain scale, dyspnoea scale, functional disability inventory.

Multidisciplinary team (MDT) in PPC

Children with life-limiting conditions have simple to complex needs which change across the disease trajectory. The goals of care for every individual child across different domains are complex. Various healthcare teams collaborate to address the complex and diverse needs of children receiving palliative care. These teams are interconnected and interdependent. The coordinated multidisciplinary team (MDT) approach is vital in tailoring for specific individual needs and optimising the use of available resources.



Core members of the multi-disciplinary team (MDT) HC=home care

The extended multidisciplinary team (MDT)

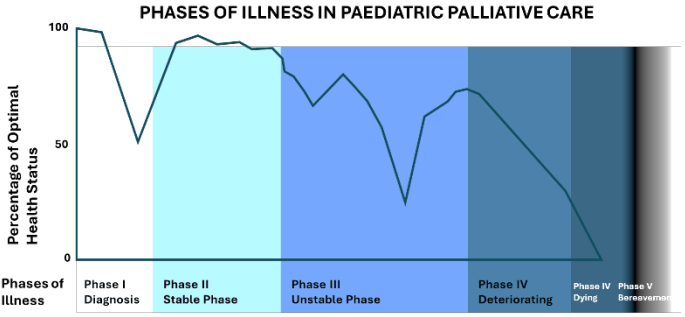
Members of the MDT meet not just the child and caregivers regularly to assess needs but also with the rest of the team members to formulate a care plan to address those needs. This enhances collaborative decision-making and sets out agreed goals of care. After the plan is executed, the outcomes should be monitored, and the care plan revised or updated as necessary.

An example of a structured MDT assessment is shown below in the form of the Paediatric Longitudinal Assessment of Needs (P.L.A.N.) Guidelines.

Multidisciplinary Team in PPC & Objectives

Team	Roles & Objective
Care Coordinator/ or coordinating team Physician/ Nurse	● Responsible for the coordination, continuity, and quality of PPC ● Bridge the gap between home, health clinic and hospital ● Organise regular MDT conference/ discussion – with patients/ parents to maximise exchange of knowledge related to the patient's care ● Formulate treatment goals ● Determine the roles and activities of each team
Occupational Therapist	● Optimise quality of life and well-being of clients through engagement and participation in daily routine activities, play, education, social interactions, and leisure, within the limit caused by the disease and its treatment to the patient ● Educate and empower patient and family to learn different assisted living techniques with and without the help of medical instruments
Physiotherapist	● Assist children to achieve maximum physical, social or vocational function ● Reduce suffering and improve the quality of life of both the child and his/her family.
Dietitian	● Identify and address nutritional factors that affect the patient's quality of life ● Provide nutritional support for individualized dietary needs without compromising patient's safety or comfort.
Clinical Psychologist/ Counsellor	● Assist in psychological assessment including assessment of patient and parent's understanding of the disease, coping mechanism, and their spiritual needs. ● Provide psychological therapy including cognitive behavioural therapy, play therapy, art therapy and counselling.
Community care and Hospice team	● Assist with transition to home, symptom management, respite care, end of life care, grief and bereavement for patient and family at home
Play Therapist	● Provide emotional and psychological care through facilitated communication and play
Spiritual care personnel	● Provide spiritual support, to allow positive emotional wellbeing and peace

Phase of Illness for Paediatric Palliative Care



Phase I: Diagnosis (at Ward/ ICU/ Home)

Phase Definition	Care Objective/ Issue	Strategies
● After breaking the diagnosis of Life-limiting illness to parents ● While still actively working up the diagnosis/ Active curative treatment	● Correct understanding of PPC Care concept ● Facilitate complex decision-making process ● Active Symptom Management ● Stress and Anxiety Management ● Social Function Readjustment ● Financial Crisis Support	● Memorial Symptom Assessment Score ● PPC Introduction ● Family / MDT Meeting in ward ● MDT clinic assessment ● Opioid /Drugs Counselling by Pharmacist ● Transition Home Process ● Symptom Care Plan ○ Police Letter ○ Consumable Item list ○ Transition Checklist ○ Hospice Referral ○ Nursing/Mobility/ Transfer Skills ○ Letter to employer ● Registration for Caregiver Education Workshop ● Mindfulness and Relaxation for patients and caregivers ● Introduction of hospice team and key contact person ● Home assessment by hospice/OT team ● Home nursing and medical equipment guidance by hospice team ● Referral to social welfare/ OKU/ NGO

Phase II: Stable Phase (at Clinic/ Ward/ Home)

Phase Definition	Care Objective/ Issue	Strategies

• Symptoms are controlled
• No new issues
• No recurrent hospital admission
	• Continue life prolonging treatment from primary team
	• To enhance quality of life and function
	• To maintain good symptom control
	• To facilitate hope of patient and caregivers (hope for better life)
		• Continue symptom Management & Compliance to medication
		• Medical equipment Review
		• Initiate Advance Care Plan Discussion
		• Communication with children
		• Child's Wish referral
		• Intensive Inpatient rehabilitation.
		• Look into schooling and learning options
		• Home visit by Hospice and Physiotherapist
		• Registration for Teenager Group Therapy
		• Sibling supportive programme at hospice
		• Health Prevention
		  ○ Dental check-up 6 monthly
		  ○ Immunization
		• Parent's job skill training (self-empowerment) at hospice
		• FCAT (Caregiver competency assessment)
		• Parents Support Group

Phase III: Unstable Phase (at ED/ Ward/ HDU/ Home)

Phase Definition	Care Objective/ Issue	Strategies
• Many emergency Symptoms need urgent intervention • New problems not anticipated before by caregivers • Rapid increase in severity of previous issues/ problems • Changes in quality of care of caregivers	• To facilitate communication with interdisciplinary teams in hospital and hospice • To reduce caregiver's burden and review their coping strategies • To support the caregiving process at home/hospital • Intensify symptom management process	• Home early symptom intervention • Zarith Burden Score • Family Conference (if conflict present) • Home Respite Care • Caregiver counselling • Reduce / Combine clinic's appointment • Renew symptom care plan • Facilitate hospital / ED admission • Phone Symptom Support • Regular home visit • Relaxation and Mindfulness for patient and caregiver

Phase IV: Deteriorating (at ED/ Ward/ Home)

Phase Definition	Care Objective/ Issue	Strategies
● Expected gradual deterioration in function or more severe symptoms ● Patient overall functional status decline ● Anticipated gradual worsening distress of symptom that impact the care	● Preparation for end-of-life care ● Mainly focus on good symptom control and comfort	● Communication with parents/ patient about end-of-life care ● Revise unhelpful medicine and equipment ● Recruit more family support ● Recruit more community supports ● Anticipatory grief facilitation

Phase V: Dying (Ward/Home)

Phase Definition	Care Objective/ Issue	Strategies
● Death is likely within days	● Good end of life care ● Provide good environment for family to be together	● Convert oral to IV/SC / Patch medication ● Activate 24 hours symptom on-call system ● Regular home visit Transfer single room in hospital ● Memory making (eg footprint) ● Plan for bereavement/ funeral

Phase VI: Deceased /Bereavement (Clinic/ Home)

Phase Definition	Care Objective/ Issue	Strategies
● Patient has died ● Caregiver in bereavement support	● Provide bereavement assessment and support for caregivers ● Facilitate grief expression and new meaningful searching	● 6 weeks phone call or home visit / bereavement clinic review ● Grief brochure and memory box ● Death café / Parent grief group support

Paediatric Longitudinal Assessment of Needs (PLAN) Guidelines

No	Domain	Issues
1	Physical / nursing care	Pain Fever Diarrhoea or Constipation Nausea or vomiting Bladder/urinary problems Wounds or pressure sores Cough Itch Swelling of arms, legs or abdomen (oedema) Breathing-related problems Insomnia / Sleeping problems Gastro-intestinal problems Diet and nutrition
2	Psycho-emotional	Acceptance, coming to terms with the disease Stress Depression, negative emotions Anticipatory grief Guilt and shame Anxiety and anger Fears of physical suffering/pain, death, treatment, abandonment, uncertainties of the future Loss of emotional control Changed body image and its associated emotions Overwhelmed by decision-making family/patient) Fulfilling patient's last wishes Bereavement support (family)

No	Domain	Issues
3	Practical / Financial	Equipment related: BIPAP, CPAP, suctioning, ventilator, O2 concentrator/cylinder Daily needs- Nutrition, Diapers Special beds (e.g hospital bed), ripple mattress Respite care Transportation (clinic, hospital, school) Extra family expenditure due to the illness Reduced family income due to the illness
4	Social / Family	Spouse Parent-child Extended family relationships (grandparents, etc) Healthcare team in the hospital Healthcare team in community School Friendship
5	Spirituality/ Existential	Sense of playing a useful role Ability to be present for others' needs Loss of faith - God or religion The meaning of life and death Loss connection with the self (i.e. self acceptance, self-esteem)
6	Legal / Ethical	Legal matters (last will and testament, insurance etc.) Ethical decision making / dilemmas

Adapted from STAR PALS (Singapore HCA Hospice Care)

Appendix

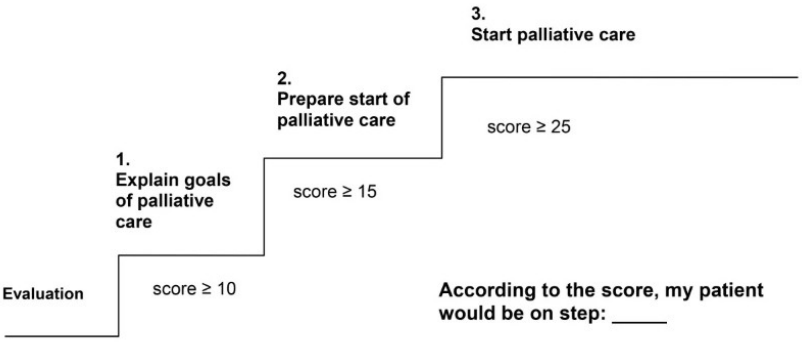
Revised PaPaS scale[11,12]

Domain 1: Trajectory of disease and impact on daily activities of the child			
1.1.1	With reference to the past 3 months, the disease trajectory of the child, in comparison with the child's own baseline, is…	…Stable	0
		…Stable, but slowly deteriorating	1
		…Unstable with slow deterioration	2
		…Unstable with significant deterioration (Please skip 1.1.2)	4
1.1.2	With reference to the past 3 months, the impact of condition on daily activities of the child, in comparison with the child's own baseline.	No impact	0
		Daily activities are impacted/ restricted	1
		Daily activities are severely impacted/restricted	2
1.2	In the past 6 months, there was a more than 50% increase in unplanned hospital admissions *(compared to previous periods)*	No	0
		Yes	3
Domain 2: Expected outcome of treatment directed at the disease and burden of treatment			
2.1	Treatment directed at the disease, even if not administered… (does not include treatment of diseaserelated complications, such as pain, dyspnea or fatigue)	…is curative.	0
		…controls disease and prolongs life with good quality of life.	1
		…does not cure or control but has a positive effect on quality of life.	2
		…does not control and has no effect on quality of life.	4

2.2	Burden of treatment, including both disease directed and symptom directed treatments. (consider frequency and skills involved; e.g. side effects, hospital stay, additional tasks for patients/caregivers)	No/minimal burden OR no treatment is planned	0 ☐
		Low level of burden (e.g. simple oral medication or diet modification)	1 ☐
		Medium level of burden (e.g. feeding tubes, catheters, medications with adverse effects)	2 ☐
		High level of burden (e.g. hospitalization, tracheostomy, BiPAP/C-PAP, PICC line, frequent suctioning)	4 ☐

Domain 3: Symptom and problem burden			
3.1.1	Symptom intensity over the past 3 months (consider unplanned hospitalization or outpatient visits, symptom crises)	Patient is asymptomatic (Please skip 3.1.2)	0 ☐
		Symptom(s) are mild	1 ☐
		Symptom(s) are moderate	2 ☐
		Symptom(s) are severe (Please skip 3.1.2)	4 ☐
3.1.2	Difficulty of symptom control over the past 3 months (consider unplanned hospitalization or outpatient visits, symptom crises)	Symptom(s) are easy to control	0 ☐
		Symptom(s) are controllable	1 ☐
		Symptom(s) are difficult to control	2 ☐
3.2	Psychological distress of patient related to symptoms	Absent	0 ☐
		Mild	1 ☐
		Moderate	2 ☐
		Significant	4 ☐

3.3	Psychological distress of parents or family related to symptoms and suffering of the child	Absent	0	
		Mild	1	
		Moderate	2	
		Significant	4	
Domain 4: Preferences of Health Professional				
4.1	Patient/parents wish to receive palliative care or formulate needs that are best met by palliative care.	No	0	
		Yes (Please skip 4.2)	4	
4.2	You or your team feel that the patient would benefit from palliative care.	No	0	
		Yes (Please skip 4.2)	4	
Domain 5: Estimated Life Expectancy				
		1 – 2 years	1	
		3 months to a year (Please skip 5.2)	3	
		Less than 3 months (Please skip 5.2)	4	
5.2	Would you be surprised if this child died in 6 months' time?	Yes	0	
		No	2	
		Total		
	Decision			



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Module 2

Symptom Management

- Pain
- Cardiorespiratory symptoms: Breathlessness, Non-invasive ventilation, chest pain, cough
- Neurological symptoms: Dystonia & Spasticity, Seizures, Insomnia, Anxiety, Drooling, Autonomic Dysfunction
- Renal failure: Uraemia
- Haematological problems: Anaemia, bleeding
- Gastrointestinal symptoms: Nausea and vomiting, constipation, diarrhoea, anorexia-cachexia
- Perinatal palliative care pathway
- Nursing care: Oral care, tube feeding, gastrostomy tube care, tracheostomy care, urinary care, bed bound patients
- Multidisciplinary paediatric palliative care
- Communication Skills for Supporting the Child and Family
- Caregiver and healthcare provider well being
- Spiritual Care

Module 2: Symptom Management

Pain Definition

Pain is any unpleasant sensory or emotional experience associated with tissue damage or described by the patient in those terms, e.g. burning, stabbing pain. [1]

Concept of total pain

Pain interacts with other forms of distress and contributes to overall suffering in patients.

Pain is multi-dimensional; it is helpful to think in terms of total pain, encompassing physical, psychological, social and spiritual aspects of suffering. [2]

Physical Pain	Psychological Pain
• Nociceptive pain • Neuropathic pain • Aggravated by other symptoms (e.g. nausea, fatigue) • Adverse effects of treatment (e.g. chemotherapy) • Concurrent multiple causes of pain	• Anger • Anxiety • Sad • Loneliness • Fear • Previous experience of pain
Spiritual Pain	**Social Pain**
• Hopelessness • Loss of faith • Fear of unknown • Anger at fate / higher power • Personal image	• Dependency on family members • Discontinuation of learning in school • Family conflict • Isolation from peers

Pathophysiology of pain

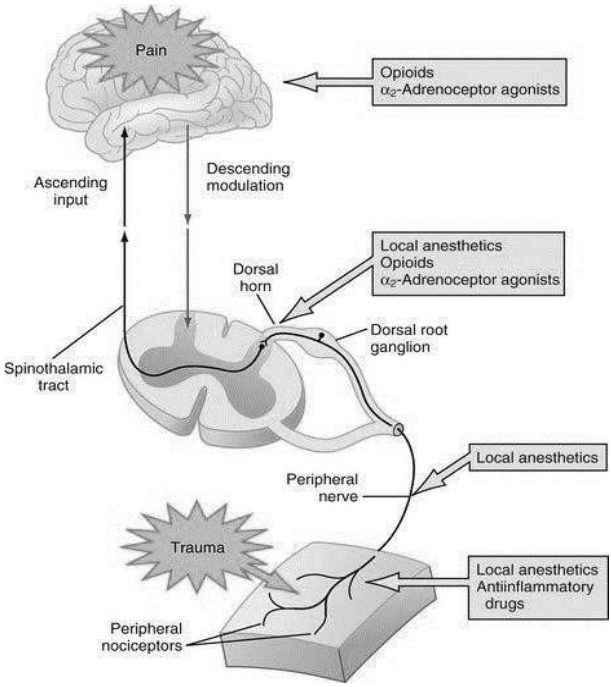
There are multiple pathways involved in pain perception:

a) Ascending myelinated and unmyelinated fibres

The pathway where pain stimulus is carried from the peripheral nociceptors to he brain

b) Descending inhibitory pathways for pain modulation

The pathway which controls the quality and perceived severity of the pain



Ascending and descending pain pathway and its analgesic[3]

Classification of pain

There are various classifications of pain.

- **Pathophysiological mechanism of pain** (nociceptive or neuropathic)
- **Duration of pain** (chronic or acute, breakthrough pain)
- **Aetiology** (cancer or non-cancer)
- **Anatomic location of pain** (myofascial, rheumatic, skeletal, neurological and vascular)

Nociceptive pain	
• Originates from mechanical, chemical or thermal damage to body tissue • Subdivided into somatic / visceral pain • Involve activation of nociceptors	
Somatic pain	Nociceptors in either surface tissues (skin, mucosa of mouth, nose, urethra, anus) Superficial somatic pain - sharp and localised Deep somatic pain - dull and aching
Visceral pain	Nociceptors located in the visceral organs (e.g. gut, ureters) Diffuse, difficult to localise May have referred pain e.g. diaphragm irritation referred to right shoulder tip
Neuropathic pain	
• Results from abnormal nerve function e.g. nerve damage by drugs, impingement by tumours, or physical damage to the nerve itself. • **Allodynia** – pain caused by stimulus which usually does not cause pain e.g. light touch. • **Hyperalgesia** – increased or excessive pain from a stimulus which can cause pain • Examples of neuropathic pain: spinal cord metastases causing pain over related somatosensory area, phantom pain after limb amputation	

Causes of pain

In palliative care, pain can generally be divided into cancer or noncancer pain.

Cancer pain	Non-cancer pain
• Pain directly associated with tumour (tumour infiltration, bone metastasis) • Pain associated with cancer therapy (chemotherapy, surgery or radiation) • Pain due to cancer debility (decubitus)	• Arthritis • Metabolic neuropathies • Chest pain • Post-traumatic injury • Post-stroke pain • Immobility • Abdominal pain • Peripheral vascular disease • Decubitus ulcers and other skin disorders

Principles of pain assessment (Q.U.E.S.T.T.)

The following are principles to guide pain assessment in a child[4]

Question the parent/ child

Use appropriate pain rating scale

Evaluate behaviour / physiologic change

Secure family involvement

Take holistic cause of pain into account

Take action and evaluate results

Question the parent/ child	"Does it hurt or is it sore anywhere?" "Can you show me where it hurts/is sore?" Use a body chart or a doll here. "Does it hurt/is it sore anywhere else?" "When did the hurt/pain start?" "Does anything make it worse?"
Use appropriate pain rating scale	According to pain assessment tool
Evaluate behaviour / physiologic change	According to pain assessment tool
Secure family involvement	Sensitise the parents to be aware of and to report pain
Take holistic cause of pain into account	Look into physical, psychological, social and spiritual causes
Take action and evaluate result	According to cause of pain

Pain Assessment Tools

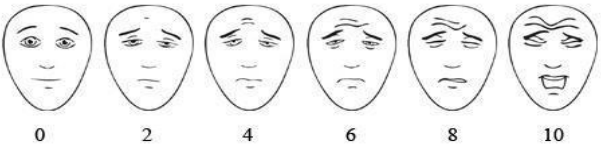
There are various tools that can be used to assess severity of pain.

Tools are chosen based on the child's developmental age and verbal ability.

Pain Assessment Tool	Age Group/Population
FLACC Scale	1 month to 4 years, Children who are unable to verbalize pain
FACES Pain Scale-Revised (IASP)	Most children aged 4 – 7 years old, Picture-based scale where the child selects 1 to 6 faces to represent their pain experience
Numerical Scale (MOH Pain Scale)	Children who understand the concept of order and number (typically 7 years and older)
Revised FLACC	Behavioural observer-rated pain scale revised for specific needs children, who are unable to verbalise pain or with developmental disabilities. It incorporates individualised pain behaviours that are unique to a child
Neonatal/Infant Pain Scale (NIPS)	Neonates and infants

Faces Pain Scale

- Can be used in children less than 7 years of age.[5]
- Say to the child, "Point to the face that shows how much you hurt (right now)"



Numeric Scale• Use zero (no pain) to 10 (worst pain you can imagine) scale for children aged 7 years and above.[6]

FLACC Scale

This is a nonverbal pain scale which can be used in children aged 1 month to 3 years.[7]

Category	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distracted	Difficult to console or comfort
Each of the five categories (F) Face, (L) Legs, (A) Activity, (C) Cry, (C) Consolability, is scored from zero to two, which results in a total score between zero and 10.			

Revised FLACC Scale

Assessments	Score		
	0	**1**	**2**
FACE **Individualised behaviour:**	No particular expression or smile	Occasional grimace or frown, withdrawn or disinterested; appears sad or worried	Consistent grimace or frown; frequent/constant quivering chin; clenched jaw; distressed-looking face; expression of fright or panic
LEGS **Individualised behaviour:**	Normal position or relaxed; usual tone & motion to limbs	Uneasy, restless, tense; occasional tremors	Kicking, or legs drawn up; marked increase in spasticity, constant tremors or jerking
ACTIVITY **Individualised behaviour:**	Lying quietly, normal position, moves easily, regular & rhythmic respirations	Squirming, shifting back/forth, tense or guarded movements, mildly agitated, shallow splinting respirations, intermittent sighs	Arched, rigid or jerking, severe agitation, head banging, shivering, breath holding, gasping or sharp intake of breaths, severe splinting
CRY **Individualised behaviour:**	No cry/ verbalization	Moans or whimpers, occasional complaint, occasional verbal outburst or grunt	Crying steadily, screams or sobs, frequent complaints, repeated outbursts, constant grunting
CONSOLABILITY **Individualised behaviour:**	Content or relaxed	Reassured by occasional touching, hugging or being talked to; distractible	Difficult to console or comfort, pushing away caregiver, resisting care or comfort measures
**Individualised pain behaviour unique to each child with severe neurological impairment as identified by carers or staff can be inserted into the most appropriate category in the left column and its severity graded accordingly to encompass pain behaviours not covered by the existing table.*			

Neonatal Pain Scale (reference from Paediatric Pain Management Guidelines KKM)

Neonatal/Infant Pain Scale (NIPS) *A score greater than 3 indicates pain*		Score
Facial expression		
0 - Relaxed muscles	Restful face, neutral expression	
1 - Grimace	Tight facial muscles, furrowed brow, jaw, chin (negative facial expression – nose, mouth and brow)	
Cry		
0 - No cry	Quiet, not crying	
1 - Whimper	Mild moaning, intermittent	
2 - Vigorous cry	Loud scream, rising, shrill continuous (note, silent cry may be scored if baby is intubated as evidenced by obvious mouth and facial movements)	
Breathing Patterns		
0 - Relaxed	Usual pattern for this infant	
1 - Change in breathing	In drawing, irregular, faster than usual, gagging and breath-holding	
Arms		
0 - Relaxed/Restrained	No muscular rigidity, occasional random movements of arms	
1 - Flexed/Extended	Tense straight legs, rigid and/or rapid extension, flexion	
Legs		
0 - Relaxed/Restrained	No muscular rigidity, occasional random movements of legs	
1 - Flexed/Extended	Tense straight legs, rigid and/or rapid extension, flexion	
State of Arousal		
0 - Sleeping/Awake	Quiet, peaceful sleeping or alert random leg movement	
1 - Fussy	Alert, restless and thrashing	

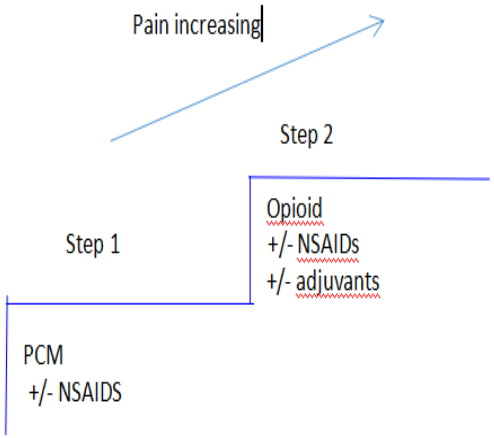
Non-pharmacological pain management

Method	Examples
Physical methods	Cuddles/hugs, massage, comfort positioning, heat, cold, TENS (Transcutaneous Electrical Nerve Stimulation)
Cognitive behavioural techniques	Guided imagery, Hypnosis, Abdominal breathing, Distraction, Biofeedback
Multi-sensory	Acupuncture, Acupressure, Aromatherapy
Infants	Nesting / Swaddling, Kangaroo care, Dimming light and noise, and Administration of breast milk or sucrose for painful procedures
Parental involvement	Soothing environment, favourite toys, distraction, books, bubbles, interactive story-telling, asking the child what helps

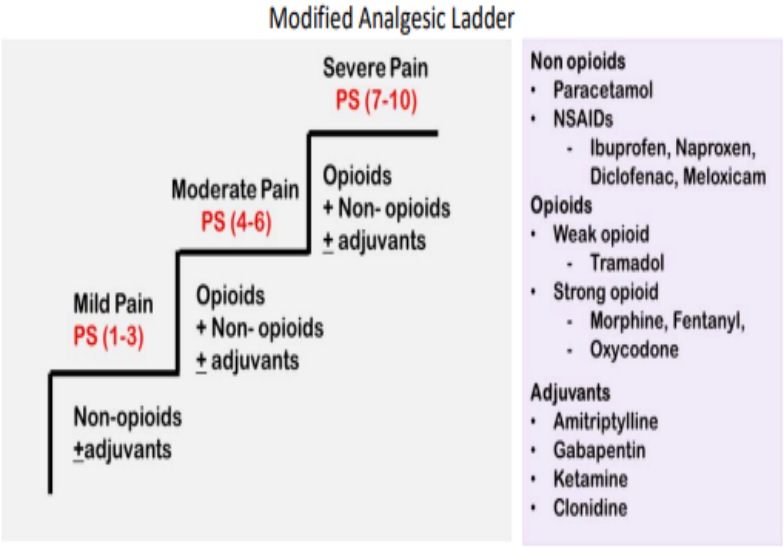
Principles for cancer pain management

Principles[8]	Description
BY THE CLOCK ***Dosing at regular intervals***	Regular scheduling ensures steady blood level, reducing peaks and troughs of PRN-dosing
BY THE INDIVIDUAL ***Adapting treatment to the individual child***	Treatment should be tailored to individual child Opioid analgesics should be titrated on individual basis
BY THE MOUTH ***Using the appropriate route of administration***	Use oral/enteral route Alternative routes: sublingual, buccal, transdermal, rectal
BY THE LADDER ***Using a 2-step strategy***	**WHO step 1:** Mild pain, use paracetamol and/or ibuprofen **WHO step 2:** Moderate to severe pain, use Morphine, Fentanyl, Oxycodone, Methadone

Pain management ladder for paediatric cancer pain (adapted from WHO guidelines)



Pain management ladder for paediatric pain (KKM Pain Guidelines 2023)



Pharmacological management

Step 1: Mild to moderate pain[8]		
Medication	**Mode of action**	**Caution**
Paracetamol	Simple analgesic and antipyretic. Weak inhibitor of the synthesis of prostaglandins (PGs) and interacts on serotonergic, opioid, nitric oxide and cannabinoid pathways in CNS.	Side effects are rare in recommended doses, hepatotoxicity if overdose
Ibuprofen	Non-steroidal antiinflammatory drugs (NSAIDs). Inhibit cyclo-oxygenase (COX) mediated prostaglandin production. Side effects are related to COX-1 inhibition.	Peptic ulcer, GI bleed, platelet dysfunction, nephrotoxicity, cardiac events
Step 2: Moderate to severe pain[8]		
Medication	**Mode of action**	**Caution**
Morphine	Strong opioid that binds to mu, kappa, gamma opioid receptors to block the release of substance P in CNS and dorsal horn of spinal cord. Duration of action: 3-4 hours Active metabolites morphine-6-glucuronide and morphine-3glucuronide can lead to neurotoxicity, especially in renal impairment.	Common side effects: Nausea, vomiting, constipation, drowsiness Uncommon side effects: Sweating, euphoria, pruritus, myoclonus, delirium
Transdermal fentanyl	Suitable for stabilised background pain. 100 times more potent than morphine. Duration of action: 48-72 hours. Preferred for patients with renal impairment – accumulation of inactive metabolites	Not for initial titration or breakthrough pain. Sedative Caution must be used in handling/ disposal of patches. Absorption affected by changes in body temperature.
Oxycodone	Short-acting and long acting preparations available Oral oxycodone is 1.5 more potent than oral morphine IV oxycodone is equipotent to IV morphine Duration of action: 3-4 hours	Side effects comparable to morphine Reserved for those who are unable to tolerate morphine due to cost considerations

Step 2: Moderate to severe pain[8]		
Medication	**Mode of action**	**Caution**
Methadone	Useful for both neuropathic and nociceptive pain. Preferable for patients with renal impairment. Only indicated if patient is unable to tolerate other opioids or poor response to morphine.	Needs experience in titration. Consult paediatric palliative care specialist.
Tramadol	By mouth, tramadol is about 1/10 as potent as morphine. Onset of action for oral dose is 30 to 60 minutes; duration of action is 4-9hours.	Causes less constipation and respiratory depression than the equivalent morphine dose. Side effects include diarrhoea, retching, fatigue and paraesthesia.
Intranasal Fentanyl	Synthetic opiate analgesic with rapid onset (5-10 minutes). Short acting (30-60 minutes)	Use with caution for patient age below 1 month old, and patients with prior allergy history to opiates. URTI may cause unreliable delivery of drug. Liver failure

Case example

Aiman is a 10-year-old boy with relapsed Acute Lymphoblastic Leukemia with bone metastasis. He complains of generalised pain with pain score of 6/10. He is opioid naïve with normal renal and liver function. His weight is 20kg and he is currently at home.

1. Please give the choice of opioid, route of administration and write the opioid prescription.

   Immediate release oral Morphine 0.2mg/kg/dose x 20kg = 4mg q4h (maximum initial dose is 5mg/dose for children) = 24mg/day

   Breakthrough dose: 1/10 to 1/6 of daily dose (2.5mg-4mg), can be served 1-2 hours after previous dose of morphine.

2. Aiman requires 4 breakthrough doses of 4mg Morphine in a day, please titrate his morphine dose.

   Total morphine 24mg + 16mg = 40mg/day

   Dose adjusted to 6mg every 4 hour, breakthrough dose 6mg prn

3. Aiman's pain is well-controlled with oral morphine 40mg/day with no breakthrough dose required, what next?

   As pain is well-controlled with oral morphine 40 mg/day, morphine can be converted to extended-release morphine with 20mg every 12h and breakthrough dose of oral morphine of 5mg prn

4. Besides pain management by opiods, components of PPC in pain management are:
    - Concurrent treatment of anxiety (e.g. play therapy, schooling, benzodiapines)
    - Management of patient's and family's pain perception (e.g. cognitive behavioural therapy)
    - Empower patients and families for breakthrough pain
    - Continuous assessment and management of pain at home by community and hospice team
    - Multidisciplinary pain assessment and management (e.g. physiotherapy, occupational therapy, counsellor)

Opioid switching

Different opioids have different side effect profiles and pharmacological properties. Individuals will have different responses to different types of opioids. Switching or rotating opioids may be indicated if:

- pain is not well controlled despite optimal titration
- intolerable side effects occur with morphine
- development of renal impairment
- patient cannot swallow oral medications
-

Opioid Conversion Table

TO FROM	Oral morphine mg/day	SC/ IV morphine mg/day	Oral oxycodone mg/day	SC/ IV oxycodone mg/day	TD fentanyl mcg/h
Oral morphine mg/ day		÷ 2	÷ 1.5	÷ 3	÷ 3
SC/ IV morphine mg/day	X 2		÷ 0.7	÷ 1.5	÷ 1.5
Oral oxycodone mg/day	X 1.5	X 0.7		÷ 2	÷ 2
SC/IV oxycodone mg/day	X 3	X 1.5	X 2		÷ 1
TD fentanyl mcg/h	X 3	X 1.5	X 2	X 1	

MULTIPLY **DIVIDE**

Adapted from Ministry of Health Malaysia. (2024). Clinical practice guidelines management of cancer pain (2nd ed.).

Examples of opioid conversion

1. Oral morphine to IV/SC morphine

Divide dose of oral morphine by 2 to convert to IV/SC morphine. 10mg of oral morphine is equivalent to 5mg of IV or SC morphine.

2. Fentanyl patch

When converting total daily oral morphine dose to fentanyl patch (divide by 3), round up to the lower adjustable dose. The lowest dose is 6.25mcg/h (half of the 12.5mcg/h patch).

Oral morphine	Fentanyl patch
45 mg /24h	12.5 mcg/h
90 mg/24h	25 mcg/h
180 mg/24h	50 mcg/h

3. Oxycodone

When converting from oral morphine to oral oxycodone, use an initial dose conversion ratio of 1.5:1

e.g. 15 mg Morphine = 10mg Oxycodone, then titrate to optimize the analgesia.

Medications for neuropathic pain

In children, neuropathic pain can be treated with NSAIDs, opioids or other agents such as gabapentinoids, anticonvulsants and tricyclic antidepressants.[10]

Medications used for neuropathic pain

Medication	Mechanism of action	Undesirable effects
Amitriptyline	Prevent re-uptake of serotonin and norepinephrine	Anti-muscarinic effects, drowsiness, postural hypotension
Gabapentin	Inhibition of glutamate excitatory system. Selective calcium- channel blockage	Drowsiness, dizziness, ataxia, headache, and myoclonus
Pregabalin	Selective calcium- channel blockage	Drowsiness, dizziness, ataxia, headache, and myoclonus
Sodium Valproate	Block influx of sodium ions, preventing depolarization and generation of an action potential.	Drowsiness, tremor, hair thinning, hair loss, menstrual irregularities, weight gain, and thrombocytopenia.
Methadone*	NMDA receptor antagonist	Nausea, vomiting, constipation, dry mouth, biliary spasm, respiratory depression, drowsiness, muscle rigidity, hypotension, bradycardia.
Ketamine	NMDA receptor antagonist	Dissociated hallucination, agitation, anxiety, dysphoria, sleep disturbance, urinary tract symptoms (dysuria, hematuria)

**(required specialist advice)*

Interventional strategies for pain control

Procedures	Indications	Benefits
Regional anaesthesia[10] (Epidural or intrathecal neurolytic blocks)	Post-operative pain Neuropathic pain Terminal pain	Modifies the neuroendocrine stress response, provides profound post-operative pain relief, ensure a more rapid recovery, shorten hospital stay, fewer opioid-induced side effects.
Percutaneous cervical cordotomy (PCC)[11]	Unilateral pain below the clavicle	Ablates the sensory pathways of the lateral spinothalamic tract

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Cardiorespiratory Symptoms

Breathlessness

Definition

Breathlessness is the **unpleasant subjective sensation of being unable to breathe adequately[1].**

Pathophysiology

It arises from **mismatch** between the need of breathing and the perceived work of breathing, related to activity of **mechanoreceptors** (stretch receptors in airways, lung parenchyma, intercostal muscles and diaphragm), **chemoreceptors** (hypoxia and hypercarbia) and **direct ascending stimulation** from respiratory centre (anxiety, claustrophobia).[2]

Possible Causes

Dyspnoea or breathlessness is a complex symptom involving physiological, psychological, environmental and functional factors.

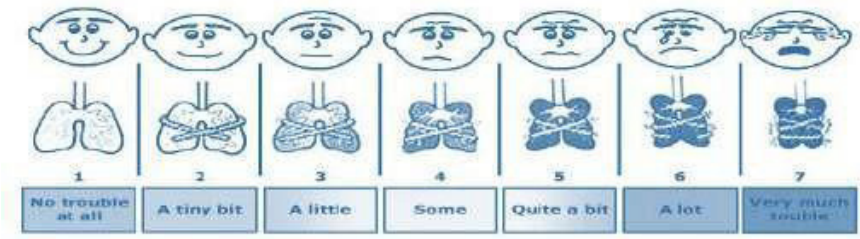
Pathophysiology	Causes
Airway obstruction	Congenital airway anomaly Bronchial asthma External compression or invasion by tumour
Intrathoracic extraparenchymal abnormalities	Pneumothorax Pleural effusion Lung empyema
Lung parenchyma abnormalities	Pneumonia Pulmonary haemorrhagic tumour Pulmonary oedema
Psychological	Anxiety
Ventilation: perfusion (VQ) mismatch	Anaemia
External compression of the diaphragm	Ascites Massive intra-abdominal tumour

Assessment

Assessing dyspnoea in children can be challenging. Children may describe dyspnoea as "chest pain", "tummy pain", or "tiredness". Usually the degree of breathlessness is interpreted clinically based on their level of activities.

Formal scoring may be done at baseline and after intervention for children who are able to understand the scale. Care should be taken in interpreting the scale as it is highly dependent on the child's understanding and perception of the symptom.

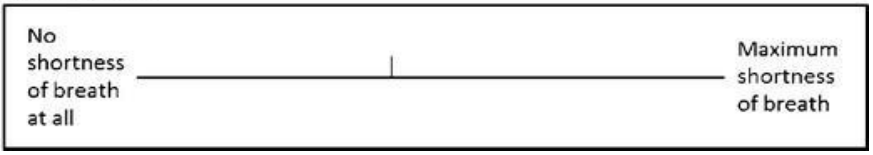
Paediatric Dyspnoea Scale[3]



Numerical rating scale (1- 10)

At rest

During activity



Non-pharmacological management

- Use a hand-held fan towards the face
- Cooling and open space (open windows, air conditioner)
- Loose and comfortable clothing
- Positioning (usually the child will choose their most comfortable position)
- Breathing techniques (deep breathing, pursed-lip breathing, abdominal breathing)
- Relaxation and distraction (music visualisation, art, play, massage) for anxiety management
- Chest physiotherapy (percussion, vibration and postural drainage).
- Encourage cough (staggered breathing technique) for patients with neuromuscular disorders.
- Calm approach to patient and family
- Consider additional non-invasive breathing support. Carefully weigh the benefits and risks of NIV for each patient because they may cause more symptoms or worsening breathlessness in certain cases. NIV may cause secretion retention, airway dryness, claustrophobia, and barotrauma.
- Plan and schedule the activities to avoid over-exertion

Pharmacological and Procedural Management

Causes	Treatment of underlying causes
Upper airway obstruction	Steroids, tracheostomy, radiotherapy
Secretion, drooling	Nebulised Ipratropium Bromide (consider withholding pre-existing anti-muscarinic medications, e.g. scopolamine patch, to avoid over-thickening of secretions)
Bronchospasm	Bronchodilators, steroids
Pneumonia	Antibiotics, Cough Assist device
Heart Failure	Diuretics
Pleural Effusion	Pleural drainage, pleurodesis
Anaemia	Blood transfusion, erythropoietin
Superior vena cava obstruction	Steroid, radiotherapy, chemotherapy

Treatment	Symptom management for dyspnoea
Oxygen	• Use if SpO_2 < 90% or patient finds oxygen supplement helpful
Non-Invasive Ventilation (NIV)	• Consider early use for children with neuromuscular disorder who are admitted for pneumonia. • Increase ventilator setting or check for machine dysfunction if child is already on 24-hour home ventilation NIV.
Opioids	• Reduces the sensation of breathlessness • Do not cause respiratory depression at recommended doses • Give 1/3 of the pain dosage (starting dose of Sy morphine 0.05 to 0.1 mg/kg/dose 4 hourly and prn). • Consider concurrent laxative to avoid constipation
Anxiolytics	For episodic anxiety: • Short acting e.g. midazolam • Intermediate acting e.g. alprazolam lorazepam For sustained anxiety: • Long-acting e.g. oral clonazepam, diazepam

Non-Invasive Ventilation (NIV)

Indications:

Category 1: Palliative with probably reversible acute respiratory distress

- Patient with acute respiratory failure (eg severe pneumonia) with Do Not Resuscitation and Intubation (DNI) as the patient's goal and ceiling of care
- NIV can be seen as an alternative to invasive (endotracheal) ventilation to improve lobar collapse secondary to impaired cough effort, impaired mucociliary clearance,

pulmonary aspiration or pneumonia, in whom intensive care is electively declined or deemed inappropriate.

- It aims to improve oxygenation and ventilation. Sometimes minor discomfort is outweighed by potential benefits.

Category 2: Palliative symptom management and comfort measures only (CMO) at the end of life

- End-stage respiratory failure for symptom relief such as end-stage renal failure with pulmonary oedema, severe lung metastasis of cancer or withdrawal from invasive ventilation support for end of life. Resuscitation and intubation are not the options of care for the patient.
- It aims to improve symptoms. NIV tolerance is a priority.

Contraindications:

Absolute: Lack of spontaneous breathing, gastrointestinal bleeding, severe hypoxemia, cardiogenic shock, anatomical airway issues.

Relative: Coma, agitation, secretion-related respiratory distress, and certain infectious diseases (e.g., tuberculosis).

Monitoring:

Patients are monitored regularly (1, 6, 12, 24, 48 hours) for comfort, respiratory effort, ventilation effectiveness, and potential side effects. Adjustments are made based on symptoms and clinical response.

Chest pain

Introduction

Chest pain in children can be very alarming for parents, but very few have a cardiac cause.[4]

Causes and pathophysiology

Common Causes	Pathophysiology of pain
Costochondritis (most common)	Inflammatory process of costochondral cartilages that causes localized tenderness and pain of the anterior chest wall due to direct trauma, aggressive exercise, repeated cough or idiopathic.
Pneumonia	Pleurisy. Worsening sharp pain after cough.

Upper gastrointestinal causes (e.g. oesophagitis, gastritis, reflux	Raised intra-abdominal or intra-gastric pressure (e.g. from dystonia, tube feeding, scoliosis), gastro-oesophageal sphincter dysfunction (e.g. NG tubes, hiatus hernia) Drugs (anticholinergics, steroids and nonsteroidal anti-inflammatory agents).
Anxiety	Children respond less well to change, uncertainty, blocked communication, stressful home and school life.
Cardiac causes: e.g. pericarditis, myocarditis	Referred pain from the heart

Assessment

Look for:

- signs of cardiorespiratory distress (poor perfusion, hypotension, hypoxia, muffled heart sound, distended neck veins).
- risk factors of underlying serious disorders.

Important causes	Associated features
Cardiac causes	Pain radiating to arm or back Associated dizziness or collapse Underlying congenital cardiac disease and connective tissue disease
Pulmonary embolism	Pleuritic pain Sudden onset dyspnoea Haemoptysis Hypoxia Possible causes: malignancy, blocked or infected central venous catheter, deep vein thrombosis.
Respiratory causes	Tachypnoea Abnormal lung examination findings e.g. pneumonia, foreign body, pneumothorax, asthma exacerbation and lung collapse.
Gastroesophageal reflux	Symptoms related to food intake and positioning

Non-pharmacological management

Costochondritis
Local analgesia (methylsalicylate or NSAID cream) Stretching exercises Application of ice for 20-minute intervals Advise to minimize activity of the patient's upper limbs

Anxiety
Listen to the child's ideas, concerns, thoughts, feelings and fears especially about death and illness
Explain to the child that anxiety is normal and acceptable when they are facing illness
Maximize normalization – keep family routine, boundaries, school activities unchanged
Advise on non-pharmacological methods for anxiety – listening or playing music, cuddling, breathing techniques, progressive muscle relaxation, guided visualization and relaxation.
Avoid false reassurance. Be honest when answering their questions and promote positive coping mechanism.
Manage the family as a whole
Consider referral for formal psychotherapy
Gastroesophageal Reflux
Diet modification: frequent small meal, food thickener (commercial or rice/corn flour)
If on tube feeding, adjust the volume, rate or frequency of feeding
Positioning: Left lateral position when not feeding. Prop up during and immediately after feeding for at least 30 minutes
Drugs: Withhold or reduce causative drugs

Pharmacological management

General
Treat the underlying causes (such as the underlying causes of persistent cough)
Costochondritis
Paracetamol and Non-steroidal Anti-inflammatory Drugs (NSAIDS)
Anxiety
Refer to section for breathlessness
Gastroesophageal Reflux
Antacids and raft forming agents such as alginates H2-antagonists (e.g. ranitidine) or proton-pump inhibitors (e.g. omeprazole or lansoprazole) Prokinetic (Domperidone / metoclopramide / erythromycin to improve gastric emptying) Consider surgery if failed medical treatment (e.g. fundoplication)

Cough

Introduction

Coughing is a physiological defence mechanism that helps to prevents pulmonary aspiration, promotes ciliary activity and clears airway debris.[5]

Pathophysiology

Cough becomes pathological and needs further assessment and management when:

- It becomes ineffective e.g. in neuromuscular diseases or poor cognitive function
- It adversely affects sleep, rest, eating and social activities
- It causes complications such as muscle strain, rib fracture, vomiting, syncope, headache or urinary incontinence Cough efficiency depends on physical/ mechanical aspects (respiratory muscles, mucus, airway calibre and larynx) and integrity of the neurophysiological pathway of cough.

Possible causes

- Infection
- Gastro-oesophageal reflux
- Post-nasal drip
- Asthma
- Impaired swallowing in neurological conditions
- Foreign bodies in the airway
- Psychogenic cough
- Congenital lung conditions e.g. cystic fibrosis

Assessment

History and physical examination to look for underlying causes and complication of cough

Distinguish between

- Episodic and recurrent cough
- Productive/wet cough and dry cough

Management

Productive/ Wet cough

Non-pharmacological management
For patients who still can cough effectively, encourage them to cough with steam inhalation or nebulized sodium chloride 0.9% PRN to loosen tenacious mucous, together with position, breathing technique and chest percussion/vibration

Pharmacological management
• N-acetylcysteine - reduce sputum viscosity • Antibiotic may be appropriate as symptomatic treatment to reduce secretion • Nebulised salbutamol for bronchospasm • Nebulised ipratropium bromide for secretions • Consider steroid and radiotherapy for lung tumours

Dry Cough

Non-pharmacological management
• Encourage fluid intake • Lozenges to sooth the throat • Avoid cigarette smoke
Pharmacological management
Cough suppression with • Non-opioid linctus, diphenhydramine • Codeine*/pholcodine* linctus • Oral morphine syrup • Promethazine

* Use with caution in children <12 years old

Neurological Problems

Dystonia and Spasticity

Introduction

Dystonia is defined as an involuntary movement disorder where sustained or intermittent muscle contractions (spasm) that cause twisting and repetitive movements or abnormal postures.[1] Spasticity is hypertonia with resistance to externally imposed movement.[1] Dystonia and spasticity often co-exist.

Pathophysiology

Dystonia is due to damage to deep structures of the brain (such as basal ganglia, thalamus and cerebellum) which alters the activity of dopamine and acetylcholine.

Spasticity can be caused by damage to the brain that reduces the activity of GABA (a relaxing neurotransmitter).

Impact of spasticity and dystonia

- Reduced or absent mobility (or even control over movements)

- Profound fatigue
- Muscle contractures leading to bone and joint deformity
- Reduced/asymmetrical bone growth leading to small and/or deformed stature
- Excessive secretions, drooling and feeding problems from impaired motility of the gastrointestinal tract.

Causes of dystonia

Inherited	Neurometabolic disorders	Disorders of biogenic synthesis (Doparesponsive dystonia AADC deficiency GLUT1 deficiency
	Organic acidemia	Glutaric aciduria type 1 Methylmalonic academia Propionic acidemia
	Heavy-metal related disorder	Wilson disease Neurodegeneration with brain iron accummulation (NBIAs)
Acquired/ sporadic	Medications	Anti-epileptic drugs (carbamazepine, phenytoin) Cinnarizine Levodopa Dopamine antagonists / agonists e.g. prochlorperazine metoclopramide Haloperidol, Risperidone, all D-2 receptor blockers
	Toxins	Bilirubin (kernicterus)
	Vascular	Stroke (haemorrhagic or ischaemic) Vascular malformation Vasculitis
	Infection	Toxoplasmosis
	Autoimmune	Anti-NMDA receptor encephalitis Anti-phospholipid syndrome Reye's syndrome Sjogren's syndrome Systemic lupus erythematosus Subacute sclerosis panencephalitis
	Structural	Abscess Arnold-Chiari malformation Atlanto-axial subluxation
	Tumours	Brain, spine tumour
	Others	Trauma Cerebral palsy Hypoparathyroidism

Assessment

Dystonia is a clinical diagnosis.

Getting the family to video episodes is very useful as children may not show dystonia when you meet them.

Assessment	Questions to ask
Confirm that dystonia is present	• How was the child's tone prior to treatment? • What is the child's level of spasticity? • Does the child have episodes of arching, posturing, "toning," or stiffening? • Does the child appear to be in pain before or during muscle spasms? • Do comfort measures such as repositioning, cuddling, or massage help lessen spasms?
Assess for comorbidities or underlying causes	• Spasticity, joint problems, signs of gastrointestinal dysmotility, and seizures.
Assess the severity of symptoms: Frequency and the level of functional impairment.	• How often does the child experience muscle spasms in a typical day? • Ask the child or family to describe, in detail, their 'typical day' for a full 24 hours. • Barthel Index of Activities of Daily Living (ADLs)
Identify potential triggers	• Anything that would make the child feel tense or stressed. • Pain, urinary retention, constipation, inter-current illness, loud noises, bright lights, unfamiliar contact or positions, seizures
Assess for complications of dystonia	• Pain, gastro-oesophageal reflux, constipation, joint problems, dental decay, recurrent chest infections, anxiety and agitation. • Severe status dystonicus may result in rhabdomyolysis, with a risk of acute renal failure.
Define the goals of treatment	• Decide at the outset on interventions, when to stop treatment, and when to consider another intervention. • This baseline information can then be used to "measure" and follow the degree of benefit from any treatment.
Assessment of treatment outcome	• What degree of benefit do you see in your child since treatment started? • Is it easier to provide care such as clothing, bathing and transferring? • Do you consider your child to be a little or a lot better— 25%, 50%, or more than 50% better? • Has there been a decrease in the frequency and severity of muscle spasms and associated features such as arching or stiffening? • Is your child more comfortable? • How does the clinical examination since treatment started compare with the initial exam?

Modified Ashworth Scale for spasticity

The Modified Ashworth Scale (MAS) measures resistance during passive soft tissue stretching and is used as a simple measure of spasticity[2]. We use this as an objective assessment.

Modified Ashworth Scale for spasticity

The Modified Ashworth Scale (MAS) measures resistance during passive soft tissue stretching and is used as a simple measure of spasticity[2]. We use this as an objective assessment.

0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release, or by minimal resistance at the end of the range of motion when the affected part is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of movement (ROM)
2	More marked increase in muscle tone through most of ROM, but affected parts easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part rigid in flexion and extension

The goals of therapy are to ameliorate involuntary movements, correct abnormal postures, reduce pain, prevent contractures, and improve overall function and quality of life.

Non-pharmacological management

- Treat any cause of anxiety or pain.
- Help the child to relax through positioning, correct seating, massage, physiotherapy, warm bathing or distraction.
- Physical and occupational therapy help to mobilize frozen joints, limit mounting contractures, establish appropriate exercise programs, and provide assistive devices.
- Sensory motor retuning, also known as constraint-induced movement therapy, may be useful in hand dystonia.

Pharmacological Management

- Stop any medication that may cause dystonia
- Diphenhydramine can be used to treat medication-induced (e.g. metoclopramide) dystonic react

Oral Medication for Dystonia (ABCD)

Intervention	Medication	Side Effects
Anti-cholinergics	Trihexyphenidyl, atropine, hyoscine hydrobromide, hyoscine butylbromide	Sedation, blurry vision, dry mouth, constipation, urinary retention
Baclofen	Baclofen (Pre-synaptic GABA receptor agonist) - Exact mechanism of action is unknown	Sedation, dizziness, urinary urgency or hesitancy
Clonazepam (Benzodiazepines)	Clonazepam	Sedation, confusion, impaired coordination
Dopaminergics	Levodopa and carbidopa (Dopa-responsive dystonia represent up to 5% of childhood dystonia) Bromocriptine	Carbidopa/levodopa: Nausea, orthostasis, constipation
Others	Gabapentin	Sedation, prolonged QT syndrome, nausea and vomiting

	Mechanism of action	Adverse effects
Botulinum toxin	Blocks the release of acetylcholine into the neuromuscular junction, thereby weakening the dystonic muscles and ameliorating dystonic symptoms. Effects generally take effect in the first 2 weeks and last for 3 – 4 months. To avoid developing resistance, injections are best performed at intervals of ≥3 months and the lowest possible doses that are effective should be used.	**Other interventions for dystonia (refer to paediatric palliative consultant)** Weakness of the injected muscles or weakness of nearby muscles due to local diffusion of the toxin. Systemic symptoms are uncommon.
Surgical treatment	Selective denervation Intrathecal baclofen DBS (deep brain stimulation) of the globus pallidus	

Emergency management for prolonged dystonia

1. If dystonia not controlled by current maintenance medications, consider admission and:

   Step 1 : Assess for dehydration and renal function (urea, creatinine, creatinine kinase)

   Step 2 : If intravenous line access is available, consider IV Midazolam infusion and IV Phenobarbitone. Otherwise, may use oral chloral hydrate and clonidine.

   Step 3 : Consider intranasal Midazolam or per rectal Diazepam for breakthrough dystonia

Details about intranasal Midazolam

Medication	Indication	Method of Delivery	Storage Method
Intranasal Midazolam	Dystonia / Seizure	Intranasal 1. Using a 1ml syringe, attach it to the mouth of the amber bottle. 2. Turn the bottle upside down and syringe out the needed volume. 3. Remove syringe and attach it to the atomiser. 4. Clear patient's nasal secretion (if any). 5. Place patient in a laying down position, with face facing up. Support patient's neck. 6. Place atomiser with syringe into nostril, with the tip facing outwards. 7. Push the plunger to administer medication into nostril. 8. Remove syringe and insert into another nostril. Repeat step 7 & 8.	Store in a dry place, away from strong light and below 25°C (room temperature).

Seizures

Introduction

Seizures in palliative care patients may be either:

Acute
Recent in onset Can be frightening to patients and families **Causes:** • cerebral metastases • infection • metabolic disorder • hypoxia **Treatment:** • antiepileptic drug (AED) • treat underlying cause

Chronic
Part of a long-standing underlying seizure disorder Worsening seizure control may indicate: • disease progression • factors related to AED dose, class, or administration • Children with severe neurological impairment (SNI), may have pseudo-seizures (episodes of arching and posturing, repeated muscle spasms and exaggerated startle reactions.)

In PPC setting, a 'good enough' outcome may be when a child is not necessarily seizure-free, but with seizures having minimum distressing impact on the child.

Causes of poor seizure control

Factors that can lower the seizure threshold	• Missed dose of an AED • Abrupt discontinuation of a benzodiazepine or AED • Starting or stopping a medication that can alter the metabolism of an AED.
Medications that can lower the seizure threshold	Baclofen, carbapenem antibiotics, metoclopramide, neuroleptics, tramadol
Neurological disorders	Brain tumours, neurological diseases, hypoxia, raised intracranial pressure
Other triggers	Illness and fever, sleep deprivation, obstructive sleep apnoea, pain and discomfort

Assessment and practical approach to the management of seizures

Seizure episodes may settle spontaneously

- **DON'T PANIC:** take a long, deep breath; breathe it out slowly and check your watch
- Ensure the child is not in immediate danger (e.g. from falls, burns, drowning)
- Do not place anything in the mouth (e.g. spoons, tongue depressors) • Ensure airway is secure and give oxygen if available
- Place child in side-lying position during the seizure to prevent aspiration
- If seizure does not stop within 5 minutes or if the child is turning blue, give either:
- Subcutaneous, buccal or IV midazolam 0.1–0.5mg/kg (the injectable form can be given buccally if the buccal preparation is not available)
- Rectal diazepam 5-10mg (slower onset of action)
- If seizures continue despite above measures for a further 5 – 10 minutes
- Repeat measures above
- Arrange for immediate transfer to hospital

Please refer to module 4 for management of terminal seizures

Insomnia

Introduction

Insomnia is a common and distressing sleep disturbance in children with life-threatening illness. Insomnia can include difficulty in initiating or maintaining sleep. It may result in fatigue, mood disorders, daytime somnolence and demoralisation. The aetiologies are multi-factorial and is often a combination of physical, psychological, drugs and environmental factors.

Causes of insomnia

Uncontrolled physical symptoms	Pain Dyspnoea Cough Nausea & vomiting Delirium Bowel & bladder symptoms
Unmet psychological issues	Depression Anxiety Anger Fear of dying in sleep Negative thought or rumination
Environmental changes	Admission to hospital Noise from beeping machines Noise from healthcare providers Night-time medication dispensing, vital signs checking
Drugs	Corticosteroids Bronchodilators Psychostimulants (Methylphenidate) Beta-blockers e.g. propranolol (nightmares) Diuretics Substance withdrawal from: Benzodiazepines Tobacco Alcohol Caffeine

Non-pharmacological management

Non-pharmacological	
Improve symptoms control	Pain, dyspnoea, cough
Lifestyle changes	Improve sleep hygiene, exercise
Establish good sleep hygiene	Regular bedtimes Minimize daytime napping Reduce evening stimulants e.g. caffeine Comfortable bedding Comfortable temperature Avoid staying in bed awake for more than 5-10 minutes; return to bed only when sleepy Avoid watching TV, reading or playing with smartphone Keeping a sleep diary to chart sleep time and other factors that might affect sleep can be helpful
Relaxation techniques	Music, meditation, massage, progressive muscle relaxation, hypnosis, aromatherapy
Cognitive behavioural therapy	Address thoughts that keep child from sleeping well, have a detailed sleep diary to help identify thoughts and behaviours that cause sleep problems and replace it with habits that promote sleep.

Sleep diary

SLEEP AND FEEDING DIARY							
Name: Date:							
Time	Mon	Tues	Wed	Thurs	Friday	Sat	Sun
6am							
7am							
8am							
9am							
10am							
11am							
12am							
1pm							
2pm							
3pm							
4pm							
5pm							
6pm							
7pm							
8pm							
9pm							
10pm							
11pm							
12pm							
1am							
2am							
3am							
4am							
5am							
√ If sleeping Δ If feeding							

Pharmacological management

Drugs[3]	Indication	Side effects
Antihistamines e.g. diphenhydramine	Transient insomnia	Anticholinergic side effects
Sleep hormones e.g melatonin	Delayed sleep onset, sleep cycle disturbances	Possible exacerbation of autoimmune disease
Benzodiazepine (GABA agonists) e.g. clonazepam, lorazepam	Interrupted sleep, insomnia associated with parasomnia, frequent arousal	Avoid in patients with OSAS – respiratory depression
Alpha-2 receptor agonist e.g. clonidine	Delayed sleep onset, interrupted sleep, REM suppression	Anticholinergic side effects, hypotension, bradycardia, rebound insomnia upon abrupt discontinuation
Selective benzodiazepine receptor agonists e.g. zolpidem	Delayed sleep onset, interrupted sleep	Rebound insomnia upon abrupt discontinuation, off-label use for children
Chloral hydrate	Transient insomnia	Allergic dermatitis, ataxia, confusion, delirium (more common on abrupt disruption), GI disorders, avoid in severe renal/ hepatic impairment

Anxiety

Introduction

Anxiety emerges in response to perceived or real threats to our physical integrity or our sense of self, that is, our identity or self-esteem.

Psychological symptoms of anxiety include dread and anticipation of negative outcomes, an inability to turn off one's thoughts, and feeling helpless. Physical symptoms include feeling tense, palpitations, chest tightness or shortness of breath, nausea, tremors, crying spells, and difficulty sleeping. Behaviourally, people may become jumpy, irritable, avoidant, talk too fast, and have trouble concentrating.

Possible precipitating factors of anxiety are separation from family, painful procedures, poorly controlled symptoms, fear of unknown and medical causes such as urinary retention, constipation, gastro-oesophageal reflux, seizures and medications.

Screening tool: Depression Anxiety Stress Test (DASS)

https://mits.moh.gov.my/Modules/Patient/public-dass/

Non-pharmacological management	Pharmacological management
Relaxation techniques e.g. guided imagery, breathing technique, stress management	**Treat specific cause if known and also treat severe cases by giving:**
Music therapy	**Short term: Benzodiazepines (Lorazepam, Clonazepam)**
Problem solving **- Address unhelpful thoughts** **- Teach useful behaviours**	**Long term: antidepressants (SSRIs, fluoxetine)** ***consider referral/ liaison with Child Psychiatrist**

Drooling

Introduction

Drooling is the uncontrolled leakage of saliva outside the mouth, generally as a result of difficulty in swallowing the saliva produced.[4]

It is normal until 18-24 months of age, though in some cases the condition can persist up to four years of age.[4] A good diagnosis of the problem must be established, with identification of the implicated factors in each case.

Complications of drooling include skin irritation or abrasions, unpleasant smell and in the more severe presentation, the need to wear bibs or frequently change clothing. Posterior drooling may also increase the risk of recurrent micro-aspirations.

Pathophysiology

An intact swallowing process comprises 3 steps:

a) Ability to close the mouth (oral)

b) Ability to retain the food or fluid in the mouth (oral)

c) Coordinated swallowing reflex (pharyngeal and oesophageal)This motor sequence is coordinated by a swallowing centre located in the brain stem.

Causes

Neurological conditions	
• Brain paralysis or mental retardation	58% of children with brain paralysis suffer drooling, 33% have severe drooling
• Neuromuscular and neurogenetic disorders	Congenital supra-bulbar paralysis, encephalitis, hypoxic encephalopathy, severe intellectual disability (ID), hydrocephalus, certain rare syndromes (e.g. Moebius syndrome, Angelman syndrome, Freeman Sheldon syndrome, Landau-Kleffner syndrome)

Local causes	
• Problems leading to an open mouth position	Lack of lip sealing, certain malocclusions (eg anterior open bite), oropharyngeal tumour
• Tongue deformities	
• Anaesthesia or hypoesthesia of the anterior sectors of the mouth	
• Body posture	Unable to maintain erect head position
• Lack of sensitivity in the oral phase of swallowing	CN VII facial nerve and CN XII hypoglossal nerve lesions
• Alterations precluding mandibular stabilization	Required for correct swallowing.
Associated factors	
Allergic rhinitis, Upper airway disorders, Gastroesophageal reflux.	

Assessment

Drooling Score

= [Drooling severity score] + [drooling frequency score]

Drooling Severity Score (Thomas-Storell & Greenberg) for measuring the intensity or grade of drooling

Score	Grade	Description
1	Dry	Never drools
2	Mild	Only wet lips
3	Moderate	Wet on lips and chin
4	Severe	Drools to extent that clothing becomes damp
5	Profuse	Clothing, hands, tray, and objects become wet

Drooling frequency

Score	Description
1	Never drools
2	Occasionally drools
3	Frequently drools
4	Constantly drools

Drooling Impact Score Scale

OVER THE PAST WEEK

1. How frequently did your child dribble?

Not at all 1 2 3 4 5 6 7 8 9 10 Constantly

2. How severe was the drooling?

Remained dry 1 2 3 4 5 6 7 8 9 10 Profuse

3. How many times a day did you have to change bibs or clothing due to drooling?

Once or not at all 1 2 3 4 5 6 7 8 9 10 10 or more

4. How offensive was the smell of the saliva on your child?

Not offensive 1 2 3 4 5 6 7 8 9 10 Very offensive

5. How much skin irritation has your child had due to drooling?

None 1 2 3 4 5 6 7 8 9 10 Severe rash

6. How frequently did your child's mouth need wiping?

Not at all 1 2 3 4 5 6 7 8 9 10 All the time

7. How embarrassed did your child seem to be about his/her dribbling?

Not at all 1 2 3 4 5 6 7 8 9 10 Very embarrassed

8. How much do you have to wipe or clean saliva from household items, e.g. toys, furniture, computers?

Not at all 1 2 3 4 5 6 7 8 9 10 All the time

9. To what extent did your child's drooling affect his or her life?

Not at all 1 2 3 4 5 6 7 8 9 10 Greatly

10. To what extent did your child's dribbling affect you and your family's life?

Not at all 1 2 3 4 5 6 7 8 9 10 Greatly

Reference: Reid SM, Johnson HM, Reddihough DS. The Drooling Impact Scale: a measure of the impact of drooling in children with developmental disabilities. Dev Med Child Neurol. 2010; 52(2):e23-8.

Management

Non-pharmacological management for drooling	
Myofunctional therapy	Physiotherapy to rehabilitate orofacial neuromuscular function from a young age. To improve nasal breathing, lip seal and oral closure. To ensure adequate control of neuromuscular groups in order to improve chewing and swallowing, facilitate correct feeding via the oral route, and secure adequate control of the position of the head
Behavioural change programmes	Behavioural reinforcement using acoustic feedback technique to reduce drooling by conditioning the patient to swallow each time a signal is heard from the electronic system equipped with a timer device. A chin humidity sensor that triggers a signal when humidity increases – thereby inducing the patient to swallow.
Nursing care	Lateral positioning to allow secretions to flow out. Use towel to absorb secretions Protect the face / skin with barrier cream Oral suctioning only if necessary May need to cut down fluids temporarily

Pharmacological Management			
Anti-cholinergic drugs	The salivary glands are controlled by autonomic nervous system. Muscarinic cholinergic receptor blockade reduces salivary flow e.g. atropine sulphate, glycopyrrolate, scopolamine. Side effects: vomiting, diarrhoea, irritability, urinary retention, mood changes and insomnia Transdermal scopolamine patch offers longer action and less side effects but precautions required in patients with cardiac and gastrointestinal disorders.		
	Med	**Method of Delivery**	**Storage Method**
	Scopolamine Patch	Transdermal patch 1. Wash hands with soap and water. 2. Apply patch to a clean, dry and intact skin area behind your ear. Choose and area with little or no hair and free of scars, cuts, pain, tenderness, or irritation. 3. Press the patch firmly in place with your fingertips to make sure that the edges of the patch stick well.	

		4. The patch should stay in place even during showering, bathing, or swimming. Apply a new patch behind the other ear if the first one becomes too loose or falls off. 5. Only one patch should be used at any time. 6. Remove the patch after 3 days. If treatment is to be continued for more than 3 days, remove the first patch and apply a new one behind the opposite ear.	Store the medication in a closed container at room temperature, away from heat, moisture and direct light. Keep from freezing
	Sublingual Atropine 1%	Under the tongue 1. Suction out excess saliva (if possible) or wipe dry saliva under the tongue with gauze. 2. Apply 1 drop of Atropine 1% solution under the tongue and let it be absorbed. 3. Do not swallow.	Store in a dry place, away from strong light and below 25°C (room temperature). Stability is 1 month from date of opening.
Botulinum injection to salivary gland	Exerts a local and temporary effect, without the risk of side effects. Can be used in selective cases of drooling characterized by a predominant spasticity component		
Surgery	Used as a last resort after carefully evaluating other possible treatment alternatives for the patient. e.g.: salivary gland resection, salivary duct ligation, salivary duct trans-positioning (most widely used option and involves fewer adverse effects) **Submandibular gland duct trans-positioning** towards the tonsillar pillars may facilitate the swallowing of saliva; **Post-operative complication:** appearance of ranulas or loss of smooth muscle function of the terminal sphincters, extreme dry mouth, loss of taste sensation, tongue mobility problems in the anterior sector, swelling and a tendency towards sialoadenitis.		

Autonomic Dysfunction

Children with severe neurological impairment are at risk for autonomic dysfunction. Signs and symptoms include temperature instability, flushing, sweating, tachycardia, retching, increased salivation and agitation.

Management

Reduce triggers for sympathetic drive, including fever, pain, anxiety, constipation and medications (e.g. nebulised salbutamol).

Treatment includes antipyretics, pain management and pharmacological treatment such as Clonidine, Gabapentin, and GABA agonists.

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Renal failure

Uraemia

Introduction

Children with end-stage renal disease may suffer uremic symptoms such as:

- Nausea and vomiting
- Hiccups
- Fatigue
- Itchiness
- Insomnia
- Peripheral neuropathy
- Agitation / confusion
- Seizures

Assessment

Children with uraemia can present with nonspecific symptoms especially in infancy, such as feeding intolerance, persistent crying and restlessness.

Blood investigations are helpful to rule out reversible causes (other than uraemia) such as metabolite derangements (calcium, phosphate, sodium, potassium, bicarbonate) and anaemia.

Management of symptoms of uraemia		
Symptoms	**Non-pharmacological management**	**Pharmacological management**
Nausea and vomiting	Avoid strong odours Small but frequent meals according to the child's appetite	Omeprazole Domperidone Promethazine (second line) Haloperidol (third line)
Hiccup	Pharyngeal stimulation	Metoclopramide Gabapentin Haloperidol
Fatigue	Consider treating anaemia Small but frequent meals Enough rest and sleep	Low-dose dexamethasone Methylphenidate
Itchiness	Avoid strong sunlight and maintain cool environment Wear soft cotton clothing Wear gloves / mittens to prevent scratching Advise patient to rub the skin instead of scratching Apply moisturizers and emollients	Trial of oral antihistamine Gabapentin (second line)
Insomnia	Aromatherapy Massage	Treat the causes (e.g. pain, anxiety, depression) Sedating antihistamines Chloral hydrate
Neuropathic pain	Lignocaine gel/patch	Gabapentin Amitriptyline

Symptoms	**Non-pharmacological management**	**Pharmacological management**
Agitation/ Confusion	Reassure the patient and family Promote a calm and restful environment e.g. limit loud voices Promote patient's orientation to his / her environment e.g. wall clock, night & day, calendar, avoid sudden changes in environment Introduce each visitor or team member to the patient each time	Haloperidol Benzodiazepine (midazolam)

Seizure	Maintain airway No fluids or food directly after a seizure Anticipate symptom and parent / carer education supported with written guidelines for antiseizure medication	Use short-acting benzodiazepine e.g. buccal Midazolam / Diazepam PR / Lorazepam IV for stop seizures Consider regular anticonvulsant medication after first seizure e.g. Levetiracetam (Keppra) / Phenytoin Consider midazolam / phenobarbitone infusion for severe terminal seizure

Haematological problems

Anaemia

Introduction Anaemia is the most frequent hematologic manifestation in patients with cancer.[1,2]

Symptoms of anaemia such as fatigue, dyspnoea, reduced effort tolerance and decreased appetite, may be debilitating and can significantly affect patients' quality of life.[2]

Causes of anaemia in palliative care patients

- Blood loss
- Impaired red cell formation by the marrow
- Excessive red cell destruction

Why do patients with cancer get anaemia?[3]

- Direct effects of cancer (bone marrow replacement, blood loss)
- Results of cancer treatment itself
- Chemical factors produced by the cancer (overproduction of cytokines inhibiting erythropoiesis)

Assessment

- It is important to identify, document and treat the cause of anaemia if possible
- Symptoms should be recorded before and after the transfusion to determine whether there has been any benefit.
- This will facilitate decision-making regarding future transfusions.

- The patient should give informed consent for the procedure and this should be documented in the patient notes.

Management

Indications for blood transfusion:

1. Patients with symptomatic anaemia, presented with respiratory and cardiac symptoms.
2. Patients with terminal illness when there is acute blood loss and symptomatic
3. Chemotherapy-related anaemia

Special considerations

- If prognosis is estimated to be short weeks, blood transfusion may not be appropriate.
- Studies have shown that pre-transfusion haemoglobin levels do not correlate with response to transfusion.[4]

Discontinuation of blood transfusion

- Some patients do not respond symptomatically to blood transfusion or may only respond for a short period of time.
- Decisions to continue blood transfusions should consider: symptoms, prognosis, response to previous transfusions and patient wishes.[4]

Bleeding

Introduction

Massive external bleeding as a mode of death in childhood is uncommon. Clinically significant bleeding occurs in 6 – 10% of patients with advanced cancer.[5] There are some specific sites, which when they bleed, are more likely to result in a major haemorrhage.[6] However, massive bleeding is extremely distressing to the patient, family and healthcare providers.

Advanced planning is necessary in all bleeding circumstances especially in patients with a poor prognosis and in those with the potential for massive bleeding. Interventions are based on prognosis, performance status, patient preferences and previous therapies.

Assessment

Patients who suffer from a malignancy should be assessed for their bleeding risk.

Risk factors for major haemorrhage[7,8]	
Anatomical	Fungating wounds Large head and neck carcinomas Large centrally-located lung cancers Site of lesion close to a major vessel
Systemic disease	Bone marrow failure Refractory acute and chronic leukaemias (M3 AML) Myelodysplasia/Myeloproliferative disorders Coagulation disorders DIVC Infection at the site of the lesion Malabsorption/reduced vitamin K Severe liver disease Uraemia Platelet count < 20,000/mm^3 Radiotherapy to a post-operative site
Medication	Chemotherapy (causing mucositis) Heparin NSAIDs Warfarin

Management

Before bleeding occurs

- Decisions regarding the future management of bleeding should be documented in the patient's case notes.[9,10] This information should be communicated to the relevant health care professionals who are involved in that patient's care.[10]
- Review all medications, including risk of bleeding. The decision and reason to continue to use anticoagulation and NSAIDs should be documented in the notes.[10]
- Midazolam can be prescribed prophylactically as an anxiolytic.
- Advise family to prepare dark towels to disguise bleeding if it should occur.[9,10]

Management of bleeding

Local measures	
Techniques	**Indications**
Packing	Bleeding from hollow organs e.g. nose, rectum Vasoconstrictors (cocaine/ epinephrine and silver nitrate) for epistaxis
Compression dressings • Alginates, foams, hydrocolloid dressings	

Topical haemostatics • Fibrin sealants (FS)	Bleeding from malignant wounds.
Astringents • Silver nitrate • Alum (|$AlH_4^{NO}{}_8^5{}_2$ or AlK(SO4)2)	
Postural modifications • Place patient in lateral decubitus position toward the site of bleeding	Refractory bleeding when patient is near death

Techniques	Indications
Radiation therapy	Gynaecologic malignancies lung cancer superficial skin tumours
Palliative transcatheter chemoembolization (TCE)	Controlling bleeding from many cancer e.g. head and neck, bladder, prostate, cervix, lung, hepatocellular, renal cell, neuroendocrine tumours, metastatic disease to lung, bone, liver and vagina (choriocarcinoma)

Systemic measures	
Examples	**Indications**
Plasma products • Fresh frozen plasma (FFP) • Cryoprecipitate.	DIVC End-stage liver disease Bleeding secondary to warfarin use
Platelet transfusions	Continuous bleeding of mouth and gums Overt haemorrhage (GI tract, gynaecologic, urinary) Extensive and painful hematoma In the setting of thrombocytopenia: • recent disturbed vision • severe and recent headache • severe anaemia
Vitamin K	Vitamin K deficiency Bleeding secondary to warfarin use Liver disease DIVC
DDAVP	Von Willebrand's disease Haemophilia A
Antifibrinolytic agents e.g. tranexamic acid aminocaproic acid	Haematuria bleeding from fungating tumours haemoptysis bleeding per rectum

Please refer to module 4 for management of terminal bleeding.

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Gastrointestinal Symptoms

Nausea and Vomiting

Introduction

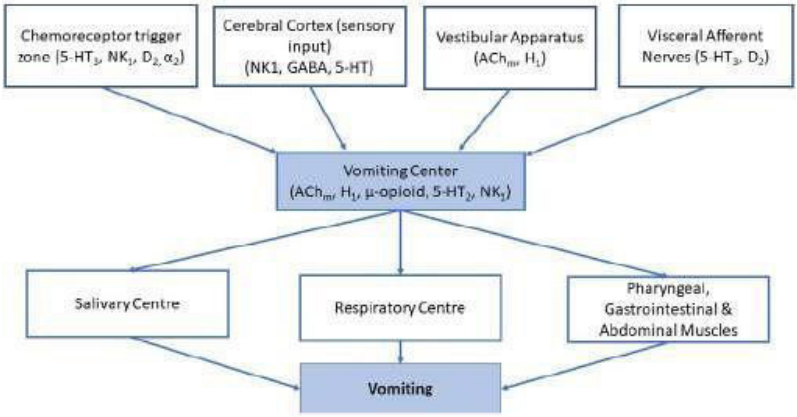
Nausea is an unpleasant sensation experienced over the pharynx and stomach with an urge to vomit.

Vomiting is the forceful expulsion of gastric or gut contents through the mouth or nasal cavity.

Pathophysiology

The vomiting centres receive afferent signals from at least four major sources:

- The chemoreceptor trigger zone (CTZ)
- Visceral afferents from the gastrointestinal tract (vagus or sympathetic nerves) - these signals inform the brain of conditions such as gastrointestinal distention (a very potent stimulus for vomiting) and mucosal irritation.
- Visceral afferents from outside the gastrointestinal tract - this includes signals from bile ducts, peritoneum, heart and a variety of other organs. For example, a stone in the common bile duct can result in vomiting.
- Afferents from extramedullary centres in the brain - certain psychic stimuli (odours, fear), vestibular disturbances (motion sickness) and cerebral trauma can result in vomiting.



Pathophysiology of Nausea & Vomiting

Assessment

- Frequency of vomiting
- Amount of vomitus
- Hydration status
- Complications (e.g. haematemesis, electrolyte imbalance)

Symptoms and causes

Vertigo and symptom association with movement	Vestibular dysfunction
Morning headache and neurological symptoms	Elevated intracranial pressure

Polyuria and polydipsia	Hyperglycaemia or hypercalcaemia
Altered mental status	Uraemia, hyponatremia, elevated ICP
Neck stiffness	Meningeal disease
Syncopal episodes, early satiety	Autonomic insufficiency
Infrequent, hard stool, abdominal fullness, straining with defecation	Constipation
Constipation, crampy abdominal pain, green colour	Bowel obstruction
Bloating, early satiety, residual gastric content	Gastric stasis
Esophageal burning, sour taste, worse lying down	GERD
Right upper-quadrant pain	Gallbladder or liver disease
Epigastric pain radiating to back	Pancreatitis
Fever, diarrhoea	Gastroenteritis
Worry, emotional responses	Anxiety
Others	Ileus, drug adverse effects, seizure

Nonpharmacological management

- Assess trigger factors
- Hot / cold packs for abdominal pain
- Encourage small amount of diet/ fluid as tolerated, chosen by child
- Provision of favourite drinks
- Hypnosis and breathing techniques
- Good oral care
- Avoid discomfort smells
- Aromatherapy
- Acupressure (P6 point)
- Nausea arising from anxiety may be reduced with behavioural therapies

Pharmacological management

- Reduce or change causative treatment or medication
- Laxative for constipation
- Regular anti-emetics depending on the cause and review symptoms by 24 – 48 hours
- Consider intravenous / subcutaneous fluid if dehydrated
- Consider anti-reflux medication
- Consider dexamethasone (post-chemo/tumour control)

Receptor activity	Medication
5-HT_3-receptor antagonists	Ondansetron, granisetron
Dopamine (D_2)-receptor antagonists	Metoclopramide, haloperidol, domperidone
Histamine (H1) / muscarinic acetylcholine (ACh_m) receptor antagonists	Diphenhydramine, promethazine, hyoscine butylbromide
Dopamine (D_2)- and histamine (H1) / muscarinic acetylcholine (ACh_m) receptor antagonists	Chlorpromazine, prochlorperazine
Neurokinin-1 (NK1) receptor antagonists	Aprepitant

Opioid induced nausea and vomiting

Mechanism:

1. Opioid-induced activation of the chemoreceptor trigger zone
2. Sensitization of the labyrinth and activation of the vestibular system
3. Gut dysmotility

Treatment:

Step 1: D2 receptor antagonist, Serotonin receptor antagonist and/or

Antihistamine/ Anticholinergic

Step 2: Opioid switch

Constipation

Introduction

- Constipation is a symptom, not a disease. It is subjective and defined differently by patients or carers.
- Characterized by difficult or painful defecation.
- Associated with infrequent bowel opening, hard and small faeces.
- Including faecal incontinence (encopresis).
- Aim to prevent constipation by the early introduction of laxatives.
- The cause of the constipation should be identified and treated. Bowel obstruction should be managed appropriately.

Causes

- In paediatrics, most patients have functional constipation (95%) with no evidence of primary or biochemical cause
- Organic causes are much more common in children with lifethreatening illness e.g. anatomic, metabolic, gastrointestinal conditions, neuropathic conditions, intestinal muscle/nerve disorders, abnormal abdominal musculature, drugs, miscellaneous

Possible underlying causes

- Immobility (e.g. bedbound)
- Dehydration (review fluid intake and diuretics)
- Neurological compromise: lower extremity motor weakness, paraesthesia, urinary retention, faecal incontinence
- Fear of opening bowel, rectal tears or pain
- Hypercalcaemia, hypokalaemia
- Medications adverse effects: opioids*, 5-HT3-receptor antagonists, anticholinergics, tricyclic antidepressants, phenothiazines, anticonvulsants

  *Must start laxatives alongside when starting opioids
- Environmental – lack of privacy
- Hypothyroidism

Assessment

- History, normal bowel habit, medication and other causative factors
- Abdominal: palpation, percussion and auscultation
- Consider using Bristol Stool Chart to monitor stool

Non-pharmacological management

- Regular bowel routine
- Increase of activity
- Increase oral fluid intake
- Abdominal massage

Pharmacological management

Class	Medications
Osmotic laxatives	Lactulose, polyethylene glycol
Stool softeners	Docusate
Stimulants	Bisacodyl, senna
Lubricant	Glycerin, liquid paraffin
Condition	**Medications**
Faecal impaction	Fleet enema, docusate, lubricant suppositories
Opioid-induced constipation	Consider osmotic or stimulant laxatives, consider opioid switch
Complete bowel obstruction	Octreotide (indicated if severe abdominal pain and vomiting)

Diarrhoea

Definition

- Passage of loose or watery stools
- Acute (< 7 days) or Chronic (> 14 days)

Causes

- Gastroenteritis
- Malabsorption (e.g. Short gut syndrome)
- Laxatives overuse
- Overflow diarrhoea (spurious diarrhoea) due to faecal impaction
- Adverse effects of medication e.g. antibiotics, chemotherapy, radiotherapy
- Concurrent illness e.g. colitis
- Anal leakage following surgical or pathological injury to anal sphincter

Management

Treat the underlying causes e.g. medication side effect, acute causes and chronic causes

Non-pharmacological management

- Oral rehydration with glucose/electrolyte (WHO) solution
- Consider decrease of milk intake
- Consider decrease of enteral intake
- Prevention of skin breakdown

Pharmacological management

- Dose reduction or discontinuation of medication with adverse side effects
- Specific directed therapy if diarrhoea is life-threatening, e.g. Antibiotic for Shigella, Campylobacter, C. difficile

Treatment options for chronic diarrhoea

Loperamide	Anti-motility agents
Cholestyramine	Short gut syndrome
Octreotide	For secretory diarrhoea
Charcoal	Absorbent agents

Anorexia-Cachexia

Definition

Anorexia: Loss of appetite and poor caloric intake

Anorexia-cachexia: Diminished caloric intake, increased basal energy expenditure, progressive depletion of lean body mass and weight loss

Causes

Common treatable causes of anorexia

- Xerostomia, mucositis, esophagitis, gastro-oesophageal reflux, pain, swallowing incoordination, dysphagia, early satiety, bulky organomegaly, intestinal obstruction
- Cancer treatment related anorexia-cachexia:
- Anorexia, nausea, vomiting, decreased oral intake, and weight loss during cancer treatment
- Anorexia-Cachexia syndrome during end stage disease:
- Pain, decreased function, immobility, stiffness, decubitus ulcers, oedema, ascites, shortness of breath, psychosocial distress, poor quality of life, poor prognosis

Management

- Provide effective cancer-directed therapy
- Treat reversible causes
- Increase appetite and nutritional intake
- Improve functional status
- Provide interdisciplinary care to address nutritional, functional and psychological issues

Strategies to increase food intake

- Offering the child favourite foods and nutritional supplements he or she enjoys
- Eliminating dietary restrictions
- Reducing portion sizes and increasing the number of meals
- Making food look more enticing
- Avoiding disliked food odours

Psychological approaches

- Encouraging child and family interaction to reduce psychological distress
- Supporting the family to distinguish between things that they can and cannot control
- Exploring the emotion components and the meaning of their child not eating and losing weight
- Assessing the impact of symptoms on the child and his or her family
- Assessing the quality of life of the child and his or her family

Non-pharmacological management

- Hypnosis
- Relaxation and Mental Imagery
- Massage
- Music Therapy

Pharmacological management

Pharmacological treatment is adjunctive to integrative and supportive management

Examples of pharmacological treatment options for anorexia

Appetite stimulants	Corticosteroids, progestogens
Anti-depressants	Mirtazapine

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Perinatal Palliative Care Pathway

Perinatal Palliative Care covers four distinct periods[1]:

Early prenatal period: Life threatening foetal diagnosis made weeks to months before birth

Late prenatal period: Life threatening foetal diagnosis made hours to days before birth

Early neonatal period: Neonatal death at the first hours until the first 7 days of life

Late neonatal period: Neonate's or infant's death from 7 until 28 days of life.

Scope and Flow of Care

Early Prenatal Period (weeks-months before birth)	
Foetus, Parents and Family	
Care Plan Action Checklist	**Content**
Birth Plan[2] Resuscitation plan -Plan A – Plan B – Pregnancy plan	Timing, location, route of baby's delivery and mother's pain management during delivery – Plan A: For natural death and no resuscitation based on certain criteria at birth – Plan B: For active resuscitation based on certain criteria at birth – Pregnancy Plan: For parents to continue or terminate the pregnancy

Flow of Care and Key Person
Step 1: Foeto-maternal specialist / obstetrician made the diagnosis of possible life-threatening conditions **Step 2:** Perinatal meeting with neonatal and palliative care team regarding birth plan, resuscitation plan and pregnancy plan **Step 3:** Foeto-maternal and palliative team meet with parents to discuss on the pregnancy and care plan. **Step 4:** Offer the option of labour room, postnatal and NICU tour for parents and family if available. **Step 5:** If parents opt for termination, obstetrician to discuss with parents about procedure of termination and grief support from palliative care team

Late Prenatal Period (hours to days before birth)	
Foetus, Parents and Family	
Care Plan Action Checklist	**Content**
Symptom Care plan (SCP) Draft NICU preterm baby procedural plan Preterm labour and emergency delivery plan	SCP includes medication for pain, respiratory distress and feeding / hydration management plan draft NICU preterm baby procedural plan include blood taking, ventilator support and blood transfusion Mother needs to be prepared for possibility of preterm and emergency delivery Need to decide on who is to be included in the delivery team on standby and key decision maker for resuscitation
Flow of Care and key person	
Step 1: If mother opts to continue with pregnancy, SCP and NICU preterm baby procedural need to be discussed. This should be done in a sensitive manner. Do not rush communication to avoid enhancing mother's guilt[3]. **Step 2:** Look into possibility of modifying environment to promote privacy, family togetherness and support grief in labour room and postnatal ward.	

Early Neonatal Period (hours to days of life)	
Neonate, Parents and Family	
Care Plan Action Checklist	**Content**
Place of Care Option Comfort plan Symptom care plan (finalized based on birth weight) Letter to Police Department for cause of death Grief support plan	Place of care options either hospital (NICU or ward) or home (with hospice team support) Comfort plan include: Warm Minimal stimulation Swaddling Kangaroo care Nesting Massage Music Noise and light reduction Nesting Minimize painful procedure Symptom care plan at home need to include the contact details of primary NICU, palliative care and home hospice/domiciliary team Grief support plan including memory making, phone call, home visit and key person who can follow up the grief process

Flow of care and key person

Step 1: Delivery standby team will decide on resuscitation plan

- Intubated/ need resuscitation → Send to NICU and and start comfort care and SCP
- Not for breathing support → Send baby to NICU inform parents

Step 2: For baby under conservative management, need to create NICU palliative corner or room equipped with bed for mother and newborn, memory making tools and space for family members to get together for family rituals.

Step 3: Discussion of place of care. If the parents chose their home for place of care, then palliative team needs to liaise with hospice / domiciliary team for home supports and prepare home symptom care plan, funeral, and death certificate/report plan (letter to police department)

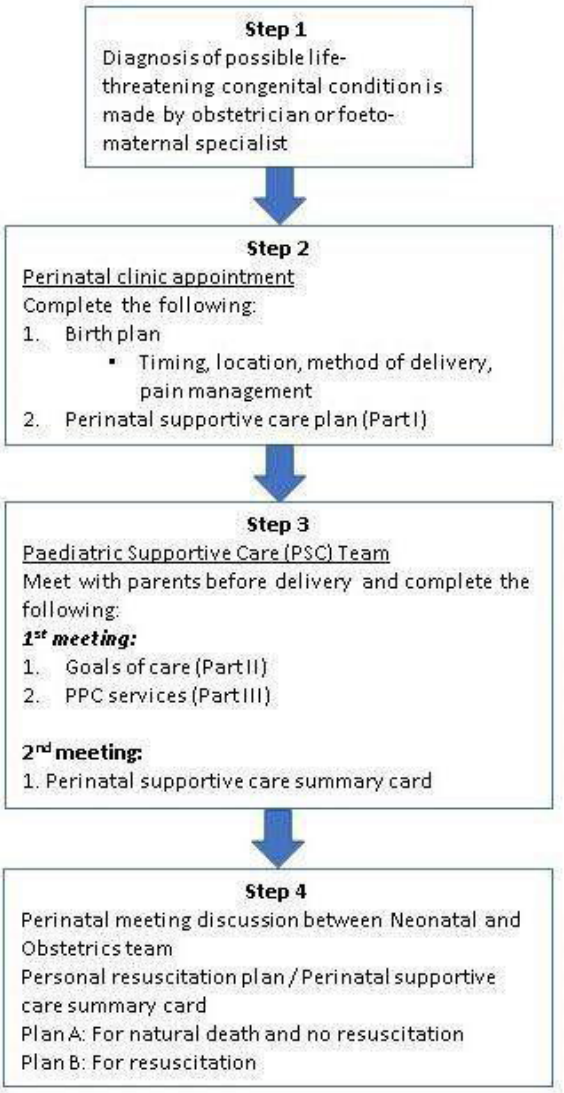
Step 4: If patient dies in hospital, explain to the parents the process of death management including transfer to mortuary and bringing the patient home.

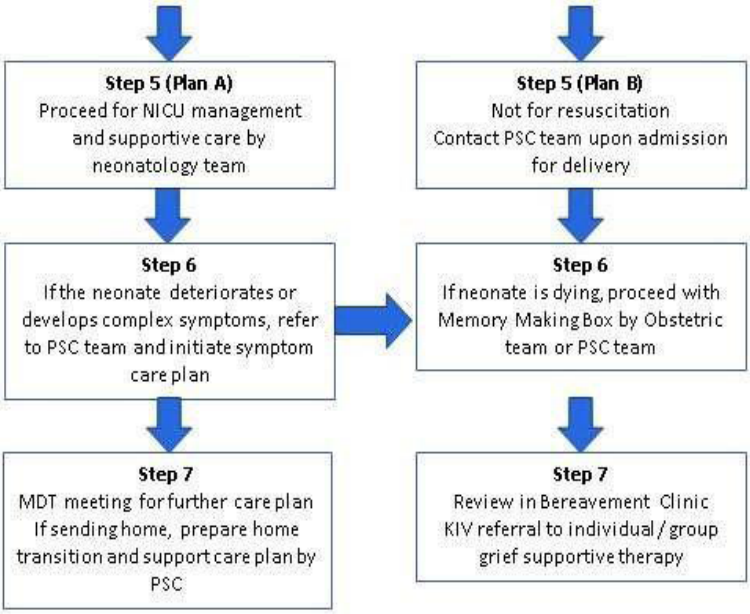
Step 5: Proceed with grief support plan

Late Neonatal Period (weeks to months)	
Neonate, Parents and Family	
Care Plan Action Checklist	**Content**
Symptom Care Plan Grief support plan Regular update meeting with parents Transition Home care plan Discussions on withholding and withdrawal of life-sustaining therapies [4]	Need to relook and add more symptoms management in the care plan during the prolonged stay in hospital such as dystonia, nausea/vomit and seizure. To support parents and family to grief starting before the child's death in hospital and create avenue for bereavement follow up either phone call, mailings, memorial service or anniversary acknowledgements after child's death Regular meetings with parents help to assess parent's evolving needs including psychosocial care (by NICU and palliative care team) Need to prepare a standard operating procedure (SOP) for: - Hospital withholding and withdrawal - Home withdrawal

Flow of care and key person
Step 1: Palliative care team should be part of the team in managing complex symptom care with ongoing modification of symptom care plan while patient in NICU/ward/home.
Step 2: Regular meeting with parents by NICU and palliative care team would elicit more needs and supports for parents and family.
Step 3: Before transfer out baby from NICU, a contingency plan should be decided by MDT team (NICU, Palliative, General Paediatrician, Hospice) if clinical condition worsening outside NICU.
Step 4: If patient is stable to go home, a transition home care plan (refer module 3 of this handbook) need to be done and pass over to home care team.
Step 5: If patient's condition is worsening in NICU, withholding and withdrawing supports may need to be discussed among MDT team and with parents. Grief support plan need to be continued.

Example of flow process for perinatal care




Step 5 (Plan A)
Proceed for NICU management and supportive care by neonatology team
Step 6
If the neonate deteriorates or develops complex symptoms, refer to PSC team and initiate symptom care plan
Step 7
MDT meeting for further care plan
If sending home, prepare home transition and support care plan by PSC
Step 5 (Plan B)
Not for resuscitation
Contact PSC team upon admission for delivery
Step 6
If neonate is dying, proceed with Memory Making Box by Obstetric team or PSC team
Step 7
Review in Bereavement Clinic
KIV referral to individual / group grief supportive therapy

Perinatal Supportive Care Plan

PART I: PERSONAL DETAILS

Name:	Date completed:
Date of Birth:	Date for review: (This document will not be valid after this date)
IC No:	Hospital RN No:
Home Address:	
Patient/family members/carers:	
Diagnosis / Clinical Issues:	
Birth plan *(route of delivery and pain management)*:	

PART II: Goal of Care

PART III: Paediatric Supportive service

☐ Visiting labour room

☐ Family conference

☐ Anticipating grief assessment and management

☐ Memory making

☐ Symptom care plan for baby

☐ Home visit/Hospice care

☐ Grief & bereavement support

☐ Others _____

_____

_____

Neonatal Supportive Care Plan (Summary) card

Neonatal Supportive Care Plan
(Summary) card

Mother Name : **Neonate RN No :**
Mother RN No :

Admission Diagnosis:
Neonatal Resuscitation Plan

☐ For active resuscitation upon delivery ☐ To decide upon delivery
☐ Do Not Resuscitate upon delivery

Overall Goals of Care

Preferred End of life care

Anticipatory Grief Support Plan

Most parents and family members value the golden chance to make good and meaningful memories with their baby during the brief time before baby's death. Others may hesitate initially but may consider taking the offer with some time for them to decide[5].

Photography
• Encourage protected photography of baby with family members
• Photography style: www.nilmdts.org www.toddhochberg.com
• Perinatal bereavement service guidelines for photographing babies at end of life[3]
Plaster Moulds
• Hand and feet 3D mould kits
Ink Prints and Other Memories
• Hands and feet prints on special birth certificates, baby book, cloth, shirts
Personal items and memory box
• Patient's voice record, hand-knit caps and blanket
Interaction of baby with family
• Touching and holding baby e.g. kangaroo care
• Rituals of blessing, naming, baptism
• Singing to baby or reading storybooks
• Taking baby for social outing

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Nursing care in Paediatric Palliative Care

Oral Care

Introduction

Oral problems such as pain, salivary gland dysfunction, dysphagia, and oral mucosal infections can occur during end of life. Therefore, oral hygiene and care should not be neglected even during active dying. Poor oral hygiene can result in multiple dental problems such as dental caries, halitosis, as well as a reservoir for infections.

Oral care is required even if the patient is no longer taking food orally, but on parenteral nutrition or tube feeding. Maintaining oral hygiene is important for a patient's comfort.

Halitosis

What is it?

Unpleasant foul-smelling breath

Possible causes

- Dry mouth
- Poor oral hygiene
- Infections of the upper respiratory tract and oral cavity
- Gastro-oesophageal reflux

Non-pharmacological management

- Brush teeth and tongue 2-3 times a day with a soft nylon toothbrush.
- Super soft toothbrushes or oral cleaning sponges/swabs which are soaked in warm water.
- If the child can gargle, dissolve 1 teaspoon of sodium bicarbonate in a glass of water and use as mouthwash.
- Gauze soaked in recommended mouthwash can be used to clean the mouth for children who cannot gargle yet. This can be fastened to the end of a tongue depressor.

Pharmacological management

- Oral cavity infections can be treated with broad spectrum antibiotics (e.g. amoxicillin-clavulanate) and anaerobic coverage (metronidazole).
- Oral candidiasis can be managed with nystatin suspension.

Xerostomia

What is it?

Excessively dry mouth

Possible causes

- Dehydration
- Hypercalcaemia
- Salivary gland dysfunction
- Infections
- Drugs (e.g. diuretics, anticholinergics, antihistamines)
- Mouth breathing
- Oxygen therapy

Non-pharmacological management

- Frequent sips of water
- Suck frozen lemon juice cubes
- Petroleum-based or beeswax-based lip balm
- Maintain oral hygiene
- Avoid medications that cause dry mouth

Pharmacological management

- Saliva stimulation (e.g. pilocarpine)
- Saliva substitution

Stomatitis

What is it?

Inflammation of the oral mucous membrane, leading to pain and ulcers

Causes

- Radiotherapy
- Chemotherapy
- Infections, especially viral infections
- Drug-induced

- Physical irritation from oral appliances
- Nutritional deficiencies

Non-pharmacological management

- Optimize oral hygiene. 0.2% alcohol-free chlorhexidine mouthwash can be used for up to 2 weeks if the child is unable to tolerate a soft toothbrush in case of mucositis to help reduce inflammation of the gingiva secondary to plaque.
- Soft food
- Avoid irritating food e.g. spicy or acidic food, very hot food

Pharmacological management

- Topical analgesics – Xylocaine viscous 4 hourly / prn, Topical antiinflammatory - choline salicylate and cetalkonium chloride gel (e.g. Bonjela or Oral Aid)
- Morphine gargle (5mg aqueous morphine dilute in 15mls boiled water and gargle for 30 seconds, may repeat 4 hourly)
- Topical hyaluronic acid gel – anti-inflammatory and angiogenic properties
- Topical triamcinolone oral paste – in children aged more than 7 years
- Treat infections – oral acyclovir for herpes simplex infections, nystatin suspension for oral candidiasis

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Tube feeding

Feeding may need to be given to the child via tubes, such as nasogastric, gastrostomy or gastrojejunostomy tubes.

Caregivers need to be shown how to prepare feeding formula and to give tube feeding correctly before discharge. Ideally, the healthcare provider should observe the caregiver demonstrating correct tube feeding technique before discharge.

Incorrect tube feeding technique and feeding formula preparation can lead to various problems such as aspiration, tube occlusion or dislodgement.

Initiation of tube feeding also may present with diarrhoea due to hyperosmolarity or lactose intolerance. Volume of feeds should be increased gradually to prevent overdistention of the stomach.

Overdistention of the stomach

Signs of overdistention

- Bloated abdomen
- Nausea and vomiting

Possible causes

- Gastroparesis, delayed gastric emptying due to medications or disease complications
- Volume or rate of feeding is too high
- Squashed stomach syndrome – compression by liver tumour or other structures in the abdomen

Management

- Consult dietician on the appropriate volume and formula for feeding. May need to temporarily reduce feed and gradually increase until target volume is reached.
- Feeding volume may be reduced but frequency of feeding increased to compensate.
- Ensure patient is kept propped up 30^{o} for at least 30 minutes after feeding.

Diarrhoea

Possible causes

- Hyperosmolarity of the formula can result in temporary diarrhoea on initiation

- Intolerance to formula contents e.g. lactose, proteins
- Gastroenteritis due to poor hygiene in formula preparation

Management

- Refer to dietician to replace with other types of feed with similar calorie and nutritional content.
- Reduce the amount of feed and gradually increase dose when tolerated.
- Ensure feeds are prepared hygienically
- Maintain skin integrity – apply barrier cream over perineum to prevent skin breakdown

Aspiration

Signs of aspiration

Can be silent – no choking or coughing

Symptoms of lung infection – coughing, fever, dyspnoea

Possible causes

- Gastro-oesophageal reflux
- Lying patient flat immediately after feeding
- Increased intra-abdominal pressure
- Tube displacement
- Worsening of dysphagia

Prevention

- Check tube placement before feeding
- Check tube placement after every tube change
- Prop patient 30^{o} up for at least 30 minutes after feeding

Management

- If aspiration pneumonia has set in, treat with antibiotics.
- If GERD, start medications e.g. domperidone, omeprazole.

Gastrostomy Tube Care

A gastrostomy tube is used to provide liquid feeds directly into the stomach. Gastrostomy tubes are preferred for long term feeding. Care for gastrostomy tubes is important to reduce risk of complications. After 3 months of creating the tract, the gastrostomy tube can be changed into button type or skin-level gastrostomy tube which is less conspicuous compared to normal gastrostomy tube.

Common problems related to gastrostomy feeding tube[1-3]

Tube obstruction or blockage

Signs of tube obstruction

- The tube cannot be flushed with water
- Prepared feeds or medications does not pass through the tube as usual
- Tube is bulging when bolus feeding is given

Possible causes

- Formula not prepared appropriately or too thick
- Medications not suitable for tube administration or inadequately crushed or dissolved
- Inadequate flushing
- Tube clamp is not released
- Defective tubing
- Infusion rate is too slow

Management

- Check that the tube clamp has been released.
- Do NOT force the feed or medication into the clogged tube.
- Flush the tube with 60ml of warm water, using a large syringe.
- Pull back the syringe plunger to create a vacuum before flushing again. This may help to dislodge the block.
- If this does not work, then the child needs to be referred to the hospital for reassessment of the tube and possibly replacement.

Tube displacement

Signs of tube displacement

- The tube is apparently out of the tract
- Child has sudden breathing difficulty
- Child has sudden symptoms of obstruction such as nausea, vomiting and abdominal pain

Possible causes

- The tube was not adequately secured
- Excessive force on the tube
- Tube migrates beyond the pylorus due to peristalsis
- Balloon deflation or rupture

Management

- Stop feeding
- If tube has migrated inside, gently pull the tube until resistance is felt. Take note of the marking of the tube and secure tube.
- If tube has completely come out, replace the tube.

Leaking tube

Signs of leaking tube

- Skin irritation around the site of insertion – may be painful, infected
- Visible hole or leak at the tube itself or around site of insertion.
- Dressing around site of insertion requires frequent change.

Possible causes

- Poorly fitted tube
- Excessive movement or tugging at exit site – resulting in enlarged tract
- Accidental cutting of the tube due to repeated clamping
- Defective or clogged tube
- Excessive pressure inside the stomach
- Skin infection surrounding the exit site

Management

- Prescribe proton pump inhibitors to reduce acidity of gastric secretion
- Barrier cream / stoma adhesive powder surrounding the insertion site.
- Secure the tube with tape.
- Possibility of using Foley's catheter temporarily to allow tract to shrink. In the meantime, other methods of feeding such as nasogastric tube feeding should be used.

Skin infection or over-granulation

Signs of infection / over-granulation

- **Infection:** Redness, tenderness, increased purulent discharge, pustule, fever
- **Over-granulation:** Moist cauliflower-like pink tissue surrounding insertion site, bleeds easily

Possible causes

- **Infection:** Poor hygiene or site care, immunocompromised state
- **Over-granulation:** excessive movement of the tube or trauma to the site

Management

- Regular dressing with proper aseptic technique
- Warm saline compress over the site – cut Y shape over 2x2cm gauze, soak in warm saline, leave on site for 3-5 minutes, repeat 3-4 times a day
- Topical antibiotics for local infection and consider systemic antibiotics if fever is present
- Prevent excessive tube movement

Emergency gastrostomy tube replacement

Emergency gastrostomy kit

Consists of:

- Foley's catheter of the same French size or smaller size and an extra G-tube button
- Water based lubricant (KY jelly)
- 5ml syringe (to fit into the balloon port) and 20ml syringe (to aspirate the stomach contents)
- Clamp from old extension set

DO NOT PANIC if the tube falls out or is pulled out.

Foley's catheters

- Insert the end of the tube into the opening of the abdominal wall gently about 3-4 inches.
- Use a 5ml syringe to fill the balloon with water into the part that inflates the balloon.
- Pull back gently on the tube until you meet some resistance.
- Slowly draw back stomach contents using 20ml syringe to assure proper placement of the tube.
- Then verify placement with free flow of small amount of water.

G-tube button

- Insert tube into stoma. *If there is any resistance, do not push. Go to the nearest hospital with your emergency kit.
- Using 5ml syringe, fill the balloon with cool boiled water or water for injection (amount depending on the G-tube button).
- Attach the extension set. Aspirate stomach content to assure placement of tube.
- Then verify placement with free flow of small amount of water.
- It is important to replace the tube as fast as possible because the tract that the G-tube enters through the stomach can close very quickly.

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Tracheostomy Care

Tracheostomy tubes may be inserted when the child requires prolonged ventilation or when upper airway obstruction cannot be removed.

Common problems with tracheostomy tubes

Obstruction or tube displacement

Causes	Management
• Early tracheostomy tube change when tract is not matured yet • Tracheostomy stenosis • Granulation tissue at tracheostoma • Obese neck with deep seated trachea • Restless or too anxious patient	• Obstruction or displaced tube leading to ventilation problems - Must remove and replace tracheostomy • Can use a smaller diameter tracheostomy tube to replace the current tube using a bougie or fibre optic scope • If track is immature (< 7 days old) blind replacement is contraindicated

Bleeding

Causes	Management
• Tracheoinnominate fistula • Bleeding from an invading tumour • DIC • Infection • Local irritation or erosion	• Call for surgical backup • All bleeding should be considered dangerous regardless of volume or cessation and should be evaluated in an OT setting. • Manage and resuscitate the patient before sending to the OT. • Over-inflate the cuff to tamponade the bleeding (successful in 85% of cases of trachea innominate fistula) • If bleeding continues, secure the airway with endotracheal intubation • Remove the tracheostomy and insert a finger into the stoma to compress the innominate artery • Digitally compress the innominate artery anteriorly

Emergency tracheostomy kit

These items should always be present in a child's emergency tracheostomy kit:

- Two clean tracheostomy tubes :
  - Tracheostomy tube of similar size to current tube
  - Tracheostomy tube one size smaller than the current tube
- Tracheostomy ties
- Small blanket or towel roll
- Blanket for mummy restraint (if needed)
- Sterile water
- Water soluble lubricant
- Saline lavage (if used at home)
- Suction and catheter kits

- Portable suction machine
- Luer-Lock syringe (if tracheostomy tube is cuffed)
- Bandage scissors
- Tissues
- Ryle's tube size 12Fr
- Wipes or hand sanitizer
- Oxygen tank
- Emergency phone numbers

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Urinary Care

Common problems in patient with diapers:

Diaper dermatitis

Red and tender skin over the buttock and perineal area, may involve thighs.

Causes

- Contact irritant: Irritation from stool and urine, chaffing or rubbing with diapers – flexures are spared as it is worst over areas with direct contact to the irritant.
- Atopic: Triggered by food, new toiletries or fabric
- Bacterial infection: presence of pustules
- Candida yeast infection – usually the redness is over the flexural areas. Presence of satellite lesions.

Non-pharmacological management

- Change diapers regularly
- Rinse the buttocks with warm water and pat dry

Pharmacological management

- Topical barrier creams e.g. Drapolene, Bepanthen, zinc oxide, Vaseline- use at every diaper change
- Powders are not recommended
- Topical antifungal if due to fungal infection

Common problems in patient with urinary catheter (intermittent/indwelling)

Bladder spasms[1]

Lower abdominal pain associated with sensation of urgency, leading to leakage or incontinence

Causes

- Irritation from the catheter balloon
- Urinary tract infection

Non-pharmacological management

- Pelvic floor muscle exercises
- Avoid irritating food e.g. spicy food, citrus, carbonated beverages

Pharmacological management

- Antispasmodics – tolterodine, oxybutynin
- Tricyclic antidepressants e.g. desipramine

Catheter blockage[2]

- Inability to advance the catheter into the bladder
- No urine flowing out from the catheter despite distended bladder
- Urinary leakage around the catheter

Causes

- Mineral deposits or crystals within the catheter
- Blood clots or sediments within the catheter
- Kinked catheter
- Constipation

Non-pharmacological management

- Check for and remove any kinks or obstruction in the catheter or the drainage bag tubing.
- Ensure the bag is positioned below the bladder when child is lying, sitting or standing.
- Check that the leg bag straps are fitted correctly and not causing bag obstruction.
- Increase fluid intake
- Increase citrate intake
- If heavy gross haematuria is seen, consider bladder irrigation
- Enema or digital evacuation of impacted stool

Urinary tract infections[3,4]

Indwelling catheters predispose the child to urinary tract infections. It is important to distinguish between a catheter-associated urinary tract infection (CAUTI) and bacterial colonisation of the catheter.

Urinary tract infection is more likely if:

- Systemic symptoms such as fever, chills, vomiting, delirium
- Local symptoms – flank pain, abdominal pain, haematuria
- Change in urine – foul-smelling, increased leakage, cloudy urine

Pyuria (leucocyte +ve) is not reliable for diagnosing UTI.

Replace the catheter and take the sample from the new catheter for urine culture and sensitivity.

A significant growth of $>10^5$ colony-forming units (CFU)

Pharmacological management4

- Trimethoprim 4mg/kg bd x 7 days
- Nitrofurantoin 0.75mg/kg qid x 7 days
- Cephalexin 12.5mg/kg bd x 7 days (first choice if upper UTI is suspected)
- Co-amoxiclav

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Bedbound patients

Common problems faced by bedbound patient

Pressure ulcers[1]

Causes

- Injuries to the skin that are caused by prolonged high pressure due to immobility.
- Aggravated by poor nutrition, shearing force during transfer, local perfusion, poor skin integrity, infection, anaemia.

Prevention

- Regular turning and repositioning of child in bed. Elevate bed head not more than 30° when not feeding.
- Cotton clothing and bedding to absorb sweat. Change clothing or diapers once soiled/soaked.
- Encourage time out of bed.
- Teach proper transfer techniques and use aids such as frames, slings or slide sheets to prevent shearing.
- Regular passive range of motion exercises to maintain joint flexibility.
- Ensure skin is moisturized adequately.
- Utilise validated risk assessment tools such as the Braden Scale of Predicting Pressure Sore Risk (Braden QD Scale applicable for paediatric population in the hospital and community) to aid in the planning of appropriate preventive interventions.

Braden Scale of Predicting Pressure Sore Risk

Sensory Perception ability to respond meaningfully to pressure-related discomfort	**1. Completely Limited:** Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation. OR limited ability to feel pain over most of body surface.	**2. Very Limited:** Responds only to painful stimuli. Cannot communicate discomfort except by moaning or restlessness. OR has a sensory impairment which limits the ability to feel pain or discomfort over 1/2 of body.	**3. Slightly Limited:** Responds to verbal commands, but cannot always communicate discomfort or need to be turned. OR has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	**4. No Impairment:** Responds to verbal commands, has no sensory deficit which would limit ability to feel or voice pain or discomfort.
Moisture degree to which skin is exposed to moisture	**1. Constantly Moist:** Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	**2. Very Moist:** Skin is often, but not always, moist. Linen must be changed at least once a shift.	**3. Occasionally Moist:** Skin is occasionally moist, requiring an extra linen change approximately once a day.	**4. Rarely Moist:** Skin is usually dry, linen only requires changing at routine intervals.
Activity degree of physical activity	**1. Bedfast:** Confined to bed.	**2. Chairfast:** Ability to walk severely limited or non-existent. Cannot bear weight and/or must be assisted into chair or wheelchair.	**3. Walks Occasionally:** Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair.	**4. Walks Frequently:** Walks outside the room at least twice a day and inside room at least once every 2 hours during waking hours.

Mobility ability to change and control body position	**1. Completely Immobile:** Does not make even slight changes in body or extremity position without assistance.	**2. Very Limited:** Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently.	**3. Slightly Limited:** Makes frequent though slight changes in body or extremity position independently.	**4. No Limitations:** Makes major and frequent changes in position without assistance.
Nutrition *usual* food intake pattern	**1. Very Poor:** Never eats a complete meal. Rarely eats more than 1/3 of any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement. OR is NPO and/or maintained on clear liquids or IV's for more than 5 days.	**2. Probably Inadequate:** Rarely eats a complete meal and generally eats only about 1/2 of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement. OR receives less than optimum amount of liquid diet or tube feeding.	**3. Adequate:** Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products) each day. Occasionally will refuse a meal, but will usually take a supplement if offered. OR is on a tube feeding or TPN regimen which probably meets most of nutritional needs.	**4. Excellent:** Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat and dairy products. Occasionally eats between meals. Does not require supplementation.
Friction and Shear	**1. Problem:** Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures or agitation lead to almost constant friction.	**2. Potential Problem:** Moves feebly or requires minimum assistance. During a move skin probably slides to some extent against sheets, chair, restraints, or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	**3. No Apparent Problem:** Moves in bed and in chair independently and has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair at all times.	

Management

- Dynamic pressure relieving surfaces eg ripple mattress.
- Repositioning chart to remind caregivers when to turn the patient.
- Appropriate dressing for ulcers. Minimize pain by giving analgesics before dressing and use non-adherent dressings. Refer to Ministry of Health Malaysia's Wound Care Manual and latest Clinical Practice Guidelines for evidence-based wound assessment and management practice in the hospital and community.

Orthostatic pneumonia

Causes

- Reduced lung expansion leading to atelectasis due to prolonged lying down position.
- Aspiration of gastric contents
- Reduced immunity

Prevention

- Frequent repositioning.
- 30^{o} elevation of bed head except when sleeping or feeding.
- Keep patient propped up $30\text{-}45^{o}$ after feeding.
- Maintain good oral hygiene
- Chest physiotherapy including use of incentive spirometry, percussion and inducing cough.

Management

Treat the infection if benefits outweigh the risks. Manage symptoms.

Constipation

Causes

- Reduced nutrition or fluid intake
- Reduced bowel motility due to medications / disease
- Immobility

Management

- Optimise feeding as tolerated
- Regular bowel habits
- Encourage mobilization
- Impacted stools may consider enema or digital evacuation
- Co-prescribing gut stimulant or laxatives if opioids are prescribed

Spasticity and contractures[3]

Causes

Joint immobility resulting in tightening of muscles or tendons, associated with hyperreflexia.

Prevention

- Active and passive range of motion exercises for joints.
- Proper support and positioning of limbs, using splints, wedges, pillows etc.

Management

- Analgesics
- Muscle relaxants e.g. baclofen, clonazepam
- Spasticity can be managed with botulinum toxin injections
- Surgical release of contractures

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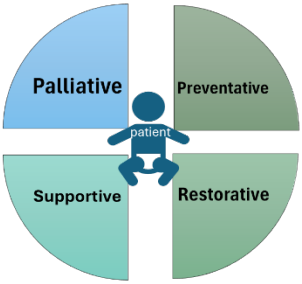
Multidisciplinary Paediatric Palliative Physical and Psychosocial Rehabilitation Services

The 4 Elements of Rehabilitation for Children who need Palliative Care



	Element	Descriptions
1.	Preventative	***Def:*** Establish a baseline functional level, identify impairments that promote physical & psychological health to reduce the incidence and/or severity of future impairments.
		Approach: Prehabilitation or early interventions program, mobility & exercise programs to encourage active participation in ADL & maintaining QOL.
2.	Restorative	***Def:*** Complete to near-complete functional recovery after surgery/ chemotherapy or radiotherapy, attempts to return patient to their previous levels of physical, psychological, social & vocational functioning.
		Approach: Early mobilization, respiratory rehabilitation, relaxation techniques & lymphedema therapy.
3.	Supportive	***Def:*** Focused care on patients with chronic condition, aim to accommodate fixed disability changes from ongoing disease, maintain self-care and maximize independent functionality.
		Approach: Facilitate functions by using self-help device, assistive measures, or alternative ways of doing things (e.g. assistive devices, motorized chair for mobility or alternative augmented communication).
4.	Palliative	***Def:*** Aims at patients in the terminal stages of illness, supports the adaptation of ADL to maintain the best independence physically, psychologically, socially & spiritually to lead a high QOL while respecting their wishes.
		***Approach*:** Therapy measures in assisting patient & their family to relieve symptoms (e.g. pain, dyspnoea, oedema, or contractures) to maximize patient comfort or functional independence & reducing caregiver burden.

Physical and psychosocial rehabilitation services could be provided by the other co-opt MDT team members in paediatric palliative care service. Co-opt members is variable depending on the availability of resources of the corresponding hospital or community-based care. In this chapter, we are focusing on:

Co-opt MDT service	Objectives in Palliative Care
Occupational therapy	To regain maximum physical, psychological, cognitive, social, and vocational functioning within the limit caused by the disease and its treatment to the patient. Educate and empower patient and family to learn different assisted living techniques with and without the help of medical instruments.
Physiotherapy	Assist in improving quality of life by maximizing functional independence and helping to provide relief from distressing symptoms such as pain, breathing, problems, weakness or mobility issues.
Psychosocial rehabilitation	Assist in psychosocial assessment including assessment of patient and parent's understanding of the disease, coping mechanism, and their spiritual needs. Provide psychosocial therapy including cognitive behavioural therapy, play therapy, art therapy, counselling and medical social worker services.

Occupational therapy

Role of the occupational therapist

Assessment

The occupational therapist (OT) will use standardized tests, purposeful play and other planned activities to examine the child's practical ability to do the tasks that enable him or her to learn like other children of the same age.

Management

Once the assessment is complete, the therapists will provide treatment services or suggestions tailored to the client's needs. In occupational therapy, rehabilitation for children generally focuses on:

- Symptom control
- Motor training
- Sensory training
- Cognitive training

Symptom control

Problem-solving strategies

This can range from physical, emotional, social and psychological problems.

If the client has any difficulty in terms of lifestyle challenges, fatigue, and self-esteem issues,

OT could help to determine their priorities, gauge energy levels, to recognize that a client's inner feelings and values, to change behaviour, and to adapt to their changed lifestyle.

Restoration activities

Relaxation

Relaxation techniques appear to increase one's sense of mastery, reduce stress, relieve muscle tension, and distract one's attention from the pain. It can be achieved through:

- **Biofeedback-Assisted Relaxation**

  Biofeedback techniques measure body functions and give you information about them so that you can learn to control them. Biofeedback-assisted relaxation uses electronic devices to teach you to produce changes in your body that are associated with relaxation, such as reduced muscle tension.

- **Deep Breathing or Breathing Exercises**

  It helps children relax by slowing their breathing rate, decreasing the heart rate and normalizing blood pressure. This technique involves focusing on taking slow, deep, even breaths.

- **Guided Imagery**

  For this technique, people are taught to focus on pleasant images to replace negative or stressful feelings. Guided imagery may be self-directed or led by a practitioner or a recording.

- **Progressive Relaxation**

  This technique, also called the Jacobson relaxation or progressive muscle relaxation, involves tightening and relaxing various muscle groups. Progressive relaxation is often combined with guided imagery and breathing exercises.

  For young children simple progressive relaxation needs to be adjusted for example "Toe Tensing" this is a method of drawing tension down to the toe. This is an exercise that involves lying on the back and allowing yourself to tense your toes. Ask the child to pull his toe muscles towards the body and hold the position for ten counts. Do 4-5 repetitions of the exercise.

Pacing activities, work simplification and energy conservation Principles

Work Simplification and Energy Conservation principles will allow the child to remain independent and be less frustrated by the illness, when their energy can last throughout the day.

Pacing involves breaking tasks down into small manageable sessions and resting between sessions to allow the body to recuperate before finishing the task. By using activity pacing, it can help the child to work with their body and understand its needs.

Example of pacing: By recording a daily log about his routine activity, a child can determine when the pain begins to worsen. The child can then reduce time for the tasks by 20%.

Body Mechanics and Ergonomics (position adjustment)

Pain can be alleviated through supportive positioning using a pressure cushion for seating, or positioning to counteract involuntary motor patterns, e.g. supporting children in a flexor position when they have a strong extensor pattern.

Splints

Making splints to help overcome various orthopaedic and neurological problems. Splint is a rigid support given to any part of the body.

Functions of splint:

- to protect the affected part and thus reduce pain.
- to strengthen any weak muscles and thus assist to carry out its action.
- to prevent formation of contractures and deformities

Examples: Resting hand splint, cock-up hand splint, knee extension splint, ankle resting splint, anti spastic hand splint and elbow extension splint.

Compensation activity

This involves the use of assistive equipment (modifications, aids and adaptive tools). The equipment aids in decreasing symptoms such as fatigue and cancer pain, and also to increase client's participation in activities.

Example: Use of table to support arm during grooming to reduce fatigue.

Interventions are targeted toward minimizing barriers to performance, which include modifications for games or activities that clients enjoy as well as appropriate positioning strategies. This may involve modifications to their home in introducing adaptive equipment.

Motor training

Motor skills are important for daily functioning of patients and strongly influences their quality of life. It can be divided into fine motor and gross motor skills.

Fine motor skills

Hand-strengthening with putty / playdough, speed improvement with competitive plays, and endurance training by increasing the time in activities are examples of mostly used trainings.

Gross motor skills

Children should develop gross motor skills as they participate in school and sports activities.

Sensory training

- Hypersensitivity
- Hyposensitivity

Desensitization or sensory re-education should be done with materials children are familiar with.

If a client has severe problems, caregiver should be well educated to prevent injuries like burn, cut, etc.

Cognitive training

Attention

Attention is needed for children to be successful in all areas of daily living but especially in school functioning.

Example: Attention should be handled in terms of selective attention, shifting attention, and divided attention. These attention parameters can be added to skills training, e.g. singing song while playing blockstacking games.

Processing speed, short-term and long-term memory, and sequencing

Processing speed, short and long-term memory, and sequencing ability should also be trained.

Examples: Memory cards, history telling, making animation, and memory training by watching cartoons and asking questions.

Category	Main symptoms/issues	Reason for referral to OT
Neuromuscular disorder	• Muscle weakness • Easy muscle fatigue • Muscle loss/atrophy • Muscle pain • Joint contractures • Functional difficulty/ disability	• Activities of daily living training(patient/caregivers) • Splinting • Wheelchair assessment • Pacing • Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer. • Home modification/Environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access) • Body mechanics and ergonomics (Positioning) • Motor training • Sensory training • Cognitive training
Severe neurologi cal impairment	• Muscle weakness • or Hypotonia • Spasticity • Joint Contractures • Pain • Impaired motor control • Impaired sensory processing • Functional difficulty/ disability	• Activities of daily living training(patient/caregivers) • Splinting • Pacing • Wheelchair assessment • Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer • Home Home modification / environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access
Severe cyanotic heart disease and chronic respiratory disease	• Breathlessness • Fatigue • Anxiety/stress • Functional difficulty	• Activities of daily living training(patient/caregivers) • Pacing • Aids and adaptation/assistive devices (e.g. light utensil, enlarge handle, cardiac table, push chair, etc.) / environmental modification (e.g. re-positioning the cardiac table, push chair, etc.) / environmental modification (e.g. re-positioning the • Home modification keeping frequently used items furniture to make walking around easier, close to hand, easy access storage to avoid bending and stretching, etc) • Body mechanics and ergonomics (positioning
Chronic Pain	• Pain • Stiffness • Fatigue • Stress • Functional difficulty	• Activities of daily living training(patient/caregivers) • Pacing • Aids and adaptation/assistive devices (grab sticks, big buttons, armchairs and highchairs, • Home modification/ Environmental modification (A raised toilet seat) • Activities of daily living training • Relaxation • Body mechanics and ergonomics (Positioning) • Splinting • Wheelchair assessment

Category	Main symptoms/issues	Reason for referral to OT
Syndromic children with slow learning	• School refusal • Functional difficulty • Developmental delay • Sensory processing difficulties • Cognitive problem/disability • Stress • Fatigue • Fine motor delay/poor hand function • Physical disabilities	• Activities of daily living training (patient/caregivers) • Splinting • Wheelchair assessment • Pacing, energy conservation and work simplification. • Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer • Home modification/ environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access) • Body mechanics and ergonomics (Positioning) • Motor training • Sensory training • Cognitive training • Relaxation

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Physiotherapy in Paediatric Palliative Care

Referral for Physiotherapy

Indication for referral	Contraindication
• Trouble in breathing • Pain • Weakness • Poor mobility	• Medical instability • Shortness of breath at rest • Resting angina • Poorly controlled epilepsy • Abnormal arterial blood gases • Acute pulmonary embolism • Acute haemorrhage
Chest physiotherapy	**Indications of positive response to chest physiotherapy**
• Breathing • Postural drainage • Percussion • Vibration • Active cycle breathing technique • Incentive spirometry • Suction	• Changes in breath sounds • Improved chest x ray • Increased oxygenation of the blood as measured by arterial blood gas sampling • The child's report of increased ease in breathing

Limb physiotherapy, transferring and positioning	Why limb physiotherapy is important
• Active free exercise • Active assisted exercise • Passive movement • Stretching • Strengthening • Balance training / proprioception training • Postural stabilization • Ambulation • Mechanical exercise **Transferring & positioning** • Independent • Stand by assist • 1-person assist • 2-person assist	• Reduces stiffness/relaxes tight muscle • Minimise muscle wasting • Prevent from contracture • Maintain joint and connective tissue mobility • Decrease restlessness • Assist circulation and vascular dynamics • Help patient awareness of movement • Can give caregivers feeling of purpose if they can help with the exercises

Musculoskeletal pain	management helps in How physiotherapy musculoskeletal pai	How to perform
Active free exercise Active assisted exercise	Maintain elasticity and connectivity of muscle Increase circulation and prevent thrombus formation	The patient can assist with opposite extremity to perform the exercises
Passive movement Passive stretching	Maintain joint and connective tissue mobility Minimize the effects of the contractures	Provided by an external source by Physiotherapist or carer.
Balance training Proprioception training	To establish an equilibrium of the body which is associated with a variety of movement and postural	Stand with one foot on the ground while the other foot is lifted up or stand on a balance board
Ambulation	Assisting a patient to walk safely and efficiently, it includes stairs climbing with or without assistance	Support with assistance devices such as parallel bar, walker, axillary crutches and forearm crutches
Electrotherapeutic modalities – heat, hydrotherapy	Management and reduction of pain or inflammation	Discuss with therapist to choose suitable modalities based on medical condition

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Communication Skills for Supporting the Child and Family

Introduction

Communication skills are a basic but crucial component in supporting children in palliative care. Good communication skills facilitate human connection and promote psychological well-being.[1,2] This section will provide brief guidance on common techniques for communicating with children and family members, including presence, listening, and responding techniques.

Techniques for communication

Presence	
Skills	**Barriers**
• Physical, mind and spiritual presence. • Attentiveness and empathy • Inner quietude, calmness • Body gestures / position e.g. sit at the same eye-level as the child	• Excessively task-oriented • Lack of concern • Cognitive/emotional reactive
Active listening	
Skills	**Barriers**
• Genuine and congruent • Unconditional/acceptance positive regards • Encourage expression of thoughts and feelings (e.g. nodding, maintain eye contact) • Check for understanding • Use child-appropriate level of language • Other medium of expression for kids: e.g. drawing, stories, cards	• Interrupting • Judging • Explaining reactively • Advising prematurely • Blocking of expression • Self-disclose/talk about own experiences
Useful ways to check understanding • Clarifying "Correct me if I'm wrong, I'm hearing…" • Repeating • Paraphrasing • Summarizing • Reflecting "Sounds like you are going through a tough time…"	

Boundary awareness	
Skills	**Barriers**
• Aware of own emotion/belief and its impact on therapeutic intervention • Have healthy emotional boundary (e.g. attentive, rested; not in overworked/ fatigue) • Have healthy relational boundary (e.g. not taking money from family)	• Projecting own value • Burnout/ exhaustion

Responding to Emotion in End of Life Communication

It is important for the health care team to be sensitive to child or family members' emotional expression, and to allow their emotional processes as part of the journey in the end of life.

Technique	Example
Normalizing and Validation	"It is normal to feel sad…" "It is understandable that you are upset…"
Empathic Observation	"You are making a difficult choice…" "It is not easy to be in what you are in now…"
Name/Acknowledge Emotion	"You look frustrated…" "You seem helpless…"
Encourage Expression	"Tell me more about how you are feeling today?" "I wonder how you have coped all this while."
Praise	"You are very brave…"
Paraphrase and Repeat Back	"If I understand you correctly, you are angry because you were told that your child's condition would not respond to antibiotics…"
Express Regret	"I am sorry that things have not turned out as we would have wished…"
Elicit Feedback	"How did you feel about our meeting today? I know that is not easy discussing death and the process of dying…"
Silence	A non-verbal way to say, "I understand" e.g. nodding head slightly Giving space for more expression
Gesture or Touch	Offering tissues; touching the patient's arm (be culturally sensitive and asked for permission before touching)

Brief Multi-Dimensional Psychosocial Assessment

The multi-dimensional psychosocial assessment helps us to understand the child's psychological state in relation to emotion, cognition, social, and spirituality.[1,3] Questions are best phrased in simple and direct manner, at child's level of understanding.

Emotions	
Area of Exploration	**Example of Open-Ended Questions**
General mood / behavioural symptoms, psychological distress (e.g. aggression, anxiety, depression)	How are you feeling today? I see your tears, would you want to share more? What you would like to do today to feel better?
Cognition	
Area of Exploration	**Example of Open-Ended Questions**
Orientation: Time, Place, People, Situation	Do you know where you are? Are you aware of what is going on now? What do the doctors or people around you tell you about your illness?
Social	
Area of Exploration	**Example of Open-Ended Questions**
Sociocultural background, social support	Would you want to tell me about your family/ friends? When you are in distress/pain, what can others do to make you feel better?
Spiritual	
Area of Exploration	**Example of Open-Ended Questions**
Religious background, beliefs, hope	**FICA spiritual history tool** **F** - Tell me about your faith **I** - What importance does your faith have in your life? **C** - Are you part of a spiritual community? **A** - How would you like me to address these issues?
Resilience	
Area of Exploration	**Example of Open-Ended Questions**
Coping mechanism, protective factors	1. What do you usually do to make yourself feel better? 2. Who do you usually go to when you need help?

Breaking Bad News

Even though breaking bad news is difficult, it is crucial to provide essential information in accordance with the child and family's needs and desires, and to tailor a more suitable treatment plan.

The 6-step SPIKES protocol is one of the methods to guide disclosure of bad news.[4,5] It is important to note that not every episode of breaking bad news will require all of the steps of SPIKES, but when they do they are meant to follow each other in sequence.

- Discuss with parents how child is best approached, with consideration of multiple factors such as age, personality etc.
- Tell the information at child's level of understanding, check with child if he/she can grasp the new information, correct immediately if misunderstanding happens.
- Be sensitive towards the child's emotion, provide support e.g. pat on arms, hugs when necessary (depending on relationship with child).

SPIKES Protocol

Step	Guidelines
Setting Up the Interview	Arrange for some privacy that involves significant others. Sit down and make connection with the child. And manage time constraints and interruptions.
Perception	Explore family's ideas, concerns and expectations.
Invitation	Adjust how much information to give based on child/family's comfort (e.g. "Would you want to know full information or should I skip the result? We can focus more on treatment plan."
Knowledge and Information	Warn child/family to prepare for bad news that is coming, (e.g. "I'm sorry to tell you that…"
Emotion with Empathic Responses	Observe and identify the emotion and the reason behind, give child period of time to express his/her emotion, be attentive and empathic
Strategy and Summary	Presenting treatment that is available and manage expectation to be realistic in sensible manner.

How Do I Handle Difficult Questions?[3]

Difficult questions may include, "Am I going to get better?" "Am I going to die?" "How long do I have?"

- Listen to and acknowledge the question and check the reason behind it and if the answer is really wanted.
- You might say, "Would you like us to talk about that today or would you like to leave it to another day?" May also answer: "That's a difficult question, there are no simple answers. We can hope to control your illness but can't hope to cure it."

The issue of "time left"

- Avoid giving a prognosis with a definite time scale or expressing the notion that "nothing more can be done."
- It is important to offer hope at some level, for example, "We cannot cure you, but we hope to control your disease" or "We will do our best to keep you as comfortable as possible." Do not be afraid to say, "I don't know."
- Communicate time in range, i.e. hours to days, days to weeks, weeks to months and months to years.
- Flexible time scale, for example, "You may have a number of months," or "You may have months rather than years."

Collusion

Definition: Withhold truth from children

Strategy: Healthcare team will not withhold truth from child but will not disclose truth in proactive manner. Truth should be told if invited by child and depending on their level of understanding.

Provide immediate follow-up (e.g. 24 hour) after consultation to child/family/significant others and help them to bridge resources as per needed, such as pastoral care, disease-specific support groups, palliative care services, counselling services and social workers.

*Be aware of the temptation to overload a patient with information. Document in the medical and nursing notes what the patient and/ or the family members/significant others have been told and their reactions.

Post breaking bad news support for parents

Common issues and concern:

- Families feel abandoned by primary team once DNAR has been signed.
- Frequently sent home by casualty thinking no more active management.

Strategies:

- Allow admission if needed.
- Give hope of ensuring comfort.
- Continue follow-up with paediatric palliative care.
- Health care workers need to be aware of their possible avoidance behaviour, either verbal or non-verbal language that might upset the family.

Procedure for referral for clinical psychology psychotherapy services:

For all government general hospital with palliative services

1. Palliative specialist/medical officer to write referral to psychiatry department
2. Patient to obtain appointment from psychiatry department
3. Psychiatrist/medical officer from psychiatry department assess and review patients
4. Psychiatrist to write referral to clinical psychologist depending on services required after assessment and review
5. Referral will be reviewed and discussed with referrer if necessary
6. Patient to obtain appointment from clinical psychologist
7. Patient to attend appointment and follow-up on pre-agreed date

For National Cancer Institute Malaysia

1. Palliative specialist to write referral to clinical psychologist depending on the services required
2. Referral will be reviewed and discussed with referrer if necessary
3. Patient to obtain appointment from clinical psychologist
4. Patient to attend appointment and follow-up on pre-agreed date

Psychosocial Intervention

The relief of suffering in palliative care patients needs a combination of good symptom control and psychosocial care. This section provides brief interventions that healthcare professionals can carry out with children for psychosocial care.[1,5-7]

Psychoeducation

- Counselling about the pain, aggravating and alleviating factors, management strategies, lifestyle factors that may influence the pain.

Self- management for child to regulate emotional distress/ pain

- 2-6y/o: Blow bubbles, watch cartoon, play with toys/friends
- 6-12y/o: Talk about favourite things/places, deep breathing and squeeze balls, guided imagery exercise and to have a hobby
- Teenagers: Self-distraction, deep breathing, squeeze balls, guided imagery relaxation/ meditation/ mindfulness and to have a hobby or interest.

Deep breathing relaxation

- Put hands on stomach and cough, the contracting muscle indicating location of diaphragm, to ensure deep breathing with expansion of diaphragm
- Shallow and fast breathing may cause adverse impacts such as vertigo and breathlessness. Pacing is important based on consistent counting.
- Counting based on 4-2-6-2
- 4 – Inhale using Nose
- 2 – Stop/ Pause
- 6 – Exhale using Mouth
- 2 – Stop
- And repeat the cycle until patient reports feeling calmer
- To be done in relaxed position (e.g. sitting, lying down)

Mindfulness of Pain

- Seek help from caregivers/doctor for analgesia
- Breathe in and out to centre yourself
- Breathe until you feel you are calmer
- Bring your attention to the pain
- Try to keep a curious mind to see what pain is
- Notice the sensations, emotions and thoughts of pain
- Pay particular attention to the unpleasantness of pain
- Notice how the mind resists pain
- Relax the resistance
- Smile to your pain

Progressive Muscle Relaxation by Edmund Jacobson[5]

Progressive muscle relaxation is an exercise that relaxes your mind and body by progressively tensing and relaxing muscle groups throughout your entire body.

- You will tense each muscle group vigorously, but without straining, and then suddenly release the tension and feel the muscle relax. You will tense each muscle for about 5 seconds.
- If you have any pain or discomfort at any of the targeted muscle groups, feel free to omit that step.
- Progressive Muscle Relaxation videos are available at: https://www.youtube.com/watch?v=t3uK039WdaM

Guided Imagery Exercise[6]

Guided imagery is a mindful and meditative process that uses visualization and imagination to bring awareness to the mind-body connection. Children can easily access this healing process because they're naturally imaginative.

By relaxing into a vivid story, children gain tools to deal with stress, pain or difficult feelings by listening to his/her inner wisdom and access their own power of healing.

Examples of scripts are available at https://www.greenchildmagazine. com/free-meditation-guided-relaxation-scripts-kids/

Expressive Art Session

- Music
- Story telling
- Drawing / colouring
- Play

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Wish fulfilment

If possible, help the child or family to decide what they would most like to do before their loved one dies. The process of fulfilling the wishes often leaves wonderful memories for the child and the family.

Supporting child with procedural pain[7]

- Preparing the caregiver and child of procedural pain
- Supportive role for caregiver, provides physical touch (e.g. stroking, hold hands) when possible
- Remain calm for the child
- "Your child needs you to keep calm for him/her, can you do it now?"

- Caregiver can take deep breaths to calm themselves and help direct child to take slow deep breaths
- Distract the child
- Singing to child/ telling a story or jokes
- Take focus away from needle
- Teaching child to recognize successful coping and praise them
- Make use of the placebo effect for child e.g. kissing or blowing away the pain
- Validate, then reframe, useful phrases for caregivers: > It's painful right now, but it's going to get better > The medicines are going to make you feel better soon > You're being very brave. I'm proud of you.

Caregiver and Palliative Health Care Provider Well Being

Caregiver Burnout

It is common for caregivers to experience physical, psychological and emotional burnout while taking care of a child in illness. Therefore, this section provides understanding to increase the awareness of caregiver burnout so their physical and psychological well-being were taken care while giving care to their children or family members.[8,9]

Risk factor for fatigue and burnout

- Care burden
- Restricted freedom/activities
- Feeling of insecurity/ loneliness / fear
- Facing death
- Lack of emotional, practical and information-related support
- Role confusion/ multiple roles (e.g. work, spouse, child)
- Unrealistic expectations
- Lack of control (e.g. money, resources, skills)
- Overly high demands on self
- Lack of awareness of burnout and fatigue

Signs of caregiver burnout

- Emotional and physical exhaustion
- Socially withdrawn

- Low mood, irritable, sense of hopelessness and helplessness
- Loss of interest in activities previously enjoyed
- Changes in appetite, sleep pattern
- Getting sick more often
- Feelings of wanting to hurt yourself or the person for whom you are caring
- Excessive use of alcohol and/or sleep medications

Protective factors to assist the caregiver

- Good social support
- Continuing previous activities
- Hope
- Keeping control (problem solving if able to)
- Satisfaction

Helpful Behaviour to Overcome Caregiver Burnout

- Have "ME" time
- Know own's limitation, get support and help when needed (e.g. family, workplace)
- Stick to routine and consistency
- Get enough rest
- Join a support group
- Use organizers (e.g. timers and reminders)

The Zarit Burden Interview, a caregiver self-report measure originated as a 29-item questionnaire (Zarit, Reever & Bach-Peterson, 1980). Each item on the interview is a statement which the caregiver is asked to endorse using a 5-point scale. Response options range from 0 (Never) to 4 (Nearly Always). For shorter administration, shorter versions, ranging from 1 to 18 items, have been developed.

Short Form Zarit Burden Interview (ZBI-12)

	"Never" (0)	"Rarely" (1)	"Sometimes" (2)	"Quite frequently" (3)	"Nearly always" (4)
Do you feel…?					
That because of the time you spend with your relative that you don't have enough time for yourself?					
Stressed between caring for your relative and trying to meet other responsibilities (work/family)?					
Angry when you are around your relative?					
That your relative currently affects your relationship with family members or friends in a negative way?					
Strained when you are around your relative?					
That your health has suffered because of your involvement with your relative?					
That you don't have as much privacy as you would like because of your relative?					
That your social life has suffered because you are caring for your relative?					
That you have lost control of your life since your relative's illness?					
Uncertain about what to do about your relative?					
You should be doing more for your relative?					
You could do a better job in caring for your relative?					

- → Short form ZBI-12 validated as screening tool in advanced illness including dementia and cancer
- → Total ZBI-12 score: summation of 12 items (0 to 4 points per item, total score range 0 to 48)
- → Copyrighted, but available for free use by clinicians and for non-funded academic research
- → Suggested guidelines for scoring:
  - 0-10: no to mild burden
  - 10-20: mild to moderate burden
  - >20: high burden

Health care provider well-being

Health care provider's well-being is easily overlooked when dealing with the emotional and physical demand as a professional when treating patients. This section provides understanding and brief assessment for burnout to ensure healthcare provider has healthy physical and emotional well-being is well taken care of to continue doing justice to their treating patients.[10,11]

Risk factors for burnout among palliative care providers

- Lack of self-confidence in professional's own communication skills with patients and relatives
- Pressure of time
- Problems with the transmission of bad news in relation to ineffective curative treatment
- Lack of education and training in palliative care
- Dealing with pain, suffering, dying and death
- Worry of patient's economic ability
- Team conflict in palliative management

Signs of clinician/support staff burnout

- Physical, psychological and emotional exhaustion
- Frequently sick
- Difficulty setting healthy boundaries
- Dreading going to work
- Feeling under-appreciated
- Lack of ambition due to burnout
- Compassion fatigue

Helpful Behavior in Overcoming Burnout

- Getting social support (family and friends).
- Keeping to a routine.
- Carve out time to relax.
- Do enjoyable activities (e.g. sports, classes)
- Read self-help books for insight and strategies for coping
- Going to see a doctor/ mental health professional/ support group.
- Reframe unhelpful thoughts to helpful ones.

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Spiritual Care

"There are a lot of people to help you usher a child into this world, but very few to help you gently accompany a child out."

- a patient's father -

Introduction

Spirituality refers to how individuals seek and express meaning and purpose in their lives, and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred.

Religion and spirituality are not the same thing, neither are they entirely distinct from one another. While spirituality may incorporate elements of religion, it is generally a broader concept. Although religion and/ or spirituality are important values for many, the influence of religion and/or spirituality on treatment decision-making or personal response to significant events remains unclear. A strong sense of spirituality may bring about positive emotions such as peace, awe, contentment, gratitude, and acceptance.[1]

Palliative care provision in Malaysia needs to consider the cultural and religious diversity which affect understanding or approach to life and death. Patients from various religious groups express their faith, specific beliefs, and values in their own way. Therefore, religious and spiritual needs are different for each person or family. Palliative care providers should refrain from assumptions and judgments.

Spiritual care assessments therefore should focus on the specific needs of every patient.

Providing Spiritual Care

The National Consensus Project for Quality Palliative Care, 2009 developed evidence-based clinical practice guidelines for managing spiritual suffering.[2]

"Spiritual screening or triage is a quick determination of whether a person is experiencing a serious spiritual crisis and therefore needs an immediate referral to a certified chaplain. Spiritual screening helps identify which patients may benefit from an in-depth spiritual assessment."[2]

Spiritual screening and assessment of the patient or family helps to uncover distress or suffering that impair the ability to experience meaning in life, connectedness with self, others, world or the Divine.

Offering spiritual care often involves creating a safe and secure or 'sacred' space, for the patient, where parents, siblings or the healthcare team are comfortable as well. In this space, the child and caregivers can express their inner emotions or suffering, know that it is all right to do so, and that they will be heard and taken seriously.

The art of good spiritual care is the art of empathetic listening - being able to be still and to hear what is not being said.

The gift of "being present" means setting aside the time to be fully available to discuss the needs and concerns of a patient. It may entail turning off your phone, or not looking at your watch.

You may practice a combination of any of the following, as appropriate to the patients' needs:

- Empathetic listening and seeking to understand worries and fears, which gives clues to their current state of spiritual health and journey.
- Touching, holding, and other forms of silent soothing – especially for those who are unable to articulate their needs and concerns.
- Addressing spiritual concerns and providing clear and consistent explanations about what is happening.
- Letting the child have a sense of control and empowerment with regards to their condition and treatment.
- Acknowledging and validating their emotions, reinforcing self-esteem and respecting privacy - especially for teenagers.
- Playing and praying together with the children and families.
- Fulfilling their secret wishes or unfinished matters they want to resolve.
- Encouraging them to explore their relationships with self / others / the Divine, along the themes of, "Thank you", "Forgive me", "I forgive you", "I love you".
- Performing religious rituals or rites together.

For patients, family members, and caregivers who draw strength from their faith, the following might be helpful for their coping:

- Remind them of the merciful loving qualities of the Divine.
- Create space for repentance, forgiveness, contemplation, reflection and gratitude.
- Refer to or bring in their community or personal religious leaders if they prefer.
- Help patients adjust by offering or teaching concessions for rituals in order to ease worship while sick – prayer, fasting, etc.
- Personalize connection with the Divine through their choice of verses of the Qur'an / Bible / other scripture. Offer to recite or listen to their recitation.
- For prayer – ask them what they want to ask the Divine for – empower them to verbalize their own wishes and prayers.
- Focus on being patient-centered, yet balancing the sensitivities of the family and culture.
- Meet patients at their own levels - no judgments / assumptions.

- Increase your own levels of spiritual, religious and cultural competency to be able to engage and connect deeper with the patient.

Understanding and Assessing Spiritual Suffering

Patients are usually preoccupied with their physical illness and treatment, making them ignore or downplay spiritual suffering or concerns. For children, spirituality is often centered around their understanding of daily life.

Infants and children with limited verbal ability and no concept of death depend on input from their physical senses and their physical relationship to the surroundings. In the preschool years, children may not be able to conceptualize their own death as they cannot grasp its irreversibility. Some may have "magical" thinking – and mention monsters, angels, imaginary friends, etc. Primary school age children would have more adult-like concepts of death and begin to understand their own mortality.

We should try to familiarize ourselves with the cues and metaphors which people may use to convey their concerns or distress, especially when facing a prolonged illness or anticipating death.

Common spiritual suffering / concerns, and their corresponding verbal cues

Spiritual Suffering / Concern	Examples of verbal cues
Concern about life after death	• What happens after we bury a dead person? • When do I get to go to Heaven? Will my cat be there?
Concern about the dying process	• Does it hurt to die? Will I die at home / hospital? • Is dying like sleeping? Will I know if I'm dead?
Lack of meaning / purpose / sense of self	• Doesn't matter if I die anyway, I don't even know why I am alive. • I can't go to school, I can't play, I can't even eat properly. I can't do anything good. • I used to be cool and popular, now I have no hair / carry a poo-bag, etc. (change in any physical appearance due to the illness).
Loneliness / separation (from parents, siblings, pets, friends)	• Nobody comes to play with me anymore. • Can I come back and play with Meow if I die? • What if I don't wake up from sleep tomorrow?
Fear of not being remembered / no legacy	• I'm worried everyone will forget me. • I haven't done much in my life yet.
Angry towards others / God	• Why did God let me get cancer? This is not fair. • My friend is meaner than me, but why didn't he get sick?
Desires relationship with God	• Will God forgive me? Where is God? Will He listen to me?

Spiritual Suffering / Concern	Examples of verbal cues
Questions / confusion about God and/or belief and value system	• Mama keeps praying to God, but I'm still sick anyway. • Why does anybody have to be sick?
Loss of future, relationships, self, sense of unfinished business	• Who is going to take care of Mama when she grows old, if I'm already gone? • I won't get to graduate with my friends and go with them to Tioman.
Feels guilt from past actions / thoughts	• Am I sick because I was a bad brother to my siblings? • Did my sister get cancer because I pushed her at the playground?
Feels guilt from present actions / thoughts	• Because of my sickness, Mummy and Daddy always fight about money. • Mummy can't go to work and kakak can't go to school because they have to take care of me.
Loss of control / autonomy over own body / space	• They keep poking me and taking me for tests, but nobody asks me or explains what they are doing! • Mama's friends come and pray for me, but I don't want them to.
Unfinished business	• I wish grandma knew I love visiting her at kampong, and I wanted to see the new babies from her pregnant cat.

Non-verbal cues are important. Body language, facial expressions, or drawings provide creative way to assess and understand what the patient / caregiver is thinking. Skillful clinicians listen intently and ask open-ended questions, granting patients the safe space to share and express their inner thoughts. Explaining to parents / guardians the relevance and meanings behind their child's cues could help them in making sense of and addressing their child's concerns, which may indirectly comfort the parents / guardians themselves.

The Spiritual Care Cycle

Spiritual care aims to build rapport and trust as a prerequisite to conducting a spiritual assessment. The process leads to the development of a care plan, taking the steps for intervention, and finally evaluating the outcome.

The assessment process is non-linear. It is agile and flexible, with no fixed time or iteration limit. There may be occasions where the assessment and interventions will happen immediately as you may have only one opportunity to meet with the patient. You may have a longer timeframe with other patients and conduct multiple visits and the opportunity for a more elaborate or comprehensive care and intervention plan.

It also creates awareness of how the patient's religious or spiritual beliefs and practices may impact their treatment choices. This will facilitate the development of an action plan for intervention to provide the best comforting care possible to the patient.

Spiritual conversations with children

Some useful tips, phrases and activities to help spiritual conversation with children:

1. **Listen to their words:** For example: God, heaven, spirit, karma, hope, wish, anger, sad, ghost, lonely, strong, weak, guilty, brave or afraid. Explore these thoughts by asking what the words mean to the child.
2. **Listen to their dreams:** The story or fears coming from dreams can give a chance to look at worries that are difficult to look at in 'real' life. Ask the child what the dream means to him/her. Do not try to explain it yourself.
3. **Listen for 'searching' phrases:** Phrases that show the child is thinking or searching deeply can give you a chance to encourage the child to talk about it more. The child may ask, "Why me?" or "I wish..." or "I wonder if...". You can help the child explore this further by asking, "What else do you wish?" or "How do you think that may happen?"
4. **Listen to their journey:** Children who are beginning to sense that they are dying often talk about going home or leaving. Talking about these feelings and exploring the journey with the child is difficult, but it needs to be done. Do not give false reassurances that they are not dying.

Spiritual Care Assessment Tools

There are several Spiritual Care Assessment tools and questionnaires publicly available, however these may be more suited to assess adolescents and adults, rather than children. But you may benefit from a general basic understanding of these tools in order to get to the heart of spiritual care, or while supporting families and caregivers.

Further details on the tools are available online.

S.P.I.R.I.T. (Maugans, Ambuel and Weissman)

S - Spiritual belief system

P - Personal spirituality

I - Integration with a spiritual community

R - Ritualized practices and restrictions

I - Implications for medical care

T - Terminal events (death) planning

F.I.C.A. (Puchalski and Romer)

F - Faith

I - Importance or Influence of religious/spiritual beliefs & practices

C - Community Connections

A - Address or Action

H.O.P.E. (Anandaraja and Hight)

H - Sources of hope, meaning, comfort, strength, peace, love

O - Organized religion

P - Personal spiritual practices

E - Effects on medical care and end-of-life care

When all else fails, remember that just your comforting and compassionate presence and accompanying of the child and caregivers is one of the most important and impactful forms of spiritual care.

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Medicines requiring Special Authorization by the Director General of Health/ Senior Director of Pharmaceutical Services (UKK Application) for MOH Hospitals

1) Scope

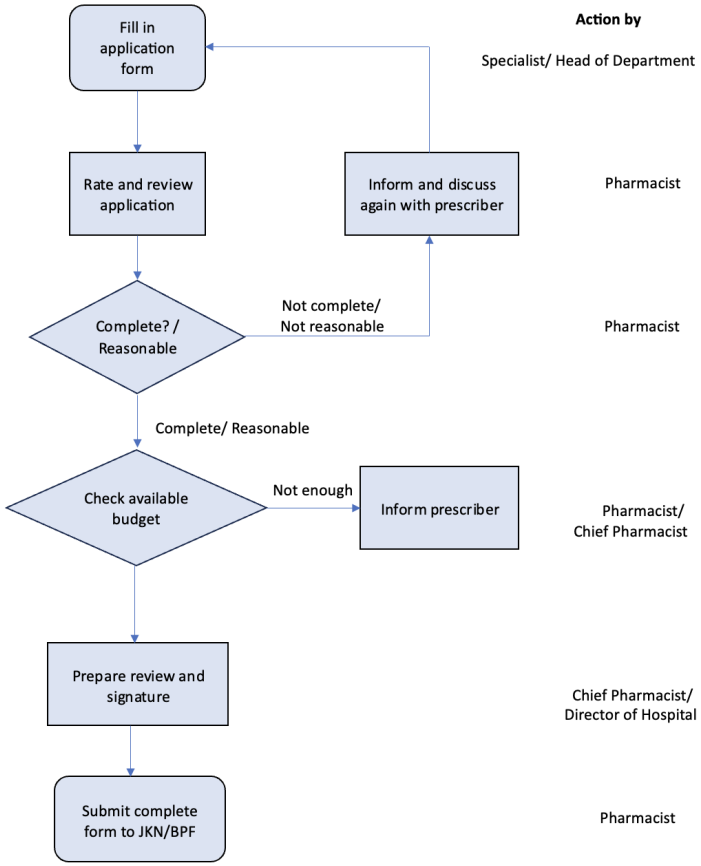
Special authorization by the Director General of Health/ Senior Director of Pharmaceutical Services is needed to procure and use the medication under the following conditions:

i. Registered but **not listed** in FUKKM
ii. Registered and listed in FUKKM but not indicated in FUKKM (**off-label FUKKM)**
iii. Registered and listed in FUKKM but the indication is not registered with Drug Control Authority (DCA) or Pihak Berkuasa Kawalan (PBKD) (off-label PBKD)
iv. Not registered with Drug Control Authority and not listed in FUKKM

Specialists are responsible for ensuring that the patient is given sufficient explanation. **Consent Form to Undergo Treatment** must be filled and signed by both the patient and the prescriber.

Application form and Consent form is available at https://pharmacy.moh.gov.my/sites/default/files/document-upload/garispanduan-permohonan-ubat-kpk-2016-final-040816.pdf

UKK Medication Application Flow Chart



Common medication in paediatric palliative care that require UKK application (up to November 2024):

I. Scopolamine patch
II. Methadone syrup
III. Glycopyrrolate tablet
IV. Melatonin tablet

Sourcing of medication outside Government Setting

Valid prescription from prescriber to patient is needed. Patients can purchase medication from private settings e.g. Selected private hospitals, compounding pharmacies etc.

Storage of UKK Medication

The Pharmacy is responsible for the storage of UKK medication. It should be stored in a specific location in the pharmacy, each drug with its own bin card.

Counselling to patient for UKK Medication

Some UKK medication requires special counselling on method of administration. Refer to pharmacists for counselling services.

Module 3

Transition Care

- Discharge planning
- Advance Care Plan
- Symptom Care Plan
- Continuation of care in the community
- Home Medications
- Transition to Adult Services

Module 3: Transition Care

Introduction

Children requiring palliative care service may need to be transitioned from the hospital to the community, or from paediatric service to adult service. Management of children with chronic and complex medical conditions require input from various teams, but with similar objectives and goals of care. Communication between team and parent, and documentation of previous or ongoing intervention would be vital as part of effective care transition for the patient.

Discharge planning

Important issues that need to be ironed out before discharge include:

- Decision on place of care and key healthcare workers involved
- Preparation of key documents: Advanced care plan including personal resuscitation plan, symptom care plan
- Caregiver preparation including essential knowledge and skills.
- Ensuring continuous supply of required medications
- Procuring equipment and consumable items.
- Financial support and community resources

Table 3.1 shows a checklist for tasks to be completed or issues to be discussed before discharge or transfer out from any service. For each item ticked "yes", the date that it has been carried out is documented.

Table 3.2 shows another checklist for consumable items for parents. This list helps the family to prepare all necessary medical consumables before the patient is discharged and helps with cost-estimation for the family.

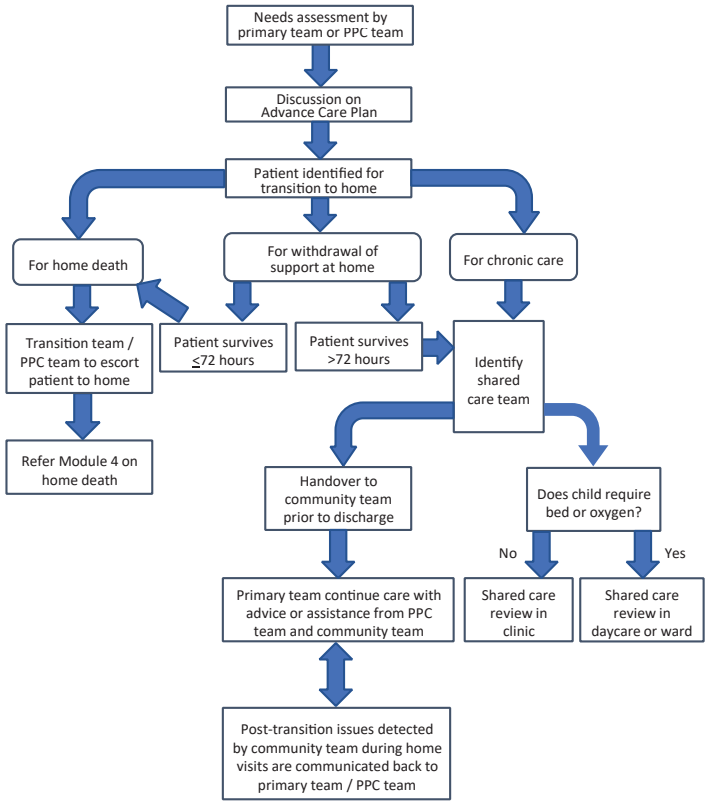
	Items
1	**Patient / Child** Medically stable for home care
2.	**Parents/ Caregiver** Family desires to have child at home
	Family has learned the necessary skills Basic Life Support Suction Feeding (Ryle's tube/ Perfusor/ Gastrostomy) Stoma Care Pressure Sore Prevention Wound Care Tracheostomy Care Oxygen Therapy/ Ventilation (refer to Consensus on Paediatric Home Ventilation/LTOT guidelines) Dialysis (refer to Peritoneal Dialysis SOP) Acute seizure treatment Clean Intermittent Self Catheterization Care of indwelling catheter Care of central line / Hickman catheter Therapies (OT/PT/SLT) Others
	Family has the finances to provide care (if not, referral made for financial assistance)
	Full time caregiver available
	Family has considered palliative care and end-of-life care options
6.	**Medications** Discharge medication review and counselling
7.	**Home Care Team** Hospital-based home care team Health clinic domiciliary care team (contacted, briefed/ trained and logistic arranged)
8..	**Written document** Written consent for home care Written agreement on equipment loan Basic Life Support attendance Patient's summary (Book) / Letter to local paediatrician/ FMS / community OT/PT Letter to school Personal Resuscitation Plan / Advance care plan / Contingency Plan Symptom Care Plan Letter to police for certification of home death (if for end of life care) List of medications/consumables/equipment

9.	**Financial assistance** (if qualified or applicable) Refer hospital medical social worker Fill up Borang OKU / Support letter for JKM Caregiver Allowance Fill up Borang C (to apply to TBP for medical and rehab equipment and milk (if on NG or gastrostomy tube feeding) for non-government servants. Fill up JPA Borang Perubatan 1/09 (for Government servant) Support letter to Pusat Zakat (Baitulmal) for purchase of milk and disposable diapers Others
10.	**Contacts,** provided for Key primary care provider Home care team (hospital or community-based) Hospice (if for palliative care) Biomedical company of equipment and supplies

Consumable Items Checklist

Category	No	Item	Size/brand	Quantity Per month
Feeding	1	Nasogastric tube		
	2	Feeding syringe (20/50cc)		
	3	Milk infusion bag+tube		
	4	Formula milk		
Respiratory	1	Suction tube		
	2	Normal saline for neb		
	3	Tracheostomy tube		
	4	Tracheostomy filter		
	5	Oxygen tubing and mask		
	6	Nebulizing set		
Dressing	1	One-use dressing set		
	2	Sterile cotton		
	3	Sterile gauze		
	4	Sterile glove		
	5	Latex glove (non-sterile)		
	6	Flavin /povidone		
	7	Saline 500ml/bottle		
Toileting	1	CIC tube /cbd tube		
	2	Diapers		
	3	Enema		
Medication	1	Alcohol swab		
	2	Medication syringes - 0CC -10CC -5CC -3CC -1CC		
Skin	1	Lotion/moisturiser		
Miscellaneous	1	Plaster		
	2	Scissor		

Transition to home - flow process



Medical social worker in paediatric palliative care

The Medical Social Worker Service's roles are:

a. To conduct the biopsychosocial assessment before the supportive therapy and practical assistance interventions are provided.

b. To provide practical assistance interventions e.g. purchase of medical equipment, purchase of medicines, funding treatment costs or general assistance, institutional placement and tracking down patients' relatives.

c. To provide supportive therapy interventions including consultation, emotional support and crisis interventions.

d. To facilitate application for eligible psychosocial assistance to patients and/or family members

e. Based on their assessment, they can recommend specific agencies or NGOs from whom the family are eligible to apply for required assistance.

Examples of governmental and non-governmental agencies that can provide aid for patients

Agency	Assistance
Tabung Bantuan Perubatan (TBP) KKM	Medical equipment/ Medication/ Special formula
Majlis Kanser Nasional (MAKNA)	Medical equipment/ Medication Transportation cost Disposable items
National Cancer Society Malaysia	Living allowance/ Transportation cost
Yayasan Tunku Laksamana Johor	Medical equipment/ Medication Transportation cost
Persatuan Paliatif Pediatrik Malaysia (MAPPAC)	Medical equipment Transportation cost / Monthly financial assistance Caregiver training / volunteer training Respite care
Baitulmal/ Lembaga Zakat Negeri	Medical equipment/ Medication Transportation cost Disposable items/ Special formula
Tzu Chi Foundation Malaysia	Medical equipment/ Medication Disposable items/ Special formula
Tabung Kebajikan Perubatan Malaysia	Medical equipment/ Medication Transportation cost
Jabatan Kebajikan Masyarakat	Monthly financial assistance
Persatuan Pemeliharaan dan Penyaraan Kanak-kanak Malaysia (MACAS)	Monthly financial assistance

Advance care plan

The advance care plan (ACP) is a record of a discussion that has been taken place between a child or adolescent (where possible), their professional care givers and those close to them about their future care.[3]

Discussing the ACP allows patient and parents to retain their autonomy when facing uncertainty in patients' disease trajectories.[3] It improves the two-way communication between patients/parents and healthcare personnel when discussing short-term and long-term goals of care and treatment plan during a sudden serious event (personal resuscitation plan).[4]

The child and parents are given the opportunity to discuss their treatment or care plan options. Sometimes, treatment or care plan decision-making is required during sudden or unplanned serious events.[5] When the child is in a stable disease phase, the goals of care may still need to be re-discussed.

Hence, the ACP should be flexible as changes may be required later (parallel planning of life sustaining treatment and palliative care supports). The ACP should be reviewed regularly (every 6 to 12 months), even in the absence of changes.

The child's primary team paediatrician should usually be involved in the discussions. The first discussion should be led by the paediatrician. However, the paediatrician is not necessarily the chairperson for subsequent discussions.

Before the discussion, the teams should prepare information regarding confirmation of diagnosis and expected prognosis of the child's disease.

If the child's care involves many teams from local and referral hospitals, the multidisciplinary teams may need to discuss among themselves even before discussions with the child and parents. Team discussion should involve all levels of staff, including the nurses. Nursing and junior staff can continue to support and follow through the ACP discussion and implementation.

Timing of ACP discussion

Discussion about ACP may be indicated if:

1. The child fulfils any of the criteria for the ACT/RCPH
2. categories for life-limiting or life-threatening conditions[5] (Refer Module 1)
3. The child's Paediatric Palliative Screening Scale (PaPaS) score is > 15[6] (Refer Module 1)
4. You would not be surprised if the child dies within a year[7,8]

OR

The child is not expected to live beyond 18 years of age

AND

Any of the following criteria:

- Previous admission to PICU
- Previous prolonged hospital admission >3 weeks
- Decline in underlying condition
- Increasing frequency of intercurrent illness and failure to return to prior baseline status
- Changes in treatment plans e.g. chemotherapy
- >3 unplanned hospital admissions in the past 12 months
- Child / family wishes to discuss ACP
- Admission from a long-term care facility
- Difficulty to control physical or emotional symptoms
- Patient, family or physician uncertainty regarding prognosis

In general, the ACP should be discussed as early as possible in the course of an illness, because it offers the greatest opportunity to explore the different possibilities that may happen as the child's illness progresses. However, the right time to introduce discussion about the ACP varies individually.

Timing of discussion should take the following into consideration:

- The preparedness and willingness to discuss by the child, parents and the physician.
- Availability of time to discuss, because the discussion should not be rushed.

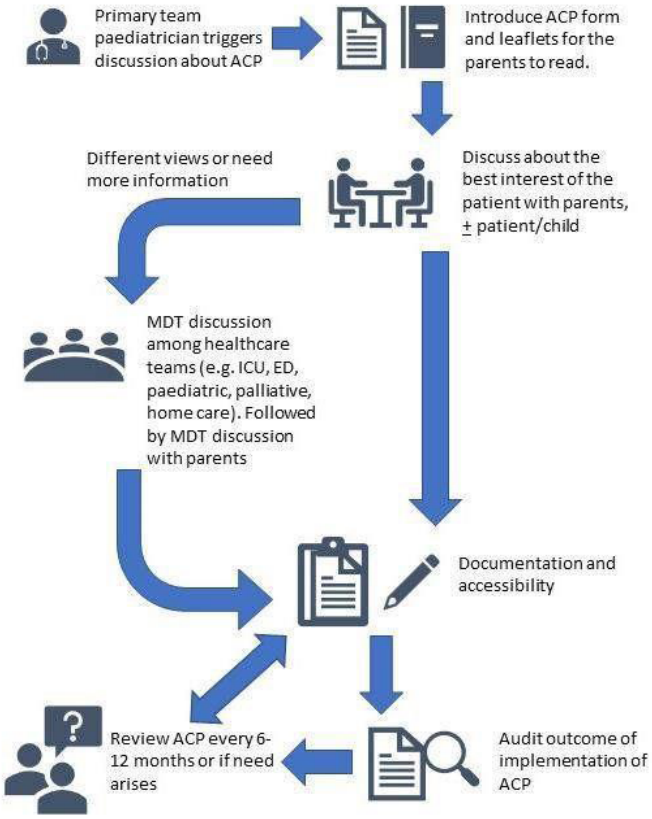
Legality of the ACP

It is the duty of clinicians, to act in the best interest of the patient. If the parent(s) or legal guardian is present when the child collapses, they may wish to deviate from the previously agreed Advance Care Plan. Under these circumstances, the parent(s) or legal guardian's wishes should be respected, provided they are deemed to be in the best interests of the child/ young person.

The child/young person or parents/guardians may change their mind about any stated preferences in the care plan at any time. The documented ACP is just a record of prior discussions.

It is recommended that the ACP document is signed by both the primary team consultant and parents. This formality increases the likelihood that the document will be executed. However, signing the ACP itself is not strictly necessary.

Flow process of discussing the ACP



Step 1

- The primary team paediatrician identifies the need of ACP discussion for the children with life limiting disease.

Step 2

- The primary team paediatrician leads the first discussion to introduce the concept of ACP to the patient and parents.
- The blank ACP form and patient information leaflets are given to the patient and parents for further reading.
- An agreed time frame is given to the patient and parents for them to discuss with other family members before the next meeting.

Step 3

- The ACP discussion involves the primary team consultant / paediatrician, the patient (where possible) and the parents.
- If the child has no adequate cognitive ability and verbal capability to be involved in the discussion, then the best interest of the child should be agreed upon between the paediatrician/clinician and the patient.

Step 4

- If the parents and patient (where possible) are unable to reach a consensus with the primary team consultant / paediatrician with regards to personal resuscitation plan and goals of care, then a multidisciplinary (MDT) team meeting should be arranged for further discussion among medical staff.
- The MDT team members may include Paediatric Intensivist, Emergency physician, related subspecialty paediatricians, palliative care physician or paediatrician, nurse in charge and home care doctors or nurses.
- If the parents and patient (where possible) has the same decision with the paediatrician/ clinician, then the ACP form should be documented and signed by both parents and the primary team paediatrician.

Step 5

- Review the ACP document regularly:

  > The child just being discharged from hospital admission

  > The child/parents wish to change or modify the ACP decision > Every 6 to 12 months duration from last review in the clinic appointment

Step 6

- Regularly audit (at least once every two years) to counter check if the ACP documented plans for a child were being carried out in your hospital whenever the child came to casualty or being admitted to ward.
- If the audit failed to prove the implementation of the ACP plan, then a root cause analysis should be sought to look into the steps of failure and the strategy to improve the implementation.

The ACP Form

Part I and II

Fill in the personal details of the patient (name, age) and parents / legal guardian (name, contact telephone number, relationship) who are involved in the ACP discussion.

Part III

Fill in the diagnosis and the bio-psycho-social issues of the patient and family in this column.

Part IV

List down all major events or possible future emergency symptoms and signs related to the disease of the patient, especially those causing suffering and cardiorespiratory distress.

Part V

In the event of immediate reversible cause of acute life-threatening deterioration such as choking, tracheostomy blockage or anaphylaxis, active resuscitation must be carried out.

Decisions are required on treatment options for two scenarios:

- resuscitation during cardiorespiratory arrest (asystole and stop breathing)
- intervention plan for acute deterioration (not cardiorespiratory arrest)

Part VI

This part documents the patient's preferred place of death, the funeral arrangement and the care support for the family members after the patient deceased.

PART VII

This part documents the preference and goals of the care process for patient and family members while the patient is at the stable phase of disease.

PART VIII

This part contains the signatures from the paediatrician and the parent/legal guardian to signify the ACP discussion has taken place. It also records the date that the ACP was signed.

Template for advance care plan

PART I: PERSONAL DETAILS

Name:	Date completed:
Date of Birth:	Date for review: (This document will not be valid after this date)
IC No:	Hospital RN No:
Home Address:	

PART II: PATIENT/FAMILY MEMBERS/CARERS INVOLVED IN ACP DISCUSSION

Name	Relationship to Patient	Age (years)	Contact number
(Main)			

PART III: DIAGNOSIS / CLINICAL ISSUES

PART IV: SYMPTOMS & SIGNS TO EXPECT IN THE EVENT OF EMERGENCY

Please refer to the symptom care plan (if available) for detailed management.

The child/young person or parents /guardian can change their mind about any of the preferences on this care plan at any time. This document is a record of discussion. Version 1: August 2019

PART V: PERSONAL RESUSCITATION PLAN

In the event of immediate reversible cause of acute life threatening deterioration such as choking, tracheostomy blockage or anaphylaxis, please intervene and treat actively.

Clinicians have a duty to act in a patient's best interests at all times. If a parent or legal guardian is present at the time of their child's collapse, they may wish to deviate from the previously agreed Advance Care Plan and under these circumstances their wishes should be respected, provided they are thought to be in the best interests of the child/ young person.

The child/young person or parents/guardian can change their mind about any of the preferences on this care plan at any time. This document is a record of discussion.

Resuscitation Status for Cardiorespiratory Arrest(Please)

- For active cardiopulmonary resuscitation (including bag and mask ventilation, chest compression, intubation and Intensive Care unit admission)
- Do not attempt cardiopulmonary resuscitation

Further Information (If any):

Intervention plan for Acute Deterioration (Non Cardiorespiratory Arrest)

(Please circle either "Yes" or "No" option)

YES	**NO**	Oxygen (Face Mask or Nasal Cannula)
YES	**NO**	Airway clearance/suction (Include Bag and Mask if required)
YES	**NO**	Analgesic / sedation for comfort
YES	**NO**	Tube feeding
YES	**NO**	Intravenous Access
YES	**NO**	Intraosseous Access
YES	**NO**	Intravenous antibiotic
YES	**NO**	Blood transfusion
YES	**NO**	Intubation and ventilation

Further Information (If any):

Further discussion is needed for any unforeseen condition that requires emergency surgical procedures.

PART VI: End of Life Care

Preferred Place of Care	**Priorities of Care** *(wishes, hope, organ donation, funeral, memories making, bereavement support)*
☐ Hospital ☐ Home ☐ No preference ☐ Undecided Others:_____	

The child/young person or parents /guardian can change their mind about any of the preferences on this care plan at any time.
This document is a record of discussion. Version 1: August 2019

PART VII: PREFERENCES DURING LIFE

Patient's Preferences *(e.g. Place of care, wish, symptom management, people to be involved [professional/ nonprofessional], activities to be continued [including spiritual and cultural] and goal-directed outcomes)*

Family's Preferences *(e.g. who you would like to be involved, sibling needs (e.g medical, spiritual or cultural backgrounds).*

PART VIII: Agreement with Discussions

Senior Clinician's agreement: I have discussed and support this care plan

Signature:

Name: Designation: Date: Phone contact:

Parent / Guardian's agreement: I have discussed and support this care plan

Signature: Relationship:

Name: Phone contact:

Date:

The child/young person or parents /guardian can change their mind about any of the preferences on this care plan at any time.
This document is a record of discussion. Version 1: August 2019

Symptom care plan

SCP is a written document that consists of plans to address distressing symptoms that might arise during the course of disease or terminal phase. This written plan has a step-wise approach consisting of non-pharmacological, pharmacological and contingency plan if symptoms persist. The SCP counselling will be provided to caregivers in hospital settings prior to discharge. This will empower caregivers to manage their symptoms at home.

Template for symptom care plan

PELAN PENJAGAAN SIMPTOM INDIVIDU

Nama	Aidil	**MyKid**	
Alamat		**Berat:**	13 kg
		Alahan:	Nil

Diagnosis: Spastic quadriplegic cerebral palsy secondary to perinatal event, scoliosis, restrictive lung disease

1. Sembelit

Aidil boleh mengalami masalah sembelit. Ambil langkah berikut jika dia kurang kerap buang air besar atau najis dia keras.

Langkah 1 : Pastikan jumlah susu dan air mencukupi.

Langkah 2 : Jika najis keras atau tidak membuang air besar melebihi 1 hari, boleh teruskan **Syrup Lactulose 5 ml dua kali sehari** sehingga najis lembut

Langkah 3 : Jika tidak beransur baik, boleh memberikan **Syrup Lactulose 5 ml sehingga 3 kali sehari** sehingga najis lembut. Jika beransur baik, kurangkan semula dua kali sehari atau sehari sekali. Jika mula cirit-birit, hentikan syrup lactulose dan minta bantuan nasihat

Langkah 4 : Jika Aidil masih sembelit selepas 2 hari, berikan **Ravin enema 1/2 tube**

Langkah 5 : Jika langkah di atas tidak berkesan, anda boleh menghubungi nombor panggilan hospital untuk bantuan nasihat.

2. Simptom 1

Aidil mempunyai risiko untuk mendapat [symptom] disebabkan oleh penyakit beliau.

Langkah 1 :

Langkah 2 :

Langkah 3 :

Langkah 4 :

3. Simptom 2

Aidil mungkin boleh mengalami [symptom 2] ..

Langkah 1 :

Langkah 2 :

Langkah 3 :

Langkah 4 :

Disediakan oleh: Dr _____ (Tel:_____)

Hospital _____

Tel: _____ Ext _____(Hubungi _____)

INDIVIDUAL SYMPTOM CARE PLAN

Nama	Aidil	**MyKid**	
Alamat		**Berat:**	13 kg
		Alahan:	Nil

Diagnosis: Spastic quadriplegic cerebral palsy secondary to perinatal event, scoliosis, restrictive lung disease

1. Constipation

Aidil may develop constipation or difficulty passing motion. Take the following steps if he passes motion less frequently, or if his stools are hard.

Step 1 : Ensure that he is taking enough milk and water.

Step 2 : If his stools are hard or he does not pass motion for more than 1 day, you may continue Syrup lactulose 5ml twice a day until the stools are soft.

Step 3 : If this does not improve, you may give Syrup lactulose 5ml three times a day until the stools are soft. If his condition is improving, reduce it to twice a day or once a day. If he starts to have diarrhoea, stop the lactulose and seek medical advice.

Step 4 : If Aidil is still constipated after 2 days, give ½ tube of Ravin enema.

Step 5 : If the above steps are not effective, you can contact the hospital for further advice.

2. [Symptom 2]

Aidil may develop [symptom 2]. Take the following steps if he...

Step 1 :

Step 2 :

Step 3 :

Step 4 :

Step 5 :

3. [Symptom 3]

Aidil may develop [symptom 3]. Take the following steps if he...

Step 1 :

Step 2 :

Step 3 :

Step 4 :

Step 5 : 5:

Prepared by: Dr _____ (Tel) :_____)

Paediatric Dept, Hospital _____

Tel: _____ Ext _____ (Contact _____)

Continuation of care in the community (Post discharge)

There are many models of collaboration between hospital and community healthcare providers, depending on resources and location. One example is the nurse-led community service. A trained nurse can become a liaison coordinator who can help the patient and family to navigate the local healthcare system. Community level palliative support may be coordinated with the local Family Medicine Specialist (FMS) or hospice. The hospital will provide additional support for crises.

It is vital for the hospital team to identify the available resources in the community before discharge. Availability of resources may be focused on urban communities. Special arrangements may be required if there are lack of necessary resources, particularly in rural communities.

Continuity of care at home (Home visit)

A home visit is a contact between a family and a nurse/doctor that allows the healthcare practitioner to analyse the home and family situations to provide the necessary nursing care. Using a multidisciplinary team (MDT) approach in home visits is crucial for tailoring to individual needs and making the best use of available resources within the community.

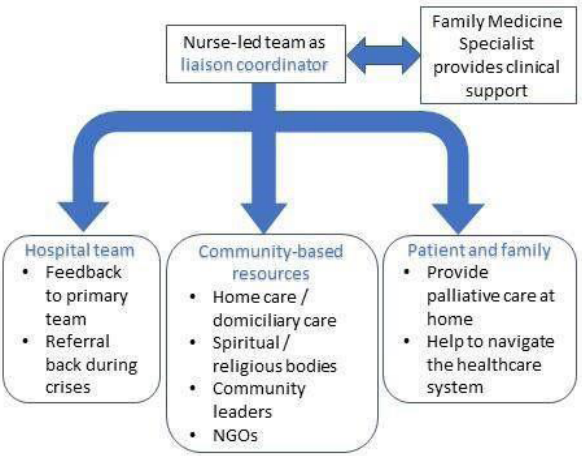
Important steps in conducting home visits.

Before home visit	During home visit	After home visit
• Familiarize with patient's case, MDT discussion • Identify reason for visit • Logistic preparations for visits: address, contact, staff, equipment, transport • Confirm timing with patient's family	• Patient assessment: symptom, functional, cognitive, psychosocial, nutritional • Caregiver assessment: caregiving practices, caregiver burden (refer module 2), caregiver competency (e.g. FCAT), family dynamics • Medication review and compliance • Medical equipment review. • Environmental assessment: safety, home modifications • Community resources and financial support e.g. child's wishes, parent support group, school and learning opportunity.	• Summarize plan of action and identify who executes it • Documentation • Feedback to primary team as necessary

Challenges and precautions during home visit:

- Adjusting clinical examination method to home setting
- Lack of equipment and investigation results
- Privacy for examination
- Privilege of assessing home dynamics

Example of nurse-led community team model



Home medications

Oral medications

The continuous supply of oral medications can be facilitated through pharmacy value-added services (VAS) available at Ministry of Health (MOH) facilities. VAS encompasses a range of innovative services offered by more than 500 MOH facilities. These programs include Medicine by Post (UMP), Drive-Through Pharmacy, Appointment Card Dispensing System, Locker4U, and the Integrated Drug Dispensing System (SPUB).

The SPUB can be used for morphine or other drugs under Dangerous Drugs Act, provided the following conditions are met:

- the health clinic / district hospital can arrange to collect the medications from the tertiary hospital
- the pharmacist in the health clinic / district hospital has a system to store, monitor and dispense DDA drugs

Parenteral medications

Medications delivered via the syringe driver may need to be constituted at the health clinic.

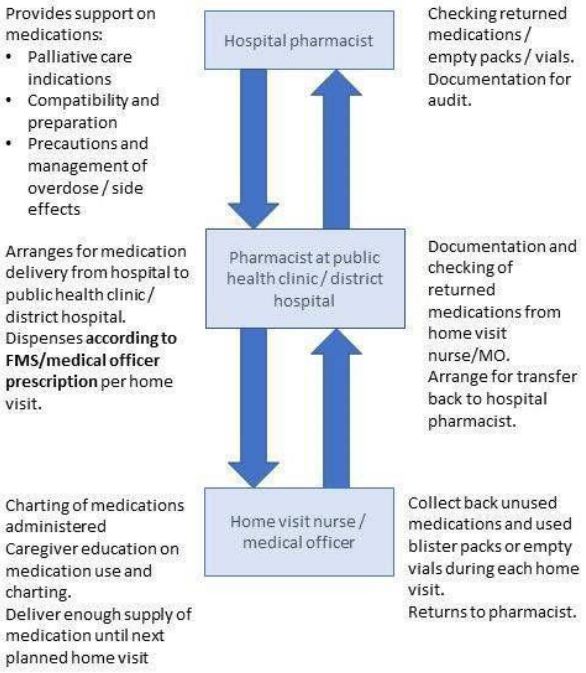
Discussions between hospital pharmacist with the local pharmacist is needed regarding:

- medications used for uncommon indications, which is common in palliative care
- compatibility of the drugs and preparation of parenteral medications
- steps to take in the event of medication error, side effects or overdose (Careful documentation is essential).

Arrangements should be made by local pharmacists to allow delivery of the medications from the tertiary hospital to their centre, and subsequently from their centre to the patient's home.

There should also be a system in place for used / unused medications to be returned from the patient to the community pharmacy, and subsequently from the community pharmacy to the tertiary hospital. This allows for accountability of the medications that have been shared between hospital and community health centre.

Example of flow process for medication provision from hospital to health clinic for PPC patients receiving home visits



* different systems may be in place in different centres

Common drugs for home parenteral medications (SC bolus / infusion):

1. SC bolus / SC infusion Morphine sulphate for cancer pain, severe nociceptive pain, opioid-sensitive pain
2. Midazolam for terminal restlessness, anxiety, refractory seizures, dystonia
3. Dexamethasone for intestinal obstruction, raised intracranial pressure, anti-inflammatory for space-occupying lesion, severe pain, nausea and vomiting
4. Haloperidol for nausea and vomiting, terminal restlessness and hallucinations
5. Hyoscine butylbromide – for secretions, colicky pain,

The medication should be integrated in the parallel planning with the primary team as part of the policy.

Community pharmacist involvement is also helpful to ensure that family members learn how to manage the storage and administration of medications correctly.

Care must be taken for medication reconciliation every time a patient is readmitted and discharged. Review all medications upon discharge from the ward and ensure that caregivers are informed about changes to their usual regime.

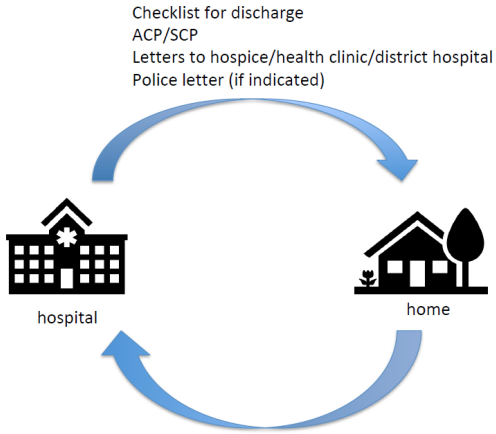
Lines of communication following discharge to home

Contingency plan

Discharge planning aims to offer support at home, reduce adverse events, improve quality of life, and prevent readmissions. To promote effective communication, the contact list should be properly recorded and maintained handy, as should written care plans.

In the event that readmission is required, an individual contingency plan should be developed based on the pathway of admission, such as direct admission to the ward or through the emergency department, depending on the hospital admission rules. The PPC provider should assist parents in navigating the healthcare system by educating and empowering them to use ACP or providing a written directory to speed admission.

When a family brings their child home for end-of-life care, it is critical that continuous on-call coverage be provided. If the family is not sufficiently supported at home, hospitalization is the default outcome in most regions, which may not be in keeping with their hopes and goals. Different communities will have different levels of home care support, such as a hospice or hospital palliative care support team. A system can be developed so that parents know who to call day and night.



Contingency plan for readmission

Transition to adult services

Principles of transition to adult services

1. Shared vision between adolescent and managing team
2. Collaboration with various agencies for health, education, housing, independent living, and social care.
3. Empowerment for the adult team to work with younger patients.
4. Engaging the community and lobbying the needs of people with life-limiting illness
5. Helping the young adult to talk about and plan for deterioration and crises, including dying.
6. Enabling adult health services to provide more patient-centred care including discussion on Advance Care Plan.
7. Improving the in-patient experience of young adults who are admitted to adult wards.
8. Supporting families during crises and bereavement.
9. Young people should have access to information.
10. Preparation for transfer should start before the child is 16 years old.
11. There are 3 phases of preparation for transfer to adult healthcare services:

Phase	Process
Phase 1 (Before 16 years old)	To introduce the concept of transition to the patient and family, including introducing the patient to the key healthcare staff in the adult team.
Phase 2 (Age 16-18 years)	Combined patient review by paediatric team and adult team in the adult clinic
Phase 3 (After 18 years old)	Adult team provides subsequent care for patient, with the support of the paediatric team.

Key information required during transfer of care to adult healthcare service:

1. Symptom profile, including pain
2. Patient's understanding of disease, preference and concerns of care
3. Support for caregivers
4. Patient's activities of daily living including mobility and nutrition
5. Multi-disciplinary assessment of needs
6. Advance care plan

Appendix

Template of letter to police officer for confirmation of death

Kepada

Pegawai Polis Daerah _____

Nama Pesakit :

No. K/P :

Penyakit :

Alamat :

Ayah :

No. K/P :

Ibu :

No. K/P :

Surat ini adalah untuk mengesahkan bahawa [nama pesakit] sedang mengidap penyakit [diagnosis] semenjak [tahun diagnosis dibuat] dan berada di bawah rawatan pihak kami di [nama hospital].

Bagaimanapun, semenjak [Tarikh], keadaan_[nama pesakit] telah menjadi semakin teruk, dan ibu bapa [nama pesakit] telah sedia maklum bahawa penyakit ini akan semakin melarat dan pesakit akan meninggal disebabkan penyakit ini.

Ibu, bapa dan [nama pesakit] telah menyatakan keinginan untuk menghabiskan masa akhirnya di rumah. Sekiranya ini terjadi, kami berharap agar surat ini dapat menerangkan situasi yang dialami oleh keluarga ini dan memudahkan mereka untuk mendapatkan sijil kematian dan permit pengebumian. Pihak tuan boleh menghubungi kami sekiranya terdapat sebarang kemusykilan. Pihak kami akan membuat apa yang boleh untuk membantu keluarga ini mengharungi masa yang sukar ini. Pegawai yang boleh dihubungi semasa waktu pejabat ialah Jururawat / Pegawai Perubatan yang menjaga [wad atau klinik berkenaan] di nombor [nombor telefon] ext: [nombor sambungan] atau di talian terus [nombor talian terus].

Segala kerjasama dari pihak tuan adalah amat dihargai dan didahului dengan ucapan terima kasih.

Yang menjalankan tugas,

_____

Pegawai Perubatan

Jabatan Paediatrik

Hospital [ ]

Template of letter to police officer for confirmation of death

To :

Police officer of ___(location)___

Patient's name :

IC number :

Diagnosis :

Address :

Father's name :

IC number :

Mother's name :

IC number :

This letter is to inform you that (patient's name) has been diagnosed with (diagnosis) since (year of diagnosis) and is receiving treatment at (hospital name).

However, since (day), the child's condition has deteriorated, and the parents are
Aware that he/she will die as a result of this ailment. Parents and (patient's name) have expressed their desire to spend the remaining time at home. If this occurs, we hope that this letter will explain the circumstances and assist the family in obtaining a death certificate and burial permit.

If any doubts arise, please contact our team. We will do everything we can to help the famil get through this difficult time. Our medical personnel who can be contacted during office hours are Staff Nurse/Medical Officer in (ward or clinic name) at (phone number).

We are grateful for the help and cooperation from your team. Thank you.

Yours truly,

_____

Medical Officer,

Paediatric Department,

(Hospital name)

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Module 4

End-of-Life Care

- Active dying
- Caring for the family
- Symptom management at end of life: pain, terminal restlessness or delirium, terminal seizures, excessive respiratory secretions, vomiting, breathlessness, terminal bleeding
- Palliative Sedation
- Basic nursing care at end of life: nutrition & hydration, oral care, skin care, home oxygen support
- Home parenteral medications: Subcutaneous route, syringe driver, elastomeric pump
- Withdrawal of Life Support
- Home extubation
- Home death
- Grief
- Ethical issues regarding end-of-life

Module 4: End-of-Life Care

Active dying

Active dying is the final phase of dying, commonly referred to as the final 48-hours of life.[1,2] The following are common signs and symptoms that may occur in last few days or hours of life:[3]

Physiological changes	Symptoms
Neurological	Increased lethargy Drowsiness Unable to talk Failure of temperature regulation Terminal delirium
Respiratory	Cheyne-Stokes breathing / apnoea Mouth breathing Death rattle / terminal congestion Gasping
Circulatory	Cool peripheries Dusky skin Feeble pulse Tachycardia / bradycardia
Gastrointestinal	Reduced appetite and thirst Dysphagia Gastric stasis Bowel incontinence
Renal	Urinary incontinence Reduced urine output

Caring for the family

Before the patient enters active dying phase:

- Discuss **goals of care** and **advance care plan** with family and patient.
- Take note of the patient and family's **preferences and wishes**, e.g. Place of care and death, spiritual rites.
- A management **plan** should incorporate the patient and family's preferences.
- Explore and address patient and family members' concerns during end-of-life.

What do I do when the child enters active dying phase?[4]

- Any treatment or intervention given is not for prolonging life.

- Inform family members regarding impending death and expected signs or symptoms.
- Educate and prepare caregivers on how to manage the anticipated symptoms.
- As far as possible, provide contact with a healthcare professional who can guide them during the active dying phase, especially if home death is desired.
- Take the family's cultural and religious beliefs into consideration on appropriate dying rituals.

How to provide medications to the dying child?

- Most medications need to be converted into subcutaneous, transdermal, sublingual or rectal routes when the child is no longer able to take orally.
- Teach caregivers how to administer the subcutaneous medications and how to operate the syringe driver, if any.
- Provide medications for anticipated end-of-life symptoms to the family and educate family on indications.

Preferred place of death

- Discuss with family members regarding suitability of preferred place of death.
- Consider availability of equipment, feasibility of symptom control, and caregiver preparedness.
- Discuss the possibility of rapid transfer and whether it is in their best interest.

Symptom management at end of life

Pain

Assessment of pain

The child is unable to communicate verbally.

Determine most likely cause of pain and whether it is reversible (refer Module 2)

Use non-verbal pain scales such as FLACC (face, legs, activity, cry, consolability) scale to measure pain intensity.[5]

Management of pain

Oral analgesics may be converted to subcutaneous morphine or transdermal fentanyl.

SC morphine can be given as bolus or as an infusion.

Transdermal fentanyl can be initiated if minimum daily oral morphine requirement is 15mg and above.[6]

Refer to opioid equivalence chart for dose conversion.

Continue oral or SC morphine for a further 8-12 hours when initiating transdermal fentanyl. After that, oral or SC morphine can be safely discontinued.[6]

Caregiver training

Teach caregivers to administer bolus doses for breakthrough pain.

Teach the caregiver how to operate the syringe driver (see Section IV).

Teach caregivers to maintain a simple pain diary and opioid charting (see Fig 4.1).

To convert oral morphine to SC morphine, divide oral morphine dose by 2.5.
e.g. oral morphine 10mg = SC morphine 4mg

Fig 4.1 Suggested format of simple pain diary and medication log

Prescription by doctor: Regular dose: Syrup morphine 2.5ml every 4 hours Breakthrough pain: Syrup morphine 2.5ml when needed for pain				
Date: 18 April 2019				
Time	Pain score	Name	Amount	Remarks
0300	4/10	Morphine	2.5ml	
0700	7/10	Morphine	2.5ml	
0930	8/10	Morphine	2.5ml	Sudden worsening of pain
1100	5/10	Morphine	2.5ml	
1500	4/10	Morphine	2.5ml	
1900	5/10	Morphine	2.5ml	Vomited after dose
2300	5/10	Morphine	2.5ml	

Terminal restlessness or delirium[7] *What is it?*

An abrupt increase in anxiety, agitation and confusion at the end of life.

Assessment

- Any symptoms that have not been relieved?
- Any medications that could have triggered the restlessness?
- Any fever or evidence of infection?

Pharmacological management

Palliative sedation may be given to alleviate patient suffering or caregiver distress without intention to shorten the patient's life.

Refer to the appendix for the doses:

- SC bolus or continuous SC infusion midazolam
- SC bolus, or SC/IV infusion haloperidol
- Intranasal Midazolam
- CSCI phenobarbitone

Non-pharmacological management

- Appropriate lighting to time of day (dark at night, bright during daytime)
- Reduce noise and light stimulation.
- Provide visual stimulus to remind of day, date and time. E.g. clock, newspaper
- Promote a familiar environment.
- Continue to talk as usual to comfort the child

Terminal seizures[8] *What is it?*

- Seizures may become more prolonged and frequent at the end of life.
- Absorption of oral anticonvulsants is poor at this stage.

Risk factors

- Underlying epilepsy
- Neurological disorders
- Brain tumours
- Metabolic derangement
- Medications that lower seizure threshold e.g. amitriptyline, tramadol, baclofen

Caregiver preparation

- Provide oral midazolam (for buccal administration) or rectal diazepam.
- Educate on immediate actions during a seizure (remove potential hazards, left lateral position, head turned to lateral, not to insert objects into mouth)

Pharmacological management

- Buccal midazolam
- Rectal diazepam
- Consider SC midazolam if not controlled
- Consider CSCI midazolam or CSCI phenobarbital if not controlled with bolus SC midazolam

Excessive respiratory secretions[9] *What is it?*

Excessive salivation can occur at the end of life, due to failure of swallowing. Secretions can pool at the throat of the patient causing a rattling sound while breathing.

Non-pharmacological measures

- Head positioning (avoid flexed neck posture, lateral position)
- Bibs or absorbent towels

Medications

- Sublingual atropine 1% eyedrops
- Hyoscine hydrobromide (Scopoderm®) patch
- SC Glycopyrronium bromide bolus or infusion
- SC hyoscine butylbromide bolus or infusion

Nausea and vomiting[9]

Assess for causes

Refer to symptom management module for assessment of causes.

At the end of life, nausea and vomiting can be due to:

- Gastric stasis
- Increased ICP in brain tumours
- Intestinal obstruction
- Side effects of medications

Non-pharmacological management

Reduce or withhold feeds if there is gastric stasis.
Nausea and vomiting is not usually a great problem at the end of life unless there is bowel obstruction or it has not been controlled previously.

Pharmacological management

Choice of medications depends on the underlying cause. At end of life, subcutaneous

- Haloperidol (first-line)
- Metoclopramide - not for intestinal obstruction
- Promethazine (subcutaneous infusion, not for bolus)
- Dexamethasone (increased ICP or intestinal obstruction)

Breathlessness[9]

Assess for causes

- Anxiety
- Physical discomfort
- Environmental factors
- Accumulated airway secretion
- Medical disorders (pneumonia, heart failure, sepsis, acidosis)

General principles

- Treat underlying cause if reversible.
- Oxygen supplementation may not be necessary or helpful, unless there is documented hypoxia.

Pharmacological management

- Bronchodilators if bronchoconstriction is present
- Nebulised saline
- Low dose short-acting morphine

Non-pharmacological management

- Direct a fan to the side of patient's face
- Open a window
- Repositioning – prop up to 45 degree
- Suctioning if necessary

Terminal bleeding[10]

Assess for causes

- Coagulopathy and rupture of oesophageal varices from liver failure
- Tumour erodes to major blood vessel
- Thrombocytopenia

General principles

- The goal of care is patient comfort.
- Calm the patient and family members.
- Appropriate analgesia and sedation may be prescribed to reduce the child's anxiety.

Pharmacological management

- SC Morphine
- SC Midazolam
- Topical Adrenaline

*Morphine and midazolam should be considered as terminal sedation if the child is restless or anxious due to bleeding.

Non-pharmacological management

- Prepare dark cloth, linen and bucket near the bedside
- When the major bleed happens, compress adrenaline-soaked cloth at the bleeding site.

Palliative sedation[21]

What is it?

Palliative sedation is a medical practice used to relieve intractable suffering in patients with terminal illnesses by reducing their consciousness. In paediatric palliative care, it's considered when a child is experiencing severe symptoms that cannot be controlled by any other means, such as intense pain, agitation, or respiratory distress. The goal is to alleviate suffering, not to hasten death, and it is used only after all other treatment options have been exhausted. Best to consult the Paediatric Palliative care team before initiation and to be done in a hospital setting.

Key considerations for palliative sedation in children include:

- Ethical and Clinical Guidelines:
  It is guided by strict ethical and clinical standards. The decision to initiate palliative sedation involves a careful evaluation of the child's symptoms, prognosis, and quality of life. Families are deeply involved in the decision-making process.

- Types of Sedation:
  Palliative sedation can be either mild or deep. Mild sedation might reduce the child's level of consciousness but still allow them to respond, while deep sedation renders them unconscious.

- Medications:
  Common medications used for sedation include midazolam, levomepromazine, or barbiturates. These are titrated carefully to achieve the desired level of sedation.

- Double effect of medications:
  Refer to its intended therapeutic benefits alongside potential unintended side effects or adverse reactions, including death.

- Communication with Family:
  It is crucial to communicate openly with the family about the goals of care, what palliative sedation entails, and how it aligns with the child's comfort and dignity in their final moments.

  Palliative sedation can be considered as part of a broader palliative care plan, focusing on holistic care for the child and family during this challenging time.

Basic Nursing Care at End of Life

Nutrition and hydration[11]

- Nutrition and hydration at the end of life is for patients comfort, and NOT for weight gain or sustaining life.
- Initiating tube feeding is not recommended during active dying.
- Gastric stasis occurs at the end of life, and may lead to vomiting.
- Subcutaneous fluid infusion can be started if dehydration is causing distress to the child. However, increasing hydration at the end of life may increase secretions or oedema.
- Advise family members to perform oral care, even if the child is no longer able to take it orally.

- Subcutaneous fluids can be given short term (≤10 days) via gravity infusion sets or syringe drivers.

Cultural considerations
Food and drink play an important role in our culture and family members become concerned when someone is no longer able to eat or drink. Explain to family members that at the end of life, hunger and thirst is no longer an issue due to reduced physiological needs.

Indications for subcutaneous hydration are:

- Hypercalcaemia
- Nausea and vomiting
- Dysphagia
- To improve myoclonus (involuntary contractions of muscles)
- Assists sedation

Oral care[12]

- Alleviates the discomfort from dry mouth, halitosis and excessive salivation.
- An active routine of mouth care is required.

Caregiver training

- Clean the mouth regularly or at least 4 times a day with wet gauze to maintain oral hygiene and prevent odour.
- Gently remove the plaque, debris or dry skin from oral mucosa with oral swab stick or wet gauze.
- Moisten the mouth regularly with water spray or ice chips as frequently as possible.
- Apply lip balm to prevent cracked lips.
- Avoid glycerine and lemon - increase dryness and may damage tooth enamel.

Skin care

Possible changes at end of life[13]

- Higher risk of pressure sore due to immobility and reduced skin perfusion
- Difficult to maintain hygiene if unable to transfer to bathroom
- Oedema and dry skin increase risk of skin breakdown and infection
- Incontinence leads to irritant contact dermatitis

Caregiver training: [14]

- Regular repositioning to prevent pressure sore.
- Use a pressure-relieving mattress.
- Regular bedside sponging for hygiene.
- Apply emollients at pressure sites or swollen peripheries to reduce friction.
- Apply moisturisers regularly on dry skin to reduce itchiness.
- Handle oedematous limbs gently.
- Apply barrier cream at the diaper area.
- Use of sliding sheet to prevent shearing force.

Home oxygen support [15]

- Indicated for breathlessness due to hypoxaemia (SpO_2< 90%)
- The aim of home oxygen therapy is to **provide comfort** rather than prolong life.
- Routine checking saturations may not be necessary for palliative care.

Guidelines for prescribing home oxygen

Hospital and healthcare workers

- Indication for the use of oxygen should be clearly documented in patient case note
- Oxygen prescription should include flow rate and route of delivery:

Route of oxygen support	Oxygen flow rate
Nasal cannula	1-2.5L/min
Face mask	4-6L/min

- Humidification of home oxygen is a must if oxygen is given via tracheostomy tube.
- For oxygen flow rate that is more than 2L/min, humidification helps to prevent drying effect on mucous membranes.
- Provide family members written information regarding dangers of using home oxygen near sources of fire.

Home assessment

- Should be arranged **BEFORE discharge** and commencement of home oxygen support.
- Regular reassessment at each home visit by community palliative care provider

Assessments should include:

- Home environment (proximity to naked flames from stoves/lamps/ cigarettes)
- Attitude toward risks
- Smoking behaviour of family members
- Advice family regarding smoking cessation and location of oxygen tank in the home.

Risks and adverse effects of home oxygen support:

- Dry nose/eyes/mouth
- Pressure sores over cheeks, ears or nose
- Claustrophobia
- Hypercapnia respiratory failure
- Fire risk

Home non-invasive ventilation (NIV)[16]:

- The aim of the use of NIV is for symptom control, not for prolonging life.
- NIV improves symptoms by:

  > reducing respiratory effort by the patient

  > reducing carbon dioxide retention
- NIV can be used when withdrawing invasive ventilation support in ICU or the ward.
- Community palliative care providers require training to operate the ventilator prior to patient discharge from hospital.

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Home parenteral medications

Subcutaneous route[1–3]

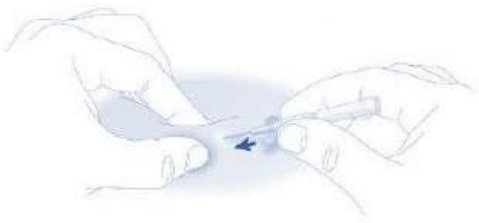
Suitable for parenteral administration of medications when:

- Unable to take orally (nausea, vomiting, dysphagia)
- Poor gastrointestinal absorption
- Intestinal obstruction
- Reduced consciousness

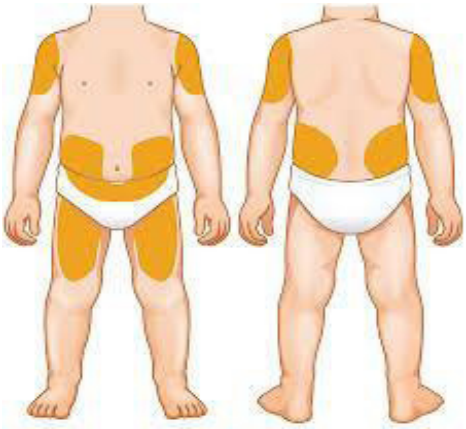
Intravenous lines are not recommended for the home setting.

Insertion[4,5]

- Use a fine gauge paediatric cannula (24G/yellow) or a butterfly needle
- For butterfly needles, grasp the textured sides of the wings and bring them together, pinching firmly.
- Using thumb and index finger, gently pinch the skin around the selected site to identify the subcutaneous tissue.
- Insert at 30-45o to the skin surface.



- Secure with adhesive tape.
- Connect to infusion line (for infusion) or yellow stopper (for bolus medications)



It is recommended for newborn until the child is 12 months old, the best site is the area of the upper thigh. For young children 12 to 36 months old, the best site is either the thigh or the back of the upper arm. Then for children older than 36 months of age may receive injections in the thighs, outer surface of upper arms and abdomen, except the naval or waistline.

Avoid inserting the line at:

- Bony prominences
- Joints
- Oedematous, infected, broken or bruised skin
- Recently irradiated skin area
- Sites in contact with wheelchair harnesses or seatbelts
- Areas with a lot of body hair

Syringe driver[6–8]

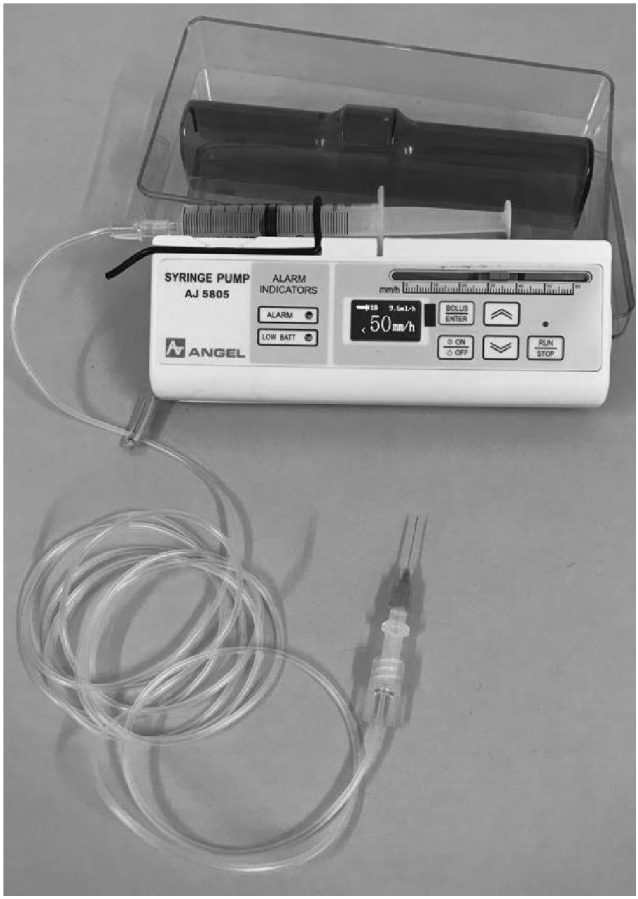
Medication preparation for use with a syringe driver

- Check for compatibility especially if combining drugs in single syringe
- Calculate the dose and volume needed for the infusion.

Volume of syringe	Volume of diluent
10ml	10ml
20ml	18ml
30ml	22ml
50ml	33ml
Take note that larger syringes need to be under filled for the syringe driver to work!	

- Label the prepared medications syringe (patient's name, name of drug(s), strength / dilution, rate ordered, date and time, name of staff who prepared the syringe).
- Both water for injection and normal saline can be used for diluting drugs. Normal saline is preferred when there is risk of skin irritation at the site of infusion but may not be suitable for some drugs. Water for injection is hypotonic and may cause skin irritation. However, it has less risk of drug incompatibility.

Caution: Promethazine and phenobarbitone cannot be given as a subcutaneous bolus due to high risk of severe irritation and tissue necrosis. However, it may be given as an infusion diluted with normal saline



Syringe driver with infusion set

Combining medications in a single syringe

- Check for compatibility before combining medications in a single syringe. Refer to your pharmacist!

- Common medications that can be combined include:
  > Midazolam
  > Morphine or other opioid
  > Hyoscine hydrobromide or Glycopyrrolate
  > Metoclopramide
  > Haloperidol

- Common medications use that are incompatible with other medications:
  - Proton pump inhibitor (eg: omeprazole)
  - Dexamethasone

- Incompatible medications can result in:
  > Precipitation / crystallisation of the drugs
  > Cannula blockage
  > Skin / tissue irritation
  > Ineffective absorption of drug into the body

Storage of the medications[7,8]

- Most drugs diluted in normal saline are physically compatible and stable for 24 hours at ambient temperature.
- Unused prepared syringes should be stored in the refrigerator for not more than 7 days.

Operating the syringe driver[9]

- Different models have different operations. Please refer to the manufacturer's manual.
- Check that the delivery rates have been calculated correctly.
- For a newly set up infusion line, let the medications fill up the whole tubing before starting the infusion (Priming the line).
- Change the infusion tubing whenever the infused medication is changed.
- If doses are altered, use a new syringe. Altering the rate of delivery is not advisable.

Caregiver education
Educate caregiver on use of syringe driver at home on: • Basic steps of operating the syringe driver • Recognizing the occlusion alarm and almost empty alarm. • How to replace empty syringes • Steps to take if occlusion occurs • How to eliminate air bubbles.

Elastomeric pump [10]

Elastomeric pumps, also known as balloon pumps or ball pumps, are commonly used to deliver liquid medication via continuous subcutaneous infusion (CSCI). The term "elastomeric" refers to the pump's balloon component, which contains a layer made of elastic material, such as natural rubber or synthetic elastomers.

The necessary pressure for delivering the drug is generated by the elastomeric layer molded within the pump. When the pump is filled, this layer stretches, and its elastic contraction forces the liquid through the tubing, passing through a flow restrictor before reaching the patient connection

Elastomeric pumps are portable, simple to use, and do not require batteries or an external power source, making them ideal for outpatient or home care settings.

However, elastomeric pumps lack alarms to notify users of issues like pump malfunctions. Additionally, they are sensitive to temperature changes; very hot or cold conditions can affect the rate at which medication is delivered, either speeding it up or slowing it down.

How it Works

- The "balloon" pump contains the prescribed medications.
- The balloon gradually becomes smaller and eventually, will see it wrinkling.
- To ensure that the balloon pump operates correctly:
  - Do not squeeze the balloon.
  - Check that there are no tangles in the tubing and that the filter is not covered.
- The nurse will tape the flow restrictor/controller to your skin. It is set at a specific rate that cannot be adjusted. The flow restrictor/controller must always be touching your skin, which allows the pump to give you medication at the right time.
- The medication in the pump should be at room temperature before the infusion begins.

Different models of elastomeric pump

Monitoring of the infusion line[9]

Monitoring of the infusion line	Steps to take
Ensure the line is secured with adhesive dressing.	Replace the adhesive dressing if dirty or less adhesive.
Check the infusion site for redness, swelling, discomfort/pain and leakage.	Remove the current line and insert a new subcutaneous line at a different location.
Check the diluted medications for precipitation, cloudiness, big air bubbles or colour change.	Replace the syringe immediately.

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Withdrawal of life support

In certain groups of severely ill children, prolonged ventilation and intensive care may no longer be in their best interests.[1] These may include:

- No chance for survival, or imminent death despite further treatment.
- Permanent severe disabilities or incapacitating conditions, resulting in a high burden of pain and suffering.
- The decision to withdraw support is led by the consultant, supported by the team of healthcare professionals involved in the care of the child and the child's parents.[1] Early involvement of a palliative care team is advisable in planning and communicating decisions with family members.

Introduction of withdrawal

- Consult a palliative care team specialist.
- Identify the appropriate clinicians and healthcare professionals to be present during family meetings to discuss withdrawal.

Important points to be discussed with family:

- Options for
  - > continuing current intensive care support vs
  - > withholding escalation of support vs
  - > withdrawal of care
  - > place for withdrawal of care (home vs hospital)

> pros and cons of withdrawal of care – child may die faster if care is withdrawn, but withdrawal allows the team to plan for better quality of end-of-life care

- Shared decision that there will be no more reintubation or cardiopulmonary resuscitation in the process of withdrawal.
- Management of symptoms after withdrawal
- Preferred place for extubation
- Timing of death is variable, the child may survive beyond expected time frame.
- Wishes family may have before extubation, e.g. taking family portraits, legacy work (hand mould, handprints etc.)
- Ensure family's concerns and values are addressed appropriately.
- Shared decision making on timing of:
- Extubation
- Discontinuation of essential life-sustaining medications Document discussions and agreed steps in case notes.

Inpatient ventilator withdrawal

Inpatient ventilator withdrawal can be conducted in 2 ways:[2]

- **Immediate extubation**
  > Endotracheal tube is immediately removed and humidified oxygen is given instead.
  > Preferred method if patient is conscious, minimal secretions, and airway patency can be maintained.
- **Terminal weaning**
  > Gradual decrease in ventilator settings (ventilation rate, PEEP and oxygen settings) while endotracheal tube is left in place.

Immediately before withdrawal

- Allow time for family rituals or memory-making.
- Turn off all alarms and monitors.
- Remove any restraints and medical devices such as nasogastric tubes.
- Discontinue parenteral medications e.g. intravenous infusions of inotropes, muscle relaxants, antibiotics, or hydration as agreed in pre-withdrawal discussions.
- Wean down any morphine and/or midazolam infusion.
- Keep intravenous access for palliative medications.
- Establish adequate symptom control before extubation.

- Prepare additional sedation for use if required after extubation.
- Give IV/SC glycopyrronium 1-2 mcg/kg/dose stat, OR IV/SC hyoscine butylbromide 0.5mg/kg around 10-15 minutes before extubation to reduce airway secretions.
- Consider IV/SC dexamethasone 0.15-0.25mg/kg stat if the child is expected to have post-extubation stridor due to prolonged intubation.

During withdrawal

- Reduce FiO^2 to 0.21 and observe for respiratory distress. If respiratory distress is present, adjust medications for symptom control.
- Give a short trial of stopping ventilator assistance before removal of the endotracheal tube.
- When removing the endotracheal tube, ensure towels and suction are available in case of secretions.
- Turn off ventilator alarms.
- Provide emotional support and presence for the family members during this process.
- Arrange for provision of grief and bereavement support for family members.

Medications to be given after extubation

- IV/SC morphine 0.1 mg/kg stat and PRN (maximum 2mg per dose)
- IV/SC midazolam 0.025mg/kg stat and PRN (maximum of 2mg per dose)
- IV/SC glycopyrronium 1-2 mcg/kg if additional dose is needed, OR
- IV/SC hyoscine butylbromide 0.5mg/kg stat if additional dose is needed

Consider to convert all these medications to 24 hours infusion if a few repeated doses are required.

Terminal Discharge

Terminal discharge is defined as a discharge of hospitalised patients for the purpose of passing away at home when death is expected to be imminent (within hours or days). It should only be considered when curative or life-prolonging treatment is futile and when patients or loved ones express their preference to be at home and there are no obvious obstacles. The aim is to help them discharge home without delay so that they can spend this critical period with loved ones.

Key points

Discharge planning similar to transition of care

- Doctor counselling, prescribe medication, prepare documentation, refer community team

- Staff nurse to conduct caregiver training
- Pharmacist to supply medication
- Family to arrange for transport

Medications

- Stop medications that are futile, potentially harmful or have little or no benefit
- Supply medications for symptom control for a period of 5-14 days for terminal discharge

Maintain a backup follow up for consult with primary team for assessment and refill medication

Terminal discharge checklist and consent form (Refer to HKL terminal discharge guideline 2023, http://library.nih.gov.my/e-doc/flipbook/hkl/terminal-discharge-guideline-12023/index.html)

Home extubation

Pre-transfer

- Discontinue unnecessary medications and parenteral access to maximise comfort and facilitate transfer.
- Identify and engage with local services to meet children and family at home, preferably during the time of extubation.
- These may include: general practitioners, family medicine specialist, hospice doctor, community / hospice nurse.
- Facilitate arrangements for transport and equipment e.g. home oxygen, suction machine, essential medications, healthcare personnel to escort in ambulance.

Caregiver preparation

- Educate regarding expected symptoms and signs at end-of-life.
- Symptom care plan – to guide caregivers and community health team for home management, if patient survives beyond expected time
- If a patient dies during transfer – extubation will take place at the home. It is not recommended to extubate in the ambulance.
- Essential medications and how to administer
- Letter to facilitate home death certification, what to do in event of home death
- Communicate the child's location and status, advance care plan to local hospice and emergency services.

- Provide a letter to inform the police about the likely cause of death / primary diagnosis, to facilitate death certification.
- Provide a copy of the child's advance care plan to the family.

During transfer

Before starting the journey home, give:

- IV/SC morphine 0.1 mg/kg stat (maximum 2mg per dose) for breathlessness, **AND**
- IV/SC midazolam 0.025mg/kg stat (maximum of 2mg per dose) as anxiolytic, **AND**
- IV/SC glycopyrronium 1-2 mcg/kg/dose stat or IV/SC hyoscine butylbromide 0.5mg/kg to reduce airway secretions

Consider IV/SC dexamethasone 0.15-0.25mg/kg stat if the child is expected to have post-extubation stridor due to prolonged intubation.

Extubation

Provide the family with time and privacy to perform cultural rituals or religious ceremonies.

Give medications to manage symptoms that are expected to occur around the time of extubation.

- IV/SC midazolam 0.025mg/kg stat (maximum of 2mg per dose)
- IV/SC glycopyrronium 1-2 mcg/kg stat if additional dose is needed,

OR

- IV/SC hyoscine butylbromide 0.5mg/kg stat if additional dose is needed
- IV/SC morphine 0.1 mg/kg stat (maximum 2mg per dose) if additional dose is needed

Post-extubation

If child develops restlessness or anxiety post-extubation:

- Repeat IV/SC midazolam 0.025mg/kg stat after 15 minutes, **OR**
- Set up IV/SC midazolam infusion 1 to 5mg/24 hours
- Provide a contact for symptom management support.

Refer to the home death transition flow process in Module 3.

After death

- Death certification by local authorities.
- Funeral arrangements by family.
- Bereavement support for family members.

No.	Medication/items	Amount / quantity	Check (√)
1	IV/SC Morphine	3	
2	IV/SC Midazolam	2	
3	IV/SC Dexamethason	3	
4	IV/SC Glycopyrronium	1	
5	IV/SC Hyoscine butylbromide	1	
6.	Infusion set	1	
7	Letter to police to support death certification	1	
8	A copy of advanced care plan	1	
9	Oxygen face mask and oxygen tank	1	
10	Portable ventilator (if available)	1	
11	Symptom care plan with contact number	1	
12	BIPAP or oxygen concentrator (optional)	1	

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Home death

Preparation for home death

- Explore what the patient and family already knows about the condition.
- Discuss on agreed goals of care for the patient and family.
- Explain what symptoms to expect or anticipate during the end of life phase. Provide medications for the symptoms.
- Provide information on what to do in case of emergencies.

- Provision of support number to call for help / guidance
- Discuss spiritual needs – identify spiritual leader, funeral arrangements
- Provide the family with a letter for purpose of death notification to police (Refer to template in Module 3)
  - > Identification details of patient
  - > Patient's diagnoses
  - > Most likely cause of death
  - > Doctor's name, institution and contact number for verification

Communication issues

Talking about death and dying with children[1,2]

Children have different understanding of death over different age groups. Use different approaches to talk about death with children based on their age group and understanding of death.[3,4]

Age	Understanding of Death	Supportive intervention
1-2 years	A dying person is sleeping and will wake up. Fear of separation from caregiver.	Keep child's daily routine unchanged. Talk to them, hold them, comfort them.
2-6 years	Death is temporary and reversible. Continuous with life— becoming less alive. Life goes on under changed circumstances. Death is personified	Provide concrete information about death. Don't use misleading terms for death, like "sleep". Young children may be afraid to go to sleep if it is associated with death. Tell the child that death is not the child's fault.
7-12 years	and a punishment. (magical thinking) Death is final and irreversible. Unpredictable, personal and can happen to them. Concrete reasoning with cause-and-effect relationships.	Reassure a sense of security by maintaining a consistent daily routine. Reassure the child. Help the child to express their emotions through activities eg art, music or conversations Acknowledge their feelings. Give honest and consistent responses.
Above 12 years old	Death is accepted as a part of life. Explore theological explanations and unrealised plans.	Acknowledge and explore their feelings. Support independence and privacy. Peer support.

Suggested books for further reading when working with children on grief issues:

- The Goodbye Book by Todd Parr; for kids 3-6 years
- How I Feel: A Coloring Book for Grieving Children by Alan Wolfelt; for kids 3-9 years.
- The Invisible String Patrice Karst; for kids 4-9 years
- When Someone Very Special Dies by Marge Heegaard; for kids 6-12 years.
- When Something Terrible Happened by Marge Heegaard; for kids 6-12 years.

Good communication skills, especially listening with empathy is vital when discussing death.

Talking about death and dying with parents[5,6]

Things to avoid	Suggestions
Saying "I know how you feel"	"It must be very difficult for you." "I can see how sad you are."
Avoid talking about the deceased	Allow the family to talk about their memories of the deceased as this helps with the grieving process.
Taking angry comments personally or being defensive	"I can see you are very upset. Would you like to share with me more on this?"
Saying the deceased is in a better place (unless voiced out by parents)	Explore regarding parents' spiritual values and beliefs. Do not impose your own beliefs on them.
Placing blame e.g. "You should have brought him/her to see a doctor earlier."	Emphasize on what can be done to comfort and support the child.

Prognostication of survival time[7,8]

When parents ask, "How much time is left?", assess the underlying reason for the question.

Providing an estimated prognosis to parents is important and valued because[7]:

- Parents want to know the child's prognosis
- Builds trust between clinician, parent and child
- Enable child and family to make decisions regarding their care plan
- Promotes hope and peace of mind
- Reduces uncertainty and distress
- Sets the platform for important discussions on child and family's concerns, values and preferences to support subsequent care planning

Communicating prognosis to the child[8]*:*

- Children should be given the opportunity to initiate discussion on prognosis in a safe and open environment

- Children should know they will not be lied to
- Children should not be forced into disclosure discussions against their wish

Prognostication is inexact and difficult[9]. There is still lack of studies to support prognostication in paediatric population.8 Tools such as the

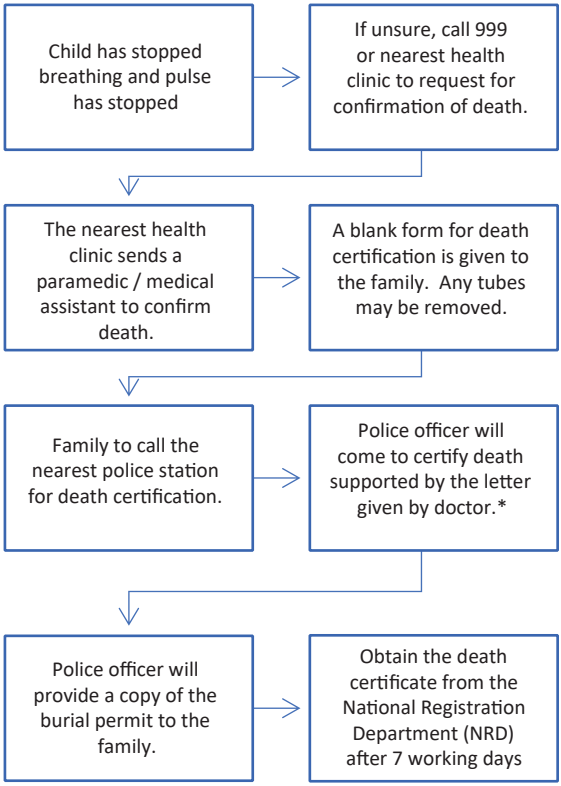
"Surprise Question" are being tested on its value for prognosis.[10]

Prognosis can be affected by various factors[11]:

- Inherent trajectory pattern of the primary diagnosis
- Acute conditions (eg sepsis, delirium, diarrhoea, vomiting)
- Comorbid organ failure
- Rate of disease progression
- Clinicians' experience in assessment
- If requested, give an estimate in units eg days to a week, weeks to a month.

Home death[12]

Process of obtaining death certification



*The police may request that the child be sent to the nearest hospital, if they are not confident to confirm the cause of death.

Alternatively, **funeral service providers** may assist the family with the documentations for death.

In Sabah and Sarawak, death must be notified to the NRD within 24 hours. There are different sets of forms for notification within 24 hours and late notification of death. In Sarawak, deaths among indigenous tribes require a certification of death by their community leaders, and police report for home deaths.12

About a month after death, the family may receive a visit from healthcare staff from the nearest health clinic who will be responsible to interview the family members regarding possible cause of death, as part of a **verbal autopsy**.[13] This occurs in deaths that have not been medically certified.

Tips for healthcare providers when informed of patient's death

- May attend funeral on a personal basis if invited
- Contact family about a week after funeral to allow for family to complete funeral proceedings
- May express own personal sorrow to family members
- Identify if any assistance or needs that can be provided to family
- Allow family members to express their grief
- Plan for follow up review for family members, more importantly if at risk of pathological grief[5]
- Offer contact information and advice to come to clinic if having symptoms of pathological grief

Grief

Normal acute grief	Complicated grief
Varies between individuals. Usually 6-12 months.	Lasts **beyond culturally accepted duration** (compare the grief symptoms with other family members, friends of the deceased), usually beyond 6 months. Also includes increasing / persistent grief intensity and living dysfunction.
• Yearning for the deceased (core symptom) • Depressed mood and guilt related to the deceased • Pangs of sadness, interspersed with periods of joy • Frequent thoughts of the deceased, including hallucination of the deceased • Somatic symptoms: insomnia, loss of appetite, dry mouth	• **Persistent** and intense symptoms of acute grief that are **excessive**. (Unable to feel positive mood) • **Affects the functioning** of the bereaved e.g. personal, family, occupational, social functioning. • Similar to mild post-traumatic stress disorder, where the stressor is the death of the deceased.
Symptom intensity reduces with a supportive environment for grieving over time. Grief support should begin before the child dies (anticipatory grief).	Grieving intensity persists if a supportive environment is not given. Require further intervention: • Screening for complicated grief (to differentiate between complicated vs prolonged grief) • Interpersonal / group psychotherapy • Treat comorbid major depression / anxiety disorder

Screening for complicated grief[14,15]

The Brief Grief Questionnaire is shown in the following page. This screening tool can be used in adults bereaved for at least 12 months or children who have been bereaved for at least 6 months

Refer family members to a mental health specialist, e.g. psychiatrist / clinical psychologist if they scored >5.

Initial:_____

Date: ___/___/___

THE CENTER FOR
COMPLICATED GRIEF

Brief Grief Questionnaire (BGQ)

Katherine Shear M.D. and Susan Essock Ph.D.
DO NOT CIRCULATE WITHOUT WRITTEN PERMISSION BY AUTHOR

1. How much are you having trouble accepting the death of _____?

0	1	2
Not at all	Somewhat	A lot

2. How much does your grief still interfere with your life?

0	1	3
Not at all	Somewhat	A lot

3.How much are you having images or thoughts of _____ when he/she died or other thoughts about the death that really bother you?

0	1	3
Not at all	Somewhat	A lot

4. Are there things you used to do when _____ was alive that you don't feel comfortable doing anymore, that you avoid? Like going somewhere you went with him/her, or doing things you used to enjoy together? Or avoiding looking at pictures or talking about _____? How much are you avoiding these things?

0	1	3
Not at all	Somewhat	A lot

5. How much are you feeling cut off or distant from other people since _____ died, even people you used to be close to like family or friends?

0	1	3
Not at all	Somewhat	A lot

*Brief Grief Questionnaire (reproduced with permission from Center for Complicated Grief, Columbia School of Social Work)

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Ethical issues regarding end-of-life care

The four pillars of medical ethics are:

- Beneficence (do good)
- Non-maleficence (do no harm)
- Patient autonomy (patient's free will)
- Justice (fair distribution of limited medical resources)

Common issues at end of life

Disclosure of diagnosis or prognosis to the child

Ethical principle(s)	Explanation
Patient autonomy, beneficence, nonmaleficence	Parents may wish to withhold the diagnosis from their child to protect them from the suffering.[1] However, many children do have some capacity to understand their condition.[2] Discuss the pros and cons of diagnosis disclosure with the child. If disclosure is done, ensure that it is given at a level that the child can understand, and the amount that is needed for the child to understand.

Withdrawal of treatment, nutrition and hydration[3]

Ethical principle(s)	Explanation
Non-maleficence and justice	Withdrawal of treatment is done when treatment is futile. Futile treatment is when treatment provides no further benefit to the patient and will not cause harm if not given.[4] Some resources can be used for other patients who may benefit from it. Children who are able to and wish to take orally should be given food and drink. Medically provided food and drink should only be withheld if it prolongs or causes more symptoms to the dying process.

Euthanasia[5]

Ethical principle(s)	Explanation
Non-maleficence Patient autonomy	In Malaysia, giving medications with intent to hasten death is not legal.[5] If a patient requests euthanasia, explore underlying reasons and optimise symptom control. Supporters of euthanasia claim that patients who request for it are suffering from existential suffering, rather than physical. However, this is still strongly debated in various countries.[6,7] If there is suspicion of existential suffering, refer to psychotherapists (narrative therapy or hypnotherapy) or pastoral care.

Preferences for place of death[8] (home vs hospital)

Ethical principle(s)	Explanation
Patient autonomy, beneficence and non-maleficence	Patient may prefer to die at home, however there may be challenges if the community lack resources to support home death.[9] Adequate caregiver preparation is required to allow home death. Family members may bring patients back to the hospital if they are unable to cope with the symptoms of active dying.

Conflict between child's and parents' preferences[2,10]

Ethical principle(s)	Explanation
Patient autonomy, decision-making competency	Have a family conference to discuss the discrepancy in an attempt to reconcile the preferences. If conflict persists after adequate discussion and deliberation, the parents' preferences take precedence due to the Child Act which states that children <18 years old are under the care of their parents or legal guardians.

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The Association for Paediatric Palliative Medicine makes no representation, express or implied that the drug doses in this formulary are correct.

Professionals must always check the product information and clinical procedures with the most up to date published product information and data sheets provided by manufacturers and the most recent codes of conduct and safety regulations. The authors and the publisher do not accept responsibility or legal liability for any errors in the text or for the misuse or misapplication of material in this work.

Professionals are reminded that at all times they must prescribe, or advise on prescribing, only within their sphere of competence and in line with the terms of their professional registration. The APPM Formulary should be used in conjunction with other appropriate, up to date literature and guidelines, supplemented where necessary by expert advice.

Every attempt has been made to ensure information presented in this formulary is accurate and up to date as of September 2023. Important updates or corrections will be posted on the APPM Formulary web-page which can be accessed by scanning the QR code.

The APPM Formulary editorial team welcomes feedback, comments, suggestions and recommendations from healthcare professionals in the UK and across the world. Please contact Lynda.Brook@alderhey.nhs.uk

The Association for Paediatric Palliative Medicine

Formulary
6th Edition
2024

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Foreword

The Association for Paediatric Palliative Medicine formulary has been the paediatric palliative care prescribers' best friend for over a decade and continues to go from strength to strength. It is now on its 6th edition with a change in the editorial leadership to Dr Lynda Brook supported by a new deputy editor Dr Ella Aidoo. This fresh perspective brings some welcomed new additions to support prescribing practice whilst maintaining the original core purpose of the formulary-to support prescribers working in paediatric palliative care. The formulary continues to provide prescriber guidance across the age range from neonates to adolescents.

Where available, and relevant to our clinical population, Medicines for Children leaflets on specific medication have been embedded. There has been an expansion in clinical indications for some medications with detailed guidance on use in some cases. There are several new additions; Codeine, Dihydrocodeine and several other monographs have been removed. Due to the welcomed growing evidence, some references will be separately held but accessible for the prescriber on the APPM website.

For opioid prescribing, there are conversion tables between routes of administration, breakthrough doses, pain in the opioid naive and example calculations to support the prescriber. Furthermore, Methadone receives more detailed guidance and direction. Practical compromise for Midazolam dosing has occurred in this edition with clearer dosing per route of administration.

The appendices have expanded to support knowledge and understanding in the management of medicines including opioid conversion tables and stewardship. There is some additional guidance on the administration of buccal medication, prolonged QT syndrome and switching medication in the same drug class (gabapentinoids and benzodiazepines).

Huge congratulations to Lynda and her team on a highly successful and ambitious expansion. Thank you also to all of those who have contributed to this, and previous editions. The formulary is largely an unfunded labour of love supported by an enthusiastic band of overstretched and underfunded colleagues working in the field of paediatric palliative care. It is a credit to them that they offer their expertise and valuable time due to their steadfast commitment to raising standards of care for the children with palliative care needs across the sector.

AK Anderson, September 2023.

Preface

Taking over as Editor for the APPM Formulary is a significant responsibility. Dr Sat Jassal is certainly a formidable act to follow!

When Sat raised his hand as I chaired the inaugural meeting of the Association for Paediatric Palliative Medicine in 2010 and suggested developing the APPM Master Formulary I don't think anyone could have imagined where this simple act would lead. Over the 12 years since the first edition of the formulary, it has grown to become a significant body of work providing definitive guidance on prescribing in paediatric palliative medicine to professionals in the UK and across the world. The first edition of the formulary, published in January 2011, contained monographs for 82 drugs with 202 references contained within 72 pages. This latest edition of the formulary includes monographs for 104 drugs, 410 references and comprises a total of 273 pages.

The growth of the formulary reflects other changes too: the increasing number of professionals working in paediatric palliative medicine in the UK and worldwide; the growth in non-medical prescribing; the increasing range of medicines available to prescribe with corresponding increases in the research evidence base to support their use; changes in technology allowing dissemination of information across the world wide web and most importantly the increasing number of children and their families benefitting from improvements in quality of life and quality of end of life care enabled through these advances.

As the new Editor, I am building on nearly 20 years of experience in paediatric palliative medicine, my original work on the first WHO list of Essential Medicines for Paediatric Palliative Care, my work as a contributor to the APPM Master Formulary and more recently my work as Deputy Editor under close support and supervision of Sat.

I would like to offer an enormous thank-you to Sat for all your hard work over the last 13 years from myself, colleagues in the UK and worldwide, and the thousands of children and their families whose lives have hopefully been made a little bit easier through the invaluable information presented in the formulary.

Here's to the next chapter.

Lynda Brook, September 2023

Contents

Introduction

Welcome to the sixth APPM Formulary. This latest edition represents a substantive revision from the previous version. The entire formulary has been reviewed and updated incorporating recent published literature, specialist advice and feedback from formulary users. Many of the monographs have been extensively rewritten and references have been brought up to date. The formulary has also been completely reformatted, including greater use of tables and with the aim of improving clarity and navigability.

Notable changes are as follows:

- Substantially revised or reformatted opioid equivalence tables including new recommended approximate equi-analgesic ratios for morphine, diamorphine and oxycodone
- Use of a QR code to link the printed formulary directly to the APPM Website for updates and supplementary information
- Substantially revised or reformatted monographs: Aprepitant, Diamorphine, Midazolam, Morphine, Octreotide, Pamidronate, Risperidone
- New monographs: Alimemazine, Famotidine, Propantheline, Prucalopride, Oxybutynin
- Archived monographs: Arthrotec, Codeine, Dihydrocodeine, Lomotil, Ranitidine (as unavailable)
- New appendices:
  - Prolonged QT syndrome
  - Opioid stewardship
  - Buccal administration of liquid preparations
  - Dosing in obesity
- The table outlining compatibility of two drugs in continuous intravenous or subcutaneous infusion has been archived. Professionals are instead advised to consult the appropriate specialist text to inform the safe practice of combining multiple drugs in a single infusion
- Referencing updated with older references archived and greater emphasis on systematic reviews where available. The full references archive will continue to be available online on the APPM website
- New additions to the formulary and significant revisions clearly marked
- More consistent referencing to drugs known to prolong the QT-interval in the individual monographs
- Consistent referencing to available patient information from Medicines for Children Leaflets

We hope that other neonatal and paediatric palliative medicine formularies in books or hospitals in the UK and worldwide will continue to be based on the APPM Formulary. As ever we welcome feedback, comments, suggestions, and recommendations from healthcare professionals in the UK and across the world. Please contact Lynda.Brook@alderhey.nhs.uk

The Formulary, together with versions translated into other languages, is available to download from the Association for Paediatric Palliative Medicine website www.appm.org.uk

Lynda Brook and Anita Aindow, September 2023

Using the formulary

Drugs are presented in alphabetical order by generic name focusing primarily on routes and indications generally used in children's palliative care in the United Kingdom. Drugs are included in the formulary only when there is sufficient evidence either in the form of published peer reviewed literature, or established professional consensus for their safety, efficacy, and cost effectiveness.

In some circumstances drug doses higher than quoted in the formulary may be recommended by specialists familiar with their use.

Dosing recommendations apply to all stated indications unless otherwise specified. The term "by mouth" refers to administration via the enteral route. See notes section for available information on administration via intra-gastric or jejunal tubes.

Common and important side effects and drug interactions are listed, particularly those likely to influence therapeutic decision making in paediatric palliative care. Clinicians are advised to consult the BNF, BNFc and relevant summary of product characteristics for a definitive list of all known side effects and drug interactions.

The most recent references are included focusing primarily on systematic reviews where available and monographs where additional justification for recommendations is required. Further references, including those archived from previous editions of the formulary, can be accessed on the APPM website by scanning the QR code below.

Patient information leaflets

Patient information leaflets are included where available. Please note however that patient information may focus on use of the drug for another indication not necessarily in paediatric palliative medicine. Professionals are advised to review the available information for appropriateness before recommending for a patient.

Prolonged QT-interval

Alerts regarding QT prolongation are provided for all drugs known to prolong QT-interval when used for the indications and doses. Other drugs that may prolong QT-interval in certain circumstances are indicated only if relevant to paediatric palliative medicine.

Relation to BNFC

Doses recommended are generally consistent with those in the British National Formulary (BNF) or British National Formulary for Children (BNFc). Dose recommendations that are different to those in the BNFc are marked together with rationale.

Accuracy of information

Every attempt has been made to ensure information presented here is accurate and up to date as of September 2023. Any critical updates or corrections will be posted on the APPM Formulary webpage which can be accessed by scanning the QR code.

We would strongly advise practitioners not to prescribe outside their expertise, and if in doubt to consult the growing network of clinicians with specialist expertise in paediatric palliative medicine via the Association of Paediatric Palliative Medicine.

Weight or age-based dosing

Over the last few years there has been a general move towards age-based rather than weight-based dosing for children: the rationale being improved patient safety by avoiding the need for drug dose calculations. However, paediatric palliative medicine patients are frequently atypical in terms of weight for age or body composition. In general weight-based dosing options should be used if possible and these have been provided where available. When no weight-based dosing options are given, and patients are extremely small for their chronological age, consider starting at doses corresponding to the age-band normally associated with the patient's weight. For dosing in obesity, see specific monographs and also Appendix 7.

Abbreviations

$5HT_2$	5 hydroxytryptamine (serotonin) type 2 receptor
$5HT_3$	5 hydroxytryptamine (serotonin) type 3 receptor
APLS	Advanced Paediatric Life Support
ALT	Alanine transaminase
AST	Aspartate transaminase
CD	Controlled drug
CIVI	Continuous intravenous infusion
cLQTS	Congenital long Q-T syndrome
CNS	Central nervous system
COX	Cyclo-oxygenase
CSCI	Continuous subcutaneous infusion
CSF	Cerebrospinal fluid
GFR	Glomerular filtration rate
IM	Intramuscular
IV	Intravenous
kg	Kilograms
MAD	Mucosal atomiser device
mg	Milligrams
MHRA	Medicines and Healthcare Products Regulatory Authority
ml	millilitres
NHS	National Health Service (UK)
NICU	Neonatal intensive care unit
NK	Neurokinin type 1 receptor
NMDA	N-methyl-D-aspartate
NSAID	Non-steroidal anti-inflammatory drug
PICU	Paediatric intensive care unit
PO	By mouth (per oral)
PRN	As required
SC	Subcutaneous
SL	Sublingual
SPC	Summary of Product Characteristics
SSRI	Selective serotonin reuptake inhibitor
TdP	Torsades de Pointes
UK	United Kingdom
WFI	Water for injection
WHO	World Health Organisation

Formulary

Acetazolamide

Use:

- Epilepsy
- Raised Intracranial Pressure-to reduce CSF production in obstructive causes, as an alternative to steroids

Dose and route:

Epilepsy

By mouth using immediate release formulations, or by slow intravenous injection:

- **Neonate:** Initially 2.5mg/kg 2-3 times daily, followed by 5-7mg/kg 2-3 times daily (maintenance dose)
- **Child 1 month-11 years:** initially 2.5mg/kg 2-3 times daily, followed by 5-7mg/kg 2-3 times daily, maximum total daily dose 750mg (maintenance dose)
- **12 years and over:** 250mg 2-4 times daily, maximum total daily dose 1g

Raised intracranial pressure

By mouth or slow intravenous injection:

- 8mg/kg 3 times daily, increased as necessary, maximum 100mg/kg total daily dose

Notes:

- Carbonic anhydrase inhibitor.

Licensing

- Licensed for childhood and adult epilepsy. Not licensed for raised intracranial pressure in children.

Therapeutics

- May give symptomatic benefit in the case of CSF obstruction including from inoperable brain tumours.
- May provide GABA-A receptor mediated analgesia at the spinal level, due to carbonic anhydrase inhibition.

Contraindications, cautions

- Contraindicated in sulphonamide sensitivity, adrenocortical insufficiency, hypokalaemia, hyponatraemia

Side effects

- Association with acute kidney injury (AKI) in critically ill children admitted to intensive care units
- May cause electrolyte disturbance with prolonged use (can be corrected with potassium bicarbonate), gastrointestinal disturbance, paraesthesia at higher doses and haematological abnormalities.
- Monitor blood count and electrolytes in prolonged use.

Interactions

- Potential for severe interactions with aspirin, lithium, valproate and zonisamide

Administration

- Tablets are scored and can be halved or quartered.
- Dissolving tablet in water produces a coarse dispersion that settles rapidly. For administration via feeding tubes, dissolve the required dose in 10ml water and rinse container to ensure the full dose is given.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Injection can theoretically be used via feeding tubes.
- Modified release capsule is not suitable for enteral tube administration.
- Alkaline pH: NOT appropriate for IM or SC administration

Available as

- Tablets 250mg, modified release capsules 250mg; 500mg injection (sodium salt, powder for reconstitution) Diamox®.

Evidence: (1–10)

Adrenaline (also known as Epinephrine)

Use:

- Small external bleeds
- Upper airway obstruction (inflammatory/oedema cause)

Dose and route:

Localised bleeding:

By topical application

- Soak gauze in 1:1000 (1mg/ml) solution and apply directly to bleeding point for up to 10 minutes

Upper airway obstruction:

By inhalation of nebulised solution:

- **Child 1 month-11 years:** 0.15-0.4ml/kg of 1:1000 (1mg/ml) solution, maximum 5ml per dose, diluted to 5ml with sodium chloride 0.9%. Repeat after 30 minutes if necessary
- **12 years and over:** 1-5ml of 1:1000 (1mg/ml) solution diluted to 5ml with sodium chloride 0.9%. Repeat after 30 minutes if necessary

Notes

Licensing

- Not licensed for upper airway obstruction, croup or localised bleeding

Side effects

- Short term use only. Risk of ischaemic necrosis and rebound vasodilation with prolonged use.

Pharmacokinetics

- Nebulised: duration of action 2-3 hours

Available as

- Ampoules solution for injection 10mg/10ml, 5mg/5ml, 1mg/1ml and 500micrograms/0.5ml

Evidence: (1–3,11)

Alfentanil

Use:

- Short acting synthetic lipophilic opioid analgesic derivative of fentanyl
- Alternative opioid in patients with end stage (4 or 5) renal failure, opioid related neurotoxicity or intolerance to other opioids
- Useful for breakthrough pain and procedure-related pain
- Used as analgesic especially intra-operatively and for patients in intensive care and on assisted ventilation (adjunct to anaesthesia)

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in patients already receiving regular strong opioids

By continuous intravenous or subcutaneous infusion

- Calculate the total daily dose (regular + PRN) of opioid administered over the previous 24 hours

  Convert to the equivalent dose of alfentanil using the table below (see also Appendix 1)

- Consider reducing the dose of alfentanil by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

Conversion		Ratio	Calculation	Example
From	To			
Morphine oral	Alfentanil CSCI or CIVI	30:1	Divide 24hour morphine dose by 30	Morphine oral 60mg/24hours ÷ 30 = alfentanil CSCI 2mg/24hours
Morphine CSCI or CIVI	Alfentanil CSCI or CIVI	15:1	Divide 24hour morphine dose by 15	Morphine CSCI 30mg/24hours ÷ 15 = alfentanil CSCI 2mg/24hours

Breakthrough pain in patients already receiving opioids

By subcutaneous, buccal and intranasal routes

- 1/10 to 1/6 (10%-16%) of the total CSCI dose as required, up to hourly

  There is no direct correlation between the effective PRN-dose and the regular background dose: start with low dose and titrate according to response

Procedure-related pain SEEK SPECIALIST ADVICE

By subcutaneous, buccal and intranasal routes

Administer at least 5 minutes before procedure, repeating if needed.

- **Child 2-11 years:** 5micrograms/kg single dose, maximum 250micrograms/dose
- **12 years and over**: 250-500micrograms single dose over 30 seconds. Subsequent doses 250micrograms

Notes:

Licensing

- Licensed for perioperative use in children. Not licensed for pain relief in palliative care. Not licensed for buccal, sublingual, or intranasal administration. Not licensed for incident or breakthrough pain.

Therapeutics

- Rapid onset of action (less than 5 minutes after subcutaneous bolus injection), and short duration of action (less than 60 minutes). Even with an optimally titrated PRN dose, frequent dosing (even every 1-2 hours) may be required. Review dose and frequency of administration regularly.
- Useful for incident and breakthrough pain as faster onset, shorter acting and smaller volumes required compared with fentanyl. Not appropriate for titration of opioid requirements against the patient's pain due to short duration of action. No direct correlation between the effective PRN dose and the regular background dose.
- Limited information or evidence for analgesic doses in palliative care, especially in children. Doses are largely extrapolated from suggested equianalgesic doses with other opioids.

- Useful in patients with severe renal failure (no dose reduction is needed). Avoid or reduce doses by 30-50% in severe hepatic impairment.
- Calculate starting doses in obese children based on ideal body-weight for height rather than actual body-weight.
- Potential alternative to diamorphine or fentanyl when higher doses of opiate are required but subcutaneous administration is difficult due to large volume of infusion.
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Contraindications, cautions

- Contraindicated in patients receiving MAOIs (monoamine oxidase inhibitors) or within 2 weeks of their discontinuation.
- Greater risk of addiction, tolerance and drug seeking behaviour particularly when administered via buccal or intranasal routes, compared with longer acting opioids.

Side effects

- Usual opioid side effects, hypothermia and muscle rigidity (which can be managed with neuromuscular blocking drugs).

Pharmacokinetics

- Half-life prolonged in neonates: risk of accumulation. Clearance may be increased in patients from 1 month to 12 years of age: higher doses may be needed.

Interactions

- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by CYP3A4 inhibitors including aprepitant, ciprofloxacin, clarithromycin, erythromycin and fluconazole. Levels reduced by CYP3A4 inducers including carbamazepine and phenobarbital. Levels potentially increased by midazolam.

Administration

- Compatible with sodium chloride 0.9% or dextrose 5% as a diluent. Physically compatible with most drugs used in a syringe driver. Possible concentration-dependent incompatibility with cyclizine: use water for injection as diluent and observe for crystallisation.

Available as

- Injection (500 micrograms/ml in 2ml, 10ml and 50ml ampoules); Intensive care injection (5mg/ml in 1ml ampoule to be diluted before use). Nasal spray with attachment for buccal / SL use (5mg/5ml bottle available as special order from Torbay Hospital Manufacturing Unit Tel: 01803 664707, torbaypharmaceuticals@nhs.net. Each 'spray' delivers 0.14ml = 140micrograms alfentanil. More costly than using injection preparation).

CD

- Schedule 2 CD

Evidence: (1–3,12,13)

Alimemazine (Trimeprazine) tartrate (NEW)

Use:

- Urticaria
- Pruritus
- Anti-emetic
- Procedural sedation
- Short term treatment of sleep disturbance in children with suspected or definite neurodevelopmental disorder where other behavioural and pharmacological measures have failed

Dose and route:

Doses as alimemazine *tartrate* (see notes below for other formulations)

Urticaria, pruritus, anti-emetic

By mouth

- **Child 6 months-1 year (specialist use only):** 250micrograms/kg, maximum 2.5mg/dose, 3–4 times daily
- **Child 2-4 years**: 2.5mg, 3–4 times daily
- **Child 5-11 years**: 5mg 3–4 times daily
- **12 years and over**: 10mg 2–3 times daily

Procedural sedation, night sedation

By mouth

1-2 hours before procedure or 1-2 hours before bed-time

- **Child 1 month-1 year (specialist use only):** 1-2mg/kg as a single dose
- **2 -11 years:** 1-2mg/kg not to exceed 60mg as a single dose
- **12 years and over**: Up to 30-60mg as a single dose

Notes:

Sedative phenothiazine antihistamine

Licensing

- Unlicensed for treatment of urticaria or pruritus in children from the age of 6 months to 2 years. Licensed for sedation in children from 2-6 years. Licensed indications may differ between formulations

Therapeutics

- Total daily doses of up to 100mg have been reported in adults

Contraindications, cautions

- Contraindicated in neonates and children under 2 years except on specialist advice, epilepsy.
- Caution in patients with cardiac disease and those with, or at risk of prolonged QT, hypotension or risk of hypotension; may lower seizure threshold; pyloroduodenal obstruction; urinary retention; hepatic impairment and/or jaundice

Side effects

- Respiratory depression, particularly at higher sedative doses, cardiac arrhythmia, mood and sleep disturbance, seizures, dystonia, photosensitivity especially at higher doses, neuroleptic malignant syndrome

Hepatic impairment, renal impairment

- Contraindicated in severe renal failure and severe hepatic failure

Interactions

- Sedative effects intensified when co-administered with other sedatives
- Increased antimuscarinic and sedative effects with anticholinergics including tricyclics, antihistamines and MAOIs
- Hypotensive effects intensified when co-administered with other hypotensive agents especially alpha adrenoreceptor blockers
- May reduce or abolish effects of clonidine

Administration

- Dilute oral solution or oral syrup with an equal volume of water before administration via feeding tube. Tablets can be crushed and mixed with water for administration. The blue film-coating can be washed off the tablets to make them easier to crush. Without crushing they disperse in one to two minutes. Flush tube well before and after administration
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy

Available as

- Oral syrup / liquid containing alimemazine tartrate 7.5mg/5ml, 10mg/5ml and 30mg/5ml; alimemazine tartrate 10mg tablets
- A variety of brands/generics available, and the syrup formulations contain high amounts of sucrose and ethanol. Check carefully. Oral solutions may be preferable to syrups in terms of sucrose and ethanol content. Liquid formulations may also contain methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed) and/or sodium sulfite anhydrous (E221) and sodium metabisulfite (E223), which may rarely cause severe hypersensitivity reactions and bronchospasm. Alimemazine tartrate is given orally; doses in the UK are given as the amount of alimemazine tartrate, while those in some other countries are expressed in terms of the equivalent amount of alimemazine. Alimemazine tartrate 25mg is equivalent to about 20mg of alimemazine

Evidence: (1,14–25)

Amitriptyline

Use:

- Neuropathic pain
- Drooling, sweating, refractory cough
- Neuropathic pruritus

Dose and route:

By mouth:

- **Child 2-11 years**: Initial dose of 200micrograms/kg (maximum 10mg) at night increased gradually, if necessary. Recommended maximum 1mg/kg/dose twice daily (under specialist supervision)
- **12 years and over**: Initial dose of 10mg at night increased gradually, if necessary, every 3-5 days to a suggested initial maximum of 75mg once daily

  Higher doses up to 150mg daily in divided doses may be used in adults under specialist advice.

  Twice daily dosing rarely needed. If necessary give 25-30% of daily dose in morning and 70-75% at night

Notes:

Licensing

- Not licensed for use in children with neuropathic pain or pruritus, drooling, sweating or cough.

Therapeutics

- Evidence of benefit for neuropathic pruritus in adults.
- Analgesic effect unlikely to be evident for several days. Improved sleep and appetite are likely to precede analgesic effect.
- Benefit generally increases with higher doses; however benefit is lost at higher doses in some patients.
- Benefit in cough probably relates to reduction in cough reflex hypersensitivity.

Contraindications, cautions

- Contraindicated in severe liver impairment.
- Contraindicated in patients receiving MAOIs (monoamine oxidase inhibitors) or within 2 weeks of their discontinuation.
- Caution in mild/moderate hepatic impairment, heart block and arrhythmias.
- Caution in epilepsy: may lower seizure threshold

Side effects

- Main side effects limiting use in children include: constipation, dry mouth, blurred vision and drowsiness.

Pharmacokinetics

- Absorbed slowly from gastrointestinal tract. Peak plasma concentration occurs 4-8 hours after oral administration.

Interactions

- Metabolised by cytochrome P450 enzymes CYP2D6 and CYP2C19. Levels increased by drugs that inhibit CYP2D6 enzymes including fluoxetine and fluconazole, particularly in those who are poor CYP2D6 metabolisers. Levels reduced by drugs that induce CYP2D6 enzymes including carbamazepine, phenobarbital and phenytoin.
- Carbamazepine reduces plasma amitriptyline by up to 60%.
- Amitriptyline increases the effects of adrenaline/epinephrine. Manufacturer advises avoid.
- May reduce effect of clonidine

Administration

- Oral solution may be administered via an enteral feeding tube (mix with equal volume of water; no data for some of the preparations). No specific data available for administration of tablets via enteral feeding tube.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet “Amitriptyline for neuropathic pain”: https://www.medicinesforchildren.org.uk/medicines/amitriptyline-for-neuropathic-pain/

Available as

- Tablets (10mg, 25mg, 50mg) and oral solution (10mg/5ml, 25mg/5ml, 50mg/5ml; other strengths may be available as ‘specials’).

Evidence: (1–3,8,26–30)

Aprepitant

Use:

- Prevention and treatment of nausea and vomiting associated with moderate or highly emetogenic cancer chemotherapy in combination with a corticosteroid (usually dexamethasone) and a 5-HT3 antagonist such as ondansetron
- Management of pruritus refractory to other treatment including paraneoplastic pruritus and drug related pruritus
- Cyclical vomiting
- Vomiting in gastrointestinal dystonia

Dose and route:

Chemotherapy induced nausea and vomiting

By mouth:

Day 1: 1 hour before chemotherapy

- **Child 6 months-11 years** (and not less than 6kg): 3mg/kg (maximum 125mg) as a single dose
- **12 years and over**: 125mg as a single dose

Days 2 & 3: 1 hour before chemotherapy or in the morning if no chemotherapy is given

- **Child 6 months-11 years** (and not less than 6kg): 2mg/kg (max 80mg) as a single dose
- **12 years and over**: 80mg as a single dose

Cyclical vomiting (NEW)

By mouth:

Prodromal phase, at least 30 minutes before emetic phase

Child 6 months-11 years (and not less than 6kg): 3mg/kg (maximum 125mg) as a single dose

- **12 years and over**: 125mg as a single dose

Days 2 & 3

- **Child 6 months-11 years** (and not less than 6kg): 2mg/kg (max 80mg) as a single dose
- **12 years and over**: 80mg as a single dose

Prophylaxis

Child 6 months-11 years (and not less than 6kg): 3mg/kg (maximum 125mg) twice weekly

- **12 years and over**: 125mg twice weekly

Vomiting in gastrointestinal dystonia refractory to other anti-emetics (NEW)

By mouth:

- **Child 6 months-11 years** (and not less than 6kg): 2mg/kg (max 80mg) once daily
- **12 years and over**: 80mg once daily

Pruritus (NEW)

By mouth:

- **Child 6 months-11 years** (and not less than 6kg): 2mg/kg (max 80mg) once daily for 3-13 days. Then stop. If symptoms return, repeat course or reduce to alternate days.
- **12 years and over**: 80mg once daily for 3-13 days. Then stop. If symptoms return, repeat course or reduce to alternate days.

Notes:

- Selective high-affinity antagonist at neurokinin-1 (NK-1) receptors in vomiting centre and chemoreceptor trigger zone.

Licensing

- Licensed for the prevention of acute and delayed nausea and vomiting associated with highly or moderately emetogenic cancer chemotherapy in adults, children, and infants from 6 months of age (>6kg).

Therapeutics

- Powerful anti-emetic but may be significantly less effective in reducing nausea

Interactions

- Aprepitant is a substrate, a moderate inhibitor and an inducer of cytochrome P450 enzyme CYP3A4. Aprepitant is also an inducer of CYP2C9. During treatment with aprepitant CYP3A4 is inhibited. At the end of treatment aprepitant causes a transient mild induction of CYP2C9, CYP3A4 and glucuronidation
- Aprepitant therefore has the potential to interact with other drugs that are metabolised by these enzymes including alfentanil, buprenorphine, carbamazepine, dexamethasone, diazepam, diclofenac, domperidone, erythromycin, fentanyl, ibuprofen, midazolam and phenobarbital. *This list is not exhaustive-seek advice.*

Side effects

- Common: include hiccups, dyspepsia, diarrhoea, constipation, anorexia, asthenia, headache and dizziness.

Available as

- Capsules 80mg and 125mg and powder for an oral suspension (125mg powder yielding on reconstitution an oral suspension 25mg/ml).

Evidence: (1–3,31–37)

Arachis Oil Enema

Use:

- Faecal softener
- Faecal impaction

Dose and route:

By rectal administration

- **Child 3-6 years**: 45-65ml as required (approximately 1/3 to 1/2 enema)
- **Child 7-11 years**: 65-100ml as required (approximately 1/2 to 3/4 enema)
- **12 years and over**: 100-130ml as required (approximately 3/4 to 1 enema).

Notes:

Licensing

- Licensed for use in children.

Therapeutics

- Generally used as a retention enema to soften hard, impacted faeces. May be instilled and left overnight to soften the stool. Can be followed by use of a stimulant suppository or osmotic enema the following morning.

Contraindications, cautions

- Derived from peanuts, do not use in children with a known allergy to peanuts.
- Caution in inflammatory bowel disease and bowel obstruction.

Administration

- Warm enema in a water bath before use.
- Administration may cause local irritation.

Available as

- Enema, arachis (peanut) oil in 130ml single dose disposable packs.

Evidence: (1–3)

Atropine

Use:

- Noisy breathing at the end of life (may be more effective if started early)
- Hypersalivation

Dose and route:

By sublingual route:

- **Neonate**: 20-40micrograms/kg/dose 2-3 times daily as required
- **Infant body-weight less than 10Kg:** 20-40micrograms/kg/dose 2–3 times daily as required
- **Child body-weight 10-19kg**: 250micrograms/dose 2–3 times daily as required
- **Child body-weight 20kg and over**: 250-500micrograms/dose, 2–3 times daily as required
- **12 years and over:** 500micrograms–1mg/dose 3-4 times daily as required

Use solution for injection 400 micrograms/ml, 600 micrograms /ml or 1mg/ml for administration of doses up to 250micrograms

Use 1% atropine eye drops (atropine 10mg/ml) for doses of 500micrograms and over. 1 drop of 1% atropine contains approximately 500micrograms of atropine

Notes:

Licensing

- Not licensed for this indication or route of administration.

Therapeutics

- Research evidence based on 0.5% eye drops, only available outside the UK.
- Use only where symptom is affecting quality of life. Used 3rd line if glycopyrronium bromide or hyoscine hydrobromide are either unavailable or ineffective.
- Monitor for anticholinergic side effects: concurrent treatment with 2 or more antimuscarinic drugs increases risk of side effects, central toxicity and worsening quality of life. Children are particularly susceptible.

Pharmacokinetics

- Bioavailability of sublingual atropine is approximately 60%

Side effects

- May result in central nervous system stimulation.

Available as

- Available in UK as 1% (10mg/ml) eye drops (10 ml or 0.5ml pack size). Outside the UK 0.5% eye drops are also available. Solution for injection 400 micrograms/ml, 600 micrograms /ml, 1mg/ml ampoules. Pre-filled syringes: 500micrograms/5ml, 1mg/5ml and 3mg/10ml.

Evidence: (1–3,11,38–53)

Baclofen

Use:

- Chronic severe spasticity and skeletal muscle spasm
- Dystonia
- Considered as third line for neuropathic pain
- Intractable hiccups

Dose and route:

By mouth:

Initial dose

- **Child 1 month and over**: 300micrograms/kg/day in 3-4 divided doses,

  Increased gradually every 3-7 days to a usual maintenance dose of

  - 750micrograms-2mg/kg/day in divided doses

  Maximum daily doses:

  - **Child 1 month-7 years**: 40mg/day in divided doses
  - **8 years and over**: 60mg/day in divided doses

By intrathecal injection:

- **Specialist teams only**. Maintenance 25-200micrograms daily via intrathecal pump.

Notes:

Licensing

- Oral preparations licensed for treatment of spasticity and skeletal muscle spasm for all ages. Intrathecal injection licensed from 4 years of age.

Therapeutics

- Review treatment for spasticity if no benefit within 6 weeks of achieving maximum dose and withdraw over at least 1-2 weeks, more gradually if symptoms occur, if ineffective.
- Less likely to result in dependence or tolerance than diazepam.
- Doses starting at approximately 50% of those for spasticity have been used in severe intractable hiccups. May have direct effect on diaphragm.
- Impact of undesirable hypotonia may be minimised by reducing daytime and increasing evening doses.
- Intrathecal use by specialist only, for severe chronic spasticity that cannot be effectively managed by enteral treatment.
- Intrathecal injection can be administered as a short term CSCI to avoid sudden withdrawal when enteral and/or intrathecal routes are unavailable.

- Abrupt withdrawal, including through loss of the enteral route, intrathecal or pump failure can precipitate life threatening withdrawal syndrome with hyperactivity, increased spasticity, autonomic dysfunction and serious psychiatric reactions.
- Limited clinical data on the use of baclofen in children under the age of one year.

Side effects

- Common: drowsiness, nausea, hypotonia. Potential effects on swallow, airway protection, posture and function. Exacerbation of epilepsy. Increased gastric acid secretion.

Contraindications, cautions

- Contraindicated in active peptic ulcer disease.

Hepatic impairment, renal impairment

- Risk of toxicity in renal impairment; use smaller oral doses and increase dosage interval if necessary.

Pharmacokinetics

- Oral bioavailability >90%, onset of action hiccup 4-8hours, muscle spasm 1-2 days, spasticity 3-4 days

Administration

- Administer after food to reduce risk of gastric irritation.
- May be administered via enteral feeding tubes including gastrostomy or jejunostomy. (Specific data only available for some makes of liquid and tablet). Use liquid formulation for small doses; dilute prior to use to reduce viscosity. Consider dispersing tablets in water for higher doses owing to the sorbitol content of the liquid formulation. (Teva brand tablets produce a fine dispersion in 10 ml water).

Patient information

- See Medicines for Children leaflet “Baclofen for muscle spasm”: https://www.medicinesforchildren.org.uk/medicines/baclofen-for-muscle-spasm/

Available as

- Tablets (10mg) and oral solution (5mg/5ml, 10mg/5ml). Solution for injection 50mg/ml. Intrathecal solution for infusion 500 micrograms/ml and 2mg/ml.

Evidence: (1,2,8,54–56,56–58)

Bethanechol

Use:

- Urinary retention including opioid-induced urinary retention

Dose and route:

By mouth:

- **Child 1-11 years**: 600micrograms/kg/day in 3 or 4 divided doses. Increasing if necessary and tolerated to a maximum of 1.2mg/kg/day in 3 or 4 divided doses. Maximum 10mg/dose.
- **12 years and over**: 10-25mg per dose 3 to 4 times daily. Increasing if necessary and tolerated to maximum of 50mg/dose

Notes

- Stimulates the parasympathetic nervous system, increasing bladder muscle tone and causing contractions which initiate urination.

Licensing

- Not licensed for use in children.

Contraindications, cautions

- Contraindicated in hyperthyroidism, peptic ulcer disease, asthma, cardiac disease and epilepsy.
- Safety and efficacy not established in children.

Interactions

- Effects antagonised by antimuscarinic agents

Pharmacokinetics

- Poorly absorbed by gastrointestinal tract. Therapeutic effect seen within 1 hour of oral administration.

Administration

- Administer 1 hour before or 2 hours after food to reduce likelihood of nausea and vomiting.
- Tablets may be crushed and dispersed in water for immediate administration via an enteral feeding tube; formulation for extemporaneous oral suspension is available.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- 10mg and 25mg tablets licensed in UK, other strengths via importation companies and NOT licensed in UK.

Evidence: (2,8,59)

Bisacodyl

Use:

• Constipation

Dose and route:

By mouth:

- **Child 4 years and over**: 5-10mg once daily (recommended to be taken at night), adjust according to response. Increased as necessary up to 20mg daily

By rectum (suppository):

- **Child 2 years and over**: 5-10mg once daily; adjust according to response

Notes:

- Stimulant laxative.

Therapeutics

- Acts by local effect on the colonic mucosa.
- Limited data exist on the safety and efficacy of regular and long term use. Prolonged or excessive use can cause electrolyte disturbance.

Pharmacokinetics

- Onset of action: tablets 10–12 hours, suppositories act in 20–60 min

Administration

- Suppositories must be in direct contact with mucosal wall.
- Enteric coated tablets. Do not crush.
- Not suitable for enteral tube administration.

Available as

- Gastro-resistant tablets (5mg) and suppositories (5mg, 10mg).

Evidence: (1,2,60)

Buprenorphine

Use:

- Moderate to severe pain
- Alternative opioid in patients with end stage (4 or 5) renal failure

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

***Stable* pain in patients already receiving regular strong opioids**

By transdermal patch:

- By titration or convert using oral morphine equivalent (OME) see Appendix 1. Not suitable for dose titration in patients with unstable pain.
- Consider reducing the dose of buprenorphine by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

Buprenorphine patches are *approximately* equivalent to the following 24-hour doses of oral morphine

7 day patches

Oral morphine 12mg/24hours	≡	Buprenorphine 5micrograms/hour
Oral morphine 24mg/24hours	≡	Buprenorphine 10micrograms/hour
Oral morphine 36mg/24hours	≡	Buprenorphine 15micrograms/hour
Oral morphine 48mg/24hours	≡	Buprenorphine 20micrograms/hour

3 or 4 day patches

Oral morphine 84mg/24hours	≡	Buprenorphine 35micrograms/hour
Oral morphine 126mg/24hours	≡	Buprenorphine 52.5micrograms/hour
Oral morphine 168mg/24hours	≡	Buprenorphine 70micrograms/hour

Systemic analgesic concentrations are generally reached within 12–24 hours after applying patch, but levels continue to rise for 32–54 hours (pharmacokinetic profile may differ slightly between preparations, check SPC for full details).

If converting from:

- 4-hourly oral morphine: administer regular morphine doses for the first 12 hours after applying the patch.
- 12-hourly slow release morphine: apply the patch and administer the final slow release dose at the same time.
- 24-hourly slow release morphine: apply the patch 12 hours after the final slow release dose.
- Continuous morphine infusion: continue the infusion for 8- 12 hours after applying the patch.

Pain in opioid naive patients

By sublingual route

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Child body-weight less than 25kg**: 5micrograms/kg/dose, maximum 100micrograms/dose, every 8 hours (using injection solution)
- **Child body-weight 25–37.5 kg**: 100micrograms every 6-8 hours
- **12 years and over body-weight 40kg and over**: 200micrograms every 6-8 hours

Titrate the dose every 4–5 days, based on analgesic requirements. Typical adult dose 800micrograms–1.2mg/24hours, given as 200–400micrograms every 6-8 hours

By subcutaneous, intramuscular or slow intravenous injection

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Child 6 months-11 years**: 3micrograms/kg/dose, maximum 300micrograms, every 6–8 hours.
- **12 years and above**: 300 micrograms every 6–8 hours.

Titrate the dose, based on analgesic requirements up to a typical adult maximum dose of 600mg every 6-8 hours.

Notes:

- Strong opioid with both agonist and antagonist properties.

Licensing

- Sublingual tablets not licensed for use in children < 6 years old. Patches not licensed for use in children.

Therapeutics

- Doses quoted for opioid naive patients reflect the lower end of ranges quoted by manufacturers and BNFc in view of equianalgesic ratios and clinical experience in both adult and paediatric palliative care.
- Ceiling effect for respiratory depression, however life- threatening respiratory depression can still occur.
- Causes less constipation than some other opioids.
- May be particularly beneficial in neuropathic pain and hyperalgesia
- Sublingual administration not appropriate for breakthrough pain due to long duration of action
- Negligible bioavailability if swallowed due to extensive first pass metabolism
- Effects only partially reversed with naloxone at conventional doses. Theoretical risk of withdrawal symptoms, including pain, in children dependant on high doses of other opioids.
- Has been given as continuous intravenous or subcutaneous infusion over 24 hours. Relatively long half-life means that equianalgesic studies based on single doses are likely to under-represent equianalgesia as a continuous infusion
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Caution

- Caution in hepatic impairment.
- Rate of absorption from patch is affected by temperature with risk of accidental overdose including respiratory depression: caution with pyrexia or increased external temperature such as hot baths.
- Remove patches before MRI scanning due to risk of burns.

Side effects

- Patches may cause contact dermatitis. This may be reduced by topical application of budesonide inhaler spray to the area where the patch is to be applied.

Pharmacokinetics

- Clearance may be faster in some children.
- Duration of action in adults 6-8 hours versus 4-5 hours for morphine. Single-dose studies are therefore likely to underestimate the relative equianalgesic ratio of buprenorphine. Opioid potencies should be considered as an approximate guide, particularly for children for whom very little pharmacokinetic data is available. See Appendix 1 for approximate opioid equivalent data

Interactions

- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by drugs that inhibit these enzymes including ciprofloxacin, erythromycin, and fluconazole. Levels reduced by drugs that induce these enzymes including carbamazepine and phenobarbital.

Administration

- MHRA advises that *fentanyl* matrix patches must not be cut due to the risk of life threatening and potentially fatal opioid toxicity. Similar considerations would be expected to apply to cutting buprenorphine patches. Buprenorphine patches should therefore not generally be cut. A decision to cut a buprenorphine matrix patch must be made on a case-by-case basis, weighing up the potential risks and benefits. Cut matrix (see Summary of Product Characteristics) patches diagonally if a smaller dose is required. Only matrix patches can be cut.
- For intravenous infusion dilute in sodium chloride 0.9% to a concentration of 15micrograms/ml. For subcutaneous infusion dilute in sodium chloride 0.9%. Limited compatibility data for mixing with other drugs used in palliative care

Available as

- *Tablets* (200micrograms, 400micrograms) for buccal administration. Tablets may be halved. Higher strength sublingual tablets also available but these are indicated as an adjunct in the treatment of opioid dependence. Take care with prescribing.
- *Patches*: several brands (and generics) of transdermal patches with 7 day, 4 day (96 hour) and 3 day (72 hour) release profiles. Patch size expressed in micrograms/hour. Only matrix patches can be cut. Prescribe by brand where possible: caution when switching between formulations.
- *7 day patches*: BuTrans®, Butec®, Bupramyl®, Panitaz®, Reletrans®, Sevodyne®. Available as 5micrograms /hour for 7 day), 10micrograms /hour for 7 days, 15micrograms/hour for 7 day) and 20micrograms/hour for 7 days
- *4 day (96 hour) patches*: Bupeaze®, Buplast®, Relevtec®, TransTec®. Available as 32.5micrograms/hour for 96 hours, 52.5micrograms/hour for 96 hours, and 70micrograms/hour for 96 hours
- *3 day (72 hour) patches*: Hapactasin®-applied every 72 hours. Available as 35micrograms/hour for 72 hours, 52.5micrograms/hour for 72 hours and 70micrograms/hour for 72 hours
- *Injection:* for intravenous or subcutaneous injection solution 300micrograms/ml

CD

- CD Schedule 3 (CD No Register). Local protocols may require safe storage.

Evidence: (1–3,10,61–72)

Carbamazepine

Use:

- Neuropathic pain
- Hyperkinetic movement disorders
- Anticonvulsant

Dose and route:

By mouth:

- **Neonates**: Experience is limited. Initial dose 5mg/kg twice daily
- **Child 1 month-11 years**: Initial dose of 5mg/kg at night or 2.5mg/kg twice daily, increased as necessary by 2.5-5mg/kg every 3–7 days; usual maintenance dose 5mg/kg 2–3 times daily.

  Total daily doses of up to 20mg/kg/day in divided doses have been used
- **12 years and over**: Initial dose of 100–200mg 1–2 times daily; increased slowly to usual maintenance of 200-400mg 2–3 times daily.

  Maximum total daily dose 1.8 g/day in divided doses

By rectum:

- **Child 1 month and over**: Use approximately 25% more than the oral dose, maximum single dose 250mg, up to 4 times daily.

Notes:

Licensing

- Not licensed for use in children with neuropathic pain. Suppositories licensed for short term use only.

Therapeutics

- May cause hyperalgesia on abrupt withdrawal.
- Different preparations may vary in bioavailability: avoid changing formulations or brands.
- Suppositories of 125mg are approximately equivalent to 100mg tablets but final adjustment should always depend on clinical response (plasma concentration monitoring recommended).
- Use ideal body weight (Appendix 7) when calculating doses in obese children

Side effects

- Can cause serious blood, hepatic, and skin disorders. Parents should be taught how to recognise signs of these conditions, particularly leucopoenia.
- Associated with osteopenia and increased risk of fractures. Consider vitamin D supplementation with long term use.
- Neuroleptic malignant syndrome

Interactions

- Induce of cytochrome P450 enzymes CYP2C9 and CYP3A4. Reduces levels of drugs metabolised by these enzymes including alfentanil, amitriptyline, buprenorphine, clobazam, clonazepam, dexamethasone, diazepam, diclofenac, domperidone, erythromycin (erythromycin also increases carbamazepine levels), fentanyl, haloperidol, methadone, midazolam, paracetamol (with increased risk of liver toxicity), risperidone and tramadol. *This list is not exhaustive-seek advice.*

Administration

- Oral liquid has been administered rectally-should be retained for at least 2 hours if possible but may have a laxative effect.
- Use the liquid preparation for administration via an enteral feeding tube. Dilute with equal volume of water to minimise adsorption to the feeding tube immediately prior to administration. There may be some tube resistance but not blockage when administering via enteral feeding tubes due to high viscosity of liquid.
- Doses above 800mg/day may cause bloating due to the sorbitol content of the liquid. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy. An increase in side effects such as dizziness is possible owing to the rapid delivery into the small bowel. Consider decreasing the dose and increasing the dosing frequency if side effects are problematic.

Patient information

- See Medicines for Children leaflet: “Carbamazepine (oral) for preventing seizures” https://www.medicinesforchildren.org.uk/medicines/carbamazepine-oral-for-preventing-seizures/

Available as

- Tablets (100mg, 200mg, 400mg), liquid (100mg/5 ml), suppositories (125mg, 250mg), and modified release tablets (200mg, 400mg).

Evidence: (1,8,73,74)

Celecoxib

Use:

- Pain, inflammatory pain, bone pain, stiffness. Not used first line
- Post-operative pain where other non-steroidal anti-inflammatory drugs (NSAIDS) are contraindicated

Dose and route:

By mouth:

- **Child over 2 years**:

  Body-weight 10-25 kg: 2-3mg/kg/dose twice daily, maximum 50mg twice daily

  Body-weight more than 25 kg: 100mg twice daily

- **Over 16 years**: 100mg twice daily, increased in severe pain to 200mg twice daily

Notes

- Selective cyclo-oxygenase-2 inhibitor.

Licensing

- Not licensed in the UK for use in children.

Therapeutics

- Dose based on management of juvenile rheumatoid arthritis.
- No difference in tolerability or efficacy has been shown between the selective cox-2 inhibitors (etoricoxib, celecoxib) and the non-selective NSAID, naproxen.
- Parecoxib may be an alternative if the enteral route is not available.
- Does not increase bleeding time.

Contraindications, cautions

- Caution in known CYP2C9 slow metabolizers.
- May mask fever and other signs of inflammation
- Caution in cardiac, hepatic or renal impairment and those with asthma
- Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure

Side effects

- All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factors or duration of NSAID use. The greatest risk may be in those receiving high doses long term.
- All NSAIDs are associated with serious gastro-intestinal toxicity. COX-2 inhibitors are associated with a lower risk of serious upper gastro-intestinal side effects than non-selective NSAIDs. Consider prescription of a proton pump inhibitor with prolonged use. May exacerbate Crohn's disease.

Hepatic impairment, renal impairment

- Caution in renal impairment: avoid in severe renal impairment.
- Caution in hepatic impairment.

Interactions

- Inhibitor of cytochrome P450 enzyme CYP2D6. May increase the plasma concentrations of other drugs metabolized by this enzyme including amitriptyline, ondansetron and oxycodone.
- Metabolised by CYP2C9. Levels increased by drugs that inhibit this enzyme including fluconazole and in known CYP2C9 slow metabolisers. Levels reduced by drugs that induce this enzyme including carbamazepine
- Reduce dose of celecoxib by 50% if administered with fluconazole.

Administration

- Capsules may be opened and contents mixed with soft food immediately before administration. For administration via an enteral feeding tube, the capsule may be opened and the contents mixed with water to form a milky suspension.

Available as

- Capsules 100mg, 200mg. Also available in UK as an unlicensed 'special' oral suspension (100mg/5ml Quantum Pharmaceuticals)

Evidence: (2,3,75–79)

Chloral hydrate

Use:

- Seizures in severe epileptic encephalopathy (seek specialist advice)
- Status dystonicus (seek specialist advice)
- Short term (up to 2 weeks) treatment of insomnia in children and young people with suspected or definite neurodevelopmental disorder where other behavioural and pharmacological measures have failed
- Procedural sedation in neonates

Dose and route:

Seizures, status dystonicus, insomnia

By mouth or rectum:

- **Neonate, child 1 month-11 years**: Initial dose of 30mg/kg as a single dose at night. May be increased to 50mg/kg at night or when required up to 6-8 hourly.

  Maximum single dose 1g

- **12 years and over**: Initial dose of 500mg as a single dose at night or when required up to 6-8 hourly. Dose may be increased if necessary to 1-2 g.

  Maximum single dose 2g

Procedural sedation in neonatal intensive care

By mouth or rectum:

- **Neonate:** for sedation for procedures in NICU: 30–50mg/kg 45–60 minutes before procedure; doses up to 100mg/kg may be used with respiratory monitoring.

Notes:

Licensing

- Not licensed for agitation, epilepsy or status dystonicus. Not licensed in infants under 2 years for insomnia. Use for treatment of severe insomnia in children and adolescents restricted by MHRA/CHM (2021) to those with a suspected or definite neurodevelopmental disorder when insomnia is interfering with daily life and other therapies have failed.

Therapeutics

- Use in insomnia only when insomnia is interfering with daily life. Long term use in insomnia only under specialist guidance
- Use in movement disorders or epileptic encephalopathy should be under the supervision of a named consultant with appropriate experience and competency in paediatric neurology, neurodisability or palliative care. The lowest effective dose should be used, at the lowest frequency and for the shortest period possible. The need for on-going use should be regularly reviewed.
- May cause agitation if withdrawn suddenly

- Enteral solution contains propylene glycol which may accumulate to potentially harmful levels with repeated dosing in neonates.

Side effects

- Allergic dermatitis; ataxia; confusion; delirium (more common on abrupt discontinuation); GI disorders
- Carcinogenic at high doses in rodents

Pharmacokinetics

- Accumulates with prolonged use
- Prolonged half-life in neonates.

Hepatic impairment, renal impairment

- Avoid in severe renal or hepatic impairment.

Administration

- By mouth: mix with plenty of juice, water, or milk to reduce gastric irritation and disguise the unpleasant taste. Light-sensitive so needs to be given as soon as it is drawn up.
- For rectal administration use oral solution or suppositories (available from 'specials' manufacturers).
- Chloral hydrate oral solution may be administered via enteral feeding tubes. Dilute with water before administration, ideally to 2 or 3 times the original volume as tolerated, to reduce risk of gastric irritation. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (chloral betaine 707mg = choral hydrate 414mg— Welldorm®), oral solution (143.3mg/5ml, 500mg/5ml). Oral solutions contain propylene glycol. The RCPCH and NPPG recommend that, when a liquid formulation of chloral hydrate is required, 500 mg/5 mL is used.
- Suppositories (available as various strengths 25mg, 50mg, 60mg, 100mg, 200mg, 500mg from 'specials' manufacturers).

Evidence: (2,11,80–85)

Chlorpromazine

Use:

- Hiccup
- Nausea and vomiting in end-of-life care (where other drugs are unsuitable)
- Agitated delirium in end-of-life care

Dose and route:

By mouth:

- **Child 1-5 years**: 500micrograms/kg 6-8 hourly, adjusted according to response, maximum 40mg daily
- **Child 6-11 years**: 10mg 6-8 hourly, adjusted according to response, maximum 75mg daily.
- **12 years and over**: 25mg 6-8 hourly adjusted according to response, maximum 150mg daily

Total daily dose can also be given once daily at night

Notes:

Licensing

- Not licensed in children for intractable hiccup.

Therapeutics

- Can be given rectally at doses of approximately twice those used via oral route

Cautions

- Caution in cardiovascular disease, neurological impairment including CNS depression, epilepsy, myasthenia gravis, severe respiratory disease, blood dyscrasias: monitor blood counts if unexplained infection or fever.

Side effects

- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval
- Photosensitisation may occur with higher dosages: avoid direct sunlight.
- Extrapyramidal side effects, neuroleptic malignant syndrome
- Risk of contact sensitisation: tablets should not be crushed; solution should be handled with care.

Hepatic and renal impairment

- Caution in hepatic impairment and jaundice: can precipitate coma.
- Caution in renal impairment: increased cerebral sensitivity. Start with small dose.

Administration

- Oral solution may be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets coated (25mg, 50mg, 100mg), oral solution (25mg/5ml, 100mg/5ml). Suppositories from specialist manufacturers

Evidence: (1,2,86–89)

Clobazam

Clo**baz**am has been confused with clo**nazep**am; care must be taken to ensure the correct drug is prescribed, dispensed and administered.

Use:

- Adjunctive therapy for epilepsy
- Short term 'add on' therapy for epilepsy exacerbations related to hormonal changes or intercurrent illness

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

By mouth:

- **Child 1 month-5 years**: Initial dose of 125micrograms/kg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 250micrograms/kg twice daily. Maximum 500micrograms/kg, 15mg single dose, twice daily
- **Child 6 years and over**: Initial dose of 5mg daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 300micrograms/kg-1mg/kg daily. Maximum 60mg daily.

  Daily doses of up to 30mg may be given as a single dose at bedtime, higher doses should be divided.

Notes:

Licensing

- Not licensed for use in children less than 6 years of age. Not licensed as monotherapy.

Therapeutics

- Avoid abrupt withdrawal, except when being used for short courses. Caution when changing between different formulations.
- Tolerance in longer term use may be managed by 'switching/rotating' benzodiazepines.

Side effects

- Risk of increased somnolence or sedation when co-administered with cannabidiol, or opiates
- Side effects similar to other benzodiazepines: children are more susceptible to sedation and paradoxical emotional reactions.

Pharmacokinetics, interactions

- Pharmacokinetics influenced by age and co-administration of other medication. Dose adjustment may be needed when co-administered with strong or moderate CYP2C19 inhibitors.

Administration

- Tablets can be administered whole, or crushed and mixed in soft food. The 10mg tablets can be divided into equal halves of 5mg. Clobazam can be given with or without food. Tablets take 1 to 5 minutes to disperse in water. Both oral liquid and tablets dispersed in water may be administered via enteral feeding tubes.

Patient information

- See Medicines for Children leaflet "Clobazam for preventing seizures" https://www.medicinesforchildren.org.uk/medicines/clobazam-for-preventing-seizures/

Available as

- Tablets 10mg, Oral liquid (10mg/5ml, 5mg/5ml-care with differing strengths), capsules and oral suspension available from special manufactures
- Clobazam is not prescribable in NHS primary care except for the treatment of epilepsy; endorse prescription 'SLS'.

CD

- CD Schedule 4, part 1 (CD4-1).

Evidence: (1,90–93)

Clonazepam

Clo**nazep**am has been confused with clo**baz**am; care must be taken to ensure the correct drug is prescribed, dispensed and administered.

Use:

- Tonic-clonic seizures
- Partial seizures
- Cluster seizures
- Myoclonus
- Neuropathic pain
- Restless legs
- Anxiety, including anxiety associated with dyspnoea, panic attacks
- Oral dysaesthesia in the adolescent

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Epilepsy

By mouth

- **Child 1 month-11 months**: Initially 250micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 500micrograms–1mg at night, or in 2-3 divided doses.
- **Child 1-4 years**: Initially 250micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance of 1–3mg at night, or in 2 -3 divided doses.
- **Child 5-11 years**: Initially 500micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 3–6mg at night or in 2 -3 divided doses
- **12 years and over**: Initially 1mg at night for 4 nights, increased over 2–4 weeks to usual maintenance of 4–8mg at night, or in 2-3 divided doses.

  Higher doses may be used in complex seizure disorders under guidance from a paediatric neurologist

Anxiolysis, neuropathic pain, myoclonus and restless legs

By mouth

- **Child 1 month-11 months**: Initially 125micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 250–500micrograms at night, or in 2-3 divided doses.
- **Child 1-4 years**: Initially 125micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance of 500micrograms-1.5mg at night, or in 2 -3 divided doses.
- **Child 5-11 years**: Initially 250micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 1.5–3mg at night or in 2 -3 divided doses
- **12 years and over**: Initially 500micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance of 2–4mg at night, or in 2-3 divided doses.

Oral dysaesthesia (burning mouth syndrome)

- Rinse with 100micrograms/ml solution

Notes

Licensing

- Licensed for use in children for status epilepticus and epilepsy. Not licensed for neuropathic pain. Tablets licensed in children. Not licensed in the UK for SC use.

Therapeutics

- Effective anticonvulsant often used as a 3rd line "add-on".
- Avoid abrupt withdrawal, except when being used for short courses. Caution when changing between different formulations
- Tolerance in longer term use may be managed by 'switching/rotating' benzodiazepines.
- Dose may be increased for short periods of 3-5 days during times of increased seizures e.g. from viral illness.
- Approximately 20 times more potent than diazepam as an anxiolytic-sedative. (i.e. 250micrograms clonazepam equivalent to 5mg diazepam orally or 2.5mg IV/SC midazolam). See Appendix 4.
- Has been used as a subcutaneous or intravenous infusion in status epilepticus resistant to other anticonvulsants. However, the injection is no longer available in the UK. Intravenous or subcutaneous doses are approximately equal to oral doses. Due to the long half -life a loading dose should be given in patients not already receiving clonazepam
- Doses of up to 1.4mg/kg/24hours have been used in status epilepticus in PICU environment.

Contraindications, cautions

- Contraindicated in myasthenia gravis.
- Avoid in acute or severe respiratory failure unless imminently dying. Caution in chronic respiratory disease or sleep apnoea.
- Avoid abrupt withdrawal.

Side effects

- Associated with salivary hypersecretion and drooling.

Pharmacokinetics

- Oral biovailability >80%; the same dose can be used when converting from PO to IV or SC routes.
- Long elimination half-life of up to 60 hours. Infusions may take up to 6 days to reach steady state. Risk of accumulation and toxicity. Consider loading dose to reach steady state more quickly.

Hepatic and renal impairment

- Caution in mild or moderate hepatic impairment: avoid in severe hepatic impairment.

Patient information

- See Medicines for Children leaflet: "Clonazepam for preventing seizures" https://www.medicinesforchildren.org.uk/medicines/clonazepam-for-preventing-seizures/

Administration

- Licensed oral liquid formulation contains alcohol. Tablets or other unlicensed non-alcohol-containing liquid preparations are therefore preferred.
- Tablets may be dispersed in water for oral administration or administration via a feeding tube.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Adheres to plastic tubing. Tablets should be dispersed in at least 30ml of water to prevent binding to enteral feeding tubes. Flush enteral feeding tubes well after administration. Use non-PVC tubing for infusions.
- Diluted clonazepam injection is stable for up to 12 hours. Infusions should ideally be changed every 12 rather than every 24 hours.
- Compatible with most drugs commonly administered via continuous subcutaneous infusion via syringe driver. Dilute with water for injection or sodium chloride 0.9%.

Available as

- Tablets (500micrograms scored, 1mg, 2mg scored); liquid (500micrograms in 5ml and 2mg in 5ml now available as licensed preparations from Rosemont, but neither are licensed for use in children due to high alcohol content; other unlicensed oral liquids are available from specials manufacturers); clonazepam drops 2.5mg/ml available from some special manufacturers; injection (1mg/ml unlicensed import).
- The RCPCH and NPPG recommend that, when a liquid special of clonazepam is required, the 2mg/5ml strength is used:

CD

- CD Schedule 4 part 1 (CD4-1).

Evidence: (1,2,11,90,94–96)

Clonidine

Use:

- Anxiety / sedation (prior to procedure)
- Pain / sedation / opioid sparing / prevention of opioid withdrawal effects
- Regional nerve block
- Spasticity / dystonia
- Status dystonicus
- Hypertensive crisis in autonomic dysreflexia
- Behavioural symptoms of irritability, impulsiveness, aggression

Doses and route:

Pain, sedation, opioid sparing, prevention of opioid withdrawal effects, spasticity, movement disorder

By mouth or intravenous bolus:

- **Child 1 month and over**: Initial dose 1micrograms/kg/dose 3-4 times daily. Increase gradually as needed and tolerated to maximum of 5micrograms/kg/dose four times daily.

  For long term use consider conversion to a transdermal patch once an effective dose has been established

By transdermal patch

Conversion from oral, intravenous or subcutaneous routes

Clonidine 100-150micrograms/24hours	≡	Clonidine 2.5mg patch (delivers 100micrograms/24hours)
Clonidine 150-250micrograms/24hours	≡	Clonidine 5mg patch (delivers 200micrograms/24hours)
Clonidine 250-350micrograms/24hours	≡	Clonidine 7.5mg patch (delivers 300micrograms/24hours)

If more than 2.5mg patch to be used i.e.200micrograms/24hours, consider using 2 smaller patches to be changed on different days of the week to reduce end of dose effect.

Therapeutic clonidine levels are achieved 2 to 3 days after initial application of patch. Oral, intravenous or subcutaneous clonidine therefore needs to be reduced gradually after applying the patch:

Apply patch on day 1.

Day 1: continue 100% of oral/IV dose

Day 2: reduce to 50% of oral/IV dose

Day 3: reduce to 25% oral/IV dose

Day 4: patient will only need patch

By continuous intravenous or subcutaneous infusion (most experience on PICU)

- **Child over 1 month**: 0.1-2micrograms/kg/hour:
  approximately 2.5-50micrograms/kg/24hours

Usual starting doses:

- **Child less than 6 months**: 0.4micrograms/kg/hour
  approximately 10micrograms/kg/24hours
- **Child 6 months and over**: 0.6micrograms/kg/hour, approximately 14micrograms/kg/24hours

Total daily dose can also be given as subcutaneous injection in two divided doses

Behavioural problems, tics, Tourette's syndrome:

By mouth:

- **Child over 4 years**: Initial dose of 25micrograms at night. Increase as necessary after 1-2 weeks to 50micrograms at night. Dose can be further increased by 25micrograms every 2 weeks. Recommended maximum 5micrograms/kg/day or 300micrograms/day

  For long term use consider conversion to a transdermal patch (see above) once an effective dose has been established

Anxiety, procedural sedation, autonomic dysreflexia:

By mouth, or buccal/sublingual (using injection solution or oral tablets):

- **Neonate**: 4micrograms/kg as a single dose
- **Child 1 month and over**: 4micrograms/kg as a single dose, maximum 150 micrograms/ dose.

Premedication given 45-60 minutes before procedure

For autonomic dysreflexia a further dose up to 2micrograms/kg can be given after an hour if required

Regional nerve block (specialist use only):

- **Child 3 months and over**: 1-2micrograms/kg clonidine in combination with a local anaesthetic.

Notes

- Mixed alpha-1 and alpha-2 agonist (mainly alpha-2). Appears to have synergistic analgesic effects with opioids and prevents opioid withdrawal symptoms. Also useful for its sedative effect. Use established in ADHD, behavioural problems and tics.

Licensing

- Not licensed for use in children. Patches not licensed in UK. Licensed for the treatment of hypertension.

Therapeutics

- Consider monitoring blood pressure and pulse on starting treatment and after each dose increase.
- Avoid abrupt discontinuation: risk of acute withdrawal symptoms including rebound hypertension.
- Can be administered by the buccal route. Some drug may be swallowed. This is unlikely to significantly affect the bioavailability but may delay the onset of action.
- Can be administered by continuous subcutaneous infusion for status dystonicus.
- Can be used as substitute for tizanidine if enteral route is unavailable due to similar mechanism of action although less hypotensive effect.
- Higher doses up to 200micrograms/kg/24hours via enteral, intravenous and transdermal routes have been reported in status dystonicus although sedation is a significant adverse effect.

Cautions

- Caution in bradycardia, Raynaud's or other occlusive peripheral vascular disease.
- Remove patches before MRI scanning: risk of burns.

Side effects

- Common side effects include constipation, nausea, dry mouth, vomiting, postural hypotension, dizziness, sleep disturbances, headache.

Interactions

- Effects abolished by drugs with alpha-2 antagonistic activity e.g. tricyclics and antipsychotic drugs. Antihypertensive effects may be potentiated by other drugs used to lower blood pressure.

Pharmacokinetics

- Oral, sublingual and rectal bioavailability 75-95%, although this may be lower in children. Generally 1:1 oral:sublingual:IV:SC:PR conversion can be used. Half-life 12-33 hours.
- Anecdotal reports of use of rectal clonidine. Pharmacokinetic studies suggest almost 100% bioavailability via this route. Single rectal doses of 2.5-4micrograms/kg have been used.
- Has also been administered via intranasal route using atomised injection solution using doses similar to oral route. Onset of action is faster than by mouth.
- Onset of action 30-60 minutes via oral, sublingual or rectal routes. Time to peak plasma concentration: oral 1.5-5 hours; epidural 20 minutes; transdermal, continuous intravenous and subcutaneous infusion 2-3 days.
- Considerable inter-individual variation in bioavailability of patches: caution when converting from other routes.

Hepatic impairment, renal impairment

- Accumulates in renal impairment. Consider reducing dose if GFR less than 30ml/min/1.73m^2

Administration

- Oral solution may be administered via an enteral feeding tube. Alternatively, tablets may be crushed and dispersed in water for administration via an enteral feeding tube. The 25microgram tablets do not appear to disperse in water as readily as the 100microgram tablets. IV solution may also be given via the enteral tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Injection can be administered by buccal or sublingual route. Alternatively oral tablets can be administered sublingually
- Rectal administration using parenteral preparation diluted to 10micrograms/ml with sodium chloride 0.9%
- Parenteral solution can be administered undiluted as a subcutaneous injection or diluted in sodium chloride 0.9% for continuous subcutaneous infusion. Can be combined with a number of other drugs commonly administered by continuous subcutaneous infusion in palliative care: consult appropriate specialist texts.

Patient information

- Patient information: see Medicines for Children leaflet: “Clonidine for Tourette’s syndrome ADHD and sleep onset disorder” https://www.medicinesforchildren.org.uk/medicines/clonidine-for-tourettes-syndrome-adhd-and-sleep-onset-disorder/

Available as

- Tablets (25micrograms, 100micrograms), oral solution (50micrograms/5ml), injection (150 micrograms/ml), transdermal patch (available via importation company)
  - 2.5mg patch (=100 micrograms clonidine/day for 7 days)
  - 5mg patch (=200 micrograms clonidine/day for 7 days)
  - 7.5mg patch (= 300 micrograms clonidine/day for 7 days)

Evidence: (3,11,58,81,97–111)

Co-danthramer (dantron and poloxamer 188)

Use:

• Constipation in end-of-life care

Dose and route:

By mouth:

Co-danthramer 25/200 suspension 5ml = one co-danthramer 25/200 capsule (Dantron 25mg, poloxamer '188' 200mg):

- **Child 2-11 years**: 2.5–5ml at night
- **Child 6-11 years**: 1 capsule at night
- **12 years and over**: 5–10ml or 1–2 capsules at night.

Strong co-danthramer 75/1000 suspension 5ml = two strong co-danthramer 37.5/500 capsules:

- **12 years and over**: 5ml or 1–2 capsules at night.

Notes

- Stimulant laxative (dantron) combined with a wetting agent (poloxamer 188)

Licensing

- Licensed for terminally ill patients of all ages

Side effects

- Avoid prolonged skin contact due to risk of irritation and excoriation (avoid in urinary or faecal incontinence, or children with nappies).
- Rodent studies indicate potential carcinogenic risk.
- Dantron can turn urine red/brown.

Administration

- Suspension can be used with enteral feeding tubes but is quite viscous, needing some pressure on syringe and to be flushed well after administration. Administration into the jejunum is unlikely to affect pharmacological response.

Available as

- Co-danthramer 25/200 suspension 5 ml = one co-danthramer 25/200 capsule (Dantron 25mg, poloxamer '188' 200mg), Strong co-danthramer 75/1000 suspension 5 ml = two strong co-danthramer 37.5/500 capsules.

Evidence: (1,2)

Co-danthrusate (dantron and docusate sodium)

Use:

- Constipation in end-of-life care

Dose and route:

By mouth:

Co-danthrusate 50/60 suspension 5ml = one co-danthrusate 50/60 capsule (Dantron 50mg/ Docusate sodium 60mg)

- **Child 6-11 years**: 5ml or 1 capsule at night
- **12 years and over**: 5–15ml or 1–3 capsules at night

Notes

- Stimulant laxative (dantron) combined with a softener (docusate sodium)

Licensing

- Licensed for terminally ill patients of all ages

Therapeutics

- Not recommended for under 6 years.

Side effects

- Avoid prolonged skin contact due to risk of irritation and excoriation (avoid in urinary or faecal incontinence, or children with nappies).
- Dantron can turn urine red/brown.
- Rodent studies indicate potential carcinogenic risk.

Administration

- No specific data on enteral tube administration are available for this preparation. If necessary use the suspension and flush tube well after use. Consider diluting with water to aid administration.

Available as

- Co-danthrusate 50/60 suspension 5ml = one co-danthrusate 50/60 capsule (Dantron 50mg/ Docusate sodium 60mg)

Evidence: (1,2)

Codeine Phosphate

Codeine is no longer indicated for palliative care in children. It has been replaced by other opioids, particularly oral morphine and buccal diamorphine or fentanyl.

Evidence: (1,2,112)

Cyclizine

Use:

- Antiemetic of choice for raised intracranial pressure.
- Nausea and vomiting of vestibular origin or where other antiemetics (metoclopramide, $5HT_3$ antagonists) have failed.

Dose and route:

By mouth or by slow intravenous injection over 3–5 min:

- **Child 1 month- 5 years**: 500micrograms–1mg/kg up to 3 times daily, maximum single dose 25mg
- **Child 6-11 years**: 25mg up to 3 times daily
- **12 years and over**: 50mg up to 3 times daily

By rectum:

- **Child 2- 5 years**: 12.5mg up to 3 times daily
- **Child 6-11 years**: 25mg up to 3 times daily
- **12 years and over**: 50mg up to 3 times daily

By continuous intravenous or subcutaneous infusion:

- **Child 1-23 months**: 1.5-3mg/kg/24hours (maximum 25mg/24hours),
- **Child 2-5 years**: 25-50mg/24hours
- **Child 6-11 years**: 37.5-75mg/24hours
- **12 years and over**: 75-150mg/24hours

Notes:

- Antihistaminic, antimuscarinic antiemetic.

Licensing

- Tablets are not licensed for use in children under 6 years old. Injection is not licensed for use in children.

Therapeutics

- Injection solution has also been given sublingually in adults using same doses as oral or rectal routes.
- Anticholinergic effects reduce effect of prokinetic antiemetics e.g. domperidone, metoclopramide

Contraindications, cautions

- Avoid in severe cardiac failure: may cause fall in cardiac output.
- Increased risk of transient paralysis with intravenous use in patients with neuromuscular disorders.

Side effects

- Antimuscarinic side effects include dry mouth, drowsiness, headache, fatigue, dizziness, thickening of bronchial secretions, nervousness.
- Risk of site reactions when administered via SC or IV route
- Rapid SC or IV bolus can lead to 'light-headedness': disliked by some but enthralling to others leading to repeated requests for IV cyclizine.

Pharmacokinetics

- Some evidence suggests 50% oral bioavailability: consider reducing dose when converting oral to IV or SC routes.
- May accumulate with continued use.

Hepatic impairment, renal impairment

- Avoid in severe liver disease.

Interactions

- Increased sedative and antimuscarinic effect when given with tricyclics, anxiolytics, MAOI's.

Administration

- For continuous subcutaneous or intravenous infusion, dilute only with water for injection or 5% dextrose*: incompatible* with 0.9% sodium chloride causing precipitation.
- Concentration dependent *incompatibility* with alfentanil, dexamethasone, diamorphine and oxycodone.
- Suppositories must be kept refrigerated.
- Tablets may be crushed for oral administration. The tablets do not disperse well in water, but if shaken in 10 ml water for 5 minutes, the resulting dispersion may be administered immediately via an enteral feeding tube. Alternatively use oral suspension. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (50mg), suppositories (12.5mg, 25mg, 50mg, 100mg from 'specials' manufacturers) and injection (50mg/ml). Oral suspension unlicensed special (50mg/5ml Nova Laboratories, 5mg/5ml). Alternative suppliers may also be available.

Evidence: (1,3,8,113)

Dantrolene

Use:

- Skeletal muscle relaxant
- Chronic severe skeletal muscle spasm or spasticity

Dose and route:

Doses should be increased *slowly*

By mouth:

- **Child 5-11 years**: Initial dose of 500micrograms/kg once daily; increase after 7 days to 500micrograms/kg/dose 3 times daily. Increase every 7 days by a further 500micrograms/kg/dose until response

  Maximum recommended dose 2mg/kg 3–4 times daily, maximum total daily dose 400mg

- **12 years and over:** Initial dose of 25mg once daily; increase after 7 days to 25mg 3 times daily. Increase by a further 500micrograms/kg/dose every 7 days until response.

  Maximum recommended dose 2mg/kg 3–4 times daily, maximum total daily dose 400mg

Notes:

Licensing

- Not licensed for use in children.

Therapeutics

- Acts directly on skeletal muscle so can be used concurrently with baclofen and diazepam.

Contraindications, cautions

- Caution in patients impaired cardiac or pulmonary function.

Side effects

- Risk of hepatotoxicity; consider checking liver function before and at regular intervals during therapy.
- Pericarditis, pleural effusion, respiratory depression, exacerbation of cardiac insufficiency, tachycardia and blood pressure changes, drowsiness, dizziness, weakness, nausea and diarrhoea.

Hepatic impairment, renal impairment

- Contraindicated in hepatic impairment: avoid in liver disease or concomitant use of hepatotoxic drugs.

Administration

- Capsules can be opened and dispersed in water for administration via gastrostomy. Alternatively use oral suspension.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Capsules (25mg, 100mg), oral suspension (extemporaneous formulation 5mg/ml).

Evidence: (1–3,114)

Dexamethasone

Use:

- Headache associated with raised intracranial pressure caused by a tumour
- Malignant spinal cord compression
- Reduction of symptoms due to peri-tumour oedema and inflammation
- Neuropathic pain due to nerve compression
- Bone pain due to malignant infiltration
- Antiemetic either as an adjuvant or in highly emetogenic cytotoxic therapies

Dose and route:

Headache associated with raised intracranial pressure, spinal cord compression

By mouth or short intravenous infusion over 15-20 minutes:

- **Child 1 month- 11 years**: 250micrograms/kg twice daily for 5 days; then stop
- **12 years and over:** 8mg twice daily (or 16mg once daily) for 5 days, then stop

If symptoms recur consider a further pulse of dexamethasone followed by a washout period to reduce side effects. Reduce to the minimum effective dose if discontinuation is not possible.

Prescribe injection or infusion as dexamethasone *base.*

Higher doses may be advised particularly in malignant spinal cord compression.

Once and twice daily doses to be given before midday to reduce likelihood of corticoid induced insomnia

Reduction of symptoms due to peri-tumour oedema and inflammation

Neuropathic pain due to malignant nerve compression

Bone pain due to malignant infiltration

By mouth, short intravenous infusion over 15–20 minutes, or subcutaneous injection

- **Child under 1 year**: Initial dose 250micrograms once or twice daily.
- **1- 5 years**: Initial dose 1mg once or twice daily.
- **6-11 years**: Initial dose 2mg once or twice daily.
- **12 years and over**: 4mg once or twice daily.

Initial therapy for 2–5 days then stop.

If symptoms recur consider a further pulse of dexamethasone followed by a washout period to reduce side effects. Reduce to the minimum effective dose if discontinuation is not possible.

Prescribe injection or infusion as dexamethasone *base.*

Once and twice daily doses to be given before midday to reduce likelihood of corticoid induced insomnia

Antiemetic

By mouth, short intravenous infusion over 15-20 minutes, or subcutaneous injection:

- **Child under 1 year**: Initial dose 250micrograms 3 times daily. This dose may be increased as necessary and as tolerated up to 1mg 3 times daily
- **1-5 years**: Initial dose 1mg 3 times daily. This dose may be increased as necessary and as tolerated up to 2mg 3 times daily
- **6-11 years**: Initial dose 2mg 3 times daily. This dose may be increased as necessary and as tolerated up to 4mg 3 times daily
- **12 years and over**: 4mg 3 times daily

Prescribe injection or infusion as dexamethasone *base*.

Notes:

Licensing

- Not licensed for use in children as an anti-emetic.

Therapeutics

- High glucocorticoid activity but relatively insignificant mineralocorticoid activity.
- Dexamethasone 1mg = 7mg prednisolone, anti-inflammatory equivalence.
- Prescribe injection or infusion as dexamethasone *base* i.e. as “dexamethasone”, not “dexamethasone phosphate” or “dexamethasone sodium phosphate”.
- Long duration of action. Can be given in a single daily dose each morning for most indications. Administration of the daily dose of dexamethasone before midday reduces the likelihood of corticosteroid induced insomnia and agitation.
- Adverse effects quickly outweigh the benefits: use short courses wherever possible or reduce as quickly as possible to lowest effective dose.
- Can be stopped abruptly if given for less than two weeks. Doses should be weaned gradually over several weeks for longer courses in order to allow recovery of the hypo-pituitary axis and avoid Addisonian crisis.
- Dexamethasone (base) 1mg = dexamethasone phosphate 1.2mg = dexamethasone sodium phosphate 1.3mg.

Side effects

- Rapid injection can cause paraesthesia and cardiovascular collapse.
- Problems of body-weight gain and Cushingoid appearance are major concerns specifically in children.
- Other side effects include: diabetes, hypertension, osteoporosis, muscle wasting, peptic ulceration and behavioural problems and agitation, also extreme exacerbation of and lability of mood (tearfulness, physical aggression), hypokalaemia.
- Consider the use of proton pump inhibitor (PPI) to prevent gastrointestinal irritation.
- Some injection formulations may contain latex: consult SPC.

Pharmacokinetics

- Oral bioavailability >80%; 1:1 oral:IV:SC conversion can be used.

Interactions

- Moderate inducer of cytochrome P450 enzyme CP3A4. May reduce levels of drugs that are metabolised by this enzyme.
- Also metabolised by CYP3A. Levels increased by drugs that inhibit this enzyme including aprepitant, ciprofloxacin, erythromycin and fluconazole. Levels reduced by drugs that induce this enzyme including carbamazepine and phenobarbital.

Administration

- Tablets may be dispersed in water if oral liquid unavailable. Oral solution or tablets dispersed in water may be administered via an enteral feeding tube.
- Alkaline drug: increased risk of precipitation when used in combination with other drugs in a syringe driver.

Patient information

- See Medicines for Children Leaflet "Dexamethasone for croup" https://www.medicinesforchildren.org.uk/medicines/dexamethasone-for-croup/

Available as

- Tablets (500 micrograms, 2mg, 4mg), soluble tablets (2mg, 4mg, 8mg, 10mg, 20mg) oral solution (2mg/5ml 10mg/5ml and 20mg/5ml) and injection dexamethasone base 3.8mg/ml and 3.3mg/ml.

Evidence: (2,3,10)

Diamorphine

Use:

- Moderate to severe pain
- Breakthrough pain where oral route is not available, or rapid onset of action is required
- Dyspnoea
- Alternative opioid where large doses need to be administered in small volume

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in patients already receiving regular strong opioids

By continuous subcutaneous or intravenous infusion

Calculate dose of diamorphine by using oral morphine equivalent (OME) from previous analgesia (See table Appendix 1).

Approximate equianalgesic ratios for oral and intravenous morphine and diamorphine

Conversion		Ratio	Calculation	Example
From	To			
Morphine oral	Diamorphine CSCI or CIVI	6:1	Divide 24hour morphine dose by 6	Morphine oral 30mg/24hours ÷ 6 = diamorphine CSCI 5mg/24hours
Morphine CSCI or CIVI	Diamorphine CSCI or CIVI	2:1	Divide 24hour morphine dose by 2	Morphine CSCI 20mg/24hours ÷ 2 = diamorphine CSCI 10mg/24hours

Breakthrough pain in patients already receiving opioids

Review background analgesia if breakthrough analgesia is required more than twice in a 24-hour period.

By subcutaneous or intravenous routes

- 1/10 to 1/6 (10-16%) of 24-hour diamorphine infusion every 1-4 hours as needed.

By intranasal or buccal route

Approximate equianalgesic ratios for intranasal or buccal diamorphine

Conversion		**Ratio**	**Calculation**	**Example**
From	**To**			
Diamorphine CIVI or CSCI	Intranasal or buccal diamorphine	**1:2**	***Multiply*** 24hour diamorphine dose by 2 *Then* administer 1/10-1/6 every 1- 4 hours as needed	Diamorphine 20mg/24hours x 2 = 40 40 ÷ 10 = 4 40 ÷ 6 = 6.6 Breakthrough dose = 4-6.6mg intranasal diamorphine
Oral morphine	Intranasal or buccal diamorphine	3:1	Divide 24hour morphine dose by 3 *Then* administer 1/10-1/6 every 1- 4 hours as needed	Morphine oral 30mg/24hours ÷ 3 = 10 10 ÷ 10 = 1 10 ÷ 6 = 1.7 Breakthrough dose = 1-1.7mg intranasal diamorphine
Morphine CIVI or CSCI	Intranasal or buccal diamorphine	1:1	Administer 1/10-1/6 24hour morphine dose every 1- 4 hours as needed	Morphine CIVI 60mg/24hours 60 ÷ 10 = 6 60 ÷ 6 = 10 Breakthrough dose = 6-10mg intranasal diamorphine

Pain in opioid naive patients

Doses refer to ***starting*** doses only[a]

Age range	Intranasal or buccal	Intravenous or subcutaneous bolus	Intravenous or subcutaneous infusion/24hours
Neonate	40micrograms/kg/dose 6 hourly	20micrograms/kg/dose 6 hourly	80micrograms/kg/24hours
1- 2 months	60micrograms/kg/dose 6 hourly	30micrograms/kg/dose 6 hourly	120micrograms/kg/24hours
3- 5 months	60micrograms/kg/dose 4 hourly	30micrograms/kg/dose 4 hourly	180micrograms/kg/24hours
6- 23 months	80micrograms/kg/dose 4 hourly	40micrograms/kg/dose 4 hourly	240micrograms/kg/24hours
2-11 years	80-100micrograms/kg maximum 5mg/dose 4 hourly	40micrograms/kg maximum 2.5mg/dose 4 hourly	240-300micrograms/kg/24hours maximum 10mg/24hours
12 years and over	80-100micrograms/kg maximum 5mg/dose 4 hourly	40-50micrograms/kg/dose 4 hourly maximum 2.5mg/dose *Alternatively* 1.25-2.5mg/dose	240micrograms/kg/24hours maximum 15mg/24hours

Injection solution can be used by intranasal or buccal routes. A Mucosal Atomiser Device (MAD) can be used for accuracy of administration.

Dyspnoea

By buccal, intranasal, subcutaneous or intravenous routes

- **Child 1 month and over:** 25-50% of pain doses

Notes:

- Pro-drug of morphine.

Licensing

- Licensed for the treatment of children who are terminally ill.

Therapeutics

- Morphine is normally considered strong opiate of first choice by mouth and for intravenous infusion or continuous subcutaneous infusion. Only benefit of diamorphine via these routes is greater solubility when high doses are required.
- Has been used via intravesical route for bladder spasms and topically in Intra-Site gel for painful skin ulcers (unlicensed indications).

[a] Doses adapted from BNFC ensuring age bands and dosing intervals are consistent, including extrapolating from morphine, taking into account longer half-life in neonates and infants, bio-availability via different routes, and ensuring consistent total daily dose across each age band

- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Pharmacokinetics

- No data directly comparing intranasal with buccal route in children. Bioavailability may be lower for buccal administration particularly if larger volumes are used for administration and some of the drug is swallowed.
- Bioavailability may be affected by developmental changes in nasal anatomy in the neonatal period and infancy

Hepatic impairment, renal impairment

- Increase dosing interval, reduce dose and administer as required rather than regularly in renal impairment. Avoid in severe renal impairment.
- Caution in hepatic impairment: consider reducing dose.

Administration

- Injection powder can be diluted in water for injection for intranasal or buccal administration (unlicensed route of administration).
- Can be given by subcutaneous infusion up to a concentration of 250mg/ml. Dilute with water for injections for CSCI: concentration-related incompatibility with 0.9% sodium chloride at concentrations above 40mg/ml.

Available as

- Injection (5mg, 10mg, 30mg, 100mg, 500mg ampoules). Supplies may be limited

CD

- CD Schedule 2.

Evidence: (1–3,115–121)

Diazepam

Use:

- Anxiety, including anxiety associated with dyspnoea, panic attacks
- Agitation
- Relief of muscle spasm or dystonia
- Status epilepticus

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Short term anxiety relief, panic attacks and agitation

By mouth:

- **Child 2-11 years**: 500micrograms-2mg 3 times daily
- **12 years and over**: Initial dose of 2mg 3 times daily increasing as necessary and as tolerated to a maximum of 10mg 3 times daily.

Relief of muscle spasm, dystonia (as rescue or short-term therapy)

By mouth:

- **Child 1-11 months**: Initial dose of 250micrograms/kg twice daily
- **1-4 years**: Initial dose of 2.5mg twice daily
- **5-11 years**: Initial dose of 5mg twice daily
- **12 years and over:** Initial dose of 10mg twice daily; maximum total daily dose 40mg.

Status epilepticus

By intravenous injection over 3–5minutes

- **Neonate**: 300-400micrograms/kg as a single dose repeated once after 10 minutes if necessary
- **Child 1 month-11 years**: 300-400micrograms/kg (max 10mg) repeated once after 10 minutes if necessary
- **12 years and over**: 10mg repeated once after 10 minutes if necessary.

By rectum (rectal solution):

- **Neonate**: 1.25–2.5mg repeated once after 10 minutes if necessary
- **Child 1 month-1 year**: 5mg repeated once after 10 minutes if necessary
- **2-11 years**: 5–10mg repeated once after 10 minutes if necessary
- **12 years and over**: 10-20mg repeated once after 10 minutes if necessary.

Notes

Licensing

- Rectal tubes not licensed for children under 1 year old.

Contraindications, cautions

- Avoid in acute or severe respiratory insufficiency unless in the imminently dying.
- Caution in muscle weakness, respiratory depression, or sleep apnoea.

Side effects

- Dose-dependent drowsiness and impaired psychomotor and cognitive skills.

Pharmacokinetics

- Almost 100% bioavailable when given orally or by rectal solution.
- Onset of action: approximately 15 minutes given orally and within 1-5 minutes given intravenously. Given as rectal solution, diazepam is rapidly absorbed from the rectal mucosa with maximum serum concentration reached within 17 minutes.
- Long plasma half-life of 24-48 hours. The active metabolite, nordiazepam, has a plasma half-life of 48-120 hours.

Hepatic impairment, renal impairment

- Caution in hepatic impairment

Interactions

- Metabolised by cytochrome P450 enzymes CYP2C19 and CYP3A4. Levels increased by drugs that inhibit these enzymes including erythromycin, fluconazole, fluoxetine, and omeprazole. Levels decreased by drugs that induce these enzymes including carbamazepine and phenobarbital.
- Risk of enhanced CNS depressant effect if co-administered with other CNS depressants including neuroleptics, antipsychotics, tranquillisers, antidepressants, hypnotics, analgesics, anaesthetics, barbiturates or sedative antihistamines.

Administration

- The oral solution may be administered via a gastrostomy tube. Dilute with water before administration to reduce viscosity. For administration via a jejunostomy tube, consider using tablets dispersed in water to reduce osmolarity.

Patient information

- See Medicines for Children leaflet "Diazepam for muscle spasm." https://www.medicinesforchildren.org.uk/medicines/diazepam-for-muscle-spasm/ and "Diazepam (rectal) for stopping seizures" https://www.medicinesforchildren.org.uk/medicines/diazepam-rectal-for-stopping-seizures/

Available as

- Tablets (2mg, 5mg, 10mg), oral solution/suspension (2mg/5ml, 5mg/5ml), rectal tubes (5mg, 10mg), and injection (5mg/ml solution and 5mg/ml emulsion)

CD

- CD Schedule 4 part 1

Evidence: (1,2,8,58,117,122)

Diclofenac Sodium

Use:

- Mild to moderate pain and inflammation
- Musculoskeletal pain

Dose and route:

By mouth or rectum:

- **Child 6 months and over** : Initial dose of 300microgram/kg 3 times daily increasing if necessary to a maximum of 1mg/kg 3 times daily (maximum 50mg single dose).

By intermittent intramuscular injection or intravenous infusion (using Voltarol® injection):

- **Child 2 years and over**: 300-500microgram/kg 1-2 times daily

  Increase, if required, to maximum 1mg/kg 1–2 times daily or 150mg/day, for a maximum of 2 days (see notes below)

Notes:

- Peripheral and central preferential COX 2 inhibitor

Licensing

- Not licensed for use in children under 1 year; suppositories not licensed for use in children under 6 years (except for use in children over 1 year for juvenile idiopathic arthritis); solid dose forms containing more than 25mg not licensed for use in children; injection licensed for short term use (up to 2 days) in adults only

Therapeutics

- Maximum intravenous and intramuscular doses quoted above refer primarily to short term use in post-operative pain. Use lower doses if longer term parenteral use is required.
- Higher doses may have a ceiling effect risking increased adverse effects, particularly with longer term use, without additional analgesic effect.

Contraindications, cautions

- May mask fever and other signs of inflammation
- Caution in cardiac, hepatic or renal impairment and those with asthma
- Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure

Side effects

- All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factors or duration of NSAID use. The greatest risk may be in those receiving high doses long term. Risks have not been quantified in children.

- All NSAIDs are associated with serious gastro-intestinal toxicity. Diclofenac is associated with an intermediate risk of gastro-intestinal toxicity. Consider prescription of a proton pump inhibitor with prolonged use.

Pharmacokinetics

- Oral bioavailability approximately 30-50%, rectal bioavailability approximately 50%

Interactions

- Metabolised by cytochrome P450 enzyme CYP2C9. Levels increased by drugs that inhibit this enzyme including fluconazole. Levels reduced by drugs that induce this enzyme including carbamazepine

Administration

- Smallest dose that can be given practically by rectal route is 3.125mg by cutting a 12.5mg suppository into quarters.
- The Palliative Care Formulary describes unlicensed CSCI use at 50% oral dose, with 0.9% sodium chloride as diluent.
- For IV infusion, dilute with 100-500ml of sodium chloride 0.9% or glucose 5%. Buffer the diluent with sodium bicarbonate (0.5ml of 8.4% or 1ml of 4.2%). Administer over 30 minutes-2 hours.
- Use oral suspension for administration via a feeding tube. There should be no reduction in bioavailability from jejunal administration.

Patient information

- See Medicines for Children leaflet “Diclofenac for pain and inflammation” https://www.medicinesforchildren.org.uk/medicines/diclofenac-for-pain-and-inflammation/

Available as

- Gastro-resistant tablets (25mg, 50mg), modified-release tablets (25mg, 50mg, and 75mg), modified release capsules (75mg and 100mg), injection (25mg/ml Voltarol® , licensed in adults for IV ***infusion*** and IM bolus only, and 75mg/ml Akis®, licensed in adults for IV, IM or SC ***bolus*** only), and suppositories (12.5mg, 25mg, 50mg and 100mg). Oral suspension 50mg in 5ml available as an unlicensed ’special’

Evidence: (1,3,8,123–126)

Dihydrocodeine

Dihydrocodeine is no longer indicated for palliative care in children. It has been replaced by other opioids, particularly oral morphine and buccal diamorphine or fentanyl.

Evidence: (1–3,127)

Docusate

Use:

- Constipation

Dose and route

By mouth:

- **Child 6 months-1 year**: Initial dose of 12.5mg 3 times daily; adjust dose according to response
- **Child 2-11 years**: Initial dose of 12.5mg 3 times daily. Increase to 25mg 3 times daily as needed. Adjust dose according to response.
- **12 years and over**: Initial dose 100mg 3 times daily. Adjust as needed according to response up to 500mg/day in divided doses

By rectum:

- **12 years and over**: 1 enema (120mg) as single dose

Notes:

Emulsifying, wetting and mild stimulant laxative

Licensing

- Adult oral solution and capsules not licensed in children < 12 years.

Therapeutics

- Generally a more powerful stimulant laxative than docusate is required for opioid induced constipation
- Oral preparations act within 1–2 days.
- Rectal preparations act within 20mins and may cause a mild localised 'burning' sensation.
- Recommended doses may be exceeded on specialist advice.

Administration

- For administration by mouth, solution may be mixed with milk or squash to disguise the unpleasant taste. Oral solution may be administered via an enteral feeding tube. Administration directly into the jejunum will not affect the pharmacological response.

Available as

- Capsules (100mg), oral solution (12.5mg/5ml paediatric, 50mg/5ml adult, 100mg/5ml adult), and enema (120mg in 10g single dose pack).

Evidence: (1–3)

Domperidone

Use:

- Nausea and vomiting where poor GI motility is the cause
- Gastro-oesophageal reflux resistant to other therapy

Important safety information

MHRA/CHM advice (updated December 2019): Domperidone for nausea and vomiting: lack of efficacy in children; reminder of contraindications in adults and adolescents

Domperidone is no longer indicated for the relief of nausea and vomiting in children aged under 12 years or those weighing less than 35 kg. A European review concluded that domperidone is not as effective in this population as previously thought and alternative treatments should be considered. Healthcare professionals are advised to adhere to the licensed dose and to use the lowest effective dose for the shortest possible duration (max. treatment duration should not usually exceed 1 week).

The use of domperidone in palliative care is excluded from these recommendations HOWEVER caution should be exercised nevertheless.

- Use the minimum effective dose.
- Avoid in known cardiac problems or other risk factors.
- Consider monitoring QTc before initiating treatment and with dose increases

Dose and route

By mouth:

- **Neonate**: 250micrograms/kg 3 times daily. Increase if necessary to 400micrograms/kg 3 times daily
- **Child over 1 month- 11 years**: Initial dose of 250micrograms/kg, maximum 10mg/dose, 3 times daily. Dose may be increased if necessary to 400micrograms/kg 3-4 times daily, maximum 80mg in 24 hours
- **12 years and over**: Initial dose of 10mg 3–4 times daily before food. Dose may be increased, if necessary, to 20mg 3-4 times daily, maximum 80mg in 24 hours.

Notes

Licensing

- Not licensed for use in gastro-intestinal stasis, not licensed for use in children for gastro-oesophageal reflux disease.

Therapeutics

- Reduced ability to cross blood brain barrier: less likely to cause extrapyramidal side effects compared with metoclopramide.
- Promotes gastrointestinal motility: diarrhoea can be an unwanted (or useful) side effect.
- Doses quoted reflect previously authorised maximum doses. Authorised doses have been since reduced due to concern regarding possible cardiac adverse effects. However benefits of higher doses may outweigh the risks in refractory symptoms in paediatric palliative care where safer alternative prokinetics are not available, and risk of cardiac adverse effects is relatively low.
- Prokinetic effect may be reduced by anticholinergic drugs including antiemetics e.g. cyclizine

Contraindications, cautions

- Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval
- Contraindicated in cardiac disease and in conditions where cardiac conduction is, or could be, impaired

Side effects

- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended.

Hepatic impairment, renal impairment

- Avoid in hepatic impairment.

Interactions

- Avoid in patients receiving other medications known to prolong QT-interval (e.g. erythromycin, ketoconazole).
- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by drugs that inhibit this enzyme including erythromycin and fluconazole.

Patient information:

- See Medicines for Children leaflet: “Domperidone for gastro-oesophageal reflux” https://www.medicinesforchildren.org.uk/medicines/domperidone-for-gastro-oesophageal-reflux/

Administration

For administration via an enteral feeding tube: use the suspension formulation, although the total daily dose of sorbitol should be considered. If administering into the jejunum, dilute the suspension with at least an equal volume of water immediately prior to administration.

Available as

- Tablets (10mg), oral suspension (5mg/5 ml).

Evidence: (1,3,8,11,128,129)

Erythromycin

Use:

- Antibiotic typically used in respiratory tract infections, and skin infections
- Gastrointestinal stasis (motilin receptor agonist) is the main indication in palliative care

Dose and route:

Antibiotic

By mouth

- **Neonate**: 12.5mg/kg every 6 hours.
- **Child 1-23 months**: 125mg 4 times daily, increased to 250mg 4 times daily in severe infections. Total daily dose may be given in two divided doses
- **2-7 years**: 250mg 4 times daily, increased to 500mg 4 times daily in severe infections. Total daily dose may be given in two divided doses
- **8 years and over:** 250–500mg 4 times daily, increased to 500mg–1g 4 times daily in severe infections. Total daily dose may be given in two divided doses

By intravenous infusion

- **Neonate**: 10–12.5mg/kg every 6 hours
- **Child 1 month-11 years**: 12.5mg/kg, maximum 1g, every 6 hours
- **12 years and over**: 6.25mg/kg every 6 hours, for mild infections when oral treatment not possible, increased to 12.5mg/kg, maximum 1g, every 6 hours in severe infections

Prokinetic

By mouth or intravenous infusion

- **Neonate, child**: 3 mg/kg 4 times a day

Benefit is often seen at lower doses. Increase if necessary and as tolerated to a maximum of 1g 4 times daily

Notes:

Licensing

- Not licensed for use in children with gastrointestinal stasis

Contraindications, cautions

- Contraindicated in patients with known clostridium difficile colonisation
- Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval
- Prokinetic effect may be reduced by anticholinergic drugs including antiemetics e.g. cyclizine

Side effects

- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in hepatic impairment or co-administration of potentially hepatotoxic drugs
- Associated with increased risk of hypertrophic pyloric stenosis in neonates and infants
- Risk of tachyphylaxis: start at lower doses where possible
- Increased risk of antibiotic associated colitis

Interactions

- Inhibitor of cytochrome P450 enzyme CYP3A4. Increases levels of drugs that are metabolised by this enzyme including alfentanil, buprenorphine, carbamazepine (also reducing erythromycin levels), dexamethasone, diazepam, domperidone, fentanyl and midazolam. This list is not exhaustive-seek advice.
- Also metabolised by CYP3A4. Levels increased by drugs that inhibit this enzyme including fluconazole. Levels reduced by drugs that induce this enzyme including carbamazepine (also increasing carbamazepine levels).

Administration

- Dilute the suspension with an equal volume of water before administration via enteral feeding tubes. Absorbed in small intestine

Patient information

- See Medicines for Children leaflet “Erythromycin for treating bacterial infections https://www.medicinesforchildren.org.uk/medicines/erythromycin-for-bacterial-infections/

Available as

- Tablets (250mg, 500mg) and gastro-resistant tablets (250mg, 500mg) and oral suspension (125mg/5ml, 250mg/5ml, 500mg/5ml). Also available as 1g powder for solution for infusion.

Evidence: (1–3,130,131)

Etoricoxib

Use:

- Anti-inflammatory analgesic
- Musculoskeletal pain

Dose and route:

By mouth:

- **Child 12-15 years**: Initial dose of 30mg once daily. Increased as necessary and as tolerated to a maximum of 60mg once daily
- **16 years and over**: Usual dose of 30-60mg once daily. Doses of 90mg daily may be used on a short term basis.

Notes:

- Oral selective cyclo-oxygenase (COX-2) inhibitor.

Licensing

- Not licensed for use in children less than 16 years of age. No pharmacokinetic data in children less than 12 years of age

Therapeutics

- No difference in tolerability or efficacy has been shown between the selective cox-2 inhibitors (etoricoxib, celecoxib) and the non-selective NSAID, naproxen.
- Doses up to 120mg have been used on a short term basis in acute gouty arthritis in adults.

Contraindications, cautions

- All NSAIDs should be used with caution in children with a history of hypersensitivity to any NSAID. Etoricoxib may be better tolerated than other NSAIDs in patients with known hypersensitivity.
- May mask fever and other signs of inflammation
- Caution in cardiac, hepatic or renal impairment and those with asthma
- Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure

Side effects

- All NSAIDs are associated with serious gastro-intestinal toxicity. Etoricoxib is associated with low risk of gastro-intestinal toxicity. Consider prescription of a proton pump inhibitor with prolonged use.
- All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factors or duration of NSAID use. The greatest risk may be in those receiving high doses long term. Risks have not been quantified in children.
- Common adverse events (1-10% patients): alveolar osteitis; oedema/fluid retention; dizziness, headache; palpitations, arrhythmia; hypertension; bronchospasm; abdominal pain; constipation, flatulence, gastritis, heartburn/acid reflux, diarrhoea, dyspepsia/epigastric discomfort, nausea, vomiting, oesophagitis, oral ulcer; increased hepatic transaminases (ALT, AST); ecchymosis; asthenia/fatigue, flu-like disease.

Hepatic and renal impairment

- Contraindicated in severe hepatic and severe renal impairment

Interactions

- Potential drug interactions include warfarin (increase in INR); diuretics, ACE inhibitors and angiotensin II antagonists (increased risk of compromised renal function). Etoricoxib does NOT appear to inhibit or induce CYP enzymes. However, the main pathway of etoricoxib metabolism is dependent on CYP enzymes (primarily CYP3A4) so co-administration with drugs that are inducers or inhibitors of this pathway may affect the metabolism of etoricoxib.

Administration

- Etoricoxib tablets may be dispersed in 10ml water and will disintegrate to give fine granules that settle quickly but disperse easily and flush down an 8Fr NG or gastrostomy tube without blockage. Particles of the film coat may remain; flush well. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Film coated tablets 30mg, 60mg, 90mg, 120mg.

Evidence: (1,2,1

Famotidine (NEW)

Use:

- Histamine H2 antagonist to inhibit / reduce gastric acid secretion
- Episodic dyspepsia
- Gastro-oesophageal reflux disease
- Prevention and treatment of peptic ulceration

Dose and route:

By mouth

Gastro-oesophageal reflux disease

- **Neonate-3 months**: 500micrograms/kg/dose once daily, increased to 1mg/kg/dose once daily if necessary
- **Child 3 months and older**: initial dose 500micrograms/kg/dose twice daily, increasing to 1mg/kg/dose twice daily if required, maximum single dose 40mg

Peptic Ulceration

- **Child 1 year and older**: 500micrograms/kg once daily at night or in 2 divided doses, maximum 40mg/day

Notes:

- Histamine H2 antagonist, reduces gastric acid secretion.

Licensing

- Not licensed for use in children in the UK. Licensed for all ages for gastro-oesophageal reflux disease, and from 1 year of age for peptic ulcer disease in the USA. Limited information of use in neonates.

Therapeutics

- No prokinetic effect, unlike ranitidine

Caution

- Increased incidence of NEC in neonates, especially very low birthweight.
- Use of gastric acid inhibitors, including proton pump inhibitors and H2 blockers, has been associated with an increased risk for development of acute gastroenteritis and community-acquired pneumonia.
- Consider monitoring blood counts and liver function in long term use.
- Continue treatment for some time after symptom relief in peptic ulcer disease.

Side effects

- Constipation; diarrhoea; dizziness; fatigue; headache; myalgia; skin reactions; confusion; agitation; decreased appetite; dry mouth; taste altered; vomiting.

Renal Impairment

- Reduce dose by 50% in severe renal impairment.

Pharmacokinetics

- Duration of effect: 10-12 hours, oral bioavailability: 40-50%.

Drug Interactions

- No clinically important pharmacokinetic drug interactions.
- Increase in gastric pH may decrease the bioavailability of certain drugs (e.g. ketoconazole, itraconazole).
- Concomitant use of antacids or sucralfate may reduce absorption of famotidine: administer antacids at least an hour and sucralfate at least 2 hours after famotidine.

Administration

- Oral: Tablets may be taken with or without food. Tablets can be crushed and mixed with water to aid oral administration (off-label). Without crushing famotidine tablets will disperse in two to five minutes.
- Enteral Feeding Tube: There is no information on administration of famotidine tablets or suspension via an enteral feeding tube. Use of suspension likely to be preferable. Consider dilution if necessary to reduce viscosity and aid administration.
- Injection (available in the USA) can be given intravenously as a slow bolus or short infusion. Has also been given as a subcutaneous bolus or continuous subcutaneous infusion.
- Single case series reporting rectal administration at a dose of 1mg/kg.

Available as

- UK: 20mg and 40mg film-coated tablets, a suspension may be available from UK ‘specials’ manufacturers; extemporaneous formulation for oral suspension available.
- US (available for importation): 10mg, 20mg and 40mg film-coated tablets and oro-dispersible wafers; 40mg in 5ml oral suspension; 10mg/ml injection concentrate.

Evidence (133–146)

Fentanyl

Use:

- Moderate to severe pain
- Transdermal fentanyl should NOT be used in opioid naive patients

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

***Stable* Pain in patients already receiving regular strong opioids**

By transdermal patch

Important safety information

MHRA/CHM advice: Transdermal fentanyl patches for non-cancer pain: do not use in opioid naive patients (September 2020)

Fentanyl is a potent opioid: a 12 micrograms per hour fentanyl patch equates to daily doses of oral morphine of approximately 30mg daily

Do NOT use fentanyl patches in opioid naive patients

Use other analgesics and other opioid medicines (opioids) for non-cancer pain before prescribing fentanyl patches

If prescribing fentanyl patches, remind patients or their carers of the importance of:

- Not exceeding the prescribed dose
- Following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application
- Not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower)
- Ensuring that old patches are removed before applying a new one
- Following instructions for safe storage and properly disposing of used patches or patches that are not needed. It is particularly important to keep patches out of sight and reach of children at all times
- Make patients and caregivers aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately (by dialling 999 and requesting an ambulance) if overdose is suspected
- Remind patients that long-term use of opioids in non-cancer pain (longer than 3 months) carries an increased risk of dependence and addiction, even at therapeutic doses (see Drug Safety Update on risk of dependence and addiction with opioids); before starting treatment with opioids, agree with the patient a treatment strategy and plan for end of treatment

Report suspected adverse drug reactions, including dependence, accidental exposure, or overdose associated with fentanyl patches, via the Yellow Card scheme

Convert using oral morphine equivalent (OME) from previous opioid analgesia see Appendix 1. NOT to be used in opioid naive patients. Not suitable for dose titration in patients with unstable pain.

72 hour Fentanyl patches are *approximately* equivalent to the following 24 hour doses of oral morphine

Oral morphine 30mg/24hours	≡	Fentanyl 12micrograms/hour
Oral morphine 60mg/24hours	≡	Fentanyl 25micrograms/hour
Oral morphine 120mg/24hours	≡	Fentanyl 50micrograms/hour
Oral morphine 180mg/24hours	≡	Fentanyl 75micrograms/hour
Oral morphine 240mg/24hours	≡	Fentanyl 100micrograms/hour

Consider reducing the dose of fentanyl by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

Systemic analgesic concentrations are generally reached within 12–24 hours after applying the first patch. If converting from:

- 4-hourly oral morphine: administer regular morphine doses for the first 12 hours after applying the patch.
- 12-hourly slow release morphine: apply the patch and administer the final slow release dose at the same time.
- 24-hourly slow release morphine: apply the patch 12 hours after the final slow release dose.
- Continuous morphine infusion: continue the infusion for 8- 12 hours after applying the patch.

Pain in patients already receiving regular strong opioids

By continuous intravenous or subcutaneous infusion

Convert using oral morphine equivalent (OME) from previous opioid analgesia, see Appendix 1

Conversion		**Ratio**	**Calculation**	**Example**
From	**To**			
Morphine oral	Fentanyl CSCI or CIVI	100:1	Divide 24hour morphine dose by 100 to give fentanyl dose in *mg/24hours* *Then* multiply fentanyl dose in mg/24hours by 1000 to convert to *micrograms/24hours*	Morphine oral 60mg/24hours ÷ 100 = 0.6mg/24hours CIVI fentanyl Fentanyl 0.6mg/24hours x 1000 = 600micrograms/24hours

Consider reducing the dose of fentanyl by 25-50% when the patient is already on a high dose of the previous opioid, when rotating due to intolerable side effects or when there has been a recent rapid escalation of the previous opioid

Breakthrough Pain in patients already receiving regular strong opioids

By buccal or intranasal administration of injection solution

- 1/10 to 1/6 of the total CSCI or CIVI dose as required, up to hourly

  There is no direct correlation between the effective PRN dose and the regular background dose: start with low dose and titrate according to response

  Maximum dose limited to 50micrograms/1ml via the intranasal route and 100micrograms/2ml via buccal route due to available concentration of injection solution (50micrograms/ml).

  Breakthrough and background (modified release, intravenous or subcutaneous infusion) doses should be reviewed if more than two breakthrough doses are required in a 24-hour period

By oromucosal application (lozenge with oromucosal applicator), buccal lozenge, buccal tablet, commercially manufactured intranasal spray

- Dose must be titrated against patient's pain. Consult product literature.

  Unlikely to be appropriate for patients receiving less than 60mg oral morphine or oral morphine equivalent per 24 hours

Pain in opioid naive patients

By continuous intravenous or subcutaneous infusion

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Neonate-11months**: 0.15-0.5micrograms/kg/hour (= 3.6-12micrograms/kg/24hours)
- **Child 1 year and over**: 0.25-1micrograms/kg/hour, maximum 50micrograms/hour (6-24micrograms/kg/24hours, maximum 1.2mg/24hours)

By buccal or intranasal administration of injection solution

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Neonate- 11 months**: 1microgram/kg as a single dose
- **Child 2 years and over**: 1-2micrograms/kg as a single dose, with initial maximum single dose of 50micrograms

Maximum dose limited to 50micrograms/1ml via the intranasal route and 100micrograms/2ml via buccal route due to available concentration of injection solution (50micrograms/ml).

By intermittent intravenous or subcutaneous injection

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Neonate- 11 months**: 0.15-0.25micrograms/kg/dose slowly over 3-5 minutes; repeated up to every 30-60 minutes
- **Child over 1 year**: 0.25–0.5micrograms/kg/dose, slowly over 3-5 minutes, repeated up to every 30-60 minutes
- **Adult** initial stat dose of 50–200micrograms, and subsequently 50micrograms, repeated up to every 30-60 minutes

Notes:

- Synthetic opioid, very different in structure from morphine, and therefore ideal for opioid switching.

Licensing

- Injection not licensed for use in children less than 2 years of age. Lozenges and nasal sprays are not licensed for use in children.

Therapeutics

- Evidence that it is less constipating than morphine has not been confirmed in more recent studies
- Buccal, intranasal and oral-transmucosal routes: onset of action 10-15 minutes and duration of action 1-2 hours depending on route and formulation. Therefore suitable for management of breakthrough pain but not ideal for titration of analgesic requirements in unstable pain.
- Some patients experience withdrawal symptoms when changed from oral morphine to transdermal fentanyl, despite adequate pain relief, due to the different mu receptor impact of the two drugs. If this occurs, small rescue doses of morphine can be used and weaned off slowly
- Intranasal administration has been reported for the treatment of dyspnoea in children
- Use adjusted body weight (Appendix 7) to calculate doses in obese children
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Contraindications, cautions

- The MHRA, CQC, and NHS England recommend NOT using transdermal fentanyl in opioid-naive patients due to numerous reports of respiratory depression.
- Greater risk of addiction, tolerance and drug seeking behaviour particularly when administered via buccal or intranasal routes, compared with longer acting opioids.

Interactions

- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by drugs that inhibit this enzyme including fluconazole. Levels reduced by drugs that induce this enzyme including carbamazepine and phenobarbital.
- Fentanyl has been reported to reduce the metabolism of IV midazolam**,** reducing the clearance by 30% and extending the half-life by 50%

Hepatic and renal impairment

- Can be safely used in poor, deteriorating or absent renal function.
- Caution in hepatic impairment: Risk of accumulation. Consider dose reduction. May be safer than other opioids in hepatic failure and hepato-renal syndrome.

Patient information

- See Medicines for Children Leaflets "Fentanyl lozenges for pain" https://www.medicinesforchildren.org.uk/medicines/fentanyl-lozenges-for-pain/ and "Fentanyl patches for pain" https://www.medicinesforchildren.org.uk/medicines/fentanyl-patches-for-pain/

Administration Intranasal

- Intranasal onset of action and duration of action are shorter than oromucosal
- Not always practical and/or well tolerated in children despite favourable pharmacokinetics.
- Intranasal route has also been used for management of respiratory distress in paediatric palliative care.
- For doses less than 50micrograms, the injection solution can be administered by the intranasal route either drop-wise (may be unpleasant) or using a mucosal atomiser device.

Lozenges, buccal / sublingual tablets

- Fentanyl products for the treatment of breakthrough pain are not interchangeable. If patients are switched from another fentanyl containing product a new dose titration is required.
- Oral transmucosal fentanyl accumulates with repeated dosing
- Usefulness of lozenges and buccal / sublingual tablets in children is limited by the dose availability, no reliable conversion factor and requirement for individual dose titration.
- Oral transmucosal products are not suitable for opioid naive patients. Use only in patients receiving at least 60mg/24hours oral morphine equivalent for at least a week.
- The lozenge must be rotated in buccal pouch, not sucked. Older children will often choose to remove the lozenge before it is completely dissolved, giving them some much-valued control over their analgesia.

Fentanyl transdermal patches

- MHRA advises that *fentanyl* matrix patches must not be cut due to the risk of life threatening and potentially fatal opioid toxicity.
- Patches are not appropriate for initiation or titration phases of opioid management in palliative care due to large dose increments and time to achieve steady state.
- Initial evaluation of the analgesic effect cannot be made before the patch is worn for 24 hours.
- Patches should be changed every 72 hours and the site of application rotated. Some children who are rapid metabolisers need patch changes every 36-48 hours.
- After an increase in dose, it may take up to 6 days for the patient to reach equilibrium on the new dose level. Therefore, after a dose increase, patients should wear the higher dose patch through two 72-hour applications before any further increase in dose level is made.
- After the patch is removed it may take 20 hours or more for serum fentanyl concentrations to decrease by 50% and significant blood concentrations persist for at least 24 hours. Replacement opioid therapy should therefore be initiated at a low dose and increased gradually
- Remove patches before MRI scanning: risk of burns.
- Absorption may be increased in pyrexia, vigorous exercise or topical application of heat including warm baths or showers
- For rapidly escalating symptoms in the last few hours and days of life, continue transdermal fentanyl and an additional 1/10 to 1/6 total daily oral morphine equivalent as required. If more than 2 PRN-doses are required in 24 hours, continue transdermal fentanyl and add morphine CSCI at a dose equivalent to the total daily morphine dose administered over the previous 24

hours. Adjust the PRN-dose taking into account the total opioid dose (i.e. transdermal fentanyl + continuous subcutaneous morphine).

Available as

- Intranasal spray Instanyl® (50micrograms/spray, 100micrograms/spray and 200micrograms/ spray). PecFent® (100micrograms/ spray and 400micrograms/spray).
- Lozenge with oromucosal applicator Actiq®, Cynril® (200micrograms, 400micrograms, 600micrograms, 800micrograms, 1.2mg and 1.6mg).
- Buccal/sublingual tablets Abstral®(100 micrograms, 200 micrograms, 300 micrograms, 400 micrograms, 600 micrograms and 800micrograms) and buccal tablets Effentora(R) (100 micrograms, 200 micrograms, 400 micrograms, 600 micrograms and 800micrograms).
- Patches: various manufacturers (12micrograms/hour, 25micrograms/hour, 37.5micrograms/hour, 50micrograms/hour, 75micrograms/hour, 100micrograms/hour); Ionys® transdermal system (40micrograms/dose)
- Injection: 50micrograms per ml

CD

- Schedule 2 CD

Evidence: (1–3,62,63,147–154)

Fluconazole

Use:

- Mucosal candidiasis infection (if nystatin not tolerated / effective), invasive candidal infections or prevention of fungal infections in immunocompromised patients

Dose and route:

Mucosal candidal infection

By mouth or intravenous infusion:

- **Neonate up to 13 days**: 3-6mg/kg on first day then 3mg/kg every 72 hours
- **Neonate 14-28 days**: 3-6mg/kg on first day then 3mg/kg every 48 hours
- **Child 1 month-11 years**: 3-6mg/kg on first day then 3mg/kg, maximum 100mg daily
- **12 years and over**: 50mg/day. Increase to 100mg/day in severe infections.

Continue treatment for 7-14 days in oropharyngeal candidiasis and 14-30 days in other mucosal infections.

Invasive candidal infections and cryptococcal infections

By mouth or intravenous infusion:

- **Neonate up to 13 days**: 6-12mg/kg every 72 hours
- **Neonate 14-28 days**: 6-12mg/kg every 48 hours
- **Child 1 month and over**: 6-12mg/kg every 24 hours maximum 800mg daily

Continue treatment for a minimum of 8 weeks with duration of treatment determined by response.

Prevention of fungal infections in immunocompromised patients

By mouth or intravenous infusion

- **Neonate up to 13 days**: 3-12mg/kg every 72 hours
- **Neonate 14-28 days**: 3-12mg/kg every 48 hours
- **Child 1 month and over**: 3-12mg/kg every 24 hours, maximum 400mg daily

Commence treatment before anticipated onset of neutropenia and continue for 7 days after neutrophil count in desirable range.

Notes:

- Fungistatic anti-fungal.

Licensing

- Licensed for treatment of fungal infections in all ages

Therapeutics

- Resistance may develop with long-term treatment. Use for 7-14 days in oropharyngeal candidiasis. Use for 14-30 days in other mucosal infections.

Side effects

- Most frequent (>1/10) reported adverse reactions are headache, abdominal pain, diarrhoea, nausea, vomiting, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased and rash.

Interactions

- Potent inhibitor of cytochrome P450 enzyme CYP2C9 inhibitor and a moderate CYP3A4 inhibitor. Fluconazole is also an inhibitor of CYP2C19. Increases levels of drugs metabolised by these enzymes including alfentanil, buprenorphine, carbamazepine, dexamethasone, diazepam, diclofenac, fentanyl, midazolam and omeprazole. *This list is not exhaustive-seek advice.*

Administration

- Intravenous infusion should be administered over 10–30 minutes at a rate not exceeding 5–10ml/minute
- Oral suspension may be administered via NG tube gastrostomy or jejunostomy. Bioavailability is unaffected by jejunal administration. Flush tube well after suspension is administered.

Patient information

- See Medicines for Children leaflet “Fluconazole for yeast and fungal infections” https://www.medicinesforchildren.org.uk/medicines/fluconazole-for-yeast-and-fungal-infections/

Available as

- Capsules (50mg, 150mg, 200mg); oral suspension (50mg/5ml, 200mg/5ml) and IV infusion (2mg/ml in 25ml, 50ml, 100ml).

Evidence: (1,2,8,155)

Fluoxetine

Use:

- Major depression (seek specialist advice)

Dose and route:

By mouth:

- **Child 5 years and over**: Initial dose 10mg once daily. May be increased after 1-2 weeks if necessary to a maximum of 20mg once daily.

Notes:

- Selective serotonin reuptake inhibitor (SSRI).

Licensing

- Licensed for use in children from 8 years of age.

Therapeutics

- Onset of benefit 3-4 weeks in depression
- Consider long half-life when adjusting dosage.
- Do not discontinue abruptly.
- May be beneficial in neuropathic pain and intractable cough.
- Undesirable effects may decrease in intensity and frequency with continued treatment and do not generally lead to cessation of therapy.

Contraindications, cautions

- Caution in children: seek specialist advice. Caution in cardiac disease and poorly controlled epilepsy.

Side effects

- Increased risk of bleeding due to antiplatelet function.
- Increased risk of anxiety for first 2 weeks.
- Suicide related behaviours have been more frequently observed in clinical trials among children and adolescents treated with antidepressants compared with placebo. Mania and hypomania have been commonly reported in paediatric trials.
- Headache, nausea, insomnia, fatigue and diarrhoea.
- Movement disorders
- Increased risk of seizures

Interactions

- Inhibits cytochrome P450 enzymes CYP2C19 and CYP2D6. Increases levels of drugs metabolised by these enzymes including amitriptyline, carbamazepine, diazepam and erythromycin. *This list is not exhaustive –seek advice.*
- Must not be used in combination with a MAOI: risk of serotonin syndrome

Administration

- Oral liquid may be administered via NG tube or gastrostomy. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet "Fluoxetine for depression, obsessive compulsive disorder and bulimia nervosa" https://www.medicinesforchildren.org.uk/medicines/fluoxetine-for-obsessive-compulsive-disorder-ocd-depression-and-bulimia-nervosa/

Available as

- Capsules (10mg, 20mg, 30mg, 40mg, 60mg) dispersible tablets (20mg) and oral liquid (20mg/5ml).

Evidence: (1–3,156)

Gabapentin

Use:

- Adjuvant in neuropathic pain
- CNS irritability
- Visceral hyperalgesia
- Management of abnormal tone and movement disorders
- Uraemic Itch
- Intractable hiccup
- Epilepsy
- Restless legs syndrome in chronic kidney disease

Important safety information

MHRA/CHM advice: Gabapentin (Neurontin®): risk of severe respiratory depression (October 2017)

Gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, and concomitant use of central nervous system (CNS) depressants, might be at higher risk of experiencing severe respiratory depression, and dose adjustments may be necessary in these patients.

Dose and route:

Neuropathic pain, all indications other than epilepsy

By mouth:

Consider introducing gabapentin more slowly in debilitated patients, or when administered with other CNS depressants

- **Neonate-23 months**: 5mg/kg/dose. Administer once daily on day 1, administer twice daily on day 2 then three times daily from day 3 onwards.

  Increase further, if necessary, in increments of 5-10mg/kg in 3 divided doses, every 3–7 days. Maximum 10mg/kg/dose

- **Child 2-11 years**: 5-10mg/kg/dose, maximum single dose 300mg. Administer once daily on day 1, administer twice daily on day 2 then three times daily from day 3 onwards.

  Increase further, if necessary, in increments of 5–10mg/kg in 3 divided doses, every 3–7 days. Maximum 20mg/kg/dose. Maximum single dose 600mg

- **12 years and over**: Initially 300mg once daily on day 1, then 300mg twice daily on day 2, then 300mg three times daily from day 3 onwards.

  Increase further, if necessary in steps of 300mg every 3-7 days given in 3 divided doses daily. Maximum 3600mg total daily dose

Gabapentin to pregabalin switch for neuropathic pain

See Appendix 5

Epilepsy

Consult BNFc or local neurology protocols. Gabapentin is now rarely used as a primary treatment for epilepsy.

Notes:

Licensing

- Licensed as an adjunct for the treatment of focal seizures in patients over 6 years and as a monotherapy for the treatment of focal seizures in patients over 12 years. Maximum licensed dose 50mg/kg/day for under 12 years. Not licensed for neuropathic pain in children.

Therapeutics

- Animal evidence suggests anti-seizure and analgesic activity of gabapentin is mediated via binding to the alpha-2 subunit of voltage gated calcium channels in the CNS with subsequent inhibition of excitatory neurotransmitter release and/or inhibition of descending inhibitory pain pathways.
- Doses can be titrated more slowly with increases every 1–2 weeks in in debilitated patients or co-administration with other CNS depressants
- Higher doses (up to 20mg/kg TDS) have been used in the management of severe dystonia. These higher doses are reached by slow upwards titration guided by the child's response.
- No consensus on dose for neuropathic pain. Doses shown are based on doses for partial seizures and authors' experience.
- Adult evidence for use in pruritus in anaemia, anxiety, hot flushes, sweating, refractory hiccups, restless legs syndrome and refractory cough.
- Risk of dependence and diversion for substance abuse

Side effects

- Very common (>1 in 10) side effects: somnolence, dizziness, ataxia, viral infection, fatigue, fever.

Pharmacokinetics

- Oral bioavailability of approximately 60%. However gabapentin absorption is saturable, leading to a non-linear pharmacokinetic profile and decrease in bioavailability with increasing gabapentin dose. Bioavailability also varies with patient population. Careful titration of dose is required.
- Peak plasma concentrations occur 2-3 hours after oral dosing.
- Bioavailability is not affected by food. Co-administration with antacids containing aluminium and magnesium can reduce bioavailability by up to 24%. Manufacturers recommend giving gabapentin two hours after antacids.

Hepatic impairment, renal impairment

- Gabapentin is solely excreted unchanged by the kidneys. Reduce dose in renal impairment (consult manufacturer's literature).

Interactions

- Morphine may increase gabapentin concentrations. Consider reducing the dose of gabapentin or opioids as clinically appropriate.

Administration

- Capsules can be opened and suspended in water or fruit juice (to hide the bitter taste) as an alternative to oral solution.
- Absorbed in proximal small bowel. The oral solution or the capsule contents (dispersed in water) can be given via a NG tube or gastrostomy. Flush tube well after administration.
- No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet “Gabapentin for neuropathic pain”: https://www.medicinesforchildren.org.uk/gabapentin-for-neuropathic-pain and “Gabapentin for preventing seizures” https://www.medicinesforchildren.org.uk/gabapentin-for-preventing-seizures

Available as

- Capsules (100mg, 300mg, 400mg); tablets (600mg, 800mg), oral solution 250mg/5 ml (Neurontin, United States import). Oral solution 50mg/ml now available as licensed preparation in UK. May contain high amount of propylene glycol as an excipient

CD

- Schedule 3 CD but exempt from safe custody requirements.

Evidence: (1,2,8,157–162)

Gaviscon®

Use:

- Gastro-oesophageal reflux, dyspepsia and heartburn.

Dose and route:

By mouth:

Gaviscon Infant® (sodium alginate with magnesium alginate) sachets:

- **Neonate-2 years, body-weight less than 4.5kg**: 1 dose (half dual sachet) when required mixed with feeds or with water for breast fed babies, maximum 6 doses in 24 hours
- **Neonate-2 years, body-weight 4.5kg and over**: 2 doses (1 dual sachet) when required mixed with feeds or with water for breast fed babies or older infants, maximum 12 doses (6 dual sachets) in 24 hours

Gaviscon Liquid and Tablets (Sodium alginate, calcium carbonate, sodium bicarbonate)

- **Child 2-11 years**: 1 tablet or 5-10ml liquid after meals and at bedtime
- **12 years and over**: 1-2 tablets or 10-20ml liquid after meals and at bedtime

Gaviscon Advance (Sodium alginate, potassium bicarbonate)

- **Child 2-11 years**: 1 tablet or 2.5-5ml suspension after meals and at bedtime (under medical advice only)
- **12 years and over**: 1-2 tablets or 5-10ml suspension after meals and at bedtime

Notes:

Licensing

- Gaviscon Infant Sachets licensed for infants and young children up to 2 years of age, but use under 1 year only under medical supervision. Gaviscon liquid and tablets are licensed for use from 2 years of age but age 2-6 years only on medical advice. Gaviscon Advance suspension and tablets are licensed for use from 12 years of age; use under 12 years on medical advice only.

Contraindications, cautions

- Gaviscon Infant should not to be used with feed thickeners, nor in patients with excessive fluid losses (e.g. fever, diarrhoea, vomiting).
- Gaviscon Liquid contains 3.1mmol sodium per 5ml; Gaviscon tablets contain 2.65mmol sodium and also contain aspartame. Gaviscon Infant Sachets contain 0.92mmol sodium per dose (half dual sachet).

Administration

- Can be administered via nasogastric tube or gastrostomy. Calcium may bind to any phosphate in an enteral feed causing tube blockage. A prolonged break in feeding is not required, but the tube should be adequately flushed to ensure that the calcium supplement does not come into contact with the feed. Not appropriate for administration via jejunostomy.

Patient information

- See Medicines for Children leaflet "Gaviscon for gastro-oesophageal reflux disease": https://www.medicinesforchildren.org.uk/medicines/gaviscon-for-gastro-oesophageal-reflux-disease/

Available as

- Gaviscon liquid and tablets; Gaviscon Advance suspension and tablets; Infant Sachets (comes as dual sachets, each half of dual sachet is considered one dose).

Evidence: (1,2,11,130)

Glycerol (glycerin)

Use:

- Constipation

Dose and routes

By rectum:

- **Neonate over 34 weeks corrected gestational age**: Tip of a glycerol suppository (slice a small chip off a 1g suppository with a blade)
- **Child 1 month-11 months**: 1g infant suppository as required
- **Child 1-11 years**: 2g child suppository as required
- **Child 12-17 years**: 4g adult suppository as required

Notes:

- Hygroscopic and lubricant actions. May also be a rectal stimulant.

Licensing

- 1g suppositories licensed for use in infants up to 1 year of age, 2g suppositories licensed for use in children aged 1-11 years, 4g suppositories licensed for use from 12 years of age.

Side effects

- Associated with necrotising enterocolitis in babies less than 34 weeks gestation.

Pharmacokinetics

- Response usually in 20 minutes to 3 hours.

Administration

- Moisten with water before insertion.

Patient information

- See Medicines for Children leaflet “Glycerin (glycerol) suppositories for constipation” https://www.medicinesforchildren.org.uk/medicines/glycerin-glycerol-suppositories-for-constipation/

Available as

- Suppositories (1g, 2g, and 4g)

Evidence: (1,2,11)

Glycopyrronium bromide

Use:

- Control of upper airways secretions
- Noisy breathing at the end of life (may be more effective if started early)
- Hypersalivation and drooling
- Bowel colic pain
- Paraneoplastic sweating or pyrexia

Dose and route:

By mouth:

Using ***Sialanar®*** glycopyrronium *bromide* 400micrograms/ml oral solution

- **Child 1 month and over**: 16micrograms/kg 3 times daily, increased in steps of 16micrograms/kg 3 times daily, every 7 days, adjusted according to response

  Maximum 80micrograms/kg 3 times daily, maximum 2.4mg/dose

Using **generic** 1mg/5ml oral solution

- **Child 1 month and over**: 20micrograms/kg 3 times daily, increased in steps of 20micrograms/kg 3 times daily, every 5-7 days, adjusted according to response

  Maximum 100micrograms/kg 3 times daily, maximum 3mg/dose

By subcutaneous or intravenous injection:

- **Child 1 month-11 years**: Initial dose of 4micrograms/kg 3-4 times daily. The dose may be increased as necessary to 10micrograms/kg 3-4 times daily,

  Maximum 200micrograms/dose 4 times daily

- **12 years and over**: 200micrograms 3-4 times daily

By continuous subcutaneous or intravenous infusion:

- **Child 1 month-11 years**: Initial dose of 12micrograms/kg/24hours, increased as necessary to 40micrograms/kg/24hours, maximum 1.2mg/24hours
- **12 years and over**: 600micrograms/24hours, increased as necessary to 1.2mg/24hours.

Notes:

- Antimuscarinic

Licensing

- Licensed oral solutions (Sialanar®, generic) are licensed for use in children from 3 years of age with a chronic neurological disorder, for chronic pathological drooling. Not licensed for use in children for control of upper airways secretion and hypersalivation.

Therapeutics

- Excessive secretions can distress the child, but more often distress those around him/her.
- Treatment is more effective if started before secretions become too much of a problem.
- More frequent subcutaneous administration, up to hourly, is occasionally required in adults.
- Adult evidence for use in smooth muscle spasm (e.g. intestine, bladder), inoperable intestinal obstruction, hyperhidrosis, para-neoplastic pyrexia and sweating.
- Injection solution has also been given sublingually in adults using same doses as subcutaneous or intravenous bolus

Side effects

- Antimuscarinic side effects including constipation, urinary retention, tachycardia, blurred vision

Pharmacokinetics

- Does not cross the blood brain barrier and therefore has fewer side effects than hyoscine hydrobromide, which is also used for this purpose. Also fewer cardiac side effects.
- Slower onset response than with hyoscine hydrobromide or butylbromide.
- Oral absorption of glycopyrronium is very poor with wide inter-individual variation.

Renal impairment

- Risk of accumulation: reduce dose or avoid

Administration

- Administration by CSCI: good compatibility data available for mixing with other commonly used palliative agents.
- Co-administration with food results in a marked decrease in systemic medicinal product exposure. Dosing should be at least one hour before or at least two hours after meals, or at consistent times with respect to food intake. High fat food should be avoided. Where the child's specific needs determine that co-administration with food is required, dosing of the medicinal product should be consistently performed during food intake.
- Tablets may be dispersed in water immediately prior to administration via feeding tubes, or use the oral solution. Flush tube immediately with 10-20 ml water. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (1mg, 2mg), oral solution 200micrograms/ml as glycopyrronium bromide (various) and 400micrograms/ml as glycopyrronium *bromide* (Sialanar®), injection (200micrograms/ml 1ml and 3ml ampoules).
- Glycopyrronium bromide tablets and oral solutions are not interchangeable on a microgram-for-microgram basis due to differences in bioavailability. Sialanar® oral solution has approximately 25% higher bioavailability and therefore equivalent doses will be lower than for tablets and generic oral solutions. The prescriber should state the specific branded or generic oral preparation to be used; care should be taken if switching between oral preparations and dosing adjusted accordingly.

Evidence: (1–3,39,42,113,163)

Haloperidol

Use:

- Nausea and vomiting where cause is metabolic, or in difficult to manage cases such as end stage renal failure.
- Delirium
- Agitation in the last hours and days of life.
- Intractable hiccups.
- Psychosis (including steroid-induced), hallucinations.
- Persistent severe aggression in autism or pervasive developmental disorders (under specialist supervision).

Dose and route:

Nausea and vomiting, delirium, agitation at end of life:

By mouth

- **Child 1 month-11 years**: 20micrograms/kg/dose, maximum 1mg, once daily at night, increased as necessary to a maximum of 180micrograms/kg/dose, maximum 10mg. Can also be given in 2 or 3 divided doses
- **12 years and over**: 1mg once daily at night, increased as necessary to 10mg at night. Can also be given in 2 or 3 divided doses

By continuous intravenous or subcutaneous infusion

- **Child 1 month-11 years**: 20micrograms/kg/24hours (maximum 1mg/24hours), increased as necessary to a maximum of 90micrograms/kg/24hours
- **12 years and over**: Initial dose of 1mg/24hours. The dose may be increased as necessary to a maximum of 5mg/24hours.

Intractable hiccups

By mouth

- **Child 1 month-11 years**: 20micrograms/kg/dose (maximum 1mg) 3 times daily, increased as necessary to a maximum of 60micrograms/kg/dose (maximum 3mg) 3 times daily. Once hiccups are controlled reduce to stop or to lowest possible maintenance dose.
- **12 years and over**: 1mg 3 times daily, increased as necessary to maximum 3mg 3 times daily. Reduce to stop or to lowest possible maintenance dose once hiccups are controlled.

Notes:

- D2 receptor antagonist and typical antipsychotic.

Licensing

- Not licensed for use in children with nausea and vomiting, restlessness and confusion or intractable hiccups. Injection is licensed only for intramuscular administration in adults

Therapeutics

- Higher doses may be used under specialist advice. If nausea and vomiting are not controlled on maximal doses via continuous infusion, review cause(s) and consider changing to levomepromazine
- For dosage in psychosis discuss with child psychiatrist.
- Dosages for agitation and confusion are often higher.
- Adult dosages can exceed 15mg/24hours in severe agitation
- Oral solution (2mg/ml) has also been given sublingually using same doses as oral or rectal routes

Contraindications, cautions

- Contraindicated in congenital long QT syndrome; history of Torsade de Pointes; history of ventricular arrhythmia; QTc-interval prolongation
- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in patients with cardiac disease and those at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, electrolyte imbalance or taking other drugs known to prolong the QT-interval

Side effects

- Associated with prolonged QT-interval and Torsades de Pointes, particularly if given intravenously or at higher than recommended doses.
- Side effects vary between age groups, with behavioural problems being common in children.
- Extrapyramidal side effects, neuroleptic malignant syndrome

Pharmacokinetics

- Oral bioavailability approximately 50%. Consider reducing dose when converting from oral to intravenous or subcutaneous routes

Interactions

- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by drugs that inhibit this enzyme including erythromycin and fluconazole. Levels may be reduced by drugs that induce this enzyme.

Administration

- Oral solutions may be administered via feeding tubes without further dilution. Flush tube well following administration. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (500 micrograms, 1.5mg, 5mg, 10mg), capsules (500 micrograms), oral liquid (200 micrograms/ml, 1mg/ml, 2mg/ml), and injection (5mg/ml).

Evidence: (1–3,8,87,113,164)

Hydromorphone

Use:

- Alternative opioid analgesic for severe pain especially if intolerant to other strong opioids.

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in patients already receiving regular strong opioids

By mouth using immediate release preparations

Convert using oral morphine equivalent (OME) from previous opioid analgesia, see Appendix 1

Conversion		Ratio	Calculation	Example
From	To			
Morphine oral	Hydromorphone oral	5:1	Divide 24hour morphine dose by 5	Morphine oral 10mg ÷ 5 = hydromorphone oral 2mg

By mouth using modified release preparations

- Calculate the total daily dose (regular + PRN) of oral hydromorphone administered over the previous 24 hours once the patient is established on regular hydromorphone for 2-3 days

  12-hourly preparations: Divide the total daily dose of oral hydromorphone by two and administer every 12 hours

  Consider reducing the dose of hydromorphine by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

  Ensure continued access to immediate release hydromorphone as required for breakthrough pain, see below.

By continuous intravenous or subcutaneous infusion

- Calculate the total daily dose (regular + PRN) of opioid administered over the previous 24 hours

  Convert to the equivalent dose of CSCI hydromorphone using the table

Conversion		**Ratio**	**Calculation**	**Example**
From	**To**			
Morphine oral	Hydromorphone CSCI or CIVI	10:1	Divide 24hour morphine dose by 10	Morphine oral 30mg ÷ 10 = hydromorphone CSCI 3mg
Morphine CSCI or CIVI	Hydromorphone CSCI or CIVI	5:1	Divide 24hour morphine dose by 5	Morphine CSCI 25mg ÷ 5 = hydromorphone CSCI 5mg
Hydromorphone Oral	Hydromorphone CSCI or CIVI	2:1	Divide 24hour hydromorphone dose by 2	Hydromorphone 10mg oral ÷ 2 = CSCI 5mg hydromorphone

  Consider reducing the dose of hydromorphone by 25-50% when the patient is already on a high dose of the previous opioid, when rotating due to intolerable side effects or when there has been a recent rapid escalation of the previous opioid

  Ensure continued access to immediate release hydromorphone as required for breakthrough pain see below

Breakthrough Pain in patients already receiving regular strong opioids

By mouth using immediate release preparations, or by intermittent intravenous or subcutaneous bolus

- 1/10 to 1/6 of total daily hydromorphone dose every 1-4 hours as required.
- If the route for breakthrough analgesia is different to the route for background analgesia (e.g. CSCI with oral breakthrough) convert the breakthrough dose as above to the required route

Breakthrough and background (modified release, intravenous or subcutaneous infusion) doses should be reviewed if more than two breakthrough doses are required in a 24-hour period

Pain in opioid naïve patients

By mouth:

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Child 1 year and above**: 25micrograms/kg per dose maximum 2mg per dose every 4 hours increasing as required.
- **12 years and above:** 1.3mg every 4 hours increasing as required

By subcutaneous or slow intravenous injection:

- **Child 1 year and above**: 12micrograms/kg per dose every 4 hours, increasing as required

Notes:

- Analogue of morphine with similar pharmacokinetic and pharmacodynamics

Licensing

- Licensed for the relief of severe pain in cancer in adults and adolescents aged over 12 years.

Side effects

- Usual opioid side effects

Pharmacokinetics

- Oral bioavailability 37-62% (wide inter-individual variation).
- Onset of action 15 min for SC, 30 min for oral. Peak plasma concentration 1 hour orally.
- Main metabolite is hydromorphone-3-glucuronide (H3G). H3G has no analgesic activity but, like morphine-3-glucuronide (see morphine), it is a CNS neuro-excitant.
- All metabolites are renally excreted and can accumulate in renal impairment.
- More soluble than morphine, and available as a high-concentration injection (50mg/ml). Alternative to diamorphine when high doses need to be administered by CSCI
- Plasma half- life 2.5 hours early phase, prolonged late phase: duration of action 4-5 hours.
- Equianalgesic ratios vary more than for other opioids: possibly due to inter-individual variation in metabolism or bioavailability.
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Hepatic impairment, renal impairment

- Caution in hepatic impairment, use at reduced doses. Avoid in severe hepatic impairment
- Caution in renal impairment, use at reduced starting doses.

Administration

- For CSCI dilute with water for injection, sodium chloride 0.9% or glucose 5%.
- Modified release capsules are given 12-hourly.

- Capsules (both types) can be opened and contents sprinkled on soft food. Do not administer via feeding tubes due to risk of blockage

Available as

- Capsules (1.3mg, 2.6mg) and modified release capsules (2mg, 4mg, 8mg, 16mg, 24mg). Injection (2mg/ml, 10mg/ml, 20mg/ml and 50mg/ml). Oral solution available as a manufacturer's special.

CD

- CD schedule 2

Evidence: (1–3,62,63,165–167)

Hyoscine butylbromide (Buscopan)

Use:

- Adjuvant where pain is caused by smooth muscle spasm of the gastrointestinal or genitourinary tract
- Antisecretory effect in bowel obstruction
- Management of secretions, especially where drug crossing the blood brain barrier is an issue
- Management of noisy breathing at the end of life (may be more effective if started early)

Dose and route:

Adjuvant in smooth muscle spasm of the gastrointestinal tract

By mouth

- **Child 1 month-1 year**: 300-500micrograms/kg 3–4 times daily, maximum 5mg per dose
- **Child 2 -4 years**: 5mg 3–4 times daily
- **5- 11 years**: 10mg 3–4 times daily
- **12 years and over**: 10–20mg 3–4 times daily

By subcutaneous bolus injection, intravenous injection or intramuscular injection

- **Child 1 month- 4 years**: 300–500micrograms/kg 3-4 times daily, maximum 5mg per dose
- **5-11 years**: 5–10mg 3–4 times daily
- **12 years and over:** 10–20mg 3–4 times daily

By continuous subcutaneous infusion:

- **Child 1 month- 4 years:** 1.5mg/kg/24hours (max 15mg/24hours)
- **Child 5-11 years**: 30mg/24hours
- **12 years and over**: Up to 60-80mg/24hours

Higher doses may be needed; doses used in adults range from 20-120mg/24hours. Maximum dose 300mg/24hours.

Adjuvant in smooth muscle spasm of gastrointestinal and urinary tract, antisecretory effect in bowel obstruction, management of respiratory secretions

By subcutaneous bolus injection, intravenous injection or intramuscular injection

- **Child 1 month-4 years**: 300–500micrograms/kg 3-4 times daily, maximum 5mg per dose
- **Child 5-11 years**: 5–10mg 3–4 times daily
- **12 years and over:** 10– 20mg 3–4 times daily

By continuous subcutaneous infusion:

- **Child 1 month- 4 years:** 1.5mg/kg/24hours (max 15mg/24hours)
- **Child 5-11 years**: 30mg/24hours
- **12 years and over**: Up to 60-80mg/24hours

Higher doses may be needed; doses used in adults range from 20-120mg/24hours. Maximum dose 300mg/24hours.

Notes:

- Antimuscarinic and has smooth muscle relaxant and antisecretory properties

Licensing

- Tablets are not licensed for use in children <6 years old. Injection is not licensed for use in children.

Therapeutics

- Does not cross blood brain barrier (unlike hyoscine hydrobromide), hence no central antiemetic effect and doesn't cause drowsiness.
- More likely to be effective in death rattle if used prophylactically

Contraindications, cautions

- Contraindicated in patients with tachycardia. Caution in cardiac disease. The MHRA recommends that patients with cardiac disease are monitored and that resuscitation equipment and trained personnel are readily available: this may not be appropriate in end of life care
- Increased risk of cardiac arrhythmia and anaphylaxis in patients with underlying cardiac disease.
- Likely to exacerbate gastro-oesophageal reflux

Side effects

- Anti-muscarinic side effects including constipation, urinary retention, tachycardia, blurred vision.

Pharmacokinetics

- Onset of action less than 10 min for SC/IV; 1-2 hours orally. Time to peak plasma concentration 15 min-2 hours orally. Plasma half-life 1-5 hours. Duration of action less than 2 hours in adult volunteers but possibly longer in moribund patients.
- Oral bioavailability, based on urinary excretion, is <1%. Thus, any antispasmodic effect reported after oral administration probably relates to a local contact effect on the GI mucosa.

Administration

- Injection solution may be given orally or via an enteral feeding tube. Administration via jejunostomy bypasses local effects on GI tract and is not recommended. Injection solution can be stored for 24 hours in the refrigerator after opening.
- Slow IV injection over 1 minute, diluted with glucose 5% or sodium chloride 0.9%.

Available as

- Tablets (10mg) and injection (20mg/ml).

Evidence: (1–3,8,42,163,168,169)

Hyoscine hydrobromide

Use:

- Control of upper airways secretions
- Noisy breathing at the end of life (may be more effective if started early)
- Hypersalivation and drooling
- Bowel colic pain
- Paraneoplastic sweating or pyrexia

Dose and routes

By mouth or buccal route:

- **Child 1 month- 11 years**: 10micrograms/kg, maximum 600micrograms, 4 times daily
- **12 years and over**: 300micrograms 4 times daily, increased gradually to a maximum of 600micrograms 4 times daily if required

By transdermal route:

- **Neonate over 32 weeks corrected gestational age, child up to 2 years**: 250micrograms (1/4 x 1mg/72hour patch) every 72 hours
- **Child 3-9 years**: 500micrograms (1/2 x 1mg/72hours patch) every 72 hours
- **10 years and over**: 1mg (1 x 1mg/72hours patch) every 72 hours

By subcutaneous or intravenous injection or infusion:

- **Child 1 month-17 years**:

  10micrograms/kg, maximum 600micrograms, every 4–8 hours OR 40

  60micrograms/kg/24hours via CSCI/IV infusion.

  Maximum suggested dose is 2.4mg in 24 hours: higher doses may be used by specialist units.

Notes:

- Antimuscarinic with smooth muscle relaxant and antisecretory properties

Licensing

- Not licensed for use in children for control of upper airways secretion or hypersalivation.

Therapeutics

- Higher doses often used under specialist advice.
- Second line, after glycopyrronium bromide, for treatment of hypersalivation in cerebral palsy

Contraindications, cautions

- MHRA (July 2023): Hyoscine hydrobromide patches (Scopoderm 1.5mg Patch or Scopoderm TTS Patch): risk of anticholinergic side effects, including hyperthermia particularly when used outside the product licence
- Transdermal patches contain metal in the backing and must be removed before MRI scanning to avoid burns.

Side effects

- Side effects: common or very common: confusion; constipation; dizziness; drowsiness; dry mouth; dyspepsia; flushing; headache; nausea; palpitations; skin reactions; tachycardia; urinary disorders; vision disorders; vomiting. Frequency unknown: neuroleptic malignant syndrome

Administration

- Apply patch to hairless area of skin behind ear.
- The patch can cause alteration of the pupil size on the side it is placed.
- Manufacturers of Scopoderm TTS patch have confirmed that it is safe to cut patches although this is outside the scope of product licence
- Injection solution may be administered orally and via feeding tubes. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (150micrograms, 300micrograms), patches (releasing 1mg/72 hours), and injection (400micrograms/ml, 600micrograms/ml).
- An oral solution is available via a ‘specials’ manufacturer.

Evidence: (1,2,42,170,171)

Ibuprofen

Use:

- Non-steroidal analgesic
- Anti-pyretic
- Adjuvant for musculoskeletal pain.

Dose and routes

Pain and inflammation

By mouth using immediate release preparations

- **Neonate**: 5mg/kg/dose every 12 hours
- **Child 1-2 months**: 5mg/kg 3–4 times daily preferably after food
- **Child 3-5 months**: 50mg 3 times daily preferably after food; in severe conditions up to 30mg/kg daily in 3–4 divided doses
- **Child 6-11 months**: 50mg 3–4 times daily preferably after food; in severe conditions up to 30mg/kg daily in 3–4 divided doses
- **Child 1-3 years**: 100mg 3 times daily preferably after food. In severe conditions up to 30mg/kg daily in 3–4 divided doses
- **Child 4-6 years**: 150mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses
- **Child 7-9 years**: 200mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4g
- **Child 10-11 years**: 300mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4g
- **12 years and over**: 300-400mg 3-4 times daily preferably after food. In severe conditions the dose may be increased to a maximum daily dose 2.4g

By mouth using modified release preparations

- **12 years and over**: 1.6g once daily, dose preferably taken in the early evening, increased to 2.4g daily in 2 divided doses if necessary.

Pain and inflammation in rheumatic diseases, including idiopathic juvenile arthritis:

By mouth using immediate release preparations

- **Child aged 3 months and over**: 30–40mg/kg daily in 3–6 divided doses preferably after food. Increased, if necessary to a maximum of 60mg/kg/day. Maximum daily dose 2.4g

Notes:

- Non-opioid analgesic, NSAID and non-selective COX inhibitor

Licensing:

- Orphan drug licence for closure of ductus arteriosus in preterm neonate. Not licensed for use in children less than 3 months of age or body-weight less than 5kg, except for up to two doses for post immunisation pyrexia. (50mg/dose given a minimum of 6 hours apart). Topical preparations and granules are not licensed for use in children.

Therapeutics

- Combines anti-inflammatory, analgesic, and antipyretic properties. It has fewer side effects than other NSAIDs but its anti-inflammatory properties are weaker.
- Alternating or combining with paracetamol may give better antipyretic effect than monotherapy but benefits in terms of analgesia are unclear.
- Use adjusted body weight (Appendix 7) to calculate doses in obese children

Contraindications, cautions

- Caution in patients with or at risk of thrombocytopenia: may impair platelet function.
- May mask fever and other signs of inflammation
- Will cause closure of ductus arteriosus; contraindicated in duct-dependent congenital heart disease
- Caution in cardiac, hepatic or renal impairment and those with asthma. Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure

Side effects

- May be associated with an increased risk of thrombotic events (e.g. myocardial infarction, thrombotic stroke) in children.
- All NSAIDs are associated with gastro-intestinal toxicity however lowest risk is likely to be with ibuprofen. Consider prescription of a proton pump inhibitor with prolonged use.

Hepatic impairment, renal impairment:

- Avoid or use with caution in severe renal failure.

Administration

- For administration via an enteral feeding tube, use a liquid preparation; dilute with an equal volume of water immediately prior to administration where possible. No specific information for jejunal administration. Administer as above and monitor for any signs of loss of efficacy or increased side effects.
- Can be used topically particularly for sprains, strains and arthritis.

Patient information

- Patient information: See Medicines for Children leaflet: “Ibuprofen for pain and inflammation” https://www.medicinesforchildren.org.uk/medicines/ibuprofen-for-pain-and-inflammation /

Available as

- Tablets (200mg, 400mg, 600mg), modified release tablet (800mg), orodispersible tablets (200mg), chewable capsules (100mg), capsules (200mg, 400mg), modified release capsules (200mg, 300mg), oral syrup (100mg/5ml), granules (600mg/sachet), topical foam (50mg per 1g) creams and gels (5%).

Evidence: (1,2,8,11,172–174)

Ipratropium Bromide

Use:

- Wheeze or breathlessness caused by bronchospasm
- Rhinorrhoea associated with allergic and non-allergic rhinitis
- Localised management of sialorrhoea (with fewer systemic side effects)

Dose and routes:

Wheeze or breathlessness caused by bronchospasm

By inhalation of nebulised solution

- **Child 1 month-5 years**: 125-250micrograms as required maximum 1mg daily
- **Child 6-11 years**: 250micrograms as required maximum 1mg daily
- **12 years and over**: 500micrograms as required maximum 2mg daily

By aerosol inhalation

Use via large volume spacer (and a close-fitting face mask in children under 3 years).

- **Child 1 month-5 years**: 20micrograms 3 times daily
- **Child 6-11 years**: 20-40micrograms 3 times daily
- **12 years and over**: 20-40micrograms 3-4 times daily

Rhinorrhoea associated with allergic and non-allergic rhinitis

By intranasal administration

- **12 years and over**: 2 sprays 2–3 times daily, dose to be sprayed into each nostril.

Notes

Licensing

- Not licensed for severe or life-threatening acute asthma. Inhalvent® not licensed for use in children under 6 years. Not licensed for rhinorrhoea

Therapeutics

- In severe acute asthma, dose can be repeated every 20-30 minutes in first two hours, then every 4-6 hours as necessary (unlicensed).
- No evidence of efficacy in infection-related bronchospasm in infants
- Use in management of sialorrhea in children not well established

Side effects

- Anti-muscarinic side effects occur with systemic absorption, including constipation, urinary retention, tachycardia, blurred vision.

Pharmacokinetics

- Maximum effects 30-60 minutes after use. Duration of action 3-6 hours. Bronchodilation can usually be maintained with treatment 3 times daily.

Administration

- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training. In acute asthma, use via an oxygen-driven nebuliser.

Available as

- Nebuliser solution (250micrograms in 1 ml, 500micrograms in 2 ml), aerosol inhaler (20micrograms per metered dose), nasal spray 21micrograms per metered dose.

Evidence: (1,2,175,176)

Ketamine

Use:

- Neuropathic pain and hyperalgesia
- Pain failing to respond to usual treatments, including opioids, non-opioids and adjuvant analgesics
- Adjuvant to strong opioids
- Severe visceral pain
- Ischaemic pain
- To reduce N-methyl-D-aspartate (NMDA) receptor wind-up pain and opioid tolerance.
- Emerging use in refractory status epilepticus.

Dose and routes

Pain including NMDA wind-up pain

By mouth, or buccal route

- **Neonate (over 37 weeks corrected gestational age)- child 11 years**: Starting dose 100micrograms/kg, as required or regularly 6–8 hourly. Increase in increments of 100micrograms/kg up to 400micrograms/kg as required.
- **12 years and over**: 5-10mg as required or regularly 6–8 hourly; increase in steps of 5-10mg up to 50mg/dose as required.

  Doses up to 200mg or 3mg/kg 4 times daily reported in adults

By continuous subcutaneous or intravenous infusion:

- **Child 1 month and over**: Starting dose 500micrograms/kg/24hours to 1mg/kg/24hours. Increase according to response; usual maximum 12mg/kg/24hours or 500mg/24hours

  Doses up to 60mg/kg/24hours have been reported, including in refractory status epilepticus.

By intravenous administration for anaesthesia

Seek specialist advice

Notes:

- Dissociative anaesthetic which has analgesic properties in sub-anaesthetic doses.
- Racemic mixture of the S(+) and R(–) stereoisomers of ketamine. The most potent NMDA-receptor–channel blocker available for clinical use

Licensing

- Not licensed for use in children with neuropathic pain.

Therapeutics

- Potential secondary benefits in adolescents with depressive symptoms.
- Continuous intravenous infusion of ketamine appears effective in refractory status epilepticus, but its place in clinical practice remains to be determined.
- Higher starting doses may be used, particularly by infusion, in anaesthesia and acute postoperative pain
- Generally administered orally or subcutaneously in palliative care. Can also be administered via intramuscular, intravenous, buccal, intranasal, spinal and rectal routes.
- Has also been administered topically for mucositis and painful wounds although RCT evidence is lacking.
- Buccal dose is effective but bitter taste. May result in increased drowsiness and slightly lower efficacy due to lack of first pass metabolism
- S-ketamine is licensed in many countries: use 50% of doses quoted above
- Short courses are preferred to long term use due to cumulative adverse effects including cognitive impairment and also renal tract damage.
- Once analgesia has been obtained, an attempt should be made to withdraw ketamine over 2–3 weeks. The benefit from a short course can last for weeks or even months, and the course can be repeated if necessary.
- Alternatively ketamine can be given as a short "burst" increasing doses stepwise rapidly over a period of 3-4 days until a therapeutic effect is achieved or side effects prevent further dose escalation and then decreasing in a similar stepwise fashion to stop after 7-10 days
- Some practitioners routinely reduce the background opioid dose by 25–50% when starting parenteral ketamine.
- Sudden discontinuation may precipitate hyperalgesia or allodynia: discontinue gradually over 2-3 weeks after prolonged use.

Side effects

- Neuropsychiatric side effects including agitation, hallucinations, anxiety and dysphoria, diplopia, nystagmus and sleep disturbance. Animal studies indicate that ketamine can induce neuronal cell death in the immature brain. Emergent phenomena occur to a lesser extent with the sub-anaesthetic analgesic doses given in palliative care, and generally can be controlled by concurrent administration of a benzodiazepine (e.g. diazepam, midazolam) or haloperidol.
- Gastrointestinal side effects include vomiting, abdominal pain, gastrointestinal bleeding, abnormal liver function tests and biliary duct dilatation
- Urological side effects include urinary frequency, urgency, dysuria, and haematuria

Pharmacokinetics

- Wide variation in clearance, mostly explained by genetic polymorphism in the activity of CYP2B6 together with increasing age
- Oral bioavailability is approximately 20% but ketamine is potentiated by first pass metabolism. In practical terms it is therefore reasonable to use a 1 to 1 ratio for conversion between oral and subcutaneous or intravenous routes.
- Onset of action 5 min IM; 15-30 min SC; 30 min PO. Duration of action 30 min–2h IM; 4-6h PO, sometimes longer. Bio-availability 93% IM; 45% nasal; 30% SL; 30% PR; 20% PO.

Hepatic and renal impairment

- Causes hepatic enzyme induction and enhances its own metabolism. Caution in severe hepatic impairment, consider dose reduction.

Interactions

- Diazepam can increase the half-life and prolong the effects of ketamine.

Administration

- Buccal doses should be prepared in a maximum volume of 2 ml. The bitter taste may make this route unpalatable. Special preparations for buccal use are available in UK.
- Dilute in 0.9% sodium chloride for subcutaneous or intravenous infusion. Can be administered as a separate infusion or by adding to opioid infusion/ PCA/NCA.
- Oral solution may be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Injection (10mg/ml, 50mg/ml, 100mg/ml) and oral solution (50mg in 5ml) from a 'specials' manufacturer. Injection solution may be given orally. Mix with a flavoured soft drink to mask the bitter taste.

CD

- Schedule 2 CD. Evidence: (1–3,165,177–184)

Ketorolac

Use:

- Short-term management of moderate to severe acute postoperative pain
- Chronic pain: limited experience of extended use

Doses and routes:

By intravenous or subcutaneous bolus

- **Child 1-15 years**: 500microgam/kg, maximum 15mg, repeated every 6 hours as required; maximum 60mg daily
- **16 years and over, body-weight over 50kg**: 10mg, every 4–6 hours as required: increased gradually to maximum of 90mg daily

By buccal route, using injection solution

- **Child 1 year and over**: 500micrograms/kg, maximum 15mg, up to 4 times daily

By continuous subcutaneous infusion

- **Child 1-15 years**: 2mg/kg/24hours, maximum 60mg daily
- **16 years and over, body-weight over 50kg**: 60mg/24hours, increased gradually to a maximum of 90mg daily

Notes:

- Non-opioid, NSAID and preferential COX-1 inhibitor with potent analgesic effects, but only moderate anti-inflammatory action. Potency approximately twice that of naproxen.

Licensing

- Licensed only for the short-term management (maximum of 2 days) of moderate to severe acute postoperative pain in adults and adolescents from 16 years of age. Not licensed for subcutaneous or buccal administration

Therapeutics

- Limited, poor quality data for indications other than post-operative pain. Anecdotal reports of effectiveness for patients with bone pain unresponsive to oral NSAIDs. Use the lowest possible dose for the shortest possible time
- High risk of gastrointestinal toxicity: co-prescription of a proton pump inhibitor strongly recommended.

Contraindications, cautions

- Contraindicated in hypersensitivity to ketorolac or other NSAIDs; history of asthma; active peptic ulcer or history of GI bleeding; severe heart, hepatic or renal failure; suspected or confirmed cerebrovascular bleeding or coagulation disorders. Do not use in combination with any other NSAID.
- May mask fever and other signs of inflammation

Side effects

- May be associated with increased risk of thrombotic events (e.g. myocardial infarction, thrombotic stroke) in children.
- All NSAIDs are associated with gastro-intestinal toxicity. Ketorolac is in the highest risk group. Co-prescription of a proton pump inhibitor is strongly recommended
- Other potential side effects; Very common (>10% patients): headache, dyspepsia, nausea, abdominal pain; Common (1-10% patients): dizziness, tinnitus, oedema, hypertension, anaemia, stomatitis, abnormal renal function, pruritus, purpura, rash, bleeding and pain at injection site. Risk of adverse effects likely to increase with prolonged use.

Interactions

- Anticoagulants (contraindicated as the combination may cause an enhanced anticoagulant effect); corticosteroids (increased risk of GI ulceration of bleeding); diuretics (risk of reduced diuretic effect and increase the risk of nephrotoxicity of NSAIDs); other potential nephrotoxic drugs.

Pharmacokinetics

- Onset of action 10-30mins IV/IM; maximal analgesia achieved within 1-2 hours and median duration of effect 4-6 hours.

Renal impairment

- Reduce dose or avoid.

Administration

- For administration by intravenous bolus administer neat or diluted in a small volume of 0.9% sodium chloride or 5% dextrose and give over at least 15 seconds
- Subcutaneous injection can be irritant therefore dilute to the largest volume possible (0.9% sodium chloride suggested). Alkaline in solution so high risk of incompatibility if mixed with acidic drugs. Some data for compatibility in 0.9% sodium chloride with diamorphine or oxycodone. ***Incompatibilities*** include with cyclizine, glycopyrronium, haloperidol, levomepromazine, midazolam and morphine.

Available as

- Injection 30mg/ml (injection contains ethanol as an excipient) and injection 10mg/ml.

Evidence: (1–3,185–189)

Lactulose

Use:

- Constipation, faecal incontinence related to constipation.
- Hepatic encephalopathy (portal systemic encephalopathy) and coma.

Dose and route:

Constipation:

By mouth:

- **Neonate**: 2.5ml twice daily, adjusted according to response
- **Child 1 month-11 months**: 2.5ml twice daily, adjusted according to response
- **Child 1-4 years:** 2.5-10ml twice daily, adjusted according to response
- **Child 5 years and over**: 5-20ml twice daily, adjusted according to response

Hepatic encephalopathy:

By mouth

- **12 years and over**: 30-50ml three times daily, adjusted to produce 2-3 soft stools per day

Notes:

- Osmotic laxative

Licensing

- Licensed for constipation in all age groups. Not licensed for hepatic encephalopathy in children.

Therapeutics

- Prebiotic: increases beneficial colonic bacteria (unlike macrogol). Macrogols are often preferable in palliative care but lactulose can be useful if large volumes are not tolerated. Generally unhelpful in opioid-induced constipation when a stimulant laxative is needed. Sickly taste. Unlikely to affect diabetic or ketogenic diets at conventional doses.

Contraindications, cautions

- Contraindicated in galactosaemia, intestinal obstruction.
- Caution in lactose intolerance.

Side effects

- Nausea, flatus, colic especially at high doses.

Pharmacokinetics

- Onset of action 36-48 hours.

Administration

- May be taken with water and other drinks. Dilute with 2-3 times the volume of water for administration via feeding tube. Therapeutic effect is unaffected by administration directly into the stomach or jejunum

Patient information

- See Medicines for Children leaflet: “Lactulose for constipation” https://www.medicinesforchildren.org.uk/medicines/lactulose-for-constipation/

Available as

- Oral solution

Evidence: (1–3,190,191)

Lansoprazole

Use:

- Gastro-oesophageal reflux disease; erosive oesophagitis; prevention and treatment of NSAID induced gastric and oesophageal irritation; treatment of duodenal and gastric ulcer.
- Fat malabsorption despite pancreatic enzyme therapy in cystic fibrosis

Dose and routes:

By mouth

- **Child body-weight less than 30 kg**: 500micrograms/kg-1mg/kg, maximum 15mg, once daily in the morning
- **Child body-weight more than 30 kg**: 15-30mg once daily in the morning

Notes:

Gastric proton pump inhibitor

Licensing

- Not licensed in the UK for infants, children or adolescents. Licensed in the US from 1 year of age. Exact doses limited by available formulations.

Therapeutics

- Inhibition of gastric acid production is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Infants and children appear to need a higher mg/kg dose to achieve therapeutic acid suppression

Cautions

- FasTabs contain aspartame and should be used with caution in known PKU patients.

Side effects

- Common adverse effects (>1 in 100 to <1 in 10): headache, dizziness; nausea, diarrhoea, stomach pain, constipation, vomiting, flatulence, dry mouth, pharyngitis, increase in liver enzyme levels, urticaria, itching, rash. Hypomagnesaemia may develop with prolonged use. PPIs are an independent risk factor for Clostridium Difficile infection. MHRA safety warning 2015: there is a very low risk of subacute cutaneous lupus erythematosus associated with use of PPIs.

Pharmacokinetics

- Oral bioavailability is good at 80-90% compared to 60% for omeprazole. Food slows down the absorption and decreases the bioavailability.

Hepatic impairment

- Reduce by 50% in moderate to severe hepatic impairment

Interactions

- Lansoprazole may interfere with absorption of drugs where bioavailability is significantly affected by gastric pH (e.g. atazanavir, itraconazole); may cause increase in digoxin levels and increase in plasma concentration of drugs metabolised by CYP3A4 (e.g. theophylline and tacrolimus). Drugs which inhibit or induce CYP2C19 or CYP3A4 may affect the plasma concentration of lansoprazole. Sucralfate and antacids may decrease the bioavailability of lansoprazole.

Administration

- Anecdotal evidence for halving Lansoprazole FasTabs to give a 7.5mg dose. For optimal effect, the single daily dose is best taken in the morning. Lansoprazole should be taken at least 30 minutes before food.
- Capsules: Capsules should be swallowed whole with liquid. Capsules may be opened and the granules mixed with a small amount of water, apple/tomato juice or sprinkled onto a small amount of soft food (e.g. yoghurt, apple puree) to ease administration.
- FasTabs: Place on the tongue and gently suck. FasTabs can be swallowed whole with water or mixed with a small amount of water if preferred.
- Lanzoprazole FasTabs can be dispersed in 10 ml water and administered via an 8Fr NG tube without blockage. For smaller bore tubes, dissolve the contents of a lansoprazole capsule in 8.4% sodium bicarbonate before administration. If the tube becomes blocked, use sodium bicarbonate to dissolve any enteric coated granules lodged in the tube. Lansoprazole less likely than omeprazole MUPS to cause blockage of small bore tubes. Administration into the jejunum is unlikely to reduce bioavailability.

Patient information

- See Medicines for Children leaflet: Lansoprazole for gastro-oesophageal reflux disease (GORD) and ulcers https://www.medicinesforchildren.org.uk/medicines/lansoprazole-for-gastro-oesophageal-reflux-disease-gord-and-ulcers/

Available as

- Capsules 15mg and 30mg and orodispersible tables 15mg and 30mg.

Evidence: (1–3,8,130,131)

Levetiracetam

Use:

- Focal seizures with or without secondary generalisation
- Epilepsy; maintenance treatment
- Convulsive status epilepticus

Dose and route:

Epilepsy: maintenance treatment

- Monotherapy of focal seizures with or without secondary generalisation
- Adjunctive therapy of focal seizures with or without secondary generalisation
- Adjunctive therapy of myoclonic seizures and tonic clonic seizures

By mouth or intermittent intravenous or subcutaneous infusion.

- **Child 1-5 months**:7mg/kg once daily increased every 2 weeks in steps of up to 7mg/kg twice daily, maximum 21mg/kg per dose, twice daily
- **6 months-17 years (body-weight up to 50 kg)**: Initially 10mg/kg once daily, then increase in steps of up to 10mg/kg twice daily (maximum per dose 30mg/kg twice daily). Dose to be increased every 2 weeks
- **18 years and over or body-weight 50 kg and above**: 250mg once daily increased every 2 weeks in steps of 250mg twice daily (maximum per dose 1.5 g twice daily).

By continuous subcutaneous or intravenous Infusion

- Administer total daily oral or intravenous dose of levetiracetam as a continuous infusion/24hours

Convulsive status epilepticus

- APLS resuscitation guideline (2021) first choice long-acting anticonvulsant after 2 doses of benzodiazepine
- Full loading dose to be given EVEN if the child is already receiving maintenance levetiracetam

By intravenous or interosseous injection over 5 minutes

- **Child 1 month and over**: 40mg/kg, maximum 3g

  Dilute 1:1 with 0.9% sodium chloride, minimum volume 10ml

Notes:

Licensing

- Not licensed for convulsive status epilepticus. Granules not licensed for use in children under 6 years, for initial treatment in children with body-weight less than 25kg, or for the administration of doses below 250mg.

Therapeutics

- Phenobarbital, not levetiracetam, remains drug of first choice long acting anticonvulsant after 2 doses of benzodiazepine for neonatal seizures
- Use adjusted body weight (Appendix 7) to calculate doses in obese children

Side effects

- Movement disorders, sedation, confusion, exacerbation of seizures, neuroleptic malignant syndrome

Interactions

- Caution when administering with other drugs with CNS depressant effects: decreases the clearance of Methotrexate

Administration

- Intravenous administration over 15 minutes at a suggested concentration of 2.5-15mg/ml. May be administered at a concentration of 50mg/ml over 5-15 minutes in an acute situation.
- Administration of levetiracetam by subcutaneous bolus or intermittent (over 15-30 minutes) or continuous subcutaneous infusion is off-label but with increasing supporting (low-grade) evidence.
- Dose conversion for oral:intravenous:subcutaneous is 1:1:1
- Continuous subcutaneous infusion: Injection has a low pH and high osmolality which increases the potential for irritation around the injection site. Dilute in water for injections or 0.9% sodium chloride to the maximum volume compatible with the infusion device. May be administered neat i.e. at a concentration of 100mg/ml but increased risk of site reactions.
- Limited compatibility data. Administer via a separate syringe driver where possible. Reported to be visually compatible at usual concentrations with diamorphine, hyoscine butylbromide, levomepromazine, midazolam, morphine or oxycodone. Seek specialist advice.

Patient information

- See Medicines for Children leaflet “Levetiracetam for preventing seizures” https://www.medicinesforchildren.org.uk/medicines/levetiracetam-for-preventing-seizures/

Available as

- Tablets 250mg, 500mg, 750mg and 1g; oral solution 100mg/ml; solution for infusion 100mg/ml. Also available as granule sachets for oral administration 250mg, 500mg, 750mg, 1g, 1.5g

Evidence: (1,2,192–199)

Levomepromazine

Use:

- Broad spectrum antiemetic where cause is unclear, or where probably multifactorial
- Second line if a specific antiemetic fails
- Antipsychotic and anxiolytic
- Sedation for terminal agitation
- Adjuvant for neuropathic pain

Dose and routes **Nausea and vomiting** By mouth:

- **Child 1 month-11 years**: 50-100micrograms/kg once daily, usually at night, or in two divided doses.

  Increase as required and tolerated in increments of 50–100micrograms/kg/24hours to a maximum of 400micrograms/kg/24hours.

- **12 years and over**: 2.5–5mg once daily, usually at night, or in two divided doses.

  Increase as required and tolerated in increments of 2.5–5mg to maximum of 25mg/24hours

By continuous intravenous or subcutaneous infusion over 24hours:

- **Child 1 month-11 years**: 100micrograms/kg/24hours. Increase as necessary to a maximum of 400micrograms/kg/24hours. Maximum dose 25mg/24hours
- **12 years and over**: 5mg/24hours. Increase as necessary to a maximum of 25mg/24hours

Infusion doses can also be given as intermittent intravenous or subcutaneous boluses in one or two divided doses

Sedation and confusion, refractory pain

By continuous subcutaneous or intravenous infusion over 24hours:

- **Child 1 year-11 years**: 350micrograms/kg/24hours, maximum initial dose 12.5mg, increasing as necessary up to 3mg/kg/24hours
- **12 years and over**: 12.5mg/24hours increasing as necessary up to 200mg/24hours.

Infusion doses can also be given as intermittent intravenous or subcutaneous boluses in one or two divided doses

Notes:

- Phenothiazine antihistamine with powerful sedative and antiemetic properties

Licensing

- Licensed for use in children with terminal illness for the relief of pain and accompanying anxiety and distress

Therapeutics

- Injection solution has also been given sublingually in adults using the same doses as oral route
- A low dose is often effective as an antiemetic. Higher doses are very sedative and not necessarily more effective as an antiemetic. Consider adding an additional antiemetic with a different mode of action e.g. dexamethasone, ondansetron.

Cautions

- May lower seizure threshold. Caution in cardiac disease, liver and renal impairment.
- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval

Side effects

- Hypotension, particularly with higher doses. Very sedating, especially at high doses.
- Paradoxical agitation, movement disorders including neuroleptic malignant syndrome.
- Constipation, vomiting

Pharmacokinetics

- Oral bioavailability 50%; consider halving dose if converting oral to subcutaneous or intravenous route in stable patient

Renal impairment

- Reduce dose and administer once daily in severe renal impairment, titrating according to response

Interactions

- Potent inhibitor of cytochrome P450 enzyme CYP2D6. May increase levels of drugs metabolised by this enzyme including amitriptyline.

Administration

- Tablets may be halved or quartered to obtain smaller doses. Tablets/segments may be dispersed in water for administration via a NG or gastrostomy tube. Flush tube well after administration. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Dilute in sodium chloride 0.9% or water for injection for subcutaneous infusion. Anecdotally associated with an increased risk of site reactions.

Available as

- Tablets (25mg) and injection (25mg/mL).

Evidence: (1–3,8,113,200–203)

Lidocaine (Lignocaine) plaster

Use:

- Localised neuropathic pain

Dose and routes

Topical:

- **Child 3-17 years**: Apply 1-2 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hours plaster free period
- **Adult 18 years and over**: Apply up to 3 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hours plaster free period

Notes:

Licensing

- Not licensed for use in children or adolescents under 18 years. Doses extrapolated from adult BNF

Therapeutics

- Lidocaine in the plaster diffuses continuously into the skin, providing a local analgesic effect. Putative mechanism of action: stabilisation of neuronal membranes by down-regulation of sodium channels
- Adult recommended maximum 3 plasters per application.
- When lidocaine 5% medicated plaster is used according to the maximum recommended dose (3 plasters applied simultaneously for 12 hours) about 3± 2% of the total applied lidocaine dose is systemically available and is similar for single and multiple administrations.
- An adequate treatment period is a minimum of 4 weeks in duration. Consider discontinuation if no response. For long-term use, treatment should be reviewed regularly to assess whether the number of plasters required can be reduced or the plaster-free period extended.
- Application to the head may be tolerated less well compared with the trunk and extremities.

Cautions

- Caution in patients with severe cardiac impairment, severe renal impairment or severe hepatic impairment.

Side effects

- The plaster contains propylene glycol which may cause skin irritation. It also contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed). Approximately 16% of patients can be expected to experience adverse reactions. These are localised reactions due to the nature of the medicinal product.

Administration

- Cut plaster to size and shape of painful area. Do NOT use on broken or damaged skin or near the eyes. The plasters must be used within 14 days of opening the sachets.

Available as

- 700mg/medicated plaster (5% w/v lidocaine) Evidence: (2,3,204–206)

Loperamide

Use:

- Diarrhoea from non-infectious cause
- Faecal incontinence
- Management of high ileostomy output

Dose and routes for management of chronic diarrhoea

By mouth:

- **Child 1-11 months**: 100micrograms/kg twice daily given 30 minutes before feeds. Increase as necessary up to a maximum of 1.25mg/kg/day given in divided doses
- **Child 1-11years**: Initial dose of 100micrograms/kg, maximum single dose 2mg, 3-4 times daily. Increase as necessary up to a maximum of 1.25mg/kg/day in divided doses, maximum 16mg total daily dose
- **12 years and over**: Initial dose of 2mg 2-4 times daily. Increase as necessary up to a maximum of 16mg/day in divided doses.

Notes

Licensing

- Not licensed for use in children with chronic diarrhoea. Capsules not licensed for use in children under 8 years. Syrup not licensed for use in children under 4 years.

Therapeutics

- Maximum therapeutic impact may not be seen for 16-24 hours.
- BNFc quotes a maximum of 2mg/kg/day in divided doses for children aged 1-11 months. However APPM has been unable to identify evidence of sufficient quality to justify this recommendation.
- Despite low bioavailability (due to almost complete first pass metabolism primarily by CYP3A4), some loperamide may be absorbed leading to life threatening toxicity in patients treated with very high doses, above the recommended maximum, for high output diarrhoeal or stoma losses

Side effects

- Constipation, nausea, flatulence.

Administration

- Orodispersible tablets can be dissolved in water. Disperse one orodispersible tablet in 4mL of water for a 0.5mg/mL suspension. For proportional doses, draw up the required dose and administer immediately. Resulting suspension can be administered without risk of blocking feeding tubes. Flush well after administration.
- Jejunal administration will not affect the therapeutic response to loperamide.

Patient information

- See Medicines for Children leaflet “Loperamide for diarrhoea” https://www.medicinesforchildren.org.uk/medicines/loperamide-for-diarrhoea/

Available as

- Tablets (2mg), capsules (2mg), orodispersible tablets (2mg).

Evidence: (1,2,8,207–209)

Lorazepam

Use

- Anxiety, including anxiety associated with dyspnoea
- Agitation and distress
- Adjuvant in cerebral irritation
- Muscle spasm
- Anticipatory nausea and vomiting in chemotherapy
- Status epilepticus

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Anxiety, agitation, cerebral irritability, muscle spasm, anticipatory nausea and vomiting

By mouth:

- **Child 1-11 months**: 25micrograms/kg 2–3 times daily
- **2-5 years**: 500micrograms 2–3 times daily
- **6-10 years**: 750micrograms 3 times daily
- **11-14 years**: 1mg 3 times daily
- **15 years and over**: 1–2mg 3 times daily.

By buccal route:

- **Child 1 month and over**: 25micrograms/kg as a single dose, as required 2-3 times daily. Increase to 50micrograms/kg, maximum 1mg/dose, if necessary
- **Adult:** 500micrograms–1mg as a single dose, repeat as required.

Status epilepticus

By slow intravenous injection:

- **Neonate**: 100micrograms/kg/dose repeated after 10 minutes if required
- **Child 1 month-11 years**: 100micrograms/kg/dose, maximum 4mg, repeated after 10 minutes if required
- **12 years and over**: 4mg repeated after 10 minutes if required.

Notes

Licensing

- Licensed in children for status epilepticus. Tablets licensed in children over 5 years for premedication, injection not licensed in children less than 12 years except for treatment of status epilepticus.

Therapeutics

- Potency in the order of 10 times that of diazepam per mg as anxiolytic/sedative.

Cautions

- May cause drowsiness and respiratory depression if given in large dose. Half-life 10–20 hours therefore risk of accumulation with frequent PRN doses. Caution in renal and hepatic failure.

Pharmacokinetics

- Well absorbed buccally with rapid onset of effect. There may however be variable absorption by this route with further variation possible depending on the formulation used.

Administration

- Specific buccal tablets are not available in the UK but generic lorazepam tablets (specifically Genus, PVL or TEVA brands) do dissolve in the mouth so can be given buccally. Tablets may be dispersed in water for administration via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (250micrograms 500micrograms, 1mg, 2.5mg) and injection (4mg/ml), oral solution (1mg/ml: Licensed in UK but not licensed for use in children, expensive and contains significant quantity of ethanol as an excipient)

CD

- CD Schedule 4

Evidence: (1,3,8,87,87,122,158,210–213)

Macrogols

Use

- Constipation.
- Faecal impaction.
- Suitable for opioid-induced constipation.

Dose and route:

Constipation, prevention of opioid-induced constipation

By mouth

Using paediatric (or half adult-size) sachets for those less than 12 years of age

- **Child under 1 year**: ½-1 paediatric sachet daily
- **Child 1-5 years**: 1 paediatric sachet daily (adjust dose according to response; maximum 4 paediatric sachets daily)
- **Child 6-11 years**: 2 paediatric sachets daily (adjust dose according to response; maximum 4 paediatric sachets daily)
- **12 years and over**: 1–3 adult sachets daily.

Using Movicol® liquid:

- **12 years and over**: 25 mL 1–3 times daily usually for up to 2 weeks; maintenance 25 ml 1–2 times daily.

Using Movicol® ready to take sachets:

- **12 years and over**: 1–3 sachets daily in divided doses usually for up to 2 weeks; maintenance 1–2 sachets daily.

Faecal impaction

By mouth:

Using paediatric (or half adult-size) sachets for those less than 12 years of age

- **Child under 1 year**: ½-1 paediatric sachet daily
- **Child 1-4 years**: 2 paediatric sachets on first day and increase by 2 sachets every 2 days (maximum 8 sachets daily). Treat until impaction resolved then switch to maintenance laxative therapy
- **Child 5-11 years**: 4 paediatric sachets on first day and increase by 2 sachets every 2 days (maximum 12 sachets daily). Treat until impaction resolved then switch to maintenance laxative therapy

- **12 years and over**: 4 adult sachets on first day, then increase by 2 sachets daily to a maximum of 8 adult sachets daily. Total daily dose should be drunk within a 6 hour period. After disimpaction switch to maintenance laxative therapy.

Notes

Osmotic laxative

Licensing

- Not licensed for use in children under 5 years with faecal impaction and under 2 years with chronic constipation.

Therapeutics

- Increased stool volume stimulates peristalsis, however no inherent stimulant action. Ensure adequate hydration.

Cautions

- Ready to take sachets have higher concentrations of electrolytes including sodium and potassium. Caution if fluid or electrolyte disturbance. Caution with high doses (volumes) in those with impaired gag reflex, reflux oesophagitis or impaired consciousness.

Administration

- Manufacturer advises dilute 25 ml of oral concentrate with 100 ml of water; after dilution the solution should be discarded if unused after 24 hours. Mix powder with water: follow manufacturers' instructions.
- For administration via a feeding tube: dissolve the powder (or liquid concentrate) in water as directed and flush down the feeding tube. Flush well after administration. Efficacy unlikely to be affected by jejunal administration

Patient information

- See Medicines for Children leaflet "Movicol for constipation" https://www.medicinesforchildren.org.uk/medicines/movicol-for-constipation/

Available as

- Movicol and Movicol Paediatric Sachets, CosmoCol and CosmoCol Paediatric Sachets, Laxido and Laxido Paediatric Sachets, Macilax and Macilax Paediatric Sachets. Movicol is also available as an oral liquid concentrate (dilute with water before administration) and 25ml oral solution sachets.

Evidence: (1–3,8,214–216)

Melatonin

Use:

- Sleep disturbance due to disruption of circadian rhythm (not anxiolytic).

Dose and route:

By mouth:

- **Child 1 month and over**: 2–3mg at night, increasing every 1–2 weeks dependent on effectiveness up to maximum 10mg.

Notes:

Licensing

- Adaflex® immediate release tablets, Ceyesto® 3mg prolonged release tablets and Colonis® melatonin liquid 1mg/ml are licensed for treatment of insomnia in children with ADHD from 6 years of age. Slenyto® is licensed in children and adolescents aged 2-18 years with Autism Spectrum Disorder and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient. All other melatonin formulations are not licensed for use in children.

Therapeutics

- Treatment should be initiated by a specialist. Ensure appropriate attention to sleep hygiene. Some prescribers use a combination of immediate-release and modified release tablets to optimise sleep patterns.
- Maximum doses are frequently outside the individual product licences

Cautions

- Caution when switching between immediate-release formulations as the peak plasma melatonin concentration may be higher with the oral solution than with tablets. Intake with carbohydrate-rich meals may impair blood glucose control.
- Reduced clearance in hepatic impairment.

Interactions

- Metabolised by cytochrome P450 enzyme CYP1A2. Levels may be increased by drugs that inhibit this enzyme including ciprofloxacin. Levels may be reduced by drugs that induce this enzyme including phenytoin.

Administration

- Modified-release tablets should be taken with or after food. The modified-release tablet Slenyto® may be mixed whole into food or drink (e.g. yoghurt, orange juice, or ice-cream) immediately before administration. Licensed immediate-release formulations should be taken on an empty stomach, 2 hours before or 2 hours after food. The immediate-release tablet Adaflex® may be crushed and mixed with water immediately before administration. Use oral liquid for administration via an enteral feeding tube No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet: Melatonin for sleep disorders https://www.medicinesforchildren.org.uk/medicines/melatonin-for-sleep-disorders/

Available as

- Prolonged release mini-tablets 1mg, 5mg (Slenyto®), prolonged release tablets 2mg, 3mg (various), immediate release tablets 1mg, 2mg, 3mg, 4mg, 5mg (Adaflex®), oral solution 1mg/1ml (Colonis®)

Evidence:(1,2,8,217–221)

Methadone

Use:

- Moderate to severe pain, particularly neuropathic pain and pain poorly responsive to other opioids.
- Not normally used as first line analgesia in the UK

Extremely important safety information

Methadone should only be commenced by practitioners experienced in its use.

This is due to wide inter-individual variation in response, very variable conversion ratios with other opioids, complex pharmacokinetics and a long half-life.

Initial close monitoring is particularly important.

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in patients already receiving regular strong opioids

By mouth:

Convert using *specific protocols* from previous opioid analgesia

Caution: Converting a patient to methadone from another opioid analgesic is a specialist skill and should only be undertaken in close collaboration with practitioners experienced in its use. There is a risk of unexpected death through overdose.

Consider other opioids first before rotating from morphine to methadone due to unacceptable side effects or inadequate analgesia. Consultation with a pain clinic or specialist palliative care service is advised

It can be difficult to convert a short or long-acting opioid to an equivalent dose of methadone. Current practice is usually to admit to a specialist inpatient unit or titrate orally at home with very close supervision. Close monitoring should be continued for a period of two weeks.

Equianalgesic doses

Dose conversion ratios from other opioids are not static but are a function of previous opioid exposure and are highly variable.

Published tables of equianalgesic doses of opioids, established in healthy non-opioid tolerant individuals, indicate that methadone is 1–2 times as potent as morphine in single dose studies. But in individuals on long-term (and high dose) morphine, methadone is closer to 10 times as potent as morphine; it can be 30 times more potent or occasionally even more. The equianalgesic ratio increases as the dose of morphine increases.

Protocols for converting patients to methadone

In adults there are several protocols for converting patients to methadone. These are not evidence based in paediatrics.

- *The reduce-and-replace* (also known as 3-day switch) protocol incorporates a transition period where the dose of the former opioid is reduced and partially replaced by methadone. The methadone dose is then titrated upwards. This approach is considered safer and may be more effective.
- *The rapid-conversion* (also known as regular-dose or stop-and-go), protocol advocates stopping previous opioid therapy completely and then starting a fixed dose of methadone at regular intervals.

Reduce-and-replace protocol

1. Calculate the average total daily oral morphine equivalent (OME)

   Add up the patient's total oral opiate requirement over the previous 48 hours. Use the equianalgesic table (Appendix 1) to calculate the oral morphine equivalent (OME). Do not include breakthrough doses for incident pain. Divide by two to give the average total daily OME

2. Convert the average total daily OME to the approximate equianalgesic dose of methadone using the table below

Total daily OME	**Equianalgesic ratio morphine(mg):methadone(mg)** Divide by this ratio
Less than 90mg/day	4:1
90-299mg/day	6:1
300-599mg/day	8:1
600-799mg/day	12:1
800mg/day or more	15:1

3. Replace original opioid with methadone, stepwise over 3 days

   - *Day 1* replace 1/3 of original opioid with equianalgesic dose of methadone in 3 divided doses
   - *Day 2* replace 2/3 of original opioid with equianalgesic dose of methadone in 3 divided doses
   - *Day 3* onwards replace all of original opioid with equianalgesic dose of methadone in 3 divided doses

4. Consider reducing the dose of methadone by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

   Example:

   Total daily OME = 900mg/day

   Equianalgesic ratio for total daily OME of 900mg/day = 15:1 (from the table above) Divide

   OME by equianalgesic ratio to obtain equianalgesic dose of methadone 900mg/day OME ÷

   15/1 = 60mg methadone

   Reduce the dose of methadone by 50% as the patient is already on a high dose of the previous opioid

   60mg methadone x 50% = 30mg methadone

Day 1: Give 2/3 original opioid (OME 600mg) and 1/3 equianalgesic dose of methadone in 3 divided doses

= 30mg ÷ 3 = 10mg methadone in 3 divided doses

= 10mg methadone ÷ 3 = 3.3mg methadone three times daily

Day 2: Give 1/3 original opioid (OME 300mg) and 2/3 equianalgesic dose of methadone in 3 divided doses

= 30mg ÷ 3 = 10mg methadone in 3 divided doses

= 10mg methadone ÷ 3 x 2 = 6.6mg methadone three times daily

Day 3: Stop original opioid and give full equianalgesic dose of methadone in 3 divided doses

= 30mg ÷ 3 = 10mg methadone three times daily

5. Use an alternative short acting opioid (such as morphine oral solution) for management of breakthrough pain. It may also be necessary to reduce the breakthrough dose by 25-50%
6. Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses may be required for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose may be sufficient.
7. To prevent adverse effects, increments in enteral dosing should be very cautious and usually by no more than 20% approximately at weekly intervals with a maximum increase of 50% (experienced practitioners may increase more frequently). Continued clinical reassessment is required to avoid toxicity as the time to reach steady state concentration following a change in dosing may be up to 12 days.
8. If excess sedation occurs reduce dose by 25-50% or omit dose. Sudden good analgesia can also indicate overdose and should trigger consideration of dose reduction or omission

Rapid-conversion-protocol

1. Calculate the average total daily oral morphine equivalent (OME)

   Add up the patient's total oral opiate requirement over the previous 48 hours. Use the equianalgesic table (Appendix 1) to calculate the oral morphine equivalent (OME). Do not include breakthrough doses for incident pain. Divide by two to give the average total daily OME

2. Convert the adjusted total daily OME (from step 1 above) to the equianalgesic dose of oral methadone by dividing by 15 (most guides say 10 so this is a cautious approach).
3. Consider reducing the dose of methadone by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation
4. Calculate the initial methadone dose by dividing the equianalgesic dose of methadone (from step 3 above) by 3.

   The initial dose would not normally exceed

- **Child body-weight less than 50kg**: 5mg three times daily
- **Body-weight 50kg and over**: 10mg three times daily

If converting from a long-acting opioid, give the first methadone dose 6 hours after the last long-acting opioid dose or 10-12 hours after opioid patch removal.

Example:

Total daily OME = 900mg/day

900mg/day OME ÷ 15 = 60mg methadone

Reduce the dose of methadone by 50% as the patient is already on a high dose of the previous opioid

60mg methadone x 50% = 30mg methadone

Calculate the initial methadone dose by dividing the equianalgesic dose of methadone by 3

= 30mg ÷3 = 10mg three times daily

5. Use an alternative short acting opioid (such as morphine oral solution) for management of breakthrough pain. It may also be necessary to reduce the breakthrough dose by 25-50%
6. Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses may be required for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose may be sufficient.
7. To prevent adverse effects, increments in enteral dosing should be very cautious and usually by no more than 20% approximately at weekly intervals with a maximum increase of 50% (experienced practitioners may increase more frequently). Continued clinical reassessment is required to avoid toxicity as the time to reach steady state concentration following a change in dosing may be up to 12 days.
8. If excess sedation occurs reduce dose by 25-50% or omit dose. Sudden good analgesia can also indicate overdose and should trigger consideration of dose reduction or omission.

By intermittent intravenous injection, continuous subcutaneous infusion, or continuous intravenous infusion:

Convert from previous opioid analgesia using appropriate methadone conversion protocol if applicable

By continuous intravenous or subcutaneous infusion

- Calculate the total daily dose of oral methadone administered over the previous 24 hours

  Divide the total daily dose of oral methadone by two and administer by continuous infusion

  Ensure continued access to immediate release morphine as required for breakthrough pain

Alternatively, the total daily dose of intravenous or subcutaneous methadone can be given as a single intravenous bolus injection over 3-5minutes or 2-3 divided doses

Seek specialist guidance if mixing with any other drug.

Pain in opioid naïve patients

By mouth:

Opioid naive patients: the maximum dose stated applies to starting dose only

- **Child 1-12 years**: 50-100micrograms/kg/dose, maximum 2.5mg, 2-3 times daily
- **12 years and over**: 2.5mg/dose, 2–3 times daily

Methadone has a long and variable half-life with potential to cause sedation, respiratory depression and even death from secondary peak phenomenon.

Consider using an alternative short acting opioid (such as morphine oral solution) for management of breakthrough pain.

Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses may be required for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose may be sufficient.

To prevent adverse effects, increments in enteral dosing should be very cautious and usually by no more than 20% approximately at weekly intervals with a maximum increase of 50% (experienced practitioners may increase more frequently). Continued clinical reassessment is required to avoid toxicity as the time to reach steady state concentration following a change in dosing may be up to 12 days.

If excess sedation occurs reduce dose by 25-50% or omit dose. Sudden good analgesia can also indicate overdose and should trigger consideration of dose reduction or omission.

Notes:

- Strong opioid with μ-opioid receptor agonist, and NMDA-receptor–channel blocker properties

Licensing

- Not licensed for use in children.

Therapeutics

- Methadone is a racemic mixture: L-isomer, analgesic active (levomethadone; L-polamidon®); R-isomer unknown action.
- In some countries levomethadone is available. It has a different strength to methadone.
- Partial replacement of former opioid is sometimes used if completing the full switch produces intolerable adverse effects: however completing the switch rather than using a combination of opioids is recommended in the first instance
- A naloxone infusion should be used to treat methadone overdose in view of the long and variable half-life
- Respiratory depressant effects may last longer than analgesic effects.
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Cautions

- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval

Monitoring

- Following concerns regarding methadone and sudden death from prolongation of QT-interval or Torsades de Pointes (especially at high doses) it is recommended that patients have an ECG prior to initiation of treatment and regularly whilst on methadone, particularly if they have any risk factors or are having intravenous treatment with methadone.

Side effects

- Usual strong opioid side effects.
- Also associated with prolonged QT-interval and ventricular arrhythmia (torsade de pointes)

Pharmacokinetics

- Limited data in paediatric patients; known to have wide inter-individual variation.
- Newer evidence suggests oral bioavailability may be as much as 80%

Hepatic impairment, renal impairment

- Reduce methadone dose by 50% in severe renal impairment and titrate according to response.
- Significant accumulation is unlikely in renal failure, as elimination is primarily via the liver.
- Avoid in severe hepatic impairment

Interactions

- Opioid antagonists naloxone and naltrexone will precipitate an acute withdrawal syndrome in methadone dependent patients. Naloxone will antagonise the analgesic, CNS and respiratory depressant effects of methadone.
- Metabolised by cytochrome P450 enzymes CYP2B6 and CYP3A4. Levels increased by drugs that inhibit these enzymes including aprepitant, ciprofloxacin, erythromycin and fluconazole. Levels may be reduced by drugs that induce these enzymes including carbamazepine, phenobarbital and phenytoin.

Administration

- If CSCI methadone causes a skin reaction, consider doubling the dilution and changing the syringe every 12 hours
- Use liquid preparations for administration via feeding tube. Absorption of methadone is unlikely to be affected by jejunal administration.

Available as

- Linctus (2mg/5ml), mixture (1mg/ml), oral solution (1mg/ml, 5mg/ml, 10mg/ml, and 20mg/ml), tablets (5mg), and injection (10mg/ml, 50mg/ml, 50mg/2 ml).

CD

- CD schedule 2.

Evidence: (2,3,8,10,120,120,222,222–233)

Methylnaltrexone

Use:

- Opioid-induced constipation when the response to other laxatives alone is inadequate and other relevant factors have been or are being addressed.

Dose and routes

By intermittent subcutaneous (or intravenous) bolus:

- **Child 1 month- 12 years or body weight less than 38kg**: 150micrograms/kg, maximum 8mg, as a single dose
- **Over 12 years, body-weight 38-61kg**: 8mg as a single dose
- **Over 12 years and body-weight over 61kg**: 12mg as a single dose

A single dose may be sufficient: repeat doses may be given with a usual administration schedule of a single dose every other day.

Doses may be given at longer intervals, as per clinical need.

Patients may receive 2 consecutive doses (24 hours apart) only when there has been no response (no bowel movement) to the dose on the preceding day.

Notes:

- μ-opioid receptor antagonist that acts exclusively in the peripheral tissues including the GI tract (increasing bowel movement and gastric emptying) and does not affect the central analgesic effects of opioids.

Licensing

- Not licensed for use in children or adolescents less than 18 years. Licensed for subcutaneous but not intravenous administration in adults.

Therapeutics

- Constipation in palliative care is usually multifactorial and other laxatives are often required in addition: continue all other laxative treatment.
- May also improve other peripheral effects of opioids, e.g. delayed gastric emptying, urinary retention. Case reports also suggest benefit in cholestatic pruritus.
- Does not cross blood brain barrier.
- Onset of action may be within 15-60 minutes: 30-50% patients have a bowel movement within 4 hours, without loss of analgesia.
- Has been used orally in adults, using a specially formulated tablet preparation, at doses of up to 450mg daily

Contraindications, cautions

- Contraindicated in known or suspected bowel obstruction other than that caused by opiate-induced constipation.

Side effects

- Common: abdominal pain/colic, diarrhoea, flatulence and nausea.

Renal impairment

- Reduce dose by 50% in severe renal impairment.

Administration

- Rotate the site of subcutaneous injection. Do not inject into areas where the skin is tender, bruised, red or hard.

Available as

- Single use vial 12mg/0.6ml solution for SC injection (Relistor®) Evidence: (2,3,216,234–237)

Metoclopramide

Use

- Prokinetic anti-emetic, in gastric compression or gastroparesis
- Hiccups

Dose and route:

By mouth, intramuscular, subcutaneous or slow intravenous injection

- **Child 1-18 years**: 100-150 microgram/kg repeated up to 3 times daily. The maximum dose in 24 hours is 500 microgram/kg (maximum 10 mg/dose; 30 mg daily).

Total daily dose may be administered as a continuous subcutaneous or intravenous infusion/24hours

Notes:

Licensing

- Not licensed for use in infants less than 1 year of age. Tablets not licensed for use in under 15 years (body-weight less than 61 kg). Not licensed for continuous infusion.

Therapeutics

- Efficacy comparable to domperidone in gastroparesis but higher incidence of adverse effects
- Use in palliative care only when alternative treatments do not work or cannot be used.
- Treatment should be limited to short term use (up to 5 days) if at all possible
- Has also been used in refractory hiccup not responsive to physical measures, or first line medication

Contraindications, cautions

- Contraindicated in children younger than 1 year, except in palliative care where no other alternative is available.
- Epilepsy: increased frequency and severity of epileptic seizures
- The EMA (2013) recommends that, due to the risk of neurological side effects, metoclopramide should only be used in children aged 1-18 as a second-line option for prevention of delayed chemotherapy-induced nausea and vomiting, and for treatment of established postoperative nausea and vomiting, and only when other treatments do not work or cannot be used.

Side effects

- Acute dystonic reactions including muscle spasms and oculogyric crises; children (especially girls, young women, and those under 10 kg) are particularly susceptible. Dystonic effects usually occur shortly after starting treatment and subside within 24 hours of discontinuation. Acute dystonic reactions can be effectively reversed using anticholinergics e.g. procyclidine and/or benzodiazepines e.g. diazepam.
- Neuroleptic malignant syndrome
- Risk of extrapyramidal effects is dose related and increased with co-administration of other drugs known to cause extrapyramidal effects

Administration

- Intravenous doses should be administered as a slow bolus over at least 3 minutes to reduce the risk of adverse effects.
- Oral liquid formulations should be given via a graduated oral syringe to ensure dose accuracy in children. The oral liquid may be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.

Available as

- Tablets (10mg), oral solution (5mg/5ml) and injection (5mg/ml).

Evidence: (1,2,8,238–240)

Metronidazole topically

Use:

- Reduction of odour caused by anaerobic bacteria associated with wounds or fungating tumours

Dose and route:

By topical application:

- Apply to clean wound 1–2 times daily and cover with non-adherent dressing.
- Cavities: smear gel on paraffin gauze and pack loosely.

Notes:

Licensing

- Off label use. Anabact® not licensed for use in children under 12 years.
- Metrogel® not licensed for use with children.

Administration

- Avoid eye area due to stinging.

Available as

- Cream and gel (Anabact® 0.75%, Metrogel® 0.75%).

Evidence: (1,2,241,242)

Miconazole oral gel

Use:

• Oral and intestinal fungal infection.

Dose and route:

Prevention and treatment of oral candidiasis

By mouth:

- **Neonate**: 1ml 2-4 times daily smeared around inside of mouth after feeds.
- **Child 1- 23 months**: 1.25 ml 4 times daily smeared around inside of mouth after food
- **Child 2 years and over:** 2.5 ml 4 times daily after meals

Continue treatment for at least 7 days after lesions have healed or symptoms have disappeared.

Prevention and treatment of intestinal candidiasis

By mouth:

- **Child 4 months and over**: 5mg/kg 4 times daily; max. 250mg (approximately 10 ml) 4 times daily.

Notes:

Licensing

- Not licensed for use in children under 4 months or during the first 5-6 months of life of an infant born preterm.
- Muco-adhesive tablet licensed in USA for child over 16 years.

Contraindications, cautions

- Contraindicated in infants with impaired swallow.

Interactions

- Increased INR/ bleeding has been reported with concomitant use of buccal miconazole and oral anticoagulants.

Administration

- Avoid applying near the back of the throat in infants and babies due to choking risk
- Retain in the mouth near lesions for as long as possible before swallowing.
- 50mg muco-adhesive buccal tablets should be applied to the upper gum just above the incisor tooth once daily for 7-14 days.
- Orthodontic appliances should be removed at night and brushed with gel.

Available as

- Oral gel (20mg per gram or 124mg per 5ml approximately 24mg/ml) in 15g and 80g tube, orange flavour. 15g oral gel can be brought over the counter

- A muco-adhesive buccal tablet of miconazole is now available. Indicated for the treatment of oropharyngeal candidiasis in immunocompromised adults, Loramyc®

Evidence: (1,2)

Midazolam

Use:

- Status epilepticus and terminal seizure control.
- Conscious sedation for procedures, to minimise awareness in terminal haemorrhage
- Management of anxiety/agitation associated with symptoms at the end of life.
- Anxiety associated with dyspnoea.
- Adjuvant for pain of cerebral irritation.
- Dystonia rescue

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Status epilepticus

<table>
<tr><th rowspan="2"></th><th>By buccal or intranasal route:</th><th>By subcutaneous or slow intravenous bolus injection</th><th rowspan="2">By continuous intravenous or subcutaneous infusion for seizure control at end of life</th></tr>
<tr><td colspan="2">Doses can be repeated once after an interval of at least 10 minutes</td></tr>
<tr><td>Neonate</td><td>300microgram/kg, maximum 1.25mg/dose</td><td rowspan="6">200micrograms/kg/dose maximum 10mg/dose</td><td>1mg/kg/24hours increasing gradually to a maximum of 7mg/kg/24hours</td></tr>
<tr><td>Child 1-2 months</td><td>300microgram/kg, maximum 2.5mg/dose</td><td rowspan="5">1mg/kg/24hours Increasing gradually to a maximum of 7mg/kg/24hours, maximum 60mg/24hours

Higher doses up to 150mg/24hours have been used. Seek specialist advice, and consider addition of other agents such as phenobarbital before increasing above 60mg/24hours.</td></tr>
<tr><td>3-11 months</td><td>2.5mg/dose</td></tr>
<tr><td>1-4 years:</td><td>5mg/dose</td></tr>
<tr><td>5-9 years:</td><td>7.5mg/dose</td></tr>
<tr><td>10 years and over</td><td>10mg/dose</td></tr>
</table>

Conscious sedation e.g. for procedures, or to minimise awareness in terminal haemorrhage

Doses can be repeated once after an interval of at least 10 minutes

	By buccal or intranasal route:	By subcutaneous or slow intravenous bolus injection	By mouth
Neonate	300microgram/kg, maximum 1.25mg/dose	200micrograms/kg/dose maximum 10mg/dose	500micrograms/kg/dose maximum 20mg
Child 1-2 months	300microgram/kg, maximum 2.5mg/dose		
3-11 months	2.5mg/dose		
1-4 years	5mg/dose		
5-9 years	7.5mg/dose		
10 years and over	10mg/dose		

Anxiety, agitation at end of life, cerebral irritation, dystonia rescue

Doses refer to ***starting*** doses only

Age range[a]	Buccal[b]	Oral[c]	Intravenous or subcutaneous bolus[d]	Continuous intravenous or subcutaneous infusion[e]
Neonate	75microgram/kg Initial maximum 300micrograms/dose As required 6 -8 hourly, maximum 2 hourly	150micrograms/kg Initial maximum 600micrograms/dose As required 6 -8 hourly, maximum 2 hourly	50micrograms/kg Initial maximum 200micrograms/dose As required 6 -8 hourly, maximum 2 hourly	200micrograms/kg /24hours Initial maximum 800micrograms/24hours
1-2 months (less than 5.5kg)	75microgram/kg Initial maximum 500micrograms/dose As required 4-6 hourly, maximum hourly	150micrograms/kg Initial maximum 1mg/dose As required 4-6 hourly, maximum hourly	50micrograms/kg Initial maximum 300micrograms/dose As required 4-6 hourly, maximum hourly	200micrograms/kg over 24hours Initial maximum 1.2mg/24hours
3-11 months (5.6-9.9kg)	500micrograms-1mg As required 4 hourly, maximum hourly	1.5mg As required 4 hourly, maximum hourly	50micrograms/kg Initial maximum 500micrograms/dose As required 4 hourly, maximum hourly	200micrograms/kg over 24hours Initial maximum 2mg/24hours
1-4 years (10-17kg)	1.5mg As required 4 hourly, maximum hourly	2.5mg As required 4 hourly, maximum hourly	50micrograms/kg Initial maximum 1mg/dose As required 4 hourly, maximum hourly	200micrograms/kg over 24hours Initial maximum 4mg/24hours
5-9 years (18kg-32kg)	2mg As required 4 hourly, maximum hourly	3.5mg As required 4 hourly, maximum hourly	50micrograms/kg Initial maximum 1.5mg/dose As required 4 hourly, maximum hourly	200micrograms/kg over 24hours Initial maximum 6mg/24hours
10 years and over (over 32kg)	2.5mg As required 4 hourly, maximum hourly	5mg As required 4 hourly, maximum hourly	50microgram/kg Initial maximum 2.5mg/dose As required 4 hourly, maximum hourly	200micrograms/kg over 24hours Initial maximum 10mg/24hours

[a] Aged based doses rounded to nearest 500micrograms for convenience of administration
[b] Based on 25% buccal seizure rescue dose
[c] Based on buccal bioavailability of 75% and oral bioavailability of 40%
[d] Based on 25% intravenous / subcutaneous seizure rescue dose
[e] Based on 4 x intravenous/subcutaneous dose for anxiety, agitation, breathlessness

Notes

Licensing

- The range of potential indications for midazolam in paediatric palliative care is very wide, but most are not licensed in infants or in children. See product literature.
- Oromucosal solution licensed only for seizure control in children 3 months of age and over. Midazolam injection is not licensed for oral or buccal administration. Midazolam injection licensed only for procedural sedation, anaesthesia and sedation in intensive care.

Therapeutics

- Doses above derived from standard doses for epilepsy via buccal and intravenous routes, taking into account recommendations in adult palliative care, and available information on bioavailability and pharmacokinetics in neonates, children and adults
- Dose recommendations in adult palliative care have been reduced over time due to recognition that lower doses were as effective and resulted in fewer adverse effects. Dose recommendations take this into account however it is important to recognise that the population of patients receiving palliative care in the adult sector is not typical of the paediatric palliative care population
- Pharmacology in children is complex and not well understood. Clearance is increased in sick patients particularly those ventilated on PICU. Tolerance/clearance may be higher in young adult males and in those already receiving other benzodiazepines and other drugs that may increase metabolism. If in doubt, start at the lowest recommended dose and titrate rapidly.
- In single dose for seizures, buccal midazolam is twice as potent as rectal diazepam. For patients who usually receive rectal diazepam for management of status, consider an initial dose of buccal midazolam that is 50% of their usual rectal diazepam dose to minimise the risk of respiratory depression
- Patients receiving midazolam by continuous infusion should continue to have buccal and/or bolus midazolam available as required for breakthrough symptoms. The background infusion can then be increased, no more often than every 12 hours, taking into account the requirement for breakthrough doses.
- Alternatively midazolam can be administered as a continuous patient controlled, patient-proxy controlled or nurse controlled infusion starting with a bolus dose equivalent to the hourly background rate and a lockout of between 5 and 15 minutes.
- Consider adding in an antipsychotic e.g. levomepromazine, before increasing midazolam above 600micrograms/kg/24hours or 30mg/24hours in agitation at end of life.

Cautions

- Caution in known hypersensitivity; renal failure; hepatic or cardiac impairment; neuromuscular respiratory weakness; pulmonary insufficiency.

Side effects

- Both high and low doses can lead to paradoxical agitation.

Pharmacokinetics

- Buccal bioavailability will be lower if some of the dose is swallowed: this is more likely when used for indications other than status epilepticus, or larger volumes
- Onset of action by buccal and intranasal route 5-15 minutes. Time to peak concentration 30 minutes. Half-life 2-5 hours.
- Onset of action by oral or gastrostomy route 10-30 minutes.
- Onset of action by IV route 2-3 minutes; SC route 5-10 minutes.
- Half-life may be shorter in patients on enzyme inducing drugs or those already receiving benzodiazepines

- Repeated dosing within an hour leads to increased peak and AUC (area under the plasma drug concentration-time curve)
- Half-life in neonates may be longer due to hepatic immaturity
- Half-life may be much longer in sick patients especially those with multi-organ system failure or critically ill on intensive care, and obese patients

Interactions

- Metabolised by cytochrome P450 enzyme CYP3A4. Levels increased by inhibitors of this enzyme including aprepitant, ciprofloxacin, erythromycin and fluconazole. Levels reduced by inducers of this enzyme including carbamazepine, phenobarbital and phenytoin
- Fatalities have occurred after concurrent administration with higher than approved doses of olanzapine
- The addition of a CYP3A4 inducer may reduce midazolam levels by ≤90%. Use of a different benzodiazepine is recommended if a moderate or potent inducer is essential
- Plasma concentrations of midazolam can be eight times higher after the addition of a CYP3A4 inhibitor. Midazolam doses may need to be reduced by ≥50%.

Administration

- For buccal administration, if possible, divide the dose so half is given into one cheek and the remaining half into the other cheek.
- Anecdotal reports of oral solution or injection administered via buccal route
- If enteral tube administration is indicated, the oral liquid or injection can be used.

Patient information

- See Medicines for Children leaflet “Midazolam for stopping seizures” https://www.medicinesforchildren.org.uk/medicines/midazolam-for-stopping-seizures/

Available as

- *Injection* (1mg/ml, 2mg/ml and 5mg/ml). *Oral solution* (5mg/ml Miprosed® and Thame generic and 2mg/ml Ozalin®). *Buccal liquid* Pre-filled oral syringes (strength 5mg/ml) available as 10mg in 2ml, 7.5mg in 1.5ml, 5mg in 1ml and 2.5mg in 0.5ml (e.g. Buccolam®, generics). Pre-filled oral syringes (strength 10mg/ml) available as 10mg in 1ml, 7.5mg in 0.75ml, 5mg in 0.5ml and 2.5mg in 0.25ml (e.g. Epistatus)
- Epistatus is also available as an unlicensed special in a 5ml multidose bottle (strength 10mg/ml) which is very useful when small doses are required
- Other oral and buccal liquids may also be available from ‘specials’ manufacturers or specialist importing companies (unlicensed)
- The buccal and oral formulations available differ in strengths-take care with prescribing and administration

CD

- CD Schedule 3 (CD No Register). Local protocols may require safe storage..

Evidence: (1–3,8,11,243–248)

Morphine

Use:

- Moderate to severe pain.
- Dyspnoea.

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in opioid naïve patients

Doses refer to ***starting*** doses only[a]

Age range	By mouth or per rectum	Intravenous or subcutaneous bolus	Intravenous or subcutaneous infusion/24hours
Neonate	80micrograms/kg/dose 6 hourly	40micrograms/kg/dose 6 hourly	160micrograms/kg/24hours
Child 1-2 months	120micrograms/kg/dose 6 hourly	60micrograms/kg/dose 6 hourly	240micrograms/kg/24hours
3-5 months	120micrograms/kg/dose 4 hourly	60micrograms/kg/dose 4 hourly	360micrograms/kg/24hours
6-23 months	200micrograms/kg/dose 4 hourly	80micrograms/kg/dose 4 hourly	480micrograms/kg/24hours
2-11 years	200-300micrograms/kg/dose maximum 10mg/dose 4 hourly	80-100micrograms/kg/dose maximum 5mg/dose 4 hourly	480-600micrograms/kg/24hours maximum 20mg/24hours
12 years and over	200micrograms/kg/dose maximum 10mg/dose 4 hourly *Alternatively* 5-10mg/dose, 4 hourly	80-100micrograms/kg/dose maximum 5mg/dose 4 hourly *Alternatively* 2.5-5mg/dose, 4 hourly	480-600micrograms/kg/24hours maximum 30mg/24hours *Alternatively* 20-30mg/24hours

Pain in patients already receiving regular strong opioids

Convert using oral morphine equivalent (OME) from previous opioid analgesia, if applicable, see Appendix 1

By mouth using modified release preparations

- Calculate the total daily dose (regular + PRN) of oral morphine administered over the previous 24 hours once the patient is established on regular morphine for 2-3 days

  12 hourly preparations: Divide the total daily dose of oral morphine by two and administer every 12 hours

  24 hourly preparations: Administer the total daily dose of oral morphine every 24 hours

  Ensure continued access to immediate release morphine as required for breakthrough pain see below

[a] Doses derived from primary research and cross referenced to BNFc ensuring age bands and dosing intervals are consistent, taking into account longer half-life in neonates and infants, equianalgesia, bio-availability via different routes, and ensuring consistent total daily dose across each age band

By continuous intravenous or subcutaneous infusion

- Calculate the total daily dose (regular + PRN) of oral morphine administered over the previous 24 hours

  Divide the total daily dose of oral morphine by ***three*** and administer by continuous infusion

  Ensure continued access to immediate release morphine as required for breakthrough pain see below

Breakthrough Pain in patients already receiving regular strong opioids

By mouth using immediate release preparations, or by intermittent intravenous or subcutaneous bolus

- 1/10 to 1/6 of total daily morphine dose every 1-4 hours as required.
- Remember to convert dose If a different route is used for breakthrough and background e.g. CSCI with oral for breakthrough

  Breakthrough and background (modified release, intravenous or subcutaneous infusion) doses should be reviewed if more than two breakthrough doses are required in a 24-hour period

Dyspnoea, cough suppressant

By mouth, subcutaneous or intravenous routes

- **Child 1 month and over:** 25-50% of pain doses

Notes:

- Strong opiate of first choice by mouth and for intravenous or continuous subcutaneous infusion

Licensing

- Oramorph® solution and MXL® capsules not licensed for use in children aged under 1 year. Sevredol ® tablets not licensed for use in children under 3 years. MST Continus® preparations licensed to treat children with cancer pain (age-range not specified by manufacturer). Actimorph® orodispersible tablets not licensed for use in children under 6 months.

Therapeutics

- Systematic review evidence suggests an equianalgesic oral to intravenous ratio of to 3:1 may be more appropriate than previously recommended ratio of 2:1.
- Some adult centres advocate giving patients on regular immediate release morphine a double dose of morphine immediate release at bed-time. This appears to be safe and reduces the likelihood of the patient waking overnight in pain.
- Can be used as a cough suppressant when treating the underlying cause is either not helpful or not possible and when other measures e.g. demulcents are not effective.
- Use ideal body weight (Appendix 7) when calculating doses in obese children
- In some circumstances, particularly opioid naïve patients at increased risk of adverse effects, it may be appropriate to start at lower doses, between $^{1}/_{10}$ and ½ of those quoted above, titrating according to response.

- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Cautions

- Caution in renal or hepatic impairment. Reduce dose and/or interval frequency. Avoid in severe
- renal impairment
- Avoid rectal administration in children with low platelets and/or neutropaenia.

Side effects

- Usual opioid side effects. Children may have a higher incidence of pruritus and urinary retention
- Toxicity often presents as myoclonic twitching.

Pharmacokinetics

- Oral absorption more variable and may be higher in neonates
- Orodispersible tablets are dissolved orally and swallowed: no significant buccal or sublingual absorption
- Higher volume of distribution in preterm and neonates especially days 2-5
- Converted to active metabolites by liver then excreted by kidneys: maturation to adult pharmacokinetics by approximately 6 months
- Clearance of morphine in some younger children may be higher than adults
- Some evidence suggests that area under time-concentration curve may be lower for subcutaneous rather than intravenous infusions. However APPM recommendation is to assume similar pharmacokinetics for intravenous and subcutaneous dosing.

Administration

- Oral solution can be administered undiluted via gastrostomy tube. Dilute with an equal volume of water for administration via a jejunostomy. Flush well to ensure total dose is delivered.
- Zomorph capsules can be opened to release the granules. The granules should not be crushed. Part doses should not be given as accuracy cannot be established. Zomorph granules can mixed with water for administration via an enteral feeding tube. The granules settle quickly in the syringe and care must be taken to deliver the complete dose. Zomorph granules can be administered via a 16Fr and above gastrostomy. Administration tubes as small as 8Fr without blockage has been reported. Caution would be advised in tubes of small diameter and a plan for unblocking the tube should be in place.
- MXL capsules can be opened and sprinkled on to food but are ***not*** suitable for administration via a feeding tube
- Morphine slow release tablets can be administered rectally.

Patient information

- See Medicines for Children leaflet “Morphine for pain” https://www.medicinesforchildren.org.uk/medicines/morphine-for-pain/

Available as

- *Tablets* (10mg-can be halved, 20mg, 50mg). Also available as *orodispersible tablets* (Actimorph®) 1mg, 2.5mg, 5mg, 10mg, 20mg, 30mg. Tablets should be placed on the tongue, and allowed to disperse before swallowing. Alternatively, tablets can be placed in a spoon and dispersed in a small amount of water before administration.
- *Oral solution* 10mg/5ml (Oramorph*)*, concentrated oral solution 100mg/5ml. An unlicensed lower strength oral solution 100micrograms/1ml is available from UK ‘specials’ manufacturers for accurate measurement of small doses especially in neonates.

- *Modified release tablets and capsules* Tablets12-hourly (5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg), modified release capsules 12-hourly (ZOMORPH 10mg, 30mg, 60mg, 100mg, 200mg), modified release capsules 24-hourly (30mg, 60mg, 90mg, 120mg, 150mg, 200mg).
- *Suppositories* (10mg): other strengths may be available from specials manufacturers.
- *Injection* (1mg/ml, 10mg/ml, 15mg/ml, 20mg/ml and 30mg/ml).

CD

- CD Schedule 2 except morphine oral solution10mg/5ml and neonatal morphine solution 100micograms/ml

Evidence: (1–3,8,11,61,62,115,117,249)

Nabilone

Use:

- Nausea and vomiting caused by cytotoxic chemotherapy (not first or second line therapy).
- Nausea and vomiting unresponsive to conventional antiemetics.
- Management of upper gastrointestinal symptoms in gut dystonia.

Dose and route:

By mouth:

- **Child less than 18 kg**: 500micrograms twice daily
- **Child 18- 30 kg**: 1mg twice daily
- **Child over 30 kg**: 1mg three times daily
- **Adult:** 1–2mg twice daily (maximum dose 6mg/day in 2-3 divided doses)

Notes:

- Synthetic cannabinoid.

Licensing

- Not licensed for use in children.

Therapeutics

- Specialist use only. Response varies between patients requiring close medical supervision on commencement and dose adjustments. Effects may persist for a variable and unpredictable period of time following oral administration.

Side effects

- Somnolence, dizziness and abdominal pain
- Adverse psychiatric reactions can persist for 48-72 hours following cessation of treatment.
- Decreased or increased appetite

Hepatic impairment, renal impairment

- Avoid in severe hepatic impairment.

Administration

- No information available regarding administration via enteral feeding tubes

Available as

- Capsules (250 micrograms, 1mg).

CD

- Schedule 2 CD. Evidence: (1–3,250,251)

Naloxone

Use:

- Emergency reversal of life threatening opioid-induced respiratory depression or opioid overdose.

Dose and route:

***Partial* reversal of respiratory depression due to acute opioid overdose**

When there is risk of acute opioid withdrawal or when a continued therapeutic effect is required By intravenous injection:

Doses approximately equal to twice the intravenous dose can be given subcutaneously or intramuscularly if intravenous access is not available, but slower onset of action

- **Neonate, child 1 month-11 years**: 1–10micrograms/kg, maximum 200micrograms per dose

  Then, if no response, repeat at intervals of 1 minute up to 5 times

  Then, if still no response, single dose of 100micrograms/kg (maximum dose 2mg)

- **12 years and over:** 100–200micrograms per dose

  Then, if no response, 100micrograms at 1 minute intervals for up to 2 doses Then, if still no response continue titrating up to a maximum of 2mg per dose

- If still no response, give a further 2mg dose: 4mg dose may be required in seriously compromised patients

Review diagnosis if still no response. Further doses, or infusion, may be required if respiratory function deteriorates following initial response.

By continuous intravenous infusion

Continued partial reversal of respiratory depression due to acute opioid overdose e.g. for long acting opioids

- 60% of the initial effective dose per hour, rate adjusted according to response

  Initial effective dose is that which maintained satisfactory self-ventilation for 15 minutes.

***Complete* reversal of respiratory depression due to acute opioid overdose**

By intravenous injection:

Doses approximately equal to twice the intravenous dose can be given subcutaneously or intramuscularly if intravenous access is not available, but slower onset of action

- **Neonate, child 1 month-11 years**: 100micrograms/kg.

  Then, if no response repeat at intervals of 1 minute to a maximum of 2mg

- **12 years and over:** initially 400micrograms.

Then, if no response, 800micrograms at 1 minute intervals for up to 2 doses

Then, if still no response, 2mg for 1 dose: 4mg dose may be required in seriously compromised patients.

Further doses, or infusion, may be required if respiratory depression deteriorates following initial response

By intranasal route

- **Child body-weight 9kg and over:** 1.8 mg, administered into one nostril Repeat dose into alternate nostril if no response after 2-3 minutes.

  Repeat dose immediately if initial response is followed by further respiratory depression. Administer into alternate nostrils.

By continuous intravenous infusion

Continued complete reversal of respiratory depression due to acute opioid overdose e.g. for long acting opioids

- 60% of the initial resuscitative dose per hour, rate adjusted according to response

  Initial resuscitative dose is that which maintained satisfactory self-ventilation for 15 minutes.

Notes

- Potent opioid antagonist.

Licensing

- Intranasal spray not licensed for children below 14 years; limited experience in children.

Therapeutics

- In some circumstances temporary discontinuation of strong opioids together with close observation may be sufficient, rather than proceeding immediately to opioid reversal
- May have a role in reversal of clonidine toxicity.

Side effects

- Arrhythmias, dizziness, headache, hypertension, hypotension, nausea and vomiting.

Pharmacokinetics

- Short duration of action; repeated doses or infusion may be necessary to reverse effects of opioids with longer duration of action.
- Naloxone acts within 2 minutes of IV injection and within 3-5 minutes of SC or IM injection.
- Intranasal bioavailability approximately 50% *depending on formulation Available as*
- Injection (20micrograms/ml, 400micrograms/ml, 21mg/2ml) and nasal spray 1.8m/0.1ml.

Evidence: (1,2,104,252–258)

Naproxen

Use:

- Non-steroidal anti-inflammatory analgesic
- Relief of symptoms in inflammatory arthritis and treatment of acute musculoskeletal syndromes

Dose and route:

By mouth

- **Child 2 years and over**: 5-7.5mg/kg/dose twice daily (maximum 1g/ day)

  Doses up to 10mg/kg twice daily (not exceeding 1g daily) have been used. Use the lowest effective dose for the shortest treatment duration possible.

Notes:

Licensing

- Licensed for use from 5 years of age for juvenile idiopathic arthritis; not licensed for use in children less than 16 years for other conditions.

Therapeutics

- Generally regarded as combining good efficacy with a low incidence of side effects.
- Anti-pyretic and anti-inflammatory actions may reduce fever and inflammation therefore reducing their utility as diagnostic signs.

Contraindications, cautions

- Contraindicated in patients with a history of hypersensitivity to any NSAID or in those with a coagulation disorder.
- May mask fever and other signs of inflammation
- Caution in cardiac, hepatic or renal impairment and those with asthma
- Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure

Side effects

- All NSAID use can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factors or duration of NSAID use. The greatest risk may be in those receiving high doses long term. Risks have not been quantified in children.
- All NSAIDs are associated with serious gastro-intestinal toxicity. Naproxen is associated with an intermediate risk of gastro-intestinal toxicity. Consider prescription of a proton pump inhibitor with prolonged use.

Hepatic impairment, renal impairment

- Use with caution in renal, cardiac or hepatic failure as this may cause a deterioration in renal function; the dose should be kept as low as possible and renal function monitored. Avoid in GFR <20ml/min/1.73m2 and in those with severe hepatic or cardiac failure.

Administration

- For administration via an enteral feeding tube, using the oral suspension or effervescent tablets. Enteric coated naproxen tablets should be swallowed whole and NOT be crushed or chewed. Naproxen should be taken with or after food.

Available as

- Tablets 250mg and 500mg; effervescent tablets 250mg; enteric coated tablets 250mg, 375mg and 500mg; oral suspension 125mg/5ml, 25mg/ml, 50mg/ml.

Evidence: (1–3,8)

Nitrous oxide (Entonox®)

Use:

- As self-regulated analgesia without loss of consciousness e.g. painful dressing changes
- Not suitable for use outside of an acute healthcare setting

Dose and route:

By inhalation:

- **Child 2 years and over**: Up to 50% to be administered using suitable anaesthetic apparatus in oxygen adjusted according to the patient's needs. Self-regulated use usually over 5 years of age.

Notes:

Therapeutics

- Normally used as a light anaesthetic. Rapid onset and then offset.
- Training, governance and supply implications may limit application in hospice settings.

Contraindications, cautions

- Contraindicated in the presence of pneumothorax or intracranial air after head injury.

Side effects

- Risk of hypoxia immediately after administration: administer supplementary oxygen for several minutes following administration.
- Prolonged exposure (including environmental exposure to relatives) by continuous or intermittent administration may result in megaloblastic anaemia. Consider assessment of plasma vitamin B12 concentration. Depression of white cell formation may also occur. Neurological toxicity may occur without preceding overt haematological changes.
- Consider assessment of plasma vitamin B12 concentration in children at risk of deficiency.

Interactions

- Avoid concomitant use with methotrexate: increased antifolate effect.
- Risk of enhanced hypotensive effect with a number of medications. Administration
- Should only be used as self-administration using a demand valve; all other situations require a specialist paediatric anaesthetist.

Patient information

- See Medicines for Children leaflet "Nitrous oxide for pain" https://www.medicinesforchildren.org.uk/medicines/nitrous-oxide-for-pain/

Available as

- Nitrous oxide 1ml per 1ml various sizes of cylinders available from medical gas suppliers Linde Gas UK and BOC Ltd. See BNFC for additional information.

Evidence: (1,259–261)

Nystatin

Use:

- Oral and perioral fungal infection.

Dose and route:

By mouth:

- **Neonate**: 100,000 units 4 times daily
- **Child 1-23 months**: 100,000-200,000 units 4 times daily
- **2 years and over:** 100,000-600,000 units 4 times daily

Notes:

Licensing

- Licensed for use in all ages. Licensed for prophylaxis against oral candidiasis in neonates at a dose of 1ml daily.

Therapeutics

- Treatment for 7 days and should be continued for 48 hours after lesions have healed.
- Higher doses allow greater mucosal contact and may therefore be more effective.

Administration

- Retain near lesions before swallowing.

Side effects

- Abdominal discomfort; angioedema; diarrhoea; facial oedema; nausea; sensitisation; skin reactions; Stevens-Johnson syndrome; vomiting
- Administer after food or feeds. If possible divide the dose between both sides of the mouth.

Available as

- Oral suspension 100,000 units/ml, 30ml with pipette.

Evidence: (1–3)

Octreotide

Use:

- Bleeding from oesophageal or gastric varices.
- Nausea and vomiting.
- Inoperable intestinal obstruction.
- Intractable diarrhoea.
- Hormone secreting tumours, ascites, bronchorrhoea.
- Chylothorax
- Hyperinsulaemic hypoglycaemia (specialist use)

Dose and route:

Gastrointestinal bleeding, chylothorax (NEW)

By continuous intravenous or subcutaneous infusion

- **Child 1 month and over**: 1microgram/kg/*hour*

  Higher doses may be required initially and for chylothorax. Usual maximum dose is 50micrograms/*hour*

  Reduce dose gradually over 24hours once there is no active bleeding.

Antiemetic, antisecretory, intractable diarrhoea, intestinal obstruction

By continuous intravenous or subcutaneous infusion

- **Child 1 month and over**: 5-10micrograms/kg/24hours. Usual maximum 750microgams/24hours

  Doses up to 30micrograms/kg/24hours may be required in intractable diarrhoea.

Hyperinsulaemic hypoglycaemia unresponsive to diazoxide and glucose (specialist use) (NEW)

By subcutaneous injection

- **Neonate**: Initially 2–5micrograms/kg every 6–8 hours, adjusted according to response; increased if necessary up to 7micrograms/kg every 4 hours, dosing up to 7micrograms/kg may rarely be required.
- **Child 1 month and over**: Initially 1–2micrograms/kg every 4–6 hours, adjusted according to response; increased if necessary up to 7micrograms/kg every 4 hours, dosing up to 7micrograms/kg may rarely be required.

Notes:

- Synthetic somatostatin analogue

Licensing

- Not licensed for use in children.

Therapeutics

- Acts as an inhibitory hormone throughout the body but particularly the gastro-enterohepatic system, increasing water and electrolyte absorption.
- Avoid abrupt withdrawal: may be associated with biliary colic and pancreatitis.
- May impair glucose tolerance: consider monitoring blood glucose.
- Rotate injection sites

Administration

- Dilute with sodium chloride 0.9% for intravenous injection and intravenous or subcutaneous infusion. Check the manufacturer's recommendations regarding dilution. Subcutaneous bolus injections may be administered undiluted but this can be painful (this can be reduced if the ampoule is warmed in the hand to body temperature before injection).

Available as

- Injection for subcutaneous or intravenous administration (50micrograms/ml, 100micrograms/ml, 200micrograms/ml, 500micrograms/ml, 1mg/5ml). Also available as depot injection for intramuscular administration every 28 days (10mg, 20mg and 30mg SandostatinLar®).

Evidence: (1–3,262–265)

Olanzapine

Use:

- Psychoses; delirium; agitation; anorexia when all other treatments have failed.
- Nausea and vomiting.

Dose and route:

Psychoses, mania

By mouth

- **Child under 12 years and up to 25kg**: Initial dose 2.5mg at night
- **Child under 12 years and greater than 25kg**: Initial dose 2.5-5mg at night.
- **12 years and over**: initial dose 5mg at night.

Increase gradually as necessary and as tolerated to a maximum of 20mg/day given usually as a single dose at night. Can be given as twice daily dose if needed.

Agitation, delirium

By mouth

- **Child under 12 years**: Initial dose 1.25mg at night and as required,
- **12 years and over**: Initial dose 2.5mg at night and as required. Increase gradually as necessary and as tolerated to maximum 10mg/day

Nausea and vomiting, anorexia

- **Child under 12 years**: Initial dose 1.25mg (or 625micrograms if 2.5mg tablets can be cut into quarters) at night and as required
- **12 years and over**: Initial dose 1.25mg-2.5mg at night and as required.

Dose may be increased as necessary and as tolerated to a suggested maximum of 7.5mg/day.

Notes:

- Atypical (second generation) antipsychotic agent and antagonist of dopamine D1, D2, D4, 5-HT2, histamine-1-, and muscarinic-receptors.

Licensing

- Not licensed for use in children and adolescents less than 18 years of age although there is general acknowledgement of 'off-label' use in adolescents for the treatment of psychosis and schizophrenia and mania associated with bipolar disorder.
- Use in the treatment of agitation, delirium, nausea and vomiting and anorexia in palliative care are all 'off-label' indications.

Therapeutics

- Five times greater affinity for $5HT_2$ receptors than for D2 receptors, resulting in fewer extrapyramidal side effects.
- Activity at multiple receptors is similar to levomepromazine.
- Titrate dose slowly to minimise sedation.
- Adolescents may be more susceptible to weight gain
- Elevated lipid and prolactin levels. Consider monitoring before and during long term use
- Onset of action is hours-days in delirium; days-weeks in psychoses.

Contraindications, cautions

- Caution in cardiovascular disease. Caution in epilepsy and conditions predisposing to seizures: lowers seizure threshold

Side effects

- Very common (> 10% patients) side effects: weight gain; elevated triglyceride levels; increased appetite; sedation; increased ALT and AST levels; decreased bilirubin; increased GGT and plasma prolactin levels. Common (1-10% patients) side effects: elevated cholesterol levels; dry mouth.
- Rare but potentially serious adverse effects include neuroleptic malignant syndrome, cardiovascular disease, severe respiratory disease and bone marrow depression, hepatitis, pancreatitis and hyperglycaemia.

Hepatic impairment, renal impairment

- Consider lower starting dose (maximum 5mg in adults) in patients with renal and/or hepatic impairment.

Interactions

- Metabolised by CYP1A2. Pharmacokinetics may be affected by co-administration of other substances using this isoenzyme e.g. carbamazepine, fluvoxamine, nicotine.

Administration

- Orodispersible tablets can be dissolved in a drink immediately before oral administration.
- Orodispersible tablets can be dissolved in water for administration via feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy. Anecdotal reports that 5mg orodispersible tablets may be halved to give a 2.5mg dose: halve immediately before administration and discard the remaining portion.
- Coated tablets: swallow whole with liquid or crushed and mixed with soft food. Orodispersible tablets contain aspartame and may be harmful for people with PKU.

Patient information

- Patient information see Medicines for Children leaflet “Olanzapine for schizophrenia bipolar disorder mania and agitation https://www.medicinesforchildren.org.uk/medicines/olanzapine-for-schizophrenia-bipolar-disorder-mania-and-agitation/

Available as

- Tablets 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg; orodispersible tablets / lyophilisate, 5mg, 10mg, 15mg, 20mg.

Evidence: (1,2,87,266,267)

Omeprazole

Use:

- Gastro-oesophageal reflux.
- Acid related dyspepsia.
- Gastrointestinal prophylaxis (e.g. with NSAID or steroids).
- Treatment of duodenal and gastric ulcers.

Dose and route:

By mouth:

- **Neonate**: 700micrograms/kg once daily; increase if necessary to a maximum of 1.4mg/kg-2.8mg/kg once daily
- **Child 1 month-1 year**: 700micrograms/kg once daily; increase if necessary to a maximum of 3mg/kg or 20mg once daily
- **Child 10-19 kg**: 10mg once daily, increase if necessary to a maximum of 20mg once daily
- **20 kg and above**: 20mg once daily, increase if necessary to a maximum of 40mg once daily.

By intravenous infusion (over 20-30 minutes)

- **Child 1 month-11 years**: initially 500micrograms/kg, maximum 20mg/dose, once daily. Increase if necessary, to 2mg/kg, maximum 40mg/dose, once daily.
- **12 years and over**: 40mg once daily.

Notes:

- Proton pump inhibitor

Licensing

- Oral formulations are not licensed for use in children except for severe ulcerating reflux oesophagitis in children > 1 year. Infusion not licensed for use in children under 12years.

Therapeutics

- Many children with life limiting conditions have gastro-oesophageal reflux disease and may need to continue with treatment long term.

Side effects

- May cause agitation. Occasionally associated with electrolyte disturbance.
- MHRA safety warning 2015: very low risk of subacute cutaneous lupus erythematosus associated with use of PPIs.
- Constipation, diarrhoea, vomiting

Interactions

- Inhibits cytochrome P450 enzyme CYP2C19. May increase levels of drugs metabolised by this enzyme including diazepam.
- Metabolised by CYP2C19 and CYP3A4. Levels may increased by drugs that inhibit these enzymes including fluconazole.

Administration

- For oral administration tablets can be dispersed in water or mixed with fruit juice or yoghurt. Capsules can be opened and mixed with fruit juice or yoghurt.
- Administer with care via enteral feeding tubes to minimise risk of blockage. Capsules may be opened and contents dispersed in 8.4% sodium bicarbonate for administration. Dispersible tablets disintegrate to give a dispersion of small granules. The granules settle quickly and may block fine-bore feeding tubes (less than 8Fr). For administration via small bore tubes use of an oral suspension (unlicensed) is recommended. Omeprazole is absorbed when administered into the jejunum with no reduction in bioavailability. Choice of formulation depends on the size of tube.
- Intermittent subcutaneous administration has been reported at doses equivalent to the intravenous route, diluted to a concentration of 400micrograms/ml in sodium chloride 0.9%

Patient information

- Patient information see Medicines for Children leaflet “Omeprazole for gastro-oesophageal reflux disease (GORD)” https://www.medicinesforchildren.org.uk/medicines/omeprazole-for-gastro-oesophageal-reflux-disease-gord/

Available as

- Gastroresistant tablets (MUPS) tablets (10mg, 20mg, 40mg), capsules (10mg, 20mg, 40mg), intravenous infusion (40mg). Oral suspensions of strengths 10mg/5ml and 20mg/5ml are now available as licensed products in the UK. Other formulations of unlicensed oral suspensions are currently still available from UK ‘specials’ manufacturers.

Evidence: (1–3,8,130,131,268)

Ondansetron

Use:

- Antiemetic, particularly in vomiting caused by damage to gastrointestinal mucosa (e.g. chemotherapy or radiotherapy, severe gastroenteritis)
- Adjunct to levomepromazine in severe nausea and vomiting
- Opioid induced pruritus

Dose and route:

Prevention and treatment of chemotherapy and radiotherapy-induced nausea and vomiting

By intravenous infusion over at least 15 minutes

- **Child 6 months and over**: 5mg/m^2 or 150micrograms/kg immediately before chemotherapy maximum 8mg/dose.

  Dose can be repeated every 4 hours for 2 further doses before changing to oral route. Alternatively change to oral route after initial intravenous dose. Maximum total daily dose 32mg by any route

By mouth following intravenous administration

Oral dosing can start 12 hours after intravenous administration

- **Child 6 months and over:**

  Surface area less than 0.6m^2 or less than 10kg: 2mg every 12 hours for up to 5 days, maximum total daily dose 32mg

  Surface area 0.6m^2-1.2m^2 or 10- 40kg: 4mg every 12 hours for up to 5 days, maximum total daily dose 32mg

  Surface area over 1.2m^2 or over 40kg: 8mg every 12 hours for up to 5 days, maximum total daily dose 32mg

Nausea and vomiting, pruritus

By mouth or slow intravenous injection over 2-5 minutes or by intravenous infusion over 15 minutes

- **Child 6 months and over**: 100-150micrograms/kg/dose every 8 -12 hours, maximum 8mg/dose

Notes:

- Serotonin ($5HT_3$) receptor antagonist

Licensing

- Injection licensed for the management of chemotherapy-induced nausea and vomiting in children over 6 months, and for the prevention and treatment of post-operative nausea and vomiting in children (as a single dose) from 1 month. Oral ondansetron licensed from 6 months of age for the management of chemotherapy-induced nausea and vomiting. Oral formulation not

recommended for post-operative nausea and vomiting in children due to a lack of data. Injection is not licensed for subcutaneous administration.

Therapeutics

- Pure $5HT_3$ antagonist, so receptor profile is complementary to levomepromazine. Consider for nausea and vomiting not controlled by regular levomepromazine.

Contraindications, cautions

- Contraindicated in patients with congenital long QT syndrome
- Prolongs QT-interval and associated with known risk of Torsades de Pointes even when taken as recommended. Caution in patients with cardiac disease and those with, or at risk of, prolonged QT-interval e.g. those with cardiac abnormalities, hypothyroidism, electrolyte imbalance or taking other drugs known to prolong the QT-interval

Side effects

- Powerfully constipating. Headache is a common adverse effect
- Possible side effects include nausea, vomiting, sweating and intestinal colic

Pharmacokinetics

- Decreased clearance in neonates (75%) in neonates and infants (50% at 3 months). Monitor closely if administered to children under 6 months. Consider increasing dosing interval and reducing dose.
- Onset of action oral less than 30 minutes, intravenous less than 5 minutes and duration 12 hours

Administration

- Orodispersible films should be placed on the tongue and allowed to disperse before swallowing. NB absorption of active drug does NOT occur via the oral mucosa, it is dependent on the dispersed tablet being swallowed
- For intravenous infusion, dilute to a concentration of 320–640micrograms/ml with dextrose 5% or sodium chloride 0.9% or Ringer's solution; give over at least 15 minutes.
- Oral solution contains sorbitol.
- Oral solution may be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Case reports of administration by continuous subcutaneous infusion, diluted in sodium chloride 0.9% at concentrations of between 100micrograms/ml and 2mg/ml. Ondansetron injection has a low (acidic) pH and the formulation may cause localised site reactions particularly at higher concentrations.

Available as

- Tablets (4mg, 8mg, orodispersible films/tablets (4mg, 8mg), oral solution (4mg/5ml, 8mg/5ml), injection (2mg/ml, 2ml and 4ml amps).

Evidence: (1,2,11,32,269–273)

Oxybutynin

Use:

- Neurogenic or overactive bladder
- Symptomatic treatment of urinary incontinence, urgency and frequency in the unstable bladder whether due to neurogenic bladder disorders or idiopathic detrusor instability

Dose and route:

By mouth

Using immediate release preparation

- **Child up to 2 years**: 100-200micrograms/kg/dose 2-3 times daily. Maximum 12.5mg/dose
- **2-4 years**: 1.25-2.5mg/dose 2-3 times daily
- **5-11 years**: initial dose 2.5-3mg/dose twice daily, increasing to 5mg 2-3 times daily if needed
- **12 years and over**: initial dose 5mg/dose 2-3 times daily, increasing up to 5mg 4 times daily if needed

Using modified-release preparation

- **Child 5 years and over**: 5mg once daily adjusted, according to response, in increments of 5mg every week to a maximum of 15mg daily

Transdermal

Using Kentera® matrix patch

Approximate equivalent doses (see also notes below)

Oral oxybutynin 2.5–5mg/24hours	≡	¼ patch (1.3mg/24hours) twice weekly
Oral oxybutynin 5-10mg/24hours	≡	½ patch (2.6mg/24hours) twice weekly
Oral oxybutynin 10-15mg/24hours	≡	1 patch (3.9mg/24hours) twice weekly

Intravesical

- **Child 2 years and over**: 5mg 2-3 times daily

Notes:

- Antispasmodic with direct effect on smooth muscle and also inhibits the action of acetylcholine on smooth muscle. Increases bladder capacity, decreases uninhibited contractions and delays desire to void therefore decreasing urgency and frequency

Licensing

- Oral oxybutynin is not licensed for use in children less than 5 years of age. Intravesical and transdermal routes are not licensed in children. Intravesical formulation is unlicensed. Cutting patches is outside product licence

Therapeutics

- Transdermal administration of oxybutynin substantially bypasses the extensive first-pass metabolism that occurs with oral administration, reducing the formation of N-desethyloxybutynin (reducing systemic exposure to the active metabolites with a suggested reduction in incidence of adverse effects)
- An exact pharmacodynamic comparison between immediate release oxybutynin and transdermal oxybutynin is not possible due to their metabolic profiles being very different. There is no study of the therapeutic equivalence of immediate release oxybutynin and transdermal oxybutynin. The suggested starting point in dosing is derived from past efficacy response and is not exact because disease syndrome, patient response and acceptability is very diverse and unpredictable. Individual patient titration upwards or downwards is warranted to obtain the best therapeutic response.

Contraindications, cautions

- Contraindicated in myasthenia gravis, glaucoma, gastrointestinal obstructive disorders including paralytic ileus or intestinal atony, toxic megacolon, severe ulcerative colitis, bladder outflow obstruction
- Young children may be more sensitive to the adverse effects of oxybutynin, particularly the CNS and psychiatric adverse reactions.

Adverse Effects

- Common adverse effects due to antimuscarinic properties include: confusion, constipation, dizziness, drowsiness, dry mouth, dyspepsia, flushing, headache, nausea and vomiting, palpitations, tachycardia, blurred vision. Oral solutions containing sorbitol may cause diarrhoea

Renal Impairment and hepatic impairment

- Use with caution due to limited experience. Possible increased risk of adverse effects

Pharmacokinetics

- Transdermal: following application of the patch, oxybutynin plasma concentration increases for ~24-48 hours; steady state concentrations are reached during application of the second patch. Thereafter, steady concentrations are maintained for up to 96 hours

Interactions

- Increased risk of anticholinergic side effects with concurrent use of other anticholinergics
- By reducing gastric motility, oxybutynin may affect the absorption of other drugs and antagonise the effect of prokinetic medication

Administration

- Tablets should be swallowed whole to avoid unpleasant taste
- Apply patches should be applied to dry, intact skin on the abdomen, hip or buttock immediately after removal from the protective sachet. A new application site should be used with each new patch (do not reapply to same site within 7 days).
- Patches can be cut without affecting the mechanism, rate or amount of oxybutynin released. Transdermal patch may contain metal-remove patch prior to MRI
- Intravesical-after emptying the bladder, administer intravesical solution directly into the bladder via a catheter
- Use liquid formulation for administration via a feeding tube. Alternatively immediate release tablets may be crushed immediately prior to administration. Oxybutynin immediate release tablets may be crushed and mixed with water for administration via an enteral feeding tube. Flush well after administration. No specific data for jejunal administration: suggest administration as for gastrostomy, using liquid preparation, and monitor for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children Leaflet “Oxybutynin for daytime urinary symptoms” https://www.medicinesforchildren.org.uk/medicines/oxybutynin-for-daytime-urinary-symptoms/

Available as

- Immediate release tablets: 2.5mg, 3mg, 5mg. Modified-release tablets: 5mg, 10mg. Oral solution: 2.5mg in 5ml, 5mg in 5ml. Intravesical solution is available as an unlicensed special. Transdermal patches: patches contain 36mg of oxybutynin and release 3.9mg oxybutynin per 24 hours (Kentera®)

Evidence: (1–3,8,274–284)

Oxycodone

Use:

- Alternative opioid analgesic for severe pain

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in patients already receiving regular strong opioids

Convert using oral morphine equivalent (OME) from previous opioid analgesia, if applicable, see Appendix 1

By mouth using immediate release preparations

Conversion		Ratio	Calculation	Example
From	To			
Morphine oral	Oxycodone oral	2:1	Divide morphine oral dose by 2	Morphine oral 20mg ÷ 2 = oxycodone oral 10mg

Consider reducing the dose of oxycodone by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation

By mouth using modified release preparations

- Use oral morphine equivalent (as above) to convert current doses of previous opioid analgesia, if applicable, *then*
- Calculate the total daily dose (regular + PRN) of oral oxycodone administered over the previous 24 hours once the patient is established on regular strong opioid analgesia for 2-3 days

  12 hourly preparations: Divide the total daily dose of oral oxycodone by two and administer every 12 hours

  24 hourly preparations: Administer the total daily dose of oral oxycodone every 24 hours

  Ensure continued access to immediate release oxycodone as required for breakthrough pain see below

By single intravenous or subcutaneous bolus injection

Conversion		**Ratio**	**Calculation**	**Example**
From	**To**			
Oxycodone oral single dose	Oxycodone SC or IV bolus single dose	1:5:1	Divide oxycodone oral dose by 1.5	Oxycodone oral 4.5mg ÷ 1.5 = Oxycodone IV/SC *bolus* 3mg

Consider reducing the dose of oxycodone by ¼-½ when the patient is already on a high dose of the previous opioid, when rotating due to intolerable side effects or when there has been a recent rapid escalation of the previous opioid

By continuous intravenous or subcutaneous infusion

Conversion		**Ratio**	**Calculation**	**Example**
From	**To**			
Morphine oral	Oxycodone CSCI or CIVI	3:1	Divide 24hour morphine dose by 3	Morphine oral 60mg/24hour ÷ 3 = oxycodone CSCI 20mg/24hours
Oxycodone oral	Oxycodone CSCI or CIVI	1.5:1	Divide 24hour dose of oral oxycodone by 1.5	Oxycodone oral 90mg/24hours ÷1.5 = oxycodone CSCI 60mg/24hours
Morphine CSCI or CIVI	Oxycodone CSCI or CIVI	1:1	Use the same dose	Morphine CSCI 50mg/24h = oxycodone CSCI 50mg/24hours

Consider reducing the dose of oxycodone by ¼-½ when the patient is already on a high dose of the previous opioid, when rotating due to intolerable side effects or when there has been a recent rapid escalation of the previous opioid

Breakthrough pain in patients already receiving opioids

By mouth using immediate release preparations, or by intermittent intravenous or subcutaneous bolus

- 1/10-1/6 of total daily oxycodone dose every 4-6 hours as required.

  Breakthrough and background (modified release, intravenous or subcutaneous infusion) doses should be reviewed if more than two breakthrough doses are required in a 24-hour period

Pain in opioid naïve patients

Opioid naive patients: the maximum dose stated applies to starting dose only By mouth using immediate release preparations:

- **Child 1 month-11 years**[a]: Initial dose 100micrograms/kg, maximum single dose 5mg, every 4 -6 hours, increase as necessary according to severity of pain.
- **12 years and over**: Initial dose 5mg every 4-6 hours, increase as necessary according to severity of pain.

Notes:

- Opioid analgesic with similar efficacy and side effects to morphine. Generally, only appropriate for patients intolerant of morphine.

Licensing

- Not licensed for use in children less than 12 years of age. Available in combination with naloxone as alternative to laxative therapy in opioid-induced constipation Targinact® (Napp) not licensed in children.

Therapeutics

- Like morphine, oxycodone is primarily a Mu opioid receptor agonist. However, differences in structure mean that it may be effective for opioid substitution
- No neonatal dose available
- Reason behind odd conversion ratio is bioavailability and rounding factors for safety
- Strong oral solution has been used sublingually in adults
- Injection solution has been administered in children via sublingual and buccal routes. Doses equivalent to those given by mouth appear to be effective with similar onset of action and bioavailability: it is unclear how much of the drug is being absorbed via the transmucosal route and how much is being swallowed.
- Modified release preparations have also been administered via the rectal route
- Oral bioavailability may be lower in younger children and infants
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Cautions

- Caution in hepatic or renal impairment.

[a] Dose modified from BNFc taking into account APPM recommendations for morphine and equianalgesia

Side effects

- Usual opioid side effects

Interactions

- Metabolised by cytochrome P450 enzymes CYP2D6 and CYP3A4. Levels increased by drugs that inhibit these enzymes including celecoxib, ciprofloxacin, erythromycin and fluconazole. Levels reduced by drugs that induce these enzymes including carbamazepine and phenobarbital.

Administration

- Oxycodone injection may be given IV or SC as a bolus or by infusion. For CSCI, dilute with water for injection, 0.9% sodium chloride or 5% dextrose.
- Oxycodone liquid may be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administration as for gastrostomy and monitor for increased side effects or loss of efficacy.
- Modified release tablets are available as 12-hourly and 24-hourly preparations. Care with prescribing and do not confuse brands.

Available as

- Capsules (5mg, 10mg, 20mg), tablets (5mg),
- Oral solution (5mg/5 ml, 10mg/ml)
- Modified release tablets ***12-hourly*** (5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg),
- Modified-release tablets ***24-hourly*** (10mg, 20mg, 40mg, 80mg)
- Injection (10mg/ml and 50mg/ml).

CD

- CD Schedule 2

Evidence: (1–3,8,62–64,71,72,113,285–287)

Oxygen

Use

- Breathlessness caused by hypoxaemia
- Pulmonary Hypertension
- Placebo effect for dyspnoea, especially where family feels need to intervene promptly
- Alternative to air blowing on face

Dose and route:

By inhalation through nasal cannula

- Flow rates of 1– 2.5L/min adjusted according to response.

  This will deliver between 24–35% oxygen depending on the patient's breathing pattern and other factors. Lower flow rates may be appropriate particularly for preterm neonates.

By inhalation through facemask

- Percentage inhaled oxygen is determined by the oxygen flow rate and/or type of mask. 28% oxygen is usually recommended for continuous oxygen delivery.

Notes:

Therapeutics

- No convincing evidence for O_2 in non-hypoxemic patients: moving air from a fan may be equally effective. Nevertheless, some patients do appear to benefit: try it and if it doesn't help stop.
- Oxygen has little effect in raising SaO_2 In cyanotic congenital heart disease and is not generally indicated. Pulmonary hypertension, in the early stages, may respond to oxygen.

Monitoring

- Oxygen saturations do not necessarily correlate with the severity of breathlessness. Observation of the work of breathing is a more reliable indicator of breathlessness where self-report is not possible.
- Decisions regarding target oxygen saturations and monitoring should be guided by the overall aims of oxygen treatment and realistic saturation levels for an individual child.
- Frequent or continuous measurement of oxygen saturations may lead to an over-reliance on technical data and distract from evaluation of the child's overall comfort, symptom relief and wellbeing.
- Usual target oxygen saturations of 92-96% are not necessarily appropriate for palliative care. More usual target oxygen saturations are above 92% in long-term oxygen therapy and 88-92% in children at risk of hypercapnic respiratory failure. Lower saturation levels may be tolerated in children with cyanotic congenital heart disease.

Side effects

- Continuous nasal oxygen can cause drying of the nasal mucosa and dermatitis.

Administration

- Nasal cannulae are generally preferable as they allow the child to talk and eat with minimum restrictions.
- Oxygen administration via a mask or via NIPPV can be claustrophobic and/or damage facial skin. This can be reduced by using a nasal mask. The duration of supply from an oxygen cylinder will depend on the size of the cylinder and the flow rate.
- An oxygen concentrator is recommended for patients requiring more than 8 hours oxygen therapy daily.
- If necessary, two concentrators can be Y-connected to supply very high oxygen concentrations.
- Liquid oxygen is more expensive but provides a longer duration of portable oxygen supply. Portable oxygen concentrators are now also available.
- Higher concentrations of oxygen are required during air travel.

Available as

- Currently Air Liquide (www.airliquidehealthcare.co.uk) and Dolby Vivisol (www.dolbyvivisol.com) provide home oxygen to the UK.

Evidence: (1–3,288–291)

Pamidronate (Disodium)

Use:

- Adjuvant for bone pain caused by metastatic disease.
- Adjuvant for bone pain due to osteopenia or osteoporosis associated with neuromuscular conditions.
- Malignant hypercalcaemia.
- Treatment of secondary osteoporosis to reduce fracture risk.
- Osteogenesis imperfecta.

Dose and route:

Malignant hypercalcaemia

By intravenous infusion:

- **Child less than 2 years**: 500microgram/kg/dose
- **2- 3 years**: 750microgram/kg/dose
- **3 years and over**: 1mg/kg/dose, maximum 90mg/dose

Ensure adequate rehydration with intravenous sodium chloride 0.9%. Dilute pamidronate to a concentration of no more than 90mg/250ml sodium chloride 0.9% and infuse over 6 hours

Repeat up to weekly, as indicated by corrected serum calcium

Bone pain, metastatic bone disease, osteopenia, osteoporosis, osteogenesis imperfecta

By intravenous infusion: Seek specialist advice

Age	Dose per infusion	Infusions per cycle	Repeat cycle	Alternative regimes
Child less than 2 years	500microgram/kg/dose	1 infusion daily for 3 consecutive days	Every 2 months	Can also be given as 750microgram/kg/infusion for 2 consecutive days every 2 months
Child 2- 3 years	750microgram/kg/dose	1 infusion daily for 3 consecutive days	Every 3 months	The same dose per infusion can also be given once every month
Over 3 years	1mg/kg/dose maximum 60mg/dose	1 infusion daily for 3 consecutive days	Every 3 months	OR the same dose per infusion can be given on 2 consecutive days every 2 months

Dilute pamidronate to a concentration of no more than 90mg/250ml 0.9% sodium chloride and infuse over 6 hours

Notes:

Licensing

- Not licensed for use in children. Not licensed for osteogenesis imperfecta.

Therapeutics

- Regimes vary between centres. Choice of regime depends on local guidelines and convenience. Some centres advise DEXA scan and investigations into calcium metabolism before and after treatment.
- Response to treatment of osteopenia or osteoporosis, and indications for on-going treatment, should be assessed after 1- 2 years treatment.
- Effectiveness of Pamidronate in bone pain does not necessarily depend on demonstrating osteoporosis, but demonstration that iatrogenic osteopetrosis has not developed afterwards can be reassuring.
- Pain may initially increase before improving.
- Improvement in bone pain may occur within two weeks in osteopenia or osteoporosis. However improvement in bone density may not be apparent for up to a year.
- Consider calcium and vitamin D oral supplements to minimise potential risk of hypocalcaemia for those with mainly lytic bone metastases and at risk of calcium or vitamin D deficiency (e.g. through malabsorption or lack of exposure to sunlight).
- Other bisphosphonates are available in different formulations, including oral, although absorption tends to be poor by the oral route and further reduced by food or fluids other than plain water. Seek specialist advice.
- Denosumab is considered second line for refractory malignant hypercalcaemia

Caution

- Monitor renal function and electrolytes; ensure adequate hydration. Risk of renal impairment is increased by concurrent use with other nephrotoxic drugs

Interactions

- Prolonged hypocalcaemia and hypomagnesaemia may occur with concurrent use of aminoglycoside and a bisphosphonate.

Side effects

- Tolerated by children, but long term effects unknown.
- Flu-like symptoms are common with first infusion, but don't necessarily recur with subsequent doses.
- Atypical femoral fractures, and of osteonecrosis especially of the jaw and the external auditory canal reported in adults. Risk in children is uncertain. Consider dental review before treatment, attention to dental hygiene together with patient and / or family education.

Administration

- Initial dose is usually given as an inpatient. Subsequent does could be given at home if necessary medical and nursing support is available.
- Can be administered by continuous subcutaneous infusion over 12-24 hours, together with subcutaneous hydration.

Available as

- Injection vials for infusion of various volumes, at 3mg/ml, 6mg/ml, 9mg/ml, 15mg/ml.

Evidence: (3,57,292–295)

Paracetamol

(US: Acetaminophen)

Use:

- Mild to moderate pain
- Pyrexia.

Dose and route:

Important safety information

MHRA advice: Paracetamol: updated dosing for children to be introduced (December 2014)

The recommended indications and doses of paracetamol have been revised to take account of MHRA and Toxbase advice that paracetamol toxicity may occur with doses between 75-150mg/kg/day.

APPM recommends body-weight-based dosing where possible because

- Many patients have lower than average body-weight for age
- Patients are more likely to be receiving paracetamol regularly
- Patients are more likely to be receiving enzyme inducing medication e.g. antiepileptics
- Patients are more likely to be at risk of hepatic and or renal impairment

By mouth:

Body-weight-based dosing: recommended

Warn parents or carers that doses may be different to "usual" doses stated on over the counter medication.

- **Neonate 28-32 weeks corrected gestational age**: 20mg/kg as a single dose then 10-15mg/kg every 8-12 hours as necessary, maximum 30mg/kg/day in divided doses
- **Neonate over 32 weeks corrected gestational age**: 20mg/kg as a single dose then 10-15mg/kg every 6-8 hours as necessary maximum 60mg/kg/day in divided doses
- **Child 1 month- 5 years**: 20-30mg/kg as a single dose then 15-20mg/kg every 4-6 hours as necessary, maximum 75mg/kg/day in divided doses
- **Child 6-11 years**: 20-30mg/kg, maximum 1 g, as a single dose then 15-20mg/kg every 4-6 hours as necessary, maximum 75mg/kg/day or 4 g/day in divided doses
- **Over 12 years**: 15-20mg/kg, maximum 500mg-1 g, every 4-6 hours as necessary, maximum 4 g/day in divided doses.

By rectum:

Body-weight-based dosing: recommended

- **Neonate 28- 32 weeks corrected gestational age**: 20mg/kg as a single dose then 10-15mg/kg every 12 hours as necessary, maximum 30mg/kg/day in divided doses.
- **Neonates over 32 weeks corrected gestational age**: 30mg/kg as a single dose then 15-20mg/kg every 8 hours as necessary, maximum 60mg/kg/day in divided doses.
- **Child 1- 2 months**: 30mg/kg as a single dose, then 15-20mg/kg every 4-6 hours as necessary, maximum 75mg/kg/day in divided doses.
- **3 months-11years**: 30mg/kg as a single dose, maximum 1 g, then 15-20mg/kg every 4-6 hours as necessary, maximum 75mg/kg/day or 4 g/day in divided doses
- **Over 12 years**: 15-20mg/kg, maximum 500mg -1 g, every 4-6 hours as necessary, maximum 4 g/day in divided doses.

By intravenous infusion over 15 minutes

- **Preterm neonate less than 32 week corrected gestational age**: 7.5mg/kg every 12 hours
- **Preterm neonate over 32 weeks corrected gestational age**: 7.5mg/kg every 8 hours
- **Neonate**: 10mg/kg every 4-6 hours, maximum 30mg/kg/day
- **Infant and child body-weight less than 10 kg**: 10mg/kg every 4-6 hours, maximum 30mg/kg/day
- **Child body-weight 10-50 kg**: 15mg/kg every 4-6 hours, maximum 60mg/kg/day
- **Body-weight over 50 kg**: 1g every 4-6 hours, maximum 4g/day

Notes:

Licensing

- Not licensed for use in children under 2 months by mouth; not licensed for use in preterm neonates by intravenous infusion; not licensed for use in children under 3 months by rectum; doses for severe symptoms not licensed; paracetamol oral suspension 500mg/5 ml not licensed for use in children under 16 years. IV infusion dose not licensed in children and neonates under 10kg.
- Oral and licensed rectal preparations are licensed for use in infants from 2 months for post immunisation pyrexia (single dose of 60mg which may be repeated once after 4-6 hours if necessary), and from 3 months as antipyretic and analgesic.
- Intravenous paracetamol is licensed for short term treatment of moderate pain, and of fever when other routes are not available.

Therapeutics

- Consider use of non-pharmacological measures to relieve pain, as alternative or in addition to analgesics.

- For management of feverish illness in children, see updated NICE clinical Guideline NG143. (Consider using either paracetamol or ibuprofen in children with fever who appear distressed and consider changing to the other agent if distress is not alleviated. Do not use antipyretic agents with the sole aim of reducing body temperature). A recent Cochrane systematic review states "there is some evidence that both alternating and combined antipyretic therapy may be more effective at reducing temperatures than monotherapy alone".
- Use adjusted body weight (Appendix 7) to calculate doses in obese children

Contraindications, cautions

- Caution in duct dependent congenital heart disease. Administration may stimulate duct closure. Seek specialist cardiology advice.

Hepatic impairment, renal impairment

- Increase dosing interval to 6 hours in moderate renal impairment. Increase dosing interval to 8 hours in severe renal impairment.

Pharmacokinetics

- Onset of action 15-30 minutes by mouth. Onset of action 5-10 minutes IV for analgesia and 30 minutes IV as an antipyretic.
- May take up to 2 hours for full effects. Duration of action 4-6 hours orally and IV.
- Oral bioavailability 60-90%. Rectal bioavailability about 2/3 of oral. Rectal absorption is slower than oral, erratic and incomplete.
- Elimination is slower in babies under 3 months.

Side effects

- Hepatotoxic in overdose (more than 75mg/kg) or prolonged high doses.

Administration

- Oral preparation can be administered rectally and is absorbed more quickly than suppositories.
- Dispersible tablets have high sodium content (over 14mmol per tablet). Consider liquid preparation for regular administration
- For administration via an enteral feeding tube: Use tablets dispersed in water for intragastric or intrajejunal administration. If the sodium content is problematic, use the liquid formulation. This can be used undiluted for intragastric administration; however, the viscosity of the paediatric liquid preparations is very high; it is difficult to administer these suspensions via a fine bore tube without dilution. If administering intra-jejunally, dilute with at least an equal quantity of water to reduce osmolarity and viscosity.

Patient information

- See Medicines for Children leaflet "paracetamol for mild to moderate pain": https://www.medicinesforchildren.org.uk/medicines/paracetamol/

Available as

- Tablets and caplets (500mg), capsules (500mg), soluble tablets (120mg, 500mg), oral suspension (120mg/5ml, 250mg/5ml), Fastabs 250mg, suppositories (60mg, 125mg, 250mg, 500mg and other strengths available from 'specials' manufacturers or specialist importing companies) and intravenous infusion (10mg/ml in 50ml and 100ml vials).

Evidence: (1,2,8,11,296–298)

Parecoxib

Use:

- Injectable NSAID
- Acute pain when the enteral route is unavailable
- Co-analgesic in cancer-related bone pain when the enteral route is unavailable

Dose and route:

By intravenous, deep intramuscular or subcutaneous bolus

- **Child 10-40kg**: 500microgram/kg/dose-1mg/kg/dose every 12 hours (maximum 40mg/dose)
- **40kg and over**: 20-40mg/dose every 12 hours By continuous subcutaneous infusion
- **Child 10-40kg**: 1-2mg/kg/24hours (maximum 80mg/24hours)
- **40kg and over**: 40-80mg/24hours

Notes:

Pro-drug of the selective COX-2 inhibitor valdecoxib

Licensing

- Licensed in adults for short term management of post-operative pain. Not licensed in children

Therapeutics

- Celecoxib may be used as an enteral alternative

Contraindications, cautions

- May mask fever and other signs of inflammation
- Caution in cardiac, hepatic or renal impairment and those with asthma
- Contraindicated: active peptic ulceration, active GI bleeding or inflammatory bowel disease, and severe heart failure
- Contraindicated in hypersensitivity to parecoxib or other NSAIDs

Side effects

- All NSAIDs are associated with serious gastro-intestinal toxicity. Parecoxib is associated with low risk of gastro-intestinal toxicity. Consider prescription of a proton pump inhibitor with prolonged use.
- All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factors or duration of NSAID use. The greatest risk may be in those receiving high doses long term. Risks have not been quantified in children.

Hepatic and renal impairment

- Reduce dose by 50% or avoid in severe renal impairment, reduce dose by 50% in moderate liver impairment, avoid in severe liver impairment

Pharmacokinetics

- Onset of action 10–15min (IV/IM), duration of action 6–12hours

Interactions

- Moderate inhibitor of cytochrome P450 enzymes CYP2C19 and CYP2D6. May increase levels drugs metabolised by these enzymes including amitriptyline, fluoxetine, haloperidol, hydromorphone, levomepromazine, omeprazole, oxycodone, risperidone, tapentadol and tramadol.
- Metabolised by CYP3A4 and CYP2C9. Levels may be increased by drugs that inhibit these enzymes including erythromycin and sodium valproate. Levels may be reduced by drugs which induce this enzyme including carbamazepine, phenobarbital and phenytoin.

Administration

- Intravenous, subcutaneous or intramuscular injection: reconstitute 40mg vial with 2ml 0.9% Sodium chloride or 5% dextrose to give solution for injection of concentration 20mg/ml. IV bolus injection is given rapidly and directly into a vein or into an existing IV line. The IM injection should be given slowly and deeply into the muscle
- For continuous subcutaneous infusion dilute with sodium chloride 0.9% to maximal volume in a 30ml syringe. Do not mix with other drugs in a syringe driver

Available as

- 40mg vial powder for solution for injection

Evidence: (2,3,299–307)

Paraldehyde (rectal)

Use:

- Treatment of prolonged seizures and status epilepticus.

Dose and route:

By rectal administration (dose shown is for premixed enema 50:50 with olive oil)

- **Neonate**: 0.8ml/kg as a single dose.
- **1 month and over**: 0.8ml/kg, maximum 20ml as a single dose.

Notes:

Licensing

- Paraldehyde enema for rectal use is an unlicensed formulation and route of administration.

Contraindications, cautions

- Contra-indicated in gastric disorders and in colitis.

Side effects

- Rectal administration may cause skin irritation.

Pharmacokinetics

- Mean half-life 7.5 hours

Patient information

- See Medicines for Children leaflet “Paraldehyde (rectal) for stopping seizures” https://www.medicinesforchildren.org.uk/medicines/rectal-paraldehyde-for-stopping-seizures/

Available as

- Paraldehyde enema: premixed solution of paraldehyde in olive oil in equal volumes from ‘special-order’ manufacturers or specialist importing companies.

Evidence:(1,2,122,308–310)

Phenobarbital

Use:

- Epilepsy including status epilepticus
- Neonatal convulsive status epilepticus: step 3 (after 2nd benzodiazepine) in APLS protocol
- Commonly used first line for seizures in neonates
- Palliation of intractable seizures in end-of-life care
- Adjuvant in cerebral irritability
- Sedation
- Agitation refractory to midazolam in end-of-life care

Dose and route:

Status epilepticus, seizures or agitation in end-of-life care

By mouth, intramuscular bolus, slow intravenous injection or subcutaneous infusion Loading dose

- Used to reach steady state quickly and avoid late toxicity due to accumulation. Phenobarbital doses will take between 5 and 30 days to achieve steady state unless a loading dose is given.
- **All ages**: 20mg/kg/dose, maximum 1g, by mouth, intramuscular bolus, slow intravenous injection or subcutaneous infusion over at least 20 minutes (but see notes below)
- In view of concerns regarding respiratory depression in patients actively dying some centres administer an initial half-loading dose of 10mg/kg followed by a further loading dose, if required, after 1-2 hours.

On-going treatment

- **Neonate**: 2.5-5mg/kg once or twice daily as maintenance.
- **Child 1month-11 years**: 2.5-5mg/kg, maximum 300mg/dose, once or twice daily. Total daily dose can also be given as a continuous infusion/24hours.
- **Child 12 years and over**: 300mg twice daily. Total daily dose can also be given as a continuous infusion/24hours.

Epilepsy, cerebral irritability

By mouth:

- **Neonate**: 2.5-5mg/kg once or twice daily
- **Child 1 month-11 years**: 1–1.5mg/kg twice daily, increased gradually as required, usual maintenance dose 2.5-4mg/kg once or twice daily
- **12 years and over:** 60–180mg once daily

Notes:

Licensing

- Licensed for seizures. Not licensed for agitation in end-of-life care.

Therapeutics

- Consider vitamin D supplementation in patients who are immobilised for long periods or who have inadequate sun exposure or dietary intake of calcium.
- For patients already on oral phenobarbital but needing parenteral treatment, doses equivalent to the patient's usual total daily dose of oral phenobarbital can be used.

Monitoring

- Monitoring therapeutic levels may not be appropriate depending on the indication for administration and because tolerance occurs.

Side effects

- Sedation, paradoxical agitation, confusion, respiratory depression, movement disorders
- Associated with osteopenia and increased risk of fractures.

Pharmacokinetics

- Elimination half-life of 2-6 days in adults, 1-3 days in children.

Interactions

- Induces cytochrome P450 enzyme CYP3A4. Reduces levels of numerous drugs including alfentanil, buprenorphine, carbamazepine, dexamethasone, fentanyl, ketamine, midazolam and paracetamol. *This list is not exhaustive –seek advice.*

Administration

- Tablets may be crushed for administration if preferred. The liquid preparations may be administered via an enteral feeding tube. For administration via a jejunostomy tube, dilution with water is recommended to reduce the liquid viscosity.
- Use a separate site to commence subcutaneous infusion. SC bolus injections should be avoided because they can cause tissue necrosis due to the high pH. Dilute injection solution 1 in 10 with water for injections (i.e. to maximum concentration of 20mg/ml) before intravenous or subcutaneous administration. Administer intravenously at not more than 1mg/kg/minute.

Patient information

- See Medicines for Children leaflet “Phenobarbital for preventing seizures”. https://www.medicinesforchildren.org.uk/medicines/phenobarbital-for-preventing-seizures/

Available as

- Tablets (15mg, 30mg, 60mg), oral elixir (15mg/5ml) and injection (15mg/ml, 30mg/ml, 60mg/ml and 200mg/ml). The licensed oral elixir of 15mg/5 ml contains alcohol 38% and it is preferable to obtain an alcohol free oral liquid (usually 50mg/5ml) via one of the specials manufacturers.

CD

- Schedule 3 CD (CD No Register Phenobarbital).

Evidence: (1–3,11,122,192,193,311)

Phenytoin

Use:

- Epilepsy: status epilepticus, tonic-clonic seizures, focal seizures and neonatal seizures
- Neuropathic pain

Dose and route:

Epilepsy, neuropathic pain

By mouth or short intravenous infusion

- **Neonate**: Initial intravenous loading dose 18mg/kg then 2.5-5mg/kg twice daily by mouth adjusted according to response and plasma phenytoin levels. Usual maximum 7.5mg/kg twice daily.
- **1 month-11 years**: 1.5-2.5mg/kg twice daily adjusted according to response and plasma phenytoin levels. Usual target maintenance dose to 2.5-5mg/kg twice daily. Usual maximum dose of 7.5mg/kg twice daily or 300mg daily.
- **12 years and over**: 75-150mg twice daily adjusted according to response and plasma phenytoin levels. Usual target maintenance dose 150-200mg twice daily. Usual maximum dose of 300mg twice daily.

Status epilepticus

By short intravenous infusion

- **Neonate**: Loading dose 20mg/kg, then 2.5-5mg/kg/dose twice daily adjusted according to response and plasma phenytoin levels.
- **1 month-11 years**: Loading dose 20mg/kg, then 2.5-5mg/kg twice daily adjusted according to response and plasma phenytoin levels.
- **12 years and over**: Loading dose 20mg/kg, maximum 1g, then 150mg twice daily adjusted according to response and plasma, phenytoin levels

Notes:

- Membrane stabiliser.

Licensing

- Suspension 90mg in 5ml is a 'special' and unlicensed. Other preparations are licensed for use in children as an anticonvulsant.

Therapeutics

- Third or fourth line for epilepsy and for neuropathic pain
- Oral doses are usually as effective as intravenous above 2 weeks old. Older babies may need higher doses.
- Cross-sensitivity is reported with carbamazepine.

- Avoid abrupt withdrawal.
- Consider vitamin D supplementation in patients at risk of osteopenia or vitamin D deficiency.
- Prescribe oral preparations by brand name: bioavailability may vary with brand.
- Use adjusted body weight (Appendix 7) to calculate doses in obese children

Side effects

- Associated with osteopenia and increased risk of fractures. Consider vitamin D supplementation with long term use.
- Arrythmias, hypotension and respiratory depression with parenteral use

Pharmacokinetics

- Narrow therapeutic index, unpredictable half-life, and non-linear relationship between dose and plasma-drug concentration. Marked variation in rate of elimination, especially in the first few weeks and months of life.
- Oral bioavailability 90-95% is roughly equivalent to intravenous, plasma half-life 7-42 hours. Poor rectal absorption.

Interactions

- Induces cytochrome P450 enzymes CYP1A2 and CYP3A4. Reduces levels of numerous drugs including alfentanil, buprenorphine, carbamazepine (also increasing levels of phenytoin), dexamethasone, diazepam, fentanyl, ketamine, melatonin midazolam and paracetamol. *This list is not exhaustive –seek advice.*
- Long term use is associated with significant side effects. No more effective than other anti-epileptics but doses can be titrated quickly.

Hepatic impairment, renal impairment

- Reduce dose in hepatic impairment. Monitor carefully if reduced albumin or protein binding e.g. in renal failure.

Administration

- Administer infusions over at least 20 minutes and at a rate not exceeding 1mg/kg/minute, maximum 50mg/minute. Monitor ECG and blood pressure during administration.
- Dilute to a concentration not exceeding 10mg/ml with Sodium Chloride 0.9% for intravenous infusion. Administer into a large vein through an in-line filter (0.22–0.50 microns); complete administration within 1 hour of preparation. Flush intravenous line with Sodium Chloride 0.9%. before and after administration,
- Preparations containing phenytoin sodium are not bioequivalent to those containing phenytoin base (such as Epanutin Infatabs® and Epanutin® suspension); 100mg of phenytoin sodium is approximately equivalent in therapeutic effect to 92mg phenytoin base. The dose is the same for all phenytoin products when initiating therapy, however if switching between these products the difference in phenytoin content may be clinically significant. Care is needed when making changes between formulations and plasma phenytoin concentration monitoring is recommended.
- Bioavailability may be reduced unpredictably by enteral feeds and/or nasogastric tube feeds, so flush with water to enhance absorption, interrupt enteral feeding for at least 1-2 hours before and after giving phenytoin, and maintain similar timings and regimes from day to day. Use the oral suspension for enteral tube administration; dilution with an equal volume of water is recommended for gastrostomy administration. Absorption is exceptionally poor via the jejunal route; plasma concentration should be monitored closely if this route is used. Dilution of the suspension is important as phenytoin suspension is hyperosmolar and may cause diarrhoea when administered into the jejunum.

Patient information

- See Medicines for Children leaflet “Phenytoin for preventing seizures”. https://www.medicinesforchildren.org.uk/medicines/phenytoin-for-preventing-seizures/

Available as

- Tablets (phenytoin sodium 100mg, generic), capsules (phenytoin sodium 25mg, 50mg,100mg, 300mg), Epanutin® Infatabs (chewable tablets of phenytoin base 50mg), oral suspension (Epanutin® phenytoin base 30mg/5ml, and 90mg/5ml phenytoin base available as an ‘unlicensed special’), and injection (phenytoin sodium 50mg/ml generic)

Evidence: (1–3,8,122,311)

Phosphate (rectal enema)

Use:

- Constipation refractive to other treatments.

Dose and route:

By rectum:

Phosphate enema BP Formula B (with standard or long rectal tube):

- **Child 3-6 years**: 45-65ml once daily.
- **Child 7-11 years**: 65-100ml once daily.
- **12 years and over**: 100-128ml once daily.

Cleen® (previously Fleet®) Ready to Use enema:

- **Child 3-6 years**: 40-60ml once daily.
- **Child 7-11 years**: 60-90ml once daily.
- **12 years and over**: 90-118ml once daily.

Notes:

Therapeutics

- Onset of action 2-5 minutes

Contraindications, cautions

- Contraindicated in acute gastro-intestinal conditions (including gastro-intestinal obstruction, inflammatory bowel disease, and conditions associated with increased colonic absorption).
- Use only in faecal impaction if all oral medications, and rectal sodium citrate have failed.

Side effects

- Risk of dehydration and electrolyte disturbance.
- Case reports of hyperphosphataemia and tetany following use of phosphate enemas in children. Risk is likely to be increased with use more than once or twice per week or higher doses.

Administration

- May be warmed to body temperature in a water bath prior to administration

Available as

- Phosphate enema BP Formula B (with standard or long rectal tube), Cleen® Ready to Use enema

Evidence: (1–3,312,313)

Pregabalin

Use:

- Epilepsy (focal seizures with or without secondary generalisation)
- Peripheral and central neuropathic pain
- Generalised anxiety disorder
- Restless legs syndrome in chronic kidney disease
- Pruritus associated with burns

Important safety information

MHRA/CHM advice: Pregabalin (Lyrica®): reports of severe respiratory depression (February 2021)

Pregabalin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, and concomitant use of central nervous system (CNS) depressants might be at higher risk of experiencing severe respiratory depression and dose adjustments may be necessary in these patients.

Dose and route:

Neuropathic pain and pruritus, adjunctive therapy for focal seizures, anxiety, restless legs

By mouth:

- **Child 1 month- 15 years:** 1mg/kg/dose twice daily

  Increase every 3-7 days by 500micrograms/kg/dose until desired therapeutic effect or side effects experienced.

  Initial maximum 5mg/kg twice daily

  Younger children under 30kg and especially those under 6 years may require up to 15mg/kg/day. Maximum 300mg twice daily

- **Adult 16 years and over:** 75mg twice daily

  Increase every 3-7 days by 75mg/dose until desired therapeutic effect or side effects experienced.

  Maximum 300mg twice daily

Gabapentin to Pregabalin switch for neuropathic pain

See Appendix 5

Notes:

Licensing

- Licensed in adults as an adjunct for partial seizures; for the treatment of peripheral and central neuropathic pain and for the treatment of generalised anxiety disorder. Not licensed for use in children or adolescents less than 18 years of age.

Therapeutics

- Binds to the alpha-2 subunit of voltage gated calcium channels in the CNS thus inhibiting the release of excitatory neurotransmitters. Six times greater receptor affinity than gabapentin
- Younger children less than 6 years may need up to 15mg/kg/day particularly for seizures
- Do not stop abruptly: discontinue gradually over a minimum of one week

Hepatic impairment, renal impairment

- Excreted unchanged via kidneys, reduce dose in renal impairment. Recommended maximum doses in renal impairment:

Body-weight	Mild renal impairment Creatinine clearance 31-60ml/min	Moderate renal impairment Creatinine clearance 15-30ml/min	Severe renal impairment Creatinine clearance <15ml/min
Less than 30kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
More than 30kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours

- No dose modification required in hepatic impairment

Pharmacokinetics

- Oral bioavailability 90% or greater. Peak plasma concentrations occur within 1.5 hours.
- Drug clearance is faster in children under 30 kg. Higher doses and/or more frequent dosing interval may therefore be needed in younger children, particularly those under 6 years of age

Side effects

- Most commonly reported adverse effects are dizziness, somnolence and headache. These are generally transient and mild to moderate in nature and may be minimised by a gradual increase to the therapeutic dose.
- Pregabalin may exacerbate seizures in patients with absence or myoclonic seizures (including juvenile myoclonic epilepsy), tonic or atonic seizures, Dravet syndrome, Lennox-Gastaut syndrome, and myoclonic-atonic seizures.

Administration

- Use the oral solution for administration via an enteral tube. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.

Available as

- Oral capsules (25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg and oral solution (20mg/ml).
- Schedule 3 controlled drug although exempt from safe storage requirements.

Evidence: (2,3,159,161,162,314–322)

Promethazine hydrochloride

Use:

- Sleep disturbance.
- Mild sedation
- Symptomatic relief of allergy
- Nausea and vomiting (including motion and opioid-induced), and vertigo
- Sedation in neonatal intensive care

Dose and route:

Important safety information

MHRA/CHM advice: Over-the-counter cough and cold medicines for children (April 2009)

Children under 6 years should not be given over-the-counter cough and cold medicines containing promethazine.

Contraindications

Promethazine should not be given to children under 2 years, except on specialist advice, due to the potential for fatal respiratory depression

Symptomatic relief of allergy:

By mouth:

- **6- 23 months:** 2.5mg–5mg twice daily (on specialist advice)
- **Child 2- 4 years**: 5mg twice daily or 5-15mg at night.
- **Child 5- 9 years**: 5–10mg twice daily or 10–25mg at night.
- **10 years and over**: 10–20mg 2–3 times daily or 25mg at night increased to 25mg twice daily if necessary.

Sedation (short term use):

By mouth:

- **6- 23 months**: 5-10mg at night (on specialist advice)
- **Child 2- 4 years**: 15-20mg at night.
- **Child 5- 9 years**: 20-25mg at night.
- **10 years and over**: 25-50mg at night.

Nausea and vomiting (particularly in anticipation of motion sickness)

By mouth

- **Child 2-4 years**: 5mg twice daily.
- **Child 5-9 years**: 10mg twice daily.
- **Child 10-17 years**: 20-25mg twice daily.

Sedation in intensive care

By mouth, by slow intravenous injection or by deep intramuscular injection

- **Neonate greater than 37 weeks corrected gestational age**: 500microgram/kg –1mg/kg 4 times daily, adjusted according to response
- **Child 1 month-11 years:** 500microgram/kg-1mg/kg 4 times daily, maximum 25mg/dose, adjusted according to response
- **12 years and over:** 25-50mg/dose 4 times daily adjusted according to response

Notes:

- Antihistamine (anti H1) with moderate muscarinic and D2 receptor antagonism. Significant antimuscarinic activity, particularly in neonates

Licensing

- Not licensed for sedation in children under 2 years

Therapeutics

- Has also been used orally for dyspnoea in adults.
- Used in neonatal units on bigger babies for oral sedation when usual IV sedation options ineffective.
- Start at 25% oral doses if administered intravenously or subcutaneously outside intensive care environment.

Contraindications, cautions

- Caution in epilepsy, asthma. Risk of hypotension if co-prescribed with opioid.

Side effects

- Respiratory depression, arrythmias, movement disorders including neuroleptic malignant syndrome, urinary retention, insomnia, seizures, nausea and vomiting.

Pharmacokinetics

- Oral bioavailability approximately 25%.

Hepatic impairment, renal impairment

- Caution in renal and severe hepatic impairment

Interactions

- Risk of drug interactions with other antimuscarinic or sedative drugs.

Administration

- Not generally recommended for subcutaneous administration due to the risk of local necrosis, but diluted in an adequate volume of sodium chloride 0.9% can usually be administered by CSCI/24hours. Do not give bolus SC injections.
- Oral preparation can be effective for up to 12 hours. Peak plasma concentration 2-3 hours after administration. Drowsiness may wear off after a few days of treatment.
- Use oral preparation for administration via gastrostomy. Dilute oral preparation with an equal volume of water for jejunal administration. Tablets will disintegrate if shaken in water for 5 minutes.

Available as

- Promethazine hydrochloride tablets (10mg, 25mg), oral elixir (5mg/5 ml), and injection (25mg/ml). (Promethazine teoclate tablets also available, 25mg, licensed for nausea, vertigo and labyrinthine disorders. Slightly longer acting than promethazine hydrochloride and dosing slightly different).

Evidence: (1,3,8,11)

Propantheline bromide (NEW)

Use:

- Smooth muscle spasm (bladder and gastrointestinal tract)
- Anti-secretory
- Hyperhidrosis

Dose and route:

By mouth

Take at least one hour before food

- **1month-11 years**: 300micrograms/kg/dose, maximum 15mg, 3-4 times daily
- **12 years and over**:: 15mg three times daily *and* 30mg at night, maximum 120mg/day

Notes:

- Quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine

Licensing:

- Not licensed for use in children

Therapeutics

- Acts by two distinct mechanisms: non-specific acetylcholine antagonist at muscarinic M1–3 receptors, *and* a direct musculotropic effect causing relaxation of smooth muscle.
- Possible clinical benefits include decreased respiratory tract secretions, decreased gastric acid production, smooth muscle relaxation. Specific benefits for hyperhidrosis (excessive sweating) and gustatory sweating are attributed to its antagonism of acetylcholine at M3 receptors of glandular tissue.

Contraindications, cautions

- Contraindicated in gastro-intestinal obstruction and ileus, urinary retention, myasthenia gravis
- Caution in arrythmias, cardiac failure, pyrexia, ulcerative colitis, gastro-oesophageal reflux

Side effects

- Antimuscarinic side effects include dry mouth, drowsiness, headache, fatigue, dizziness, thickening of bronchial secretions, nervousness.

Administration

- Can be administered via gastrostomy. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.

Available as

- Tablets 15mg, oral suspension and oral solution from special-order manufacturers. Evidence:

(1,323–329)

Prucalopride (NEW)

Use:

- Prokinetic agent for treatment of constipation when laxatives are ineffective / inadequate
- Second line prokinetic for upper gastrointestinal dysmotility

Dose and route:

By mouth

- **Child up to 12 years or less than 50kg**: 30-40micrograms/kg/dose, maximum single dose 2mg, once daily
- **12 years and over *and* 50kg or over**: 2mg once daily

Notes:

- Selective 5-HT4 receptor agonist with and enterokinetic effect increasing GI motility.

Licensing:

- Not licensed for use in children under 18 years of age.

Contraindications, cautions

- Contraindicated in Crohn's disease; intestinal obstruction; intestinal perforation; toxic megacolon; ulcerative colitis.
- Caution in history of arrhythmias

Hepatic impairment, renal impairment

- Reduce dose in severe renal and/or hepatic impairment.

Side effects:

- Headache, dizziness, fatigue and gastrointestinal symptoms (abdominal pain, decreased appetite, GI discomfort, nausea and diarrhoea). Adverse effects occur predominantly at the start of therapy and usually disappear within a few days within continued treatment.

Administration:

Tablets may be crushed and dispersed in water to aid administration (off-label) but may have an unpleasant taste. No information on administration via an enteral feeding tube.

Available as

- 1mg and 2mg tablets.

Evidence:(2,330–352)

Risperidone

Use:

- Severe neuro-irritability
- Dystonia and dystonic spasms refractory to first and second line treatment
- Delirium
- Short term treatment of persistent aggression in conduct disorder in children and in autism or moderate to severe dementia
- Psychosis in Battens disease
- Treatment of acute mania or psychosis (under specialist supervision)

Dose and routes

Severe neuro-irritability, refractory dystonia, delirium, aggression

By mouth:

- **Child 1 month-11 years, body-weight up to 50kg**: 10micrograms/kg once daily, maximum 500micrograms/dose, increasing if necessary to 20micrograms/kg once daily after 3-7 days

  Increase gradually if required, every 7-14 days in increments of 10micrograms/kg/day to a maximum of 60micrograms/kg/day, maximum 3mg/day

- **12 years and over, body-weight over 50kg:** 500micrograms once daily increasing if necessary to 1mg once daily after 3-7 days

  Increase gradually if required, in increments of 500micrograms every 7-14 days to a maximum of 3mg/day

Acute mania or psychosis (under specialist supervision), psychosis in Batten's disease

Higher doses, more rapid titration By mouth:

- **Child 1 month-11 years, body-weight up to 50kg**: 10micrograms/kg, maximum 500micrograms/dose, twice daily; increased on day 2 to 20micrograms/kg, maximum 1mg/dose, twice daily and 30micrograms/kg, maximum 1.5mg/dose, twice daily from day 3

  Increase further if required, and as tolerated. Usual maximum 3mg twice daily

- **12 years and over, body-weight over 50kg:** 500micrograms twice daily, increased on day 2 to 1mg, twice daily and 1.5mg twice daily from day 3

  Increase further if required, and as tolerated. Usual maximum 3mg twice daily

Notes

- Dopamine D2, 5-HTA, alpha-1 adrenoceptor and histamine-1 receptor antagonist.

Licensing

- Not licensed for use in children for psychosis, mania, or autism..

Therapeutics

- Usual maintenance dose in adolescents and adults with psychosis or mania is 4-8mg/day.
- Children with Juvenile Battens Disease may need up to 1.5mg 3 times daily during crises with hallucinations: this dose can be reduced or stopped as symptoms settle (episodes usually last 1-6 weeks).
- Maximum adult dose 16mg/day however doses above 10mg/day have not been shown to be more effective and side effects are more likely.
- Some experience as an anti-emetic in refractory nausea and vomiting in adults; not evaluated in children
- Total daily dose can be given once at bedtime.

Contraindications, cautions

- Caution in epilepsy (lowers seizure threshold) and cardiovascular disease; extrapyramidal symptoms less frequent than with older antipsychotic medications; can cause orthostatic hypotension; withdraw gradually after prolonged use.

Side effects

- Weight gain. Other common side effects include anxiety, depression, sleep disorders, hypertension, oedema, malaise, constipation.
- Neuroleptic malignant syndrome

Hepatic impairment, renal impairment

- Initial and subsequent doses should be halved in renal or hepatic impairment.

Pharmacokinetics

- Oral bioavailability 99%. 1-2 hours to peak plasma concentration. Onset of action hours to days in delirium; days to weeks in psychosis. Plasma half-life 24 hours. Duration of action 12-48 hours.

Administration

- Oral liquid may be diluted in any non-alcoholic drink except tea. Orodispersible tablets should be placed on the tongue, allowed to dissolve and swallowed. Use oral liquid for administration via enteral feeding tubes. Tablets also disintegrate in water within 5 minutes for easy administration via enteral feeding tubes. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet “Risperidone for psychological disorders”. https://www.medicinesforchildren.org.uk/medicines/risperidone-for-psychological-disorders /

Available as

- Tablets (500micrograms, 1mg, 2mg, 3mg, 4mg, 6mg), orodispersible tablets (500micrograms, 1mg, 2mg, 3mg, 4mg), oral solution 1mg/ml.

Evidence: (2,3,8,87,353–362)

Salbutamol

Use:

- Breathlessness or wheeze caused by bronchospasm including exacerbations associated with respiratory tract infection.
- Prevention and treatment of chronic lung disease in premature infants
- Hyperkalaemia.

Dose and route:

Exacerbation of reversible airway obstruction, prevention of allergen-or exercise-induced bronchospasm

By aerosol inhalation:

Use via large volume spacer (and a close-fitting face mask in children under 3 years).

- **Child 1 month and over**: 100-200micrograms (1-2 puffs) up to four times daily.

By inhalation of nebulised solution:

- **Neonate:** 1-2.5mg up to four times daily
- **Child 1 month-4 years**: 2.5mg up to four times daily
- **5-11 years**: 2.5-5mg, up to four times daily.
- **12 years and over**: 5mg, up to four times daily

Emergency treatment of moderate to severe acute asthma
N.B. Use in this context typically given in hospital setting to enable escalation of treatment if required. See separate detailed guidance in standard texts for use in acute life-threatening asthma

By aerosol inhalation:

- **Child 1 month and over**: 200-1000micrograms (2–10 puffs), each puff is to be inhaled separately, repeat every 10–20 minutes or when required, give via large volume spacer (and a close-fitting face mask in children under 3 years).

By inhalation of nebulised solution (*inpatient settings only*)

- **Child 1 month-4 years**: 2.5mg, repeated every 20-30minutes, or when required and administered by oxygen-driven nebuliser if available.
- **5-11 years**: 2.5-5mg, repeated every 20-30minutes, or when required and administered by oxygen-driven nebuliser if available.
- **12 years and over**: 5mg, repeated every 20-30minutes, or when required and administered by oxygen-driven nebuliser if available.

Hyperkalaemia

See separate detailed guidance in standard texts

Notes

Short acting beta 2 adrenergic receptor agonist

Licensing

- Salbutamol is not licensed for use in hyperkalaemia; injection is not licensed for use in children.

Therapeutics

- Spirometry should normally be used to confirm a possible underlying asthma diagnosis.
- In palliative care, if airflow obstruction is suspected, a pragmatic approach may be to give a trial (e.g. 1–2 weeks) of a bronchodilator and evaluate the impact on symptoms.
- Clinical efficacy of salbutamol in infants <18 months is uncertain, presumably due to the immaturity of the receptors; ipratropium may be more helpful in those less than 1-2 years. No evidence of efficacy in infection-related bronchospasm in infants
- Oral liquid is generally used only in the context of slowing rate of degradation of motor neurone proteins in neuromuscular disease. Seek specialist advice
- In children over the age of 5 years with mild and moderate acute asthma attacks, a pressurised metered-dose inhaler with a spacer is at least as effective as nebulisation.
- Ipratropium bromide is an appropriate alternative if side effects prevent use
- Advise family to seek advice if a previously effective dose fails to provide at least 3 hours relief, and warn of the dangers of exceeding prescribed inhaler and nebuliser doses.

Contraindications, cautions

- Risk of tachycardia and risk of QT prolongation at increasing doses.

Side effects

- Increased heart rate; feeling “edgy” or agitated; tremor. Rarely paradoxical bronchospasm can occur in response to beta-2-adrenoceptor agonists, hypokalaemia

Pharmacokinetics

- Onset of action 5 minutes via inhalation of aerosol, 3-5 minutes nebulised. Peak response 0.5-2 hours. Duration of action 4-6 hours. Only 10-20% of inhaled dose reaches lower airways.

Interactions

- Increased risk of hypokalaemia with corticosteroids, diuretics, theophylline.

Administration

- Inhaled product should be used with a suitable spacer device. The carer, and child where appropriate, should be given appropriate training. Inhaler technique should be explained and checked. The HFA (hydrofluoroalkane) propellant now used in multi-dose inhalers tends to clog the nozzle, so weekly cleaning is recommended.
- Salbutamol nebules are intended to be used undiluted. However, if prolonged delivery time (more than 10 minutes) is required, the solution may be diluted with sterile 0.9% Sodium chloride. Salbutamol can be mixed with nebulised solution of ipratropium bromide.

Patient information

- See Medicines for Children leaflet “Salbutamol for asthma and wheeze”. https://www.medicinesforchildren.org.uk/medicines/salbutamol-inhaler-for-asthma-and-wheeze/

Available as

- Nebuliser solution (2.5mg/2.5ml, 5mg in 2.5 ml), respirator solution (5mg/ml), aerosol inhalation (100 micrograms/puff) by metered dose inhaler (MDI), with various spacer devices. Various types of dry powder inhaler are also available, 100 and 200 micrograms per puff., injection (500 micrograms/ml), intravenous infusion (1mg/ml) oral solution (2mg/5ml), tablets (2mg and 4mg).

Evidence: (1,2,11,363,364)

Senna

Use:

- Constipation (stimulant laxative)

Dose and route:

By mouth:

Start at low dose, increasing as necessary after 24–48 hours

- **Child 1 month-3 years:** 3.75-15mg once daily, adjusted according to response.
- **4-5 years:** 3.75-30mg once daily, adjusted according to response.
- **6-17 years:** 7.5-30mg once daily, adjusted according to response.

Notes:

- Stimulant laxative acting on large bowel.

Licensing

- Oral solution is not licensed for use in children < 2 years and tablets are not licensed for use in children <6 years

Therapeutics

- Improves intestinal motility and increases water secretion into bowel lumen. Senna passes unchanged into large bowel. Hydrolysed by bacterial flora in the large bowel to yield the active compound.
- NICE Guidance CG99: Constipation in children and young people advocates the use of polyethylene glycol 3350 containing laxatives prior to a trial of a stimulant laxative. However, senna is considered the drug of first choice for opioid induced constipation in palliative care
- Optimise dose before adding a second agent
- Doses can be exceeded on specialist advice: opioid induced constipation often requires higher doses than in manufacturer's Product Information.
- Onset of action 8-12 hours.
- Available in the UK as an "over the counter" medicine for short courses in adults only

Contraindications, cautions

- Contraindicated in atony, intestinal obstruction, undiagnosed abdominal pain

Side effects

- Abdominal pain. Prolonged use or excessive use can cause hypokalaemia.

Administration

- Oral liquid may be administered via an enteral feeding tube; flush well before and after the dose. Therapeutic effect will be unaffected by jejunal administration.

Patient information

- See Medicines for Children leaflet “Senna for constipation”. https://www.medicinesforchildren.org.uk/medicines/senna-for-constipation/

Available as

- Tablets (7.5mg sennoside B) and oral suspension (7.5mg/5ml sennoside B)

Evidence: (1–3,8,313,365,366)

Sodium Citrate

Use:

- Constipation (osmotic laxative)

Dose and routes:

By rectum

Micolette Micro-enema

Sodium citrate 450mg, sodium lauryl sulfoacetate 45mg, glycerol 625mg, together with citric acid, potassium sorbate, and sorbitol in a viscous solution, in 5ml

- **Child 3 years and over**: 5–10ml as a single dose

Micralax Micro-enema

Sodium citrate 450mg, sodium alkylsulfoacetate 45mg, sorbic acid 5mg, together with glycerol and sorbitol in a viscous solution in 5ml

- **Child 3 years and over**: 5ml as a single dose

Relaxit Micro-enema

Sodium citrate 450mg, sodium lauryl sulfate 75mg, sorbic acid 5mg, together with glycerol and sorbitol in a viscous solution in a 5ml single dose pack with nozzle.

- **Child 1 month and over:** 5ml as a single dose (insert only half nozzle length in child 2 years or under).

Notes

- Osmotic laxative

Licensing

- Licensed for treatment of constipation for all ages

Therapeutics

- Usually combined with faecal softener (e.g. sodium lauryl sulphate, sodium alkylsulfoacetate) in micro-enemas.
- Sodium citrate is an osmotic agent. Sodium lauryl sulfoacetate is a faecal softener.
- Used where oral laxatives are ineffective or not feasible. Micro-enema, often used in combination with oral laxatives, particularly in neuromuscular disorders, faecal loading and faecal impaction.

- NICE Guidance for the management of constipation in children and young people advocates the use of polyethylene glycol 3350 containing laxatives and stimulant laxatives before the use of rectal measures. Sodium Citrate is considered the first line rectal measure, in preference to phosphate enemas.
- Usually acts within 15 minutes of administration

Contraindications, cautions

- Contraindicated in acute gastro-intestinal conditions
- Caution: can cause harmful sodium and water retention in susceptible patients.

Side effects

- Abdominal discomfort

Available as

- Micro-enema (5ml). All currently marketed preparations include sodium citrate 90mg/ml, but other constituents vary.

Evidence: (1,2,313)

Sodium Picosulfate

Use:

- Constipation (stimulant laxative).

Dose and routes:

By mouth:

- **Child 1 month-3 years**

  Less than 10kg: 250micrograms/kg once daily More than 10kg: 2.5mg once daily

  Increase as necessary according to response to a suggested maximum of 10mg daily

- **Child 4 years and over**: Initial dose of 2.5mg once daily increase as necessary according to response to a suggested maximum of 20mg daily.

Notes

- Stimulant laxative

Licensing

- Oral suspension is licensed for use in children; capsules are not licensed for use in children less than 4 years of age.

Therapeutics

- NICE Guidance CG99: Constipation in children and young people advocates the use of polyethylene glycol 3350 containing laxatives prior to a trial of a stimulant laxative. However, for opioid induced constipation in palliative care, senna is a considered the first line choice. If ineffective at first, dose should be optimised and only add a second agent if not adequately effective.
- Effectiveness dependent upon breakdown by gut flora-previous effectiveness may therefore be lost during courses of antibiotics and ensuing altered gut flora.
- Onset of action 6-12 hours.

Contraindications, cautions

- Contraindicated in intestinal obstruction and undiagnosed abdominal pain

Side effects

- Prolonged use or excessive use can cause hypokalaemia.

Administration

- Use the liquid preparation for administration via an enteral feeding tube; dilute with an equal volume of water. Sodium picosulfate reaches the colon without any significant absorption; therefore, the therapeutic response will be unaffected by jejunal administration.

Patient information

- See Medicines for Children leaflet " sodium picosulfate for constipation" https://www.medicinesforchildren.org.uk/medicines/sodium-picosulfate-for-constipation/

Available as

- Oral solution (5mg/5ml) and capsules (as Dulcolax PicoPerles 2.5mg). Also available mixed with Magnesium citrate for bowel evacuation prior to procedures (Picolax and Citrafleet).

Evidence: (1,2,8,313)

Sucralfate

Use:

- Prophylaxis of stress ulcer.
- Prophylaxis of bleeding from oesophageal or gastric varices
- Adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration,
- Upper gastro intestinal tract bleeding of unknown cause.
- Haemostasis (topical use).

Dose and route:

Prophylaxis and adjunctive treatment of upper GI tract bleeding

By mouth

- **Child 1 month-1 year**: 250mg four to six times daily.
- **2-11 years**: 500mg four to six times daily.
- **12-14 years**: 1g four to six times daily.
- **15 years and over**: 1g six times daily (maximum 8g/day).

Topical haemostasis

- Sucralfate suspension (1g/5ml) can be applied to the affected area twice daily e.g. as mouth wash, orally for oesophageal lesions, rectally for rectal lesions.
- Sucralfate paste (2 x 1g tablets crushed in 5ml aqueous jelly lubricant, or water) applied to the affected area twice daily

Notes:

- Complex of aluminium hydroxide and sulphated sucrose.

Licensing

- Not licensed for use in children less than 15 years; tablets are not licensed for prophylaxis of stress ulceration.

Therapeutics

- In the gut it seems to act by protecting mucosa from acid-pepsin attack. Minimal antacid properties. Acts locally and is minimally absorbed.
- Spread doses evenly throughout waking hours.

Side effects

- Case reports of bezoar formation with sucralfate.

Contraindications, cautions

- Caution in seriously ill patients, especially those receiving concomitant enteral feeds or those with predisposing conditions such as delayed gastric emptying.
- Caution: absorption of aluminium from sucralfate may be significant in patients on dialysis or with renal impairment.

Pharmacokinetics

- Onset of action 1-2 hours, duration of action 6 hours.

Administration

- Administration of sucralfate suspension and enteral feeds via a NG or gastrostomy tube should be separated by at least 1 hour to avoid formation of an insoluble complex that may block fine-bore feeding tubes. By mouth sucralfate should be given 1 hour before meals to reduce chance of bezoar formation. Suggest diluting with water before administration. Not appropriate for jejunal administration as the site of action is gastric and duodenal.
- Tablets may be crushed and dispersed in 10-15 ml water.

Available as

- Oral suspension (1g/5ml special order), tablets (1g). Oral suspension, cream, powder and enema available as special order.

Evidence:(1–3,8,367–369)

Sucrose

Use:

- Analgesia for procedural pain in babies.

Dose and route:

By mouth:

- **Neonate over 32 weeks**: 0.5-2ml of 24% sucrose orally 2 minutes before the procedure (alternatively a pacifier/dummy could be placed in the sucrose solution).

  Incremental doses 0.1ml can be used up to the maximum of 2ml. Multiple doses can be given during a single procedure.

- **Preterm infants**: administer a maximum of 4 times per 24 hours
- **Neonates and babies**: administer a maximum of 8 times in 24 hours

Notes

Licensing

- Algopedol® is licensed for use in term and preterm infants less than 4 months of age

Therapeutics

- Dextrose 25% in similar volumes may achieve the same effect.
- Effect enhanced when combined with other non-pharmacological techniques for providing analgesia including non-nutritive sucking and behavioural measures such as swaddling.
- Limited evidence to guide dosing in very premature babies
- May have a role in managing pain in infants up to 12 months.
- Sucrose given orally, for procedural pain management within the recommended dosing, does not alter blood glucose levels.
- Neonates and infants of mothers maintained on methadone may have altered endogenous opiate systems, resulting in a lack of analgesic effect of oral sucrose in the first days to weeks of life.

Contraindications, cautions

- Contraindicated in babies with oesophageal atresia, tracheo-oesophageal fistula, confirmed or suspected intra-abdominal pathology (e.g. NEC), fructose intolerance.
- Use with caution in infants with altered gag or swallow reflex or swallowing problems, cardio-respiratory instability or any major GI pathology.

Administration

- Oral administration using vial dispenser directly onto the anterior portion of the tongue. If needed, the vial can be closed and laid flat after first opening and be used again in the same infant within a period of 8 hours.
- Infants who are nil by mouth (NBM) or have an endotracheal tube in situ can (with medical approval) have the dose of oral sucrose applied with a small swab directly onto the tongue.
- Not appropriate for administration via feeding tube

Available as

- Preservative-free oral solution of sucrose 24% (Algopedol®) in 2 ml vials for single patient use, or sucrose 24% (Sweet-Ease) in 15ml cups which can be used to dip a pacifier into or draw up into dropper/syringe.

Evidence: (11,370–373)

Tapentadol

Use:

- Opioid analgesic

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

Pain in opioid naïve patients

By mouth using immediate release preparations

- **Child 2-17 years and body-weight over 16 kg:** 1.25mg/kg/dose every 4 hours. Maximum initial dose 50mg, can be increased to body-weight adjusted dose for subsequent dosing

  The dose for children with a high BMI must not exceed the calculated dose for a body-weight at the 97.5 percentile for the given age.

  Maximum total daily dose 7.5mg per kg body-weight (*see notes below)

- **18 years and older**: Initially 50mg every 4–6 hours, adjusted according to response, on the first day of treatment, an additional dose of 50mg may be taken 1 hour after the initial dose; maximum 700mg in the first 24 hours; maximum 600mg daily.

By mouth using modified release preparations

- **18 years and above**: Initially 50mg every 12 hours, adjusted according to response; maximum 500mg daily.

Notes:

- Opioid analgesic. Approximately 3 times less potent than morphine i.e.50mg oral tapentadol is approximately equivalent to 15mg oral morphine

Licensing

- Tapentadol oral solution is licensed for the relief of moderate to severe acute pain in children from 2 years of age (>16 kg body-weight) for a maximum of 72 hours. Use of tablet formulations or for treatment of chronic pain or for a duration >72 hours in children is off-label. Data on safety and efficacy of long-term use in children is not yet available and clinical trials are on-going.
- Tapentadol oral solution, immediate-release and modified-release tablets are licensed in adults for treatment of moderate to severe acute and chronic pain.

Therapeutics

- Dual action centrally acting opioid analgesic; agonist at the μ-opioid receptor and inhibitor of noradrenaline reuptake. The latter enhances the action of the descending pain inhibitory pathway contributing to a synergistic analgesic effect.
- Care needed if switching from another μ-agonist to tapentadol as this may cause low-grade opioid withdrawal. As required doses of the original opioid should be used to counter this (e.g. give an immediate release product at 25-50% of the original dose).
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Cautions

- MHRA/CHM advice: Tapentadol (Palexia): risk of seizures and reports of serotonin syndrome when co-administered with other medicines (January 2019). Tapentadol can induce seizures and should be prescribed with caution in patients with a history of seizure disorders or epilepsy. Seizure risk may be increased in patients taking other medicines that lower seizure threshold, for example, antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants, and antipsychotics.

Side effects

- Potential adverse effects as for other opioids. However GI side effects are reportedly less than with oxycodone or morphine.

Hepatic and renal impairment

- Dosage adjustment is not required in mild or moderate renal impairment. not recommended in severe renal impairment (lack of clinical trial data).
- Dosage adjustment is not required in mild hepatic impairment. Reduce initial dose in moderate hepatic impairment. Not recommended in severe hepatic impairment (lack of clinical trial data).

Pharmacokinetics

- Based on immediate release tablets-onset of action is less than 1 hour with time to peak serum concentrations around 75 minutes. Duration of action 4-6 hours. Duration of action of modified-release tablets is 12 hours.
- Tapentadol is rapidly and completely absorbed after oral administration. However mean absolute bioavailability after a single-dose administration is ~32% due to extensive first-pass metabolism.
- The major elimination pathway for tapentadol is glucuronide conjugation. Tapentadol does not have any active metabolites.

Administration

- Tapentadol oral solution 20mg/ml can be taken undiluted or diluted in water or any non-alcoholic drink. Use the dosing pipette (5ml subdivided in 0.1ml (2mg) intervals) provided to ensure the exact dose can be accurately measured.
- Tapentadol oral solution can be administered via an enteral feeding tube. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.
- Tapentadol oral solution contains 2mg/ml propylene glycol.
- Modified-release tapentadol tablets should be swallowed whole; crushing or chewing will lead to a rapid release of an overdose of tapentadol.

Available as

- Oral solution 20mg/ml (licensed from 2 years) Palexia®, immediate-release tablets 50mg, 75mg (licensed from 18 years only) Palexia®, Modified-release tablets (licensed from 18 years only) 25mg, 50mg, 100mg, 150mg, 200mg, 250mg Palexia®, Ationdo®. Modified-release capsules (licensed from 18 years only) 50mg, 100mg, 150mg, 200mg, 250mg Tapimio® As for all modified release opioids, brand prescribing is recommended to reduce the risk of confusion and error in dispensing and administration

CD

- CD Schedule 2

Evidence: (2,3,374–381)

Temazepam

Use:

- Sleep disturbance (short term use), especially where anxiety is a cause.
- Premedication before surgery and investigations

Important safety information

For all benzodiazepines

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and route:

By mouth:

- **Child 12-17 years**: 10-20mg 1 hour before procedures.
- **Adult:** 10-20mg at night. Dose may be increased to 40mg at night in exceptional circumstances.

Notes:

- GABA mimetic, anxiolytic sedative.

Licensing

- Tablets not licensed for use in children.

Therapeutics

- Correct contributory factors to insomnia if possible. Use in association with non-pharmacological methods.

Side effects

- Can cause paradoxical increased hostility and aggression requiring dose adjustment. Can also paradoxically increase anxiety. May impair judgement and reaction time.

Contraindications, cautions

- Contraindicated in severe hepatic impairment (unless in imminently dying)
- Caution in renal impairment, shorter half-life benzodiazepines may be preferable
- Contraindicated in respiratory depression, compromised airway and untreated sleep apnoea syndrome, except in the imminently dying.

Pharmacokinetics

- Oral bioavailability at least 90%; peak plasma concentration within 50 minutes of oral administration. Long plasma half-life of 8-15 hours.

Administration

- Oral solution may be administered via an enteral feeding tube. If administered via the jejunum monitor for loss of efficacy or increased side effects.

Available as

- Tablets (10mg, 20mg) and oral solution (10mg/5 ml).

CD

- Schedule 3 controlled drug (CD No register).

Evidence:(1–3,8)

Tizanidine

Use:

- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

Dose and route:

By mouth

- **Child 18 months-6 years**: 1mg/day in divided doses; increase if necessary, according to response.
- **7-11 years**: 2mg/day in divided doses; increase if necessary, according to response.
- **12 years and over**: 2mg/day in divided doses increasing in increments of 2mg at intervals of 3–4 days

  Usual adult total daily dose 24mg. Maximum total daily dose 36mg.

Administer as 3-4 divided doses. Timing and frequency of dosing is specific to individual patient as maximum effect is seen 2-3 hours after administration.

Titrate doses slowly over 2-4 weeks to reduce side effects

Notes:

Licensing

- Not licensed for use in children.

Therapeutics

- Limited research evidence in children. Paediatric doses largely extrapolated from adult doses
- Usually prescribed and titrated by neurologists.
- Peak response not seen until approximately 8 weeks.
- Avoid abrupt withdrawal-risk of rebound hypertension and tachycardia.

Contraindications, cautions

- Use with caution with drugs known to prolong the QT-interval.

Monitoring

- Monitor liver function monthly for first 4 months.

Side effects

- Drowsiness, weakness, hypotension and dry mouth are common side effects.

Hepatic impairment, renal impairment

- Use with caution in liver disease, monitor liver function regularly.
- Caution in renal impairment

Interactions

- Metabolised by cytochrome P450 enzyme CYP1A2. Levels increased by drugs that inhibit this enzyme including ciprofloxacin and possibly famotidine potentially leading to severe hypotension. Levels may be reduced by drugs that induce this enzyme including phenytoin.

Administration

- Tablets may be crushed and administered in water if preferred. May be administered via an enteral feeding tube. Tablets do not disperse readily, but will disintegrate if shaken in 10 ml of water for 5 minutes. The resulting dispersion will flush via an 8Fr NG tube without blockage. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.

Available as

- Tablets (2mg, 4mg).

Evidence: (2,3,8,382–385)

Tramadol

Use:

- Weak opioid with additional non-opioid analgesic actions

The WHO now advises there is insufficient evidence to make a recommendation use of weak opioids in children and recommends moving directly from non-opioids to low dose strong opioids for the management of moderate uncontrolled pain in children

Important safety information

For all opioids

MHRA/CHM advice: Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (March 2020)

The MHRA reminds healthcare professionals that opioids co-prescribed with benzodiazepines and benzodiazepine-like drugs can produce additive CNS depressant effects, thereby increasing the risk of sedation, respiratory depression, coma, and death.

The APPM recognises that in paediatric palliative care co-prescription of opioids and benzodiazepines is frequently necessary and appropriate. In these circumstances the lowest effective doses should be used. Doses should be increased gradually wherever possible, changing the dose of only one drug at a time, and allowing sufficient time for the changes to take effect before making further dose adjustments.

Dose and routes

By mouth, subcutaneous, intramuscular or slow intravenous injection:

- **Child 4-11 years**: 1mg/kg/dose every 6 hours. Maximum 50mg/dose.

  Increased if required to 1.5mg/kg/dose every 6 hours and then to 2mg/kg/dose every 6 hours. Maximum 100mg/dose

- **12 years and over**: Initial dose of 50mg every 4-6 hours. Increase if necessary to a maximum of 400mg/day given in divided doses every 4-6 hours.

Total daily dose can also be given as a continuous intravenous or subcutaneous infusion/24hours.

Notes:

Licensing

- Not licensed for use in children under 12 years.

Therapeutics

- By mouth tramadol is approximately 1/10 as potent as morphine. However equianalgesic ratios may be unreliable due to inter-individual variation in CYP2D6 activity.
- Has been given by sublingual route at similar doses
- May be helpful in neuropathic pain and visceral hyperalgesia
- Tramadol itself has analgesic properties. It is also metabolized in the liver by CYP2D6 to the active metabolite desmethyltramadol which has a higher affinity for the mu-opioid receptor. Unlike codeine, poor metabolisers experience only slightly diminished analgesic effect. The risk of respiratory depression may be higher in the 5% of the western European population who are ultra-metabolisers. However, the risk is likely to be significantly less than with codeine.
- Refer to Principles of Opioid Stewardship, Appendix 2
- Ensure access to an appropriate stimulant laxative if administered regularly

Side effects

- Causes less constipation and respiratory depression than the equivalent morphine dose. Risk of respiratory depression may be increased in paediatric patients who are obese or have conditions such as obstructive sleep apnoea or severe lung disease, or who are ultrarapid metabolizers of the drug
- Side effects include diarrhoea, retching, fatigue and paraesthesia.

Pharmacokinetics

- Onset of action after an oral dose is 30 to 60 minutes. Duration of action is 4-6 hours.

Interactions

- Analgesic effect may be reduced by ondansetron. Increased risk of serotonin syndrome with co-administration of tramadol and ondansetron

Hepatic impairment, renal impairment

- Avoid or reduce dose

Administration

- Orodispersible tablets should be sucked and then swallowed or they may be dispersed in water. Modified release capsules may be opened and the capsule contents swallowed immediately without chewing.
- Soluble or orodispersible tablets may be dissolved in water for administration via an enteral feeding tube or use the oral drops or disperse capsule contents. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.
- For subcutaneous infusion dilute in sodium chloride 0.9% or water for injection

Patient information

- Patient information see Medicines for Children leaflet “Tramadol for pain” https://www.medicinesforchildren.org.uk/medicines/tramadol-for-pain/

Available as

- Soluble tablets 50mg, Orodispersible tablets 50mg, Immediate release capsules 50mg, Oral solution 10mg/ml, oral drops 100mg/ml, modified-release 12hr tablets 50mg, 100mg, 150mg, 200mg, 300mg, 400mg, modified release 12hr capsules 50mg, 100mg, 150mg, 200mg, modified-release 24hr tablets 150mg, 200mg, 300mg, 400mg, solution for injection 100mg/2ml

- Brand prescribing of modified release preparations is recommended to reduce the risk of confusion and error in dispensing and administration. Care with prescribing preparations due to availability of both 12-hour and 24 hour modified release formulations

CD

- Schedule 3 CD

Evidence: (1,2,8,10,61–63,120,187,386–393)

Tranexamic acid

Use:

- Inhibition of fibrinolysis
- Oozing of blood (e.g. from mucous membranes or capillaries), particularly when due to thrombocytopenia or platelet dysfunction
- Menorrhagia

Dose and route:

Inhibition of fibrinolysis

By mouth:

- **Child 1 month and over**: 15-25mg/kg (maximum dose 1.5 g) 2–3 times daily.

By intravenous injection over at least 10 minutes:

- **Child 1 month and over**: 10mg/kg (maximum dose 1 g) 2-3 times daily.

By continuous intravenous infusion:

- **Child 1 month and over**: 45mg/kg/24hours.

Menorrhagia

By mouth:

- **Child 12 years and over**: 1g 3 times daily for up to 4 days.

  Up to 4g in divided doses can be used for very heavy bleeding. Treatment should not be initiated until menstruation has started.

Prevention or treatment of oral bleeding

For use as mouthwash (5% solution):

- **Child 6 years and over**: 5-10ml 4 times daily for 2 days. Not to be swallowed.

Topical treatment of bleeding:

- Apply gauze soaked in 100mg/ml injection solution to affected area.

Notes:

Licensing

- Injection not licensed for use in children under 1 year or for administration by intravenous infusion.

Side effects

- Urinary tract clots resulting from use in presence of haematuria can result in urinary tract obstruction and clot 'colic'
- Diarrhoea, nausea and vomiting

Hepatic impairment, renal impairment

- Reduce dose in mild to moderate renal impairment and avoid in severe renal impairment.

Administration

- For administration via an enteral feeding tube, the oral suspension (unlicensed) or injection solution is preferred. Tablets may be dispersed in water for tube administration without blockage. No specific information for jejunal administration.
- Parenteral preparation can be used topically.

Patient information

- See Medicines for Children leaflet "Tranexamic acid for heavy bleeding during periods" https://www.medicinesforchildren.org.uk/medicines/tranexamic-acid-for-heavy-bleeding-during-periods/ and Medicines for Children leaflet "Tranexamic acid for the treatment or prevention of bleeding in haemophilia and other clotting problems"
- https://www.medicinesforchildren.org.uk/medicines/tranexamic-acid-for-the-treatment-or-prevention-of-bleeding-in-haemophilia-and-other-clotting-problems/

Available as

- Tablets (500mg), syrup (500mg/5 ml available from 'specials' manufacturers) and injection (100mg/ml ampoules). Mouthwash only as extemporaneous preparation.

Evidence: (1–3,394)

Trihexyphenidyl

Uses:

- Dystonia
- Sialorrhoea (drooling)
- Antispasmodic.

Dose and route:

By mouth

- **Child 3 months and over**: 1–2mg daily in 1-2 divided doses, increased every 3-7 days by 1mg daily; adjusted according to response and side effects, maximum 2mg/kg (or 100mg) daily

  Doses needed to control drooling are generally much lower than those needed for dystonia

Notes:

- Reduces the effects of the relative central cholinergic excess that occurs in dopamine deficiency.

Licensing

- Not licensed for use in children.

Therapeutics

- Use in conjunction with careful observation and a full non-drug management programme including positioning, massage, holding, distraction, checking for causes of exacerbations etc. Seek specialist neurological advice.
- May have limited efficacy in children with cerebral palsy and dystonia.
- Start at a low dose and increase gradually to minimise the incidence and severity of side effects.
- May take several weeks for maximal effect on dystonic movements to be seen.
- Do not withdraw abruptly in children who have been on long-term treatment.

Contraindications, cautions

- Contraindicated in myasthenia gravis

Side effects

- Side effects are very common. Mouth dryness, constipation, blurring of vision, dizziness and nausea can occur in 30-50% patients. Less common side effects include urinary retention, tachycardia, confusion, insomnia and with very high doses CNS disturbance including oculogyric crisis

Hepatic impairment, renal impairment

- Use with caution in children with renal or hepatic impairment.

Pharmacokinetics

- Onset of action is usually within 1 hour, maximum effect occurs within 2-3 hours and duration of effect approximately 6-12 hours.

Administration

- Tablets may be crushed and mixed in soft food.
- Administration with or after food may help minimise gastrointestinal adverse effects
- The oral liquid may be used for administration via feeding tubes. Alternatively the tablets will disperse readily in water. No specific data for jejunal administration: suggest administering as for gastrostomy and monitoring for increased side effects or loss of efficacy.

Patient information

- See Medicines for Children leaflet "Trihexyphenidyl hydrochloride for dystonia" https://www.medicinesforchildren.org.uk/medicines/trihexyphenidyl-hydrochloride-for-dystonia/

Available as

- Tablets 2mg and 5mg; oral liquid 5mg in 5 ml.

Evidence: (1,2,8,39,58,81,158,395)

Vitamin K (Phytomenadione)

Use:

- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice)
- Reversal of coumarin anticoagulant (warfarin) overdose

Dose and route:

By mouth or intravenous:

- **Neonate**: 100micrograms/kg.
- **Child 1 month and over**: 250-300micrograms/kg (maximum 10mg) as a single dose.

Notes:

Contraindications, cautions

- Caution with intravenous use in premature infants less than 2.5 kg, increased risk of kernicterus

Administration

- Risk of cardiovascular collapse with rapid administration. Preferably dilute with Glucose 5% and give over 15-20 minutes. Can also be given as a slow intravenous injection over 3-5 minutes
- Injection should be protected from the light.

Available as

- Capsules 1mg, oral drops 200 micrograms/ml and injection 10mg/ml. Many other forms and strengths available from special order manufacturers.

Evidence: (1,2)

Appendices

1. Opiate conversion tables

- Opioid conversion tables can be used to calculate approximate equianalgesic doses of opioids when switching from a weak opioid to morphine, or from one strong opioid to another.
- Caution is *always* necessary. Conversion ratios are never more than an approximate guide due to:
    - Wide inter-individual variation in opioid pharmacokinetics
    - Limited data on opioid equi-analgesia in children
    - Differences between opioid pharmacokinetics in adults and children
    - Data largely derived from single dose studies
    - Potential for opioid tolerance related to dose and duration of opioid treatment
    - Direction of switch in opioid
    - Concurrent medications
- If switching from an opioid other than morphine to another opioid, convert the dose of the first opioid to morphine equivalent, and then use that quantity to determine the dose of the second opioid.
- Consider reducing the dose of the new opioid by 25-50% when rotating opioids due to intolerable side effects or lack of efficacy. This is especially important if the patient is already on a high dose of the previous opioid, or there has recently been rapid dose escalation.

Notes

- Equianalgesic ratios for methadone are dose dependent and highly variable: see methadone monograph
- Mean oral bio-availability of oxycodone is 75% (range 60–87%). For safety, recommended equianalgesic ratios are therefore either rounded down to 1.5:1 or up to 2:1 depending on direction of switch and rounding errors
- Newer systematic review evidence suggests using a ratio of 3:1 when converting morphine from oral to intravenous morphine
- Bioavailability of some drugs may be lower for subcutaneous versus intravenous administration, particularly for infusions. However the APPM recommendation is to assume similar pharmacokinetics for intravenous and subcutaneous dosing.
- Oral tapentadol is approximately 3 times less potent than morphine e.g. 30mg tapentadol is approximately equivalent to 10mg oral morphine. However experience in children is currently too limited to make clear recommendations regarding opioid conversion

Evidence: (1–3,117,117,396,397)

Conversion from oral morphine

Conversion		Ratio	Calculation	Example
From	To			
Morphine oral	Alfentanil CSCI or CIVI	30:1	Divide 24hour morphine dose by 30	Morphine oral 60mg/24hours ÷ 30 = alfentanil CSCI 2mg/24hours
Morphine oral	Buprenorphine sublingual	80:1	Divide 24hour morphine dose *in mg* by 80 to give 24hour buprenorphine dose *in mg* Then multiply 24hour buprenorphine dose *in mg* by 1,000 to give 24hour buprenorphine dose *in micrograms* *Then* divide 24hour buprenorphine dose *in micrograms* into 3 or 4 divided doses for 8 or 6 hourly administration	Morphine oral 60mg/24hours ÷ 80 = buprenorphine SL 0.75mg/24hours Buprenorphine 0.75mg/24hours x 1000 = buprenorphine 750micrograms/24hours Buprenorphine 750micrograms/24hours ÷ 3 = 250micrograms 8 hourly *Round down* to 200micrograms SL 8 hourly
Morphine oral	Buprenorphine transdermal	100:1	Divide 24hour morphine dose *in mg* by 100 to give 24hour buprenorphine dose *in mg* *Then* multiply 24hour buprenorphine dose *in mg* by 1,000 to give 24hour buprenorphine dose *in micrograms* *Then* divide 24hour buprenorphine dose in micrograms by 24 to give patch strength in micrograms/hour	Morphine oral 300mg/24hours ÷ 100 = buprenorphine transdermal 3mg/24hours Buprenorphine 3mg/24hours x 1000 = buprenorphine 3,000micrograms/24hours Buprenorphine 3,000micrograms/24hours ÷ 24 = buprenorphine 125micrograms/hour *Round down* to 70+35microgram/hour buprenorphine patches
Morphine oral	Diamorphine CSCI or CIVI	6:1	Divide 24hour morphine dose by 6	Morphine oral 30mg/24hours ÷ 6 = diamorphine CSCI 5mg/24hours
Morphine oral	Diamorphine intranasal	3:1	Divide PRN morphine dose by 3	Morphine oral 3mg PRN ÷ 3 = Diamorphine intranasal 1mg PRN

Conversion from oral morphine

Conversion		Ratio	Calculation	Example
From	**To**			
Morphine oral	Fentanyl CSCI or CIVI	100:1[a]	Divide 24hour morphine oral *in mg* dose by 100 to give fentanyl dose in *mg/24hours* *Then* multiply fentanyl dose in mg/24hours by 1000 to convert to *micrograms/24hours*	Morphine oral 60mg/24hours ÷ 100 = fentanyl CIVI 0.6mg/24hours CSCI Fentanyl CIVI 0.6mg/24hours x 1000 = fentanyl CIVI 600micrograms/24hours
Morphine oral	Fentanyl transdermal patch	100:1	Divide 24hour morphine oral dose by *in mg* 100 to give fentanyl transdermal dose in mg *Then* multiply by 1,000 to give fentanyl transdermal dose in micrograms *Then* divide by 24 to give fentanyl transdermal dose in micrograms/hour	Morphine oral 90mg/24hours ÷ 100 = fentanyl transdermal 0.9mg/24hours Fentanyl 0.9mg/24hours x 1000 = fentanyl 900micrograms/24hours Fentanyl 900micrograms/24hours ÷ 24 = fentanyl 37.5mg/hour = fentanyl 12+25micrograms/hour patches
Morphine oral	Hydromorphone oral	5:1	Divide morphine oral dose by 5	Morphine oral 10mg ÷ 5 = hydromorphone oral 2mg
Morphine oral	Oxycodone oral	2:1	Divide morphine oral dose by 2	Morphine oral 20mg ÷ 2 = oxycodone oral 10mg
Morphine oral	Oxycodone CSCI or CIVI	3:1	Divide morphine oral dose by 3	Morphine oral 30mg/24hours ÷ 3 = oxycodone CSCI or CIVI 10mg/24hours
Morphine oral	Tramadol oral	1:10	*Multiply* the total daily dose of oral morphine by 10	Morphine oral 10mg **x**10 = tramadol oral 100mg

[a] Some centres use equianalgesic ratio of 150:1 depending on circumstances

Conversion from continuous intravenous or subcutaneous morphine

Conversion		Ratio	Calculation	Example
From	**To**			
Morphine CSCI or CIVI	Alfentanil CSCI or CIVI	15:1	Divide 24hour morphine dose by 15	Morphine CSCI 30mg/24hours ÷ 15 = alfentanil CSCI 2mg/24hours
Morphine CSCI or CIVI	Diamorphine CSCI or CIVI	2:1	Divide 24hour morphine dose by 2	Morphine CSCI 15mg/24hours ÷ 2 = diamorphine CSCI 7.5mg/24hours
Morphine CSCI or CIVI	Fentanyl CSCI or CIVI	50:1[a]	Divide 24hour morphine dose by 50 to give fentanyl dose in *mg/24hours* *Then* multiply fentanyl dose in mg/24hours by 1000 to convert to *micrograms/24hours*	Morphine CIVI 25mg/24hours ÷ 50 = fentanyl CIVI 0.5mg/24hours Fentanyl CIVI 0.5mg/24hours x 1000 = 500micrograms/24hours
Morphine CSCI or CIVI	Fentanyl patch	50:1	Divide 24hour morphine dose by 50 to give fentanyl dose in *mg/24hours* *Then* multiply fentanyl dose in mg/24hours by 1000 to convert to *micrograms/24hours* *Then* divide by 24 to convert to micrograms/hour	Morphine CSCI 30mg/24hours ÷ 50 = fentanyl transdermal 0.6mg/24hours Fentanyl 0.6mg/24hours x 1000 = 600micrograms/24hours Fentanyl CIVI 600micrograms/24hours ÷ 24 = 25micrograms/hour patch
Morphine CSCI or CIVI	Hydromorphone CSCI or CIVI	5:1	Divide 24hour morphine dose by 5	Morphine CSCI 25mg ÷ 5 Hydromorphone CSCI =5mg
Morphine CSCI or CIVI	Oxycodone CSCI or CIVI	1:1	Use the same dose	Morphine CSCI 50mg/24h = oxycodone CSCI 50mg/24hours

[a] Some centres use equianalgesic ratio of 75:1 depending on circumstances

Change of route

Conversion		Ratio	Calculation	Example
From	**To**			
Buprenorphine sublingual	Buprenorphine IV or SC *bolus*	2:1	Divide sublingual buprenorphine by 2	Buprenorphine SL 200micrograms ÷ 2 = buprenorphine SC bolus 100micrograms
Diamorphine intranasal	Diamorphine IV or SC bolus	2:1	Divide intranasal diamorphine by 2	Diamorphine intranasal 2mg ÷ 2 = Diamorphine intravenous 1mg
Hydromorphone oral	Hydromorphone CSCI or CIVI	2:1[a]	Divide 24hour hydromorphone dose by 2	Hydromorphone oral 10mg ÷ 2 = hydromorphone CSCI 5mg
Morphine oral	Morphine CSCI or CIVI	3:1	Divide 24hour morphine oral dose by 3	Morphine oral 15mg ÷ 3 = morphine CSCI 5mg
Methadone oral	Methadone CIVI or CSCI	2:1	Divide 24hour methadone dose by 2	Methadone oral 2mg ÷ 2 = methadone CSCI 1mg
Oxycodone oral single dose	Oxycodone SC or IV bolus single dose	1.5:1	Divide oxycodone oral dose by 1.5	Oxycodone oral 4.5mg ÷ 1.5 = oxycodone IV/SC *bolus* 3mg
Oxycodone oral	Oxycodone CSCI or CIVI	1:5:1[b]	Divide 24hour dose of oral oxycodone by 1.5	Oxycodone oral 90mg/24hours ÷1.5 = oxycodone CSCI 60mg/24hours
Tramadol oral	Tramadol CIVI or CSCI	1:1	Use the same dose	Tramadol oral 10mg/24hours = tramadol CSCI 10mg/24hours

[a] Some centres use equianalgesic ratio of 3:1 depending on circumstances

[b] Some centres use a equianalgesic ratio of 2:1 for infusions

2. Opioid stewardship

- Opioids are high-risk medicines which are widely used in the field of paediatric palliative care. The concept of opioid stewardship is based on the principles of antibiotic stewardship in that opioids should be used for the right patient in the right way at the right time. Recent evidence shows an increasing trend in global opiate use which has seen a corresponding increase in harm. Opioid stewardship entails a set of systematic and coordinated interventions designed to improve the health of and minimise harm to our patients.
- Key aspects to opiate stewardship that should be followed include:
    - Patient information gathering and shared decision making
    - Effective communication with the patient or their proxy and between members of the multidisciplinary team
    - Thorough assessment and regular re-assessment of the indication(s) for opioid therapy
    - Risk-benefit analysis
    - Appropriate prescribing and dispensing, ideally by a single prescribing team.
    - Monitoring and management of opioid adverse effects
    - Clear documentation
    - Regular review of therapy
    - Appropriate storage
    - Disposal of unused opioids

Evidence (398)

3. Prolonged QT syndrome

- Polypharmacy in paediatric palliative care is common. Therefore prescribers must be aware of potential risks, including prolongation of the QT-interval. This is particularly relevant to paediatric patients receiving palliative care where there may be additional risk factors for prolonged QTc including cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT-interval
- Although the frequency of serious life-threatening arrhythmias, including Torsades de pointes (TdP), in this population appears to be low, it should be considered carefully when prescribing medications known to prolong QTc.

Drugs associated with prolonged QT-interval

- Drugs that may affect the QT-interval can be subdivided into four categories

    1. Known risk of serious life-threatening arrhythmias -These drugs prolong the QT-interval AND are clearly associated with a known risk of TdP, even when taken as recommended.
    2. Possible risk of TdP-These drugs can cause QT prolongation BUT currently lack evidence for a risk of TdP when taken as recommended.
    3. Conditional risk of TdP-These drugs are associated with TdP BUT only under certain conditions of their use (e.g. excessive dose, in patients with conditions such as hypokalaemia, or when taken with interacting drugs) OR by creating conditions that facilitate or induce TdP (e.g. by inhibiting metabolism of a QT-prolonging drug or by causing an electrolyte disturbance that induces TdP).
    4. Drugs to avoid in congenital long QT syndrome (cLQTS)-These drugs pose a high risk of TdP for patients with cLQTS and include all those in the above three categories PLUS additional drugs that do not prolong the QT-interval per se but which have a special risk because of their other actions.

- Drugs in group 1, (as of July 2023*) but not those in the other categories* are identified in the notes section of the relevant monograph in the formulary. However the list of drugs associated with prolonged QT-interval is being continually updated. Professionals are strongly advised to check the most up to date list on https://www.crediblemeds.org/ when prescribing or advising on prescribing for patients at increased risk of prolonged QT-interval

Safe prescribing

- When prescribing drugs which are known to prolong the QT-interval it is important to gather information about any additional risk factors in order to make an informed decision about the risks and benefits of the proposed drug.
- Co-administration of two or more drugs that prolong the QTc should be avoided where possible.
- For high risk patients consider a 12 lead ECG before starting treatment and repeating once the medication has reached steady state.

Evidence: (222,227,399,400)

4. Benzodiazepines

Approximate equivalent oral anxiolytic sedative doses[ab]

Benzodiazepine	Approximate equivalent oral dose
Clobazam	10mg
Clonazepam	250micrograms
Diazepam	5mg
Lorazepam	500micrograms
Midazolam	2.5mg[b] *intravenous or subcutaneous*
Temazepam	10mg

Comparative pharmacokinetic data

Diazepam[a]

	Bioavailability	Onset of action (minutes)	Time to peak plasma concentration (minutes)	Duration of action (hours)	Half-life (hours) (including active metabolites)
Diazepam oral	>90%	15-30[c] 30-90	30-90	3-30	25-50 20-100[c]
Diazepam intravenous		1-5	≤15 (oil) ≥15 (emulsion)	15-60	
Diazepam rectal	65-85% 90%[c]	<30	10-30[c] <30		

[a] BNF 85: March-September 2023. London: Pharmaceutical Press; 2023.

[b] Charlesworth S, Howard P, Wilcock A, editors. PCF8: palliative care formulary. Eighth edition. London: Pharmaceutical Press; 2022.

[c] Medicines for Children 2003

Lorazepam[a]

	Bioavailability	Onset of action (minutes)	Time to peak plasma concentration (minutes)	Duration of action (hours)	Half-life (hours) (including active metabolites)
Lorazepam sublingual		5	150		
Lorazepam oral	90%[a,b]	10-15	150 120[b]	6-72 8[b]	10-20[a,b]
Lorazepam intravenous		2-5[b] 10		4-6[b]	12-16

Midazolam[a,b]

	Bioavailability	Onset of action (minutes)	Time to peak plasma concentration (minutes)	Duration of action (hours)	Half-life (hours) (including active metabolites)
Midazolam buccal	85% 75%[c]	15 5[b]	≤30		
Midazolam oral	40%	20-30 10-30[b]	30-60	<4 20-90[3] minutes	1-4 2-5 [a,b]
Midazolam Sub-cutaneous	95%	5-10	30		
Midazolam intravenous		2-3[a,b]		30-60mins[b]	

[a] Charlesworth S, Howard P, Wilcock A, editors. PCF8: palliative care formulary. Eighth edition. London: Pharmaceutical Press; 2022
[b] Medicines for Children 2003
[c] Kienitz R et al. Benzodiazepines in the Management of Seizures and Status Epilepticus: A Review of Routes of Delivery, Pharmacokinetics, Efficacy, and Tolerability. CNS Drugs. 2022 Sep;36(9):951–75.

5. Gabapentin to pregabalin switch

- Gabapentin and pregabalin have similar mechanisms of action. However, gabapentin absorption is saturable, leading to non-linear pharmacokinetics, whereas pregabalin possesses linear pharmacokinetics. Furthermore, clearance of pregabalin is faster in children under 30 kg and particularly those under 6 years of age. Higher doses and/or more frequent dosing interval may therefore be needed. As a consequence, switching between gabapentin and pregabalin is not straight-forward.

- There is limited evidence in the literature with regard to managing a switch, with no evidence in children. However many pain centres in the UK have developed local protocols for a switch in adults, with no reports of adverse effects. The following conversion factors have been used:
  - 1/6 is generally accepted as a standard conversion however a range of factors from 1/4 to 1/9 have been used to accommodate practical dosing schedules
  - Lower conversion factors of 1/6 to 1/9 used for higher gabapentin dosing to accommodate the non-linear kinetics of gabapentin

- The table below details a switch from gabapentin to pregabalin for neuropathic pain in children extrapolated from available adult data. Conversion factors allow for practical dosing.

Table 2: Gabapentin to Pregabalin switch

<table>
<tr><th>Age</th><th>Gabapentin
APPM formulary dose</th><th>Recommended conversion ratio[a]</th><th>Pregabalin
APPM formulary dose</th><th>Recommended initial maximum pregabalin dose</th></tr>
<tr><td>1-23 months</td><td>5-10mg/kg/dose
3 times daily</td><td>1/6</td><td>1-5mg/kg/dose
2 times daily</td><td>5mg/kg/dose
2 times daily</td></tr>
<tr><td>2-11 years</td><td>5-30mg/kg/dose
3 times daily</td><td>1/6</td><td>1-5mg/kg/dose
2 times daily</td><td>5mg/kg/dose[b]
2 times daily
Maximum 100mg/dose</td></tr>
<tr><td rowspan="3">12 years and over</td><td>300mg
3 times daily</td><td>1/5</td><td rowspan="3">12-15 years
1-5mg/kg/dose
2 times daily
16 years and over
75mg-300mg
2 times daily</td><td>100mg
2 times daily</td></tr>
<tr><td>400mg
3 times daily</td><td>1/6</td><td>100mg
2 times daily</td></tr>
<tr><td>600mg-1.2g
3 times daily</td><td>1/6-1/9</td><td>200mg
2 times daily</td></tr>
</table>

[a] From adult literature and taking into account recommended doses of gabapentin and pregabalin in neonates and children
[b] Children with body-weight less than 30Kg and especially those under 6 years may require up to 15mg/kg/24hours, giving a conversion ratio that may be as much as 1/3

- Using the table:
    1. Calculate the child's total daily gabapentin dose in mg/24hours
    2. Multiply by the relevant conversion ratio to get the approximate equivalent dose of pregabalin in mg/24hours. Divide the total daily dose of pregabalin by two for twice daily administration
    3. The dose of pregabalin would be expected to fall within the range given in the formulary and should not exceed the recommended initial maximum dose

Evidence (3,401–406)

6. Buccal administration of liquid preparations

- Buccal or sublingual administration is increasingly accepted as a convenient, painless method of drug delivery. Potential advantages of administration by these routes include rapid absorption without the need to swallow and by-passing first pass metabolism. Absorption of drugs via the buccal or sublingual routes is influenced by a number of important factors with the potential for differences in bioavailability between patients and in the same patient over time.
- Factors affecting absorption via buccal or sublingual routes
  - Volume of the oral cavity
  - pH of the oral cavity
  - Rate of saliva production
  - Site of drug delivery: the sublingual mucosa has higher permeability than the buccal mucosa but small volume for administration
  - Relative lipophilic (transcellular absorption) versus hydrophilic (paracellular absorption) properties of the molecule
  - Molecular size: molecules (molecules greater than 500 Da are unlikely to be absorbed)
  - Excipients
  - Volume of administration
  - Ability to swallow or co-operate with not swallowing
  - Palatability
- The volume of liquid preparation that can be tolerated in the buccal or sublingual cavity without swallowing has been estimated as 2ml in adult patients. No equivalent data exists for children and extrapolating to the paediatric population is complex. The table below provides approximations based on scaling by weight, body surface area and head circumference. In general liquid preparations for buccal or sublingual administration should be administered in the smallest measurable volume

Age range	Estimated maximum volume for buccal or sublingual administration
Neonate -11 months	0.5ml
1-5 years	1ml
6-10 years	1.5ml
11 years and over	2ml

Evidence: (121,407–409)

7. Dosing in obesity

- Patients requiring paediatric palliative care are frequently atypical in terms of weight for age or body composition. Childhood obesity, defined as body weight greater than or equal to the 98th centile for age, is increasing. Even patients who are seemingly a normal weight for age may have relatively more body fat and less lean muscle mass if they are almost completely and permanently immobile and non weight-bearing.
- Children are usually dosed according to their body-weight or age, as a surrogate of 'normal' size and function. However, in children with obesity there is a risk of drug overdose if total body weight is used. Therefore, for a small selection of drugs it is recommended to use either ideal body weight (IBW) or adjusted body weight (AdjBW))

Weight (kg)	Definition
Total Body Weight (TBW)	Weight in kg (no adjustment necessary)
Ideal Body Weight (IBW)	Cross reference height centile to weight for that centile If height is not available, use length or arm span.
Adjusted Body Weight (AdjBW)	IBW + Adjustment Factor (0.3) x (TBW-IBW)

Analgesics

- Fentanyl (AdjBW)
- Ibuprofen (AdjBW)
- Morphine (IBW)
- Paracetamol (AdjBW)

Anticonvulsants

- Carbamazepine (IBW)
- Levetiracetam (maintenance) (AdjBW)
- Phenytoin (maintenance) (AdjBW)

Evidence: (410)

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