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PALLIATIVE PHARMACOTHERAPY GUIDELINE FOR PHARMACISTS

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Ministry of Health (MOH) Malaysia
Lot 36, Jalan Profesor Diraja Ungku Aziz,
46200 Petaling Jaya,
Selangor, Malaysia
Tel: 603 – 7841 3200
Website: www.pharmacy.gov.my

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PREFACE

YBRS. PUAN ZUHAINI BINTI MUKRIM
DIRECTOR
PHARMACY PRACTICE AND DEVELOPMENT DIVISION
PHARMACEUTICAL SERVICES PROGRAMME
MINISTRY OF HEALTH MALAYSIA

Palliative care has become an increasingly recognised and essential part of the Malaysian healthcare system, providing comprehensive support to patients with life-limiting illnesses. It encompasses not only the management of physical symptoms, but also addresses psychological, emotional, and spiritual needs. Within this multidisciplinary framework, pharmacists play a critical role in ensuring the safe, effective, and appropriate use of medications, with the ultimate aim of improving patients' quality of life.

Palliative pharmacy is a specialised area of practice that demands advanced knowledge in pharmacotherapy for symptom control, rational discontinuation of medications and medication safety—particularly in patients with progressive disease and altered pharmacokinetics. Beyond clinical expertise, it also requires sensitivity, empathy, and close collaboration with healthcare teams to ensure patient-centred care aligned with individual goals and preferences.

This guideline aims to provide pharmacists with a structured reference on their roles and responsibilities in palliative care. It outlines key clinical and technical aspects of palliative pharmacy services, aligned with national and international standards of practice. By adopting evidence-based approaches and best practices, pharmacists can contribute meaningfully to improving patient outcomes, ensuring comfort, and supporting dignified end-of-life care.

I would like to express my sincere appreciation to all contributors who were involved in the development of this guideline. It is my hope that this document will serve as a practical resource and professional guide for pharmacists involved in palliative care, and that it will continue to support the advancement of pharmacy practice within the palliative care setting in Malaysia.

ACKNOWLEDGEMENT

Zuhaini binti Mukrim
Director of Pharmacy Practice and Development Division
Pharmaceutical Services Programme, MOH

Syahida binti Che Embi
Deputy Director of Pharmacy Practice and Development Division
Pharmaceutical Services Programme, MOH

Lee Mei Wah
Senior Principal Assistant Director
Pharmacy Practice and Development Division
Pharmaceutical Services Programme, MOH

EDITORIAL BOARD

CONTRIBUTORS

Nur Hazalina binti Md Salleh
Hospital Sultan Ismail

Prita Nambbiar
National Cancer Institute

Khoo Lee Phei
Hospital Tuanku Ja'afar

Elaine Kan Mei Ying
Hospital Kuala Lumpur

Vivien Sow Yik Xin
Hospital Kuala Lumpur

Felicia Loh Yuan Ye
Hospital Selayang

Sanggetha Ramasamy
Hospital Sultanah Bahiyah

Alison Chai Ling Pao
Hospital Umum Sarawak

EXTERNAL REVIEWERS

Dr. Fazlina binti Ahmad
Senior Palliative Care Consultant
Hospital Sultanah Bahiyah
(Head of Palliative Medicine Subspecialty)

Dr. Richard Lim Boon Leong
Senior Palliative Care Consultant
Hospital Selayang

Dr. Saiful Adni bin Abd Latif
Palliative Care Specialist
National Cancer Institute

Dr Sherizalzwa binti Zainuddin
Palliative Care Consultant
Universiti Malaya, Kuala Lumpur

Dr. Teoh See Wie
Family Medicine Specialist
Salak Health Clinic

Dr. Nazedah binti Ain @ Ibrahim
Pharmacist
Hospital Tunku Azizah

Nik Zurianiarina binti Mohd Zaki
Senior Principal Assistant Director
Pharmacy Enforcement Division
Pharmaceutical Services Programme, MOH

Aidah Abdul Hassan Chin
Pharmacist
Hospis Malaysia

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1.0 INTRODUCTION

Palliative care is a cornerstone of compassionate healthcare, offering a holistic approach to those confronting serious, life-limiting illnesses. It addresses not only physical symptoms but also the emotional, social, and spiritual dimensions of a patient's journey. By prioritising dignity, quality of life and a patient-centred approach, palliative care ensures that patients and their families can better navigate the challenges of serious illness with comfort and resilience.

The need for palliative care in Malaysia is significant and growing, driven by an increase in chronic illnesses and an ageing population. With over 70% of deaths in the country attributed to non-communicable diseases, it is estimated that the demand for palliative care will more than double by 2030. Currently, less than 10% of these needs are being met, underscoring the urgent necessity to expand services and ensure equitable access across the nation.

The National Palliative Care Policy and Strategic Plan, launched in 2019, provides a crucial framework for this expansion, emphasising the integration of palliative care into all levels of the healthcare system and highlighting the vital role of a multidisciplinary approach to meet these challenges. Medications are essential to enhance the quality of life for those dealing with serious illnesses. As an integral part of the healthcare landscape, pharmacists must adapt their skills and knowledge to support this expansion, ensuring compassionate and effective care is accessible throughout the continuum of care.

This handbook is a practical resource designed to equip pharmacists with the necessary knowledge and skills for palliative care pharmacotherapy. It outlines the pharmacist's role within interdisciplinary teams and provides insights into optimising medication management, handling symptoms, and navigating the care pathways. It is hoped that this book will enhance the pharmacist's ability to contribute meaningfully to the wellbeing of patients and their families during challenging times.

2.0 OBJECTIVES

a) Equip pharmacists with a comprehensive understanding of the principles and philosophy of palliative care.

b) Provide expertise in managing commonly encountered symptoms in palliative care through effective pharmacological interventions.

c) Offer practical guidance on tailoring medication regimens to individual patient needs, considering factors such as age, comorbidities, and treatment goals.

d) Accentuate the role of pharmacists in interdisciplinary teams, fostering effective communication and collaboration to enhance the overall quality of palliative care.

3.0 ACRONYMS AND ABBREVIATIONS

ACE	Angiotensin-Converting Enzyme
ADR	Adverse Drug Reactions
ALS	Amyotrophic lateral sclerosis
BD	Twice daily
CIVI	Continuous Intravenous Infusion
COPD	Chronic Obstructive Pulmonary Disease
CR	Controlled Release
CSCI	Continuous Subcutaneous Infusion
CV	Cardiovascular
GERD	Gastroesophageal Reflux Disease
GI	Gastrointestinal
IR	Immediate Release
IV	Intravenous Injection
MYMAAT	Malaysia Medication Adherence Assessment Tool
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OD	Once daily
ON	Once at night
PO	Per Oral
PR	Per Rectum
PRN	When necessary
QID	Four times a day
SC	Subcutaneous Injection
SL	Sublingual
TD	Transdermal
TDS	Three Times a Day
WHO	World Health Organization

4.0 GLOSSARY

Term	Definition
Palliative Care[1]	Palliative care according to WHO is an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual.
Domiciliary palliative care[2]	A community based palliative care service provided by the ministry of health to ensure continuity of patient care who are discharged early, support the patient's family through caregiver training in aspect of patient's care at home and reduce hospital readmissions through quality health care at home and in the community.
Palliative Medicine[3]	The medical speciality which concerns itself with the appropriate medical care of patients with progressive disease. This should be distinguished from "Palliative Care" which is the approach to care for patients with progressive disease.
Terminal phase of dying[4]	Actively dying patients that are imminent to death and exhibit many signs and symptoms of near death.
Terminal discharge[5]	Refers to the process of discharging a patient home from a hospital or hospice in the last hours or days of their life, so that they can pass away at home.
Off-label Indication	Refers to indications not registered by any regulatory body and not listed in the Ministry of Health Medicines Formulary (MOHMF).
Indication not in MOHMF	Refers to indications not listed in the Ministry of Health Medicines Formulary (MOHMF).

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5.0 SCOPE OF SERVICES

5.1 Inpatient Services	5.2 Outpatient Services	5.3 Community Services
Deliver comprehensive medication management and support within hospital settings, to ensure optimal symptom control and quality of life for inpatients	Work with patients and caregivers in outpatient clinics, to manage medications, dispense and counsel patients, as well as address any palliative care concerns.	Visits to patients at home as part of the hospital/ domiciliary palliative care team, to assess medication use and adherence, identify side effects, and ensure continuity of care.

6.0 ROLES AND RESPONSIBILITIES OF PHARMACIST IN PALLIATIVE CARE

A pharmacist plays a crucial and multidimensional role in palliative care. As members of an interdisciplinary team, pharmacists bring specialised expertise in medication management, symptom control, and patient safety, essential for the holistic care of palliative patients. It can be classified into three roles as below: [1,2,3]

Clinical

- Optimise the outcome of symptoms management with the concept of evidence-based and patient-centred medication therapy
- Anticipate the transition of care from prescribing to deprescribing medications.
- Patient education and medication counselling
- Coordinate seamless care from hospital (inpatient/ outpatient) to community care (hospice/ domiciliary) in terms of medication supply, storage and education
- Preparation and dispensing of medications
- Facilitation of ADR and medication errors reporting
- Employ medication adherence strategies using suitable tool (e.g. MYMAAT)
- Perform opioid equianalgesic conversions[4]

Administrative

- Perform drug utilisation review
- Develop network among pharmacists who are involved in palliative care services for information sharing and continuous education
- Assist in medications procurement and shortage management

Education & Quality Improvement

- Implementing educational and training activities in palliative pharmacotherapy for the multidisciplinary team, as well as peers
- Participate in continuous pharmacy education such as pharmacy grand round or presentation
- Participate in development and review of guidelines, policies and protocols
- Conduct pharmacist-led research and quality improvement initiatives to support the implementation of National Standards of Palliative Care in Malaysia

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7.0 PALLIATIVE CARE IN VARIOUS POPULATIONS

7.1 CANCER PATIENTS

Cancer is an important cause of morbidity and mortality, particularly in industrialised and developing countries. In 2020, there were 48,639 new cancer cases reported in Malaysia. By 2040, the incidence of cancer in Malaysia is predicted to double. Approximately 1 in every 10 individuals in Malaysia will receive a cancer diagnosis in their lifetime.[1] Cancer incidence increases exponentially with age; with increasing life expectancy, cancer will become an even more common problem in the future.

Traditionally, palliative care services were only 'offered' to patients when 'there is nothing more that can be done'. A new "bow tie model" to describe palliative care is as shown in **Figure 1**, the model consists of two overlapping triangles resembling a bow tie, with an arrow pointing from left to right. The first triangle represents disease management and the second triangle is palliative care. The arrow indicates that this is a dynamic process with a gradual switch in focus.[2]

Figure 1. Basic Model of Integrated Palliative Care

The disease management triangle may be used to illustrate the role of supportive care interventions along with anti-cancer treatments **(Figure 2)**, while maintaining a visible reminder of the existence of the palliative care triangle and possibility of dying throughout. Similarly, as shown in **Figure 3**, the palliative care triangle can be enhanced to illustrate where the various components of modern supportive and palliative care fit into the patient's journey.[2]

Figure 2. Disease management-enhanced model

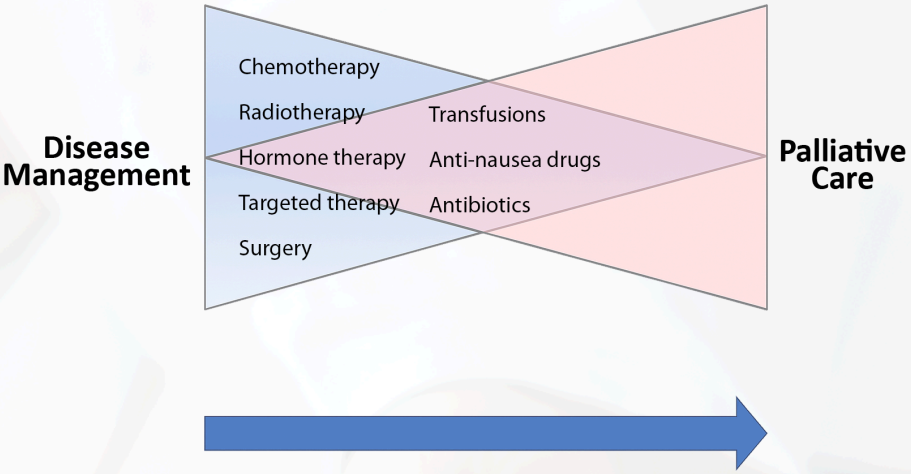
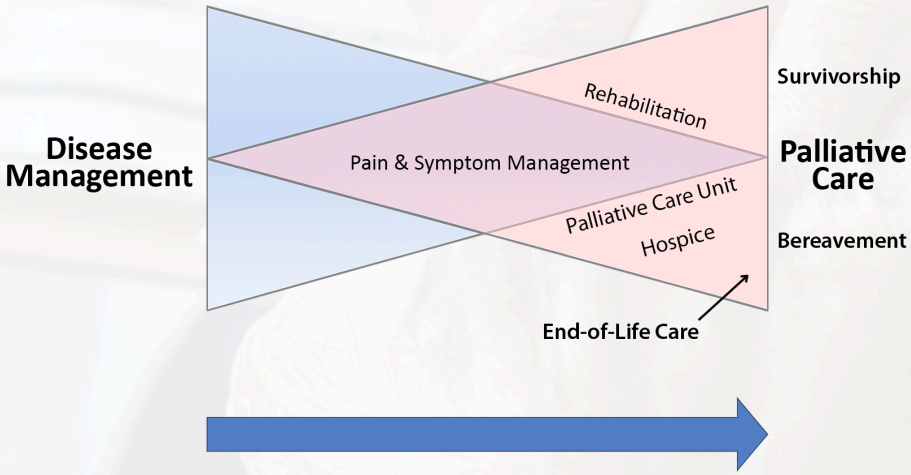


Figure 3. Palliative care-enhanced model



7.2 NON-CANCER PATIENTS

Non-oncology palliative care addresses the needs of patients with chronic, progressive illnesses outside of cancer, focusing on symptom management, quality of life, and holistic support for patients and families. This care spans a wide range of conditions:

Heart Failure	Manages symptoms like breathlessness, fatigue, and fluid overload while addressing emotional distress and end-of-life care.
Renal Failure	Provides symptom relief for patients opting for conservative management (not on dialysis) and improves quality of life.
Liver Disease	Offers care for patients with cirrhosis or liver failure, targeting ascites, encephalopathy, and nutritional needs.
Lung Disease	Manages conditions like chronic progressive lung disease and COPD, focusing on dyspnoea, oxygen therapy, and psychological support.
Neurodegenerative Disease	Addresses complex needs in conditions like ALS, Parkinson's, or dementia, providing care for mobility issues, cognitive decline, and caregiver support.
Retroviral Disease	Have complex care needs therefore integrating palliative care into multidisciplinary HIV models addresses symptom burden, comorbidities, psychosocial distress, and optimizes quality of life.

This interdisciplinary approach ensures comprehensive care for patients with diverse non-cancer diagnoses. By addressing physical, emotional, and psychosocial needs, it ensures dignity, comfort, and holistic care across all stages of illness.

7.3 GERIATRIC PALLIATIVE CARE

The current life expectancy for Malaysia in 2023 is 76.65 years, a 0.19% increase from 2022. The continuous rise in life expectancy indicated that Malaysia would experience an ageing population by 2030. According to the Department of Statistics Malaysia, the country will have an ageing population of 5.6 million seniors, or 15 per cent of the total population, by 2035. Geriatric patients are very different from younger patients because of physiological changes associated with aging, atypical presentation of disease, dependence on a range of health care providers, and a continuum of care settings. Caring for these elderly patients is a complex endeavour involving medical, social, and psychological issues, and is best achieved by the interdisciplinary and patient-centred approach of geriatric palliative care.

Geriatrics is the branch of medicine that deals with the diagnosis and treatment of diseases and problems specific to the aged. Palliative care is an approach that improves the quality of life of patients and their families as they face the problems associated with serious illness. The goal is to prevent and relieve suffering by means of early identification, assessment, and treatment of pain and other symptoms, including physical, psychosocial, and spiritual domains. Palliative care is offered throughout the continuum of illness and strives to facilitate patient autonomy, access to information, and choice. Geriatric palliative care combines these two specialties and is based on their shared core principles.

As a result of age-related changes by organ system and their clinical implications, clinicians caring for the geriatric patient population must treat the whole person in the context of the patient's family and community, and not just the illness or syndrome. It is essential to be vigilant in regard to multiple contributing factors that can have a cumulative and deleterious impact on a geriatric patient in the domains of care shown in **Table 1**.

Table 1. Domains of Care[3]

Domain	Conditions	Impact on Patient
Medical	• Diseases and disorders in elderly patients, as well as geriatric syndromes, are usually multifactorial, involve multiple organ systems, and encompass physical, social, and psychosocial elements • Typical disorders have atypical presentations	• Chronic illness(es) • Comorbidities, with polypharmacy • Geriatric syndromes • Depression risk • Sensory losses (hearing, vision)
Functional	• Multisystem comorbidities • Osteoarthritis affects gait and use of hands, causes chronic pain, creates a	• Consideration of alternative care settings

Domain	Conditions	Impact on Patient
	fall risk, and limits functional independence in activities such as dressing, driving, shopping, housekeeping, etc.	• Need for special equipment and assistive devices • Safety risks must be evaluated (indoor and outdoor) • Dependence on others for activities of daily living
Social	• Multiple comorbidities can lead to serious impact on overall quality of life • Causes for social withdrawal include medications, disorders of bladder or bowel, gait dysfunction, hearing and visual impairment • Social interactions also affected by isolation, death of spouse and friends, limited access to transportation, move to alternate care setting, forced migration to live with adult children or other relatives	• Social isolation • Unacceptable quality of life • Accumulated losses • Depression risk • Functional decline • Loss of family and community support Family caregiver burden
Economic	• Fixed income/pensions after retirement are often not sufficient • Investment reverses can lead to difficulty managing finances • Increased cost of health care • Reduced ability to afford to stay at home with home care, but with increased debility, causing ever-increasing need for care/ assistance • May need long-term care • Elders are at increased risk for financial fraud and scams	• Difficulty managing cost of personal long-term care, health insurance and medications • Inability to identify and afford foods with adequate nutrition • Limited funds to visit friends/family or to seek entertainment can lead to depression risk • Stress of having to choose between rent, medications, and food

A cornerstone of comprehensive geriatric palliative care is multidimensional assessment. Early identification of physical, cognitive, or psychosocial problems enables clinicians to plan timely and appropriate interventions to maintain or improve functional status, address debilitating symptoms such as pain or depression, prevent complications, reduce risks associated with chronic disease states, and avoid unnecessary hospitalization for the older patient. In pursuit of a comprehensive geriatric assessment, a palliative care pharmacist who is caring for older adults should conduct a Medication Review of medications by reviewing all medications and supplements. This helps to advise patients to take medications correctly and identify/avoid medication errors and drug interactions; especially since these patients are likely to have multiple appointments with different specialist teams.

7.4 PAEDIATRIC PALLIATIVE CARE

The WHO defines palliative care appropriate for children as "The active total care of 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".[4] As with adult palliative care, paediatric palliative care goes hand-in-hand alongside curative treatment, with varying levels of involvement at different stages of illnesses.

The principles of palliation apply to all chronic paediatric disorders such as children with:[5]

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. It begins when the illness is diagnosed and continues regardless of whether the child receives treatment directed at the disease.

Palliative care needs for children is unique and different from adult palliative care in terms of:[5]

Types of Health Conditions	While some conditions overlap with those in adult palliative care, many chronic non-communicable diseases are congenital in nature and may have genetic causes. The prognosis and life expectancy may be unclear especially for the rarer conditions.
Developmental Milestones	Palliative care needs will change as the child grows older, depending on the child's developmental milestones. These needs involve age-appropriate information, recreation/ play, education and coping mechanisms.
Duration	The survival time scale can be highly variable. Therefore, care can be delivered over a longer period, sometimes for months or years.
Dilemmas in Decision-Making	Children's status as minors from a legal viewpoint puts decision-making in the hands of their parents or legal guardians. The level of maturity required for making decisions will evolve as the child grows older, with issues involving the child's wishes and rights.

Paediatric palliative care is relevant for children from the perinatal period until the age of 18 years. Similar to adult palliative care, the scope of paediatric palliative care encompasses:[5] Refer **Appendix 1** for pediatrics dose recommendations for commonly used medications in palliative care.

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8.0 PALLIATIVE PHARMACOTHERAPY

8.1 PAIN

Pain is one of the most common and distressing symptoms experienced by palliative care patients. Pain is defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.[1] The prevalence of pain was 55% for patients undergoing anticancer treatment, and 66.4% for those with advanced, metastatic or terminal cancer. Pain was rated as moderate to severe in 38% of all patients.[2]

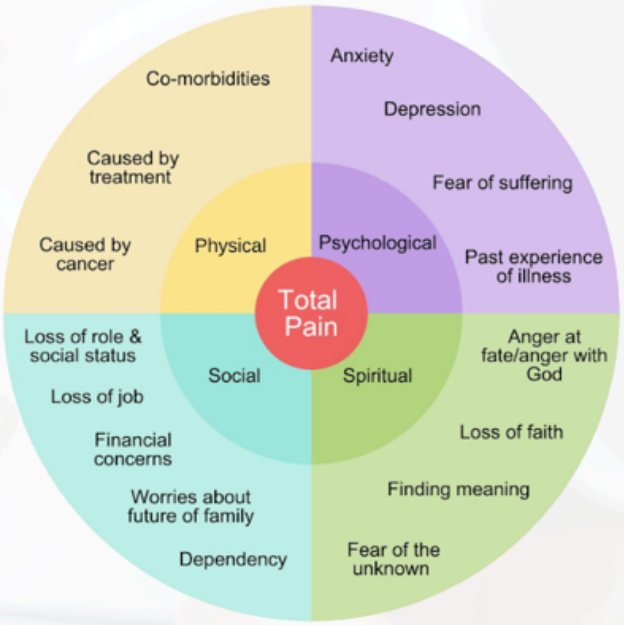
Pain is one of the most common symptoms in patients with advanced diseases. The prevalence of pain in cancer patients is 35–96%, heart disease is 41–77%, AIDS is 63–80%, chronic obstructive pulmonary disease is 34–77%, and renal disease is 47–50%.[3]

Possible Causes[4,5,6]

- **Tumour-related pain:** direct invasion of tissues, bones, or nerves by the tumour
- **Metastatic pain:** spread of cancer to distant sites such as bones or organs
- **Treatment-induced pain:** side effects of chemotherapy and radiotherapy, or pain following oncological surgeries or procedures
- **Visceral pain:** pain from organ involvement or obstruction (e.g., bowel obstruction)
- **Lymphedema-related pain:** swelling caused by blocked lymphatic drainage
- **Chronic pain conditions:** degenerative joint diseases, arthritis, or other chronic pain syndromes

While addressing the physical causes of pain is crucial, it is equally important to recognise that pain in cancer patients can extend beyond the physical. Dame Cicely Saunders pioneered the concept of "total pain," recognising that pain in patients with palliative needs also encompasses the physical, psychological, and spiritual dimension, thus necessitating a holistic approach to its management. Employing the biopsychosocial model **(Figure 4)** in cancer pain management can help ensure a more comprehensive and holistic treatment strategy.

Figure 4. The Biopsychosocial Model of Total Pain[7]



Management[4,5,6,8]

The goal of pain management is to relieve pain to a level that allows for an acceptable quality of life. While the mainstay of management is pharmacological interventions, non-pharmacological approaches can prove useful too.

Non-Pharmacological Management

- **Physical Therapies**
  - Stretching or physiotherapy exercises
  - Heat or cold packs
  - Gentle massage
- **Relaxation Techniques**
  - Deep breathing exercises
  - Guided imagery
  - Progressive muscle relaxation
- **Behavioural and Psychological Strategies**
  - Cognitive-behavioural therapy (CBT)
  - Mindfulness meditation
- **Complementary and Alternative Therapies**
  - Acupuncture

- Aromatherapy with essential oils
- Music or art therapy

- **Environmental Modifications**
  - Adjusting lighting, noise, and temperature
  - Proper positioning and use of supportive cushions/props

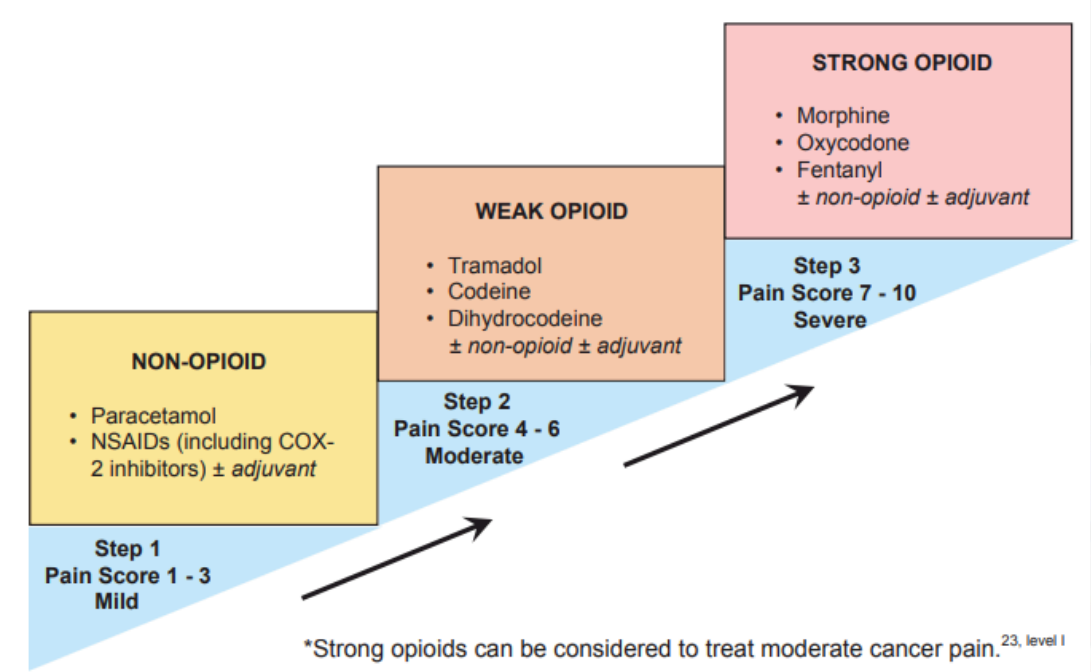
Pharmacological Management

It is common for palliative patients to present with mixed pain that constitutes both nociceptive and neuropathic pain. Treatment approaches will depend on the nature and type of pain.

<table>
<tr><th colspan="2">Types of Pain</th><th>Description</th><th>Causes</th><th>Pharmacological Option(s)</th></tr>
<tr><td rowspan="3">Nociceptive</td><td>Somatic</td><td>● Aching, stabbing, throbbing.
● Usually well localised.</td><td>● Bone metastases
● Skin/ soft tissue infiltration</td><td>● Nonsteroidal anti-inflammatory drugs (NSAIDs)
● Opioids</td></tr>
<tr><td rowspan="2">Visceral</td><td>● Aching, sharp, throbbing.
● May be referred to other sites.</td><td>● Damage to viscera, e.g. liver, intestines, bladder
● Capsular distension, e.g. liver metastasis</td><td rowspan="2">Good response to opioids</td></tr>
<tr><td>● Cramping, gnawing.
● Poorly localised.</td><td>● Obstruction of hollow viscous e.g. intestinal obstruction</td></tr>
<tr><td colspan="2">Neuropathic</td><td>● Burning, electric-like, shooting, allodynia, dysaesthesia, hyperalgesia.</td><td>● Injury to nerves in peripheral or central nervous system e.g. spinal cord compression, brachial plexopathy</td><td>● Adjuvant analgesics.
● Partially responsive to opioids.</td></tr>
</table>

The World Health Organisation's Analgesic ladder **(Figure 5)** is a useful tool to guide the choice of pharmacological agent(s) to treat cancer pain, based on the patient's scoring of their pain.

Figure 5. Modified WHO Analgesic Ladder[9]



- Paracetamol or NSAIDs may be used for mild cancer pain (Step 1 of the World Health Organization analgesic ladder).
- Weak opioids such as tramadol or dihydrocodeine may be used for moderate pain (step 2 of the WHO analgesic ladder) in cancer pain.
- Oral morphine is the preferred choice in moderate to severe cancer pain.
- Oxycodone and fentanyl can be used as alternatives to morphine.
- Adjuvant analgesics refer to medications that have primary indications other than pain but have analgesic properties in some painful conditions. They may be used alone or in combination with other analgesics including strong opioids at any step of the WHO analgesic ladder, based on the pathophysiology of pain.

The pattern and intensity of cancer pain often fluctuates and can include episodes of pain exacerbations or flare-ups called "breakthrough" pain, superimposed on a background of continuous pain. Adequate management of cancer pain will require a regular analgesic regimen for background pain as well as a supplemental dose as needed for breakthrough pain.[8,10]

Effective pain management requires a multidisciplinary approach that addresses physical, social, psychological and spiritual needs of the patient and those important to them.[6]

Step 1 Analgesics

Medication	Recommended Dosage	Side Effects	Remarks
Paracetamol#*	**PO/IV**: 0.5-1g TDS/QID Max: 4g/day	Rare	Generally favourable safety profile.
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)			
Ibuprofen*	**PO:** 200 - 400mg TDS Max: 1200mg/day	• Gastrointestinal (Nausea, Vomiting, Dyspepsia, Abdominal Pain) • Gastrointestinal bleeding/ ulcer • Platelet dysfunction • Renal impairment • Cardiac events	Use the lowest possible dose for the shortest possible duration.
Mefenamic acid*	**PO:** 250-500mg TDS Max: 1500mg/day		
Diclofenac sodium*	**PO/ IV:** 50mg TDS Max: 150mg/day		
Naproxen*	**PO:** 250-500mg BD Max: 1000mg/day		
Celecoxib*	**PO:** 200mg OD/BD Max: 400mg/day	• Hypertension • Mild gastrointestinal discomfort (dyspepsia, nausea) • Renal impairment • Cardiac events	COX-2 selective NSAIDs have lower gastrointestinal (GI) risk but higher cardiovascular (CV) risk.
Etoricoxib*	**PO:** 60-120mg OD Max: 120mg/day		
Parecoxib (IV)#*	**IV:** 40-80mg OD Max: 80mg/day		Only for short-term use in post-operative pain.

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

Step 2 Analgesics

Medication	Recommended Dosage	Side Effects	Remarks
Opioids			
Tramadol*	**PO/ IV:** 50-100mg TDS/ QID Max: 400mg/day	• Nausea • Vomiting • Constipation • Drowsiness	• Dual mechanism of action (opioid agonist and serotonin-norepinephrine reuptake inhibitor). • Use with caution in patients with a history of seizures or risk of serotonin syndrome.
Dihydrocodeine*	**PO:** 30-60mg TDS/QID Max: 240mg/day		• May be better tolerated than tramadol in patients sensitive to CNS effects • Suitable in patients where tramadol is contraindicated due to seizure risk or serotonergic drug interactions
Combination of Opioids and Paracetamol			
Panadeine* (Codeine 8mg + Paracetamol 500mg)	**PO: 1**-2 tabs TDS/QID Max: 8 tabs/day	• Nausea • Vomiting • Drowsiness • Constipation	• Combination of opioid with paracetamol for additive analgesic effect. • Risk of opioid-related side effects (sedation, nausea, constipation). • Monitor total daily paracetamol dose.
Ultracet* (Paracetamol 325mg + Tramadol 37.5mg)	**PO:** 1-2 tabs TDS/QID Max: 8 tabs/day		

*Consider dose reduction in renal impairment.

Step 3 Analgesics

Medication	Recommended Dosage	Side Effects	Remarks
Opioids			
Morphine#*	**PO:** Starting dose 3-5 mg 4-hourly of IR morphine, and titrated up accordingly Can be converted to long acting opioid once opioid requirements are stable. **Prolonged-release oral morphine:** to be given in 12-hourly dosing **IV/SC:** Starting dose 1-3 mg 4-hourly, and titrated up accordingly	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Pruritus (more noticeable with IV/SC routes) • Apnoea • Bradycardia	• PRN doses should be prescribed for breakthrough pain, on top of regularly dosed opioids for background pain. • PRN doses can be taken up to every hour if needed. • There is no maximum dose in cancer pain management. Dose titration should be continued until adequate analgesia is achieved or until further dose escalation is limited by the development of unacceptable adverse effects.
Oxycodone#*	**PO:** Starting dose 3-5 mg 4-hourly of IR oxycodone, and titrated up accordingly Can be converted to long acting opioid once opioid requirements are stable. **CR oral oxycodone:** to be given in 12-hourly dosing **IV/SC:** Starting dose 1-3 mg 4-hourly, and titrated up accordingly	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Pruritus (more noticeable with IV/SC routes) • Apnoea • Bradycardia	

Medication	Recommended Dosage	Side Effects	Remarks
Opioids			
Fentanyl#*	Parenteral Fentanyl should be administered as a continuous infusion as it is very short acting. **CIVI/CSCI:** Starting dose 100 - 200mcg/ 24 hours, and titrated up accordingly Transdermal fentanyl can only be used when opioid requirements are stable, and never in an opioid naïve patient. **TD:** Equianalgesic dose of total 24 hours' opioid requirement. Refer **Appendix 2** for Opioid Conversion Table.	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Pruritus (more noticeable with IV/SC routes) • Apnoea • Bradycardia	• PRN doses of short acting morphine or short acting oxycodone should be prescribed for breakthrough pain, on top of regularly dosed opioids for background pain. • PRN doses can be taken up to every hour if needed. • There is no maximum dose in cancer pain management. Dose titration should be continued until adequate analgesia is achieved or until further dose escalation is limited by the development of unacceptable adverse effects.
Methadone#*	As an adjunct to another primary opioid: **PO:** Start with 2.5mg OD-BD, titrate as needed ≥ 3 days. Usual max: 10-20mg BD For a complete rotation to methadone, previous opioid is stopped and methadone is initiated at 1/10 of the total daily PO morphine dose, up to a maximum of 30mg.	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness S/C doses at >25mg or CSCI can cause local inflammation, necessitating site rotation.	• Generally used in patients who do not respond adequately to morphine. Should only be managed by palliative care/ pain specialists, as it has complex pharmacokinetic properties. • For patients in severe pain who

Medication	Recommended Dosage	Side Effects	Remarks
Opioids			
	The first dose may be given > 2 hours after the last dose of morphine if the patient is in pain. PRN doses may be taken up to 3 hourly, at 1/30 of the total daily PO morphine dose, up to a maximum of 30mg.* On Day 6, the total amount of methadone taken over the last 48 hours is divided by 4 to give a new 12 hourly dose. 1/6 to 1/10 of this 24-hour dose can be given every 3 hours PRN. *		need more analgesia in <3 hours, the previously used opioid may be used hourly PRN.

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

Adjuvant Analgesics

Medication	Recommended Dosage	Side Effects	Remarks
Tricyclic Antidepressants (TCA)			
Amitriptyline*	**PO:** 12.5-50mg ON Max: 150mg ON	• Drowsiness/ sedation • Dry mouth • Dizziness • Tachycardia • QT prolongation	• Seldom requires a maximum dose. The usual effective dose is 25mg to 75mg ON. • Use with caution in elderly and patients with cardiac disease, glaucoma, renal impairment and seizure risk.
Corticosteroids			
Dexamethasone	**PO:** 8-16mg/day (initial) Then reduce to the lowest possible dose (usually 2mg/day) Usual max: 16mg/day	• Poor glycaemic control • Sleep disturbances • Delirium • Susceptibility to infections • Bleeding	Try to give earlier in the day to minimise sleep disruption at night.
Anticonvulsants			
Gabapentin*	**PO:** Start with 300mg ON and increase by 300mg/day every 2-3 days if necessary Max: 3600mg/day	• Drowsiness • Dizziness • Ataxia • Weight Gain • Oedema • Cognitive Impairment • Drug Abuse/ Dependance • Withdrawal Symptoms • Suicidal ideation • Angioedema/ Anaphylaxis	Usual effective dose >600mg TDS
Pregabalin*	**PO:** 50-75mg BD Max: 300mg BD		Increased risk of suicidal ideation and tendencies

Medication	Recommended Dosage	Side Effects	Remarks
Sodium valproate	**PO:** Start with 200mg BD and increase by 200-400mg/day every 2-3 days if necessary Max: 1600mg/day	• Drowsiness • Nausea • Vomiting • Loss of appetite	Not the first-line choice for neuropathic pain.
Bisphosphonates			
Pamidronate*	**IV:** 30-90mg as a single IV infusion over 2-4 hours	• Flu-like symptoms • Transient pyrexia • Fatigue • Nausea	Can only be repeated after 7 days if response is inadequate
Zolendronic acid*	**IV:** 4mg as a single IV infusion over 15 mins		Can only be repeated after 7 days if response is inadequate

*Consider dose reduction in renal impairment.

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8.2 RESPIRATORY SYMPTOMS

Respiratory symptoms are frequently encountered in advanced illnesses and can arise from lung disease or systemic conditions such as cardiac or metabolic abnormalities.[1] These symptoms can include breathlessness, coughing, hiccups and secretion. A comprehensive clinical examination including a detailed history and physical examination is crucial. Radiological and blood investigations can also help identify potentially reversible causes. This is particularly important for palliative care patients, as alleviating respiratory symptoms can significantly reduce distress.[2]

8.2.1 BREATHLESSNESS

Breathlessness or dyspnoea, is a prevalent and distressing symptom for individuals nearing the end of life.[3] It is reported as the most debilitating symptom by 95% of patients with Chronic Obstructive Pulmonary Disease (COPD). It is commonly seen in those with lung fibrosis, heart failure, and terminal cancer. Effective management of breathlessness requires the identification and treatment of reversible causes, along with a thorough evaluation and addressing of the patient's physical, psychological, emotional and environmental factors to ensure the optimisation of comfort and enhancement of overall quality of life.[4]

Possible Causes[5]

- **Cancer related:** bronchial obstruction, superior vena cava obstruction, lymphangitic carcinomatosis, pleural effusion, pulmonary embolism, pneumonitis
- **Non-cancer related:** pneumonia, fibrosis, COPD, hypertension, hypercapnic respiratory failure
- **Others:** cardiac causes (congestive heart failure, arrhythmia), neuromuscular disease, anaemia, acidosis, panic attack, deconditioning

Management[5]

Effective management of breathlessness in palliative care combines both non-pharmacological and pharmacological management to alleviate discomfort and improve quality of life.

<u>Non-Pharmacological Management</u>

- Breathing techniques
- Relaxation techniques
- Environmental adjustment

- Oxygen therapy
- Positioning
- Fan therapy

Pharmacological Management[5,6,7]

Pharmacological management of breathlessness in palliative care focuses on alleviating symptoms through medications that target both the sensation of dyspnoea and its associated anxiety or distress.

Medication	Recommended Dosage	Side Effects	Remarks
Strong Opioids			
Morphine#*†	**PO:** 2.5mg-5mg PRN **SC:** 2 mg PRN and titrate as needed. **CSCI:** Initiate with 10mg/24 hours then titrate as needed	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Pruritus (more noticeable with IV/SC routes) • Apnoea • Bradycardia • Bronchospasm	• If dyspnoea is continuous, opioids should be given around the clock every 4 hours or as continuous infusion. • Can be converted to long acting opioid once opioid requirements are stable. • Consider a lower dose of opioid to relieve dyspnea than is needed for pain.
Fentanyl#*†	**CSCI:** Initiate with 100mcg/24 hours then titrate as needed		• Can be converted to long acting opioid once opioid requirements are stable. • Consider a lower dose of opioid to relieve dyspnea than is needed for pain.
Benzodiazepines **For refractory breathlessness and dyspnoea-related anxiety**			
Lorazepam#*†	**SL/PO:** 0.5mg - 1mg BD/PRN	• Drowsiness • Sedation • Dizziness	• Not recommended for long term use • Contraindicated for

Medication	Recommended Dosage	Side Effects	Remarks
		• Muscle weakness • Memory impairment • Hypotension (more common in midazolam) • Paradoxical arousal/ agitation • Respiratory depression	severe hepatic impairment
Midazolam#†	**SC:** 2.5 -10mg **CSCI:** Initiate with 10mg/24 hours then titrate as needed		

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.
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8.2.2 COUGH

Coughing is the body's natural response to clear airways of mucus and foreign particles when the mucociliary transport is insufficient. However, when a cough becomes chronic, it can disrupt daily life activities causing distress and physical exhaustion.[1] Chronic cough may also interfere with sleep, impact social interactions and potentially lead to underlying health problems that require medical attention.

Possible Causes[2,3]

- **Primary disease:** lung cancer, COPD, pulmonary fibrosis, asthma
- **Infections:** pneumonia, bronchitis
- **Cardiac causes:** heart failure, pulmonary oedema
- **Gastrointestinal causes:** GERD, aspiration
- **Medication side effects:** angiotensin-converting-enzyme (ACE) inhibitors
- **Treatment-related causes:** radiation-induced lung injury, chemotherapy-induced lung toxicity

Management[2,3]

Effective management of cough focuses on relieving discomfort and improving well-being through a combination of non-pharmacological and pharmacological management tailored to individual needs.

Non-Pharmacological management

- Airway clearance techniques
- Hydration
- Positioning
- Breathing technique
- Chest physiotherapy

Pharmacological management[4]

Pharmacological management aims to address the underlying cause of the cough, alleviate symptoms, and improve patient comfort. There are different types of medications used to manage cough:

Medication	Recommended Dosage	Side Effects	Remarks
Mucolytics			
Nebulised saline (Sodium Chloride 0.9%)†	2.5ml QID/PRN	• Coughing • Hoarseness • Reversible bronchoconstriction	• Productive cough • Safe for all ages
Bromhexine#*†	**PO:** 8-16 mg TDS Max: 48mg/day	• Nausea • Upper abdominal pain • Headache • Dizziness • Urticaria • Hypersensitivity reaction	• Productive cough
N-Acetylcysteine (NAC)†	**PO (Granules):** 200mg BD/TDS **PO (Effervescent tab):** 600mg OD Max: 600mg/day	• Nausea • Abdominal pain • Headache • Rash • Pruritus • GI Haemorrhage	• Productive cough

Medication	Recommended Dosage	Side Effects	Remarks
Antihistamines			
Diphenhydramine Hydrochloride	**PO:** 10ml BD-TDS (Strength: 14mg/5ml) Max: 60ml/day	• Dry Mouth • Dizziness • Loss of coordination • Constipation	• Productive and non-productive cough
Opioids			
Dihydrocodeine#*	**<u>As a single agent:</u>** Start with 30mg PO q4-6h. If necessary, increase to 60mg q4-6h.	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Apnoea • Bradycardia	• Non-productive cough • Not recommended to prescribe dihydrocodeine in patients already taking morphine or any other strong opioid • If a greater effect is needed, the regular and PRN doses of morphine (or another strong opioid) should be increased

Medication	Recommended Dosage	Side Effects	Remarks
Aqueous Morphine#*†	**<u>Opioid naïve:</u>** **PO:** 2-5 mg q4-6h **<u>Already on Prescribed Morphine:</u>** Use existing Aqueous Morphine for breakthrough pain/ breathlessness/ cough up to 6 times a day.	• Constipation • Nausea • Vomiting • Drowsiness • Dizziness • Abdominal Pain • Apnoea • Bradycardia	• Non-productive cough • Titrate background and breakthrough morphine as required.

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*Consider dose reduction in renal impairment.
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8.2.3 HICCUPS

Hiccup is an abnormal respiratory reflex characterised by spasm of one or both sides of the diaphragm, causing sudden inspiration with associated closure of the vocal cords. This reflex involves the phrenic nerve, vagus nerve, thoracic sympathetic fibres, brainstem and hypothalamus. This reflex arc is usually inhibited by pharyngeal and glossopharyngeal nerves. Any disturbance to this reflex arc may cause hiccups. A single episode can last for a few seconds to as long as several days. When they last longer than 48 hours, hiccups are termed *persistent*; longer than one month, *intractable*. Persistent and intractable hiccups can be very distressing to patients and families and diminish the quality of life.

Possible Causes[1]

- **Via vagus nerve:** gastric distension, gastritis, GERD, hepatic tumours, ascites/ abdominal distension/ intestinal obstruction
- **Via phrenic nerve:** diaphragmatic irritation, intracranial tumours (especially brainstem lesions), leptomeningeal disease, traumatic brain injury, stroke.
- **Systemic:** renal failure, electrolyte imbalance (hyponatraemia, hypokalaemia, hypocalcaemia), corticosteroids.

Management[2,3,4]

Proper assessment is essential for identifying the underlying cause and determining the appropriate management strategy.

Non-Pharmacological Management

- Pharyngeal stimulation e.g. eating granulated sugar, sipping cold water, applying pressure to the soft palate with an inverted spoon, Valsalva manoeuver.
- Reduce gastric distension: Encourage small, frequent meals.
- Nasogastric tube aspiration to decompress the stomach

Pharmacological Management[2,3,4]

There is a lack of comprehensive studies on the management of hiccups. Many medications and interventions are proposed as effective for treating hiccups. So far, the only medication approved by the US Food and Drug Administration is chlorpromazine.

Medication	Recommended Dosage	Side Effects	Remarks
Prokinetics			
Metoclopramide #*†	**PO:** 10mg TDS-QID **IV:** 10-20mg IV stat given ≥ 3mins	• GI side effects • Somnolence/ Drowsiness • Headache • Asthenia • Altered taste sense • Nausea/Vomiting • Fluid retention • Extrapyramidal Symptoms • Tardive Dyskinesia • Neuroleptic Malignant Syndrome	• Use with caution in patient with suspected bowel obstruction
Antipsychotics			
Chlorpromazine†	**PO:** 25–50mg TDS-QID **IV:** 25–50 mg IVI in 500-1000 ml NS over several hours	• Dry mouth • Constipation • Postural hypotension • Weight gain • Urinary retention • Mydriasis • Agitation • Insomnia • Gynaecomastia • Amenorrhoea • Hyperglycaemia • Raised Serum Cholesterol • Convulsions • Tardive dyskinesia (on long-term therapy) • ECG changes • Allergic skin reaction • Depression	

Medication	Recommended Dosage	Side Effects	Remarks
Haloperidol#†	**PO:** 1.5-3 mg ON	• Extrapyramidal syndrome • Somnolence • CNS depression • Orthostatic hypotension • Anticholinergic effects • Motor or sensory instability • Hyperprolactinaemia • Oesophageal dysmotility and aspiration	
Anticonvulsants			
Gabapentin*†	**PO:** 300mg TDS for 3 days, 300mg OD for 3 days Elderly: 100mg TDS	• Drowsiness • Dizziness • Ataxia • Weight Gain • Oedema • Cognitive Impairment • Drug Abuse/ Dependance • Withdrawal Symptoms • Suicidal ideation • Angioedema/ Anaphylaxis	

Medication	Recommended Dosage	Side Effects	Remarks
Smooth Muscle Relaxants			
Baclofen*†	**PO:** 5–20 mg TDS	• Drowsiness • Dizziness • Weakness • Fatigue • Nausea • Constipation • Insomnia • Confusion or hallucinations • Depression of mood changes • Hypotension • Respiratory depression	
Calcium Channel Blockers			
Nifedipine#†	**PO:** 10–20 mg TDS Dose ≤160mg/day has been used with concurrent PO fludrocortisone 0.5–1 mg to overcome associated orthostatic hypotension in intractable hiccups	• Peripheral oedema • Symptomatic hypotension with or without syncope • Deterioration of heart failure	

Medication	Recommended Dosage	Side Effects	Remarks
Benzodiazepines			
Midazolam#†	**SC:** Initiate with 10mg/24 hours then titrate as needed by CSCI	• Drowsiness • Sedation • Dizziness • Muscle weakness • Memory impairment • Hypotension • Paradoxical arousal/ agitation • Respiratory depression	• For intractable hiccups

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*Consider dose reduction in renal impairment.
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8.2.4 SECRETIONS

Excessive or thick respiratory secretions are common in patients with pulmonary and neurologic diseases and for many patients in the last few days of life. The airway surface liquid, often referred to as mucus, is a thin layer of fluid covering the luminal surface of the airway. The major function of mucus is to protect the lung through mucociliary clearance against foreign particles and chemicals entering the lung. For patients with ineffective mucociliary clearance, poor cough, or excessive/abnormal mucus production, dyspnoea, cough, tachypnoea, or sensations of choking/gagging may occur.[1]

Possible Causes[1,2]

- As consciousness decreases in the dying process, patients lose their ability to swallow and clear oral secretions. Air moves over these pooled secretions resulting in noisy ventilation.
- Increased production of saliva, or decreased clearance of secretions in patients who are not imminently dying (e.g. brain injuries or amyotrophic lateral sclerosis)

Management[2]

Effective management of respiratory secretions in palliative patients focuses on maintaining comfort, minimising distress, and addressing symptoms like noisy ventilation, choking sensations, or dyspnoea caused by impaired secretion clearance.

Management of Secretions in the Last Days of Life

In patients who are imminently dying, explain to family members that this is due to secretions collecting in airways which are no longer able to be coughed or cleared. Often, these secretions do not cause discomfort, choking or distress to the patient.

<u>Non-Pharmacological Management</u>[2]

- Postural drainage (i.e. re-positioning the patient on their side to facilitate drainage)
- Reducing fluid intake or intravenous fluid administration
- Maintaining adequate oral hygiene
- Superficial suctioning might be useful for pooled secretions in the oral cavity
    - Suctioning is generally not recommended in the last days of life. Deep suctioning will not improve secretions and may cause further distress to patients.

Pharmacological Management[2]

Medication	Recommended Dosage	Side-Effects	Remarks
Anticholinergic agents			
Hyoscine butylbromide*	**CSCI:** 60–120mg/day **SC:** 20mg TDS and 20 mg PRN	• Anticholinergic side-effects (e.g. dry mouth, urinary retention) • Over-drying, which may cause overly thick mucus and mucus plugging	• To reduce secretion production
Glycopyrrolate	**CSCI:** 600–1200mcg/day **SC:** 200–400mcg TDS and PRN		
Others			
Atropine 1% ophthalmic solution†	**PO/SL:** 1–2 drops SL q2–4 hours PRN	• Very dry mouth and throat • Blurred vision, palpitations, constipation and urinary retention	• For excessive pooling of saliva

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8.3 GASTROINTESTINAL SYMPTOMS

8.3.1 LOSS OF APPETITE

Anorexia is a medical condition marked by a lack of appetite or loss of interest in food often occurs in advanced disease. This results a progressive depletion of lean body mass and weight loss.

Possible Causes:

- Pain and discomfort
- Nausea and vomiting
- Altered taste due to candidiasis, dry mouth, medications
- Dysphagia, swallowing issues
- Cancer related anorexia-cachexia syndrome
- Anxiety and depression

Management

The management of anorexia is generally to improve comfort, quality of life, and provide symptom relief.

Non-Pharmacological Management

- Address and manage patient's pain
- Treat reversible cause
- Advice small meals on small plate, food with strong flavours, offering food of patients' favourite or he or she enjoys
- Relaxation technique
- Improve functional status
- Exercise

Pharmacological Treatment[1,2]

Medication	Recommended Dosage	Side-Effects	Remarks
Prokinetics			
Metoclopramide*	**PO:** 10-20 mg TDS-QID	• GI side effects • Somnolence/ Drowsiness • Headache • Asthenia • Altered taste sense • Nausea/Vomiting • Fluid retention • Extrapyramidal Symptoms • Neuroleptic Malignant Syndrome	• Use with caution in patients with bowel obstruction
Appetite Stimulant			
Megestrol Acetate†	**PO:** 80mg-160mg OD	• Weight Gain • Fluid Retention • GI Upset • Hyperglycaemia • Venous Thrombosis	• May increase thromboembolic risk, adrenal suppression, hepatotoxicity, cardiovascular disease • Should consider to stop if there is no benefit after 1 to 2 weeks

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*Consider dose reduction in renal impairment.
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8.3.2 CONSTIPATION

Constipation is a symptom characterised by difficult or painful defecation It is associated with infrequent bowel opening, hard and small faeces. Aim is to identify and treat the cause of constipation and to early prevention of constipation by use of laxatives.

Possible Causes

- Poor oral intake
- Immobility (bedbound)
- Dehydration
- Environmental (lack of privacy, unfamiliar toilet arrangements)
- Hypercalcaemia, hypokalaemia
- Bowel obstruction
- Spinal cord compression
- Visceral neuropathy
- Medication: opioids, antimuscarinics, tricyclic antidepressants, chemotherapy, NSAIDs, hematinics

Management

Healthcare providers should proactively anticipate the development of opioid-induced constipation and initiate prophylactic laxative therapy at the outset of treatment.

Non-Pharmacological Management

- Encourage fluid intake
- Mobilise the patient if possible

Pharmacological Management[1]

Medication	Recommended Dosage	Side Effects	Remarks
Osmotic Laxatives			
Lactulose	**PO:** 10-20ml OD-TDS	• Flatulence • Abdominal cramps • Nausea and Vomiting • Electrolyte imbalance • Hypokalemia • Hyperphosphatemia	• Does not affect management of diabetes mellitus • Use with caution in lactose intolerance
Macrogol 4000 Powder	**PO:** 10-30g daily in divided doses		• Maintaining usual fluid intake while using macrogol
Glycerin Enema	**PR:** 1 enema PRN		
Monobasic sodium phosphate 48%, Diabasic Sodium Phosphate 18% (Oral Fleet)*	**PO:** 30ml PRN if severe constipation		
Stimulant Laxatives			
Bisacodyl	**PO:** 5-10mg OD-TDS **PR:** 10-20mg OD	• Abdominal Pain • Diarrhoea • Flatulence	• Precaution in GI obstruction, perforation or severe impaction.
Sennaŧ	**PO:** 15-30mg OD-TDS		

Medication	Recommended Dosage	Side Effects	Remarks
Lubricant Softener			
Oral Liquid Paraffin	**PO:** 10-30ml daily	• Abdominal Pain • Diarrhoea • Flatulence	• Use with caution in elderly as it can cause lipoid pneumonia

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.
†The use of medications not registered with Drug Control Authority (DCA), medications for off-label indications and medications not listed in the MOH Medicines Formulary (MOHMF) requires prior submission of a Special Approval Medicine (SAM) application to the Pharmacy Practice and Development Division, Ministry of Health (MOH). This requirement does not apply to medications that have been granted exemption from SAM application by the MOHMF Panel.

References:

1. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.

8.3.3 DIARRHOEA

This typically refers to **frequent loose or watery stools** caused by an increase in intestinal motility, reduced absorption, or increased secretion in the intestines. It is often the result of infections, medications, inflammation, or malabsorption.

Possible Causes

- Diet /enteral feeling
- Overflow due to constipation
- Laxative overdose
- Medication: antibiotics, chemo drugs, metformin, tyrosine kinase inhibitors
- Anxiety
- Gastroenteritis
- Irritable bowel syndrome
- Clostridium difficile diarrhoea
- Carcinoid syndrome
- Malabsorption/ cholegenic
- Hyperthyroidism
- Visceral neuropathy

Management

Managing diarrhoea in palliative care can be complex due to the variety of underlying causes. Treat the underlying cause e.g. medication side effects, acute and chronic causes. It is important to rule out overflow diarrhoea before starting any anti-diarrhoea medications.

Non-Pharmacological Management

- Ensure adequate hydration and electrolyte balance.

Pharmacological Management[1,2]

Medication	Recommended Dosage	Side Effects	Remarks
Antimotility agent			
Diphenoxylate 2.5mg/ Atropine 0.025mg	**PO:** 1-2 tab TDS	• Abdominal distress • Nausea • Lethargic	Usually first line
Loperamide	**PO:** 2 mg BD/ PRN	• Abdominal Cramps • Nausea • Dizziness	• More potent than Lomotil • Contraindicated in clinically used colitis and acute dysentery
Used in severe, persistent, secretory diarrhoea			
Octreotide#*	**SC/CSCI:** 300–1200 mcg/day	• Sinus bradycardia • Hyperglycaemia • Abdominal distress	• For intractable diarrhoea

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

References:

1. Katiman D, Lim RBL, editors. Handbook of palliative medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.
2. Wilcock A, Howard P, Charlesworth S, editors. Palliative Care Formulary. Eighth Edition. London: Pharmaceutical Press; 2022.

8.3.4 NAUSEA AND VOMITING

Nausea and vomiting are prevalent and distressing symptoms frequently encountered in palliative care, and while they are related, they are distinct phenomena. Nausea is described as the unpleasant sensation that one needs to vomit, while vomiting refers to the forceful expulsion of stomach contents through the mouth. Additionally, retching is a related but separate experience characterised by the effort to vomit without actually expelling any contents.

Despite being distinct, nausea and vomiting often occur together, compounding the discomfort for patients. According to Stephenson et al., 62% of patients with advanced cancer report experiencing these symptoms[1]. When examined individually, the prevalence of nausea in patients with advanced cancer varies significantly, ranging from 6% to 68%[2], whereas vomiting is reported in approximately 4% in palliative care patients[1]. These symptoms can significantly impact a patient's quality of life, making effective management crucial in palliative care settings.

Possible Causes

Nausea and vomiting in palliative care often arise from multiple, overlapping factors. According to Stephenson et al., their study identified several key causes[1]:

- **Chemical (44%):** medications (opioids, antibiotics), toxins (gut ischaemia, infection), metabolic (hypercalcaemia, renal failure)
- **Impaired gastric emptying (33%):** medications (opioids, tricyclics), autonomic dysfunction
- **Visceral/serosal (31%):** obstruction of hollow viscus, stretched liver capsule
- **Cranial (8%):** raised intracranial pressure (tumour, infarction)
- **Vestibular:** medications (opioids) base of skull tumour
- **Cortical (7%):** anxiety, pain

Management

A focussed history and examination is essential, supported by appropriate investigations (e.g. biochemistry, radiology). The objectives of assessment should be to identify the likely cause of nausea and vomiting, establish the response to previous antiemetic therapy and identify any complications of nausea and vomiting. Depending on individual patient circumstances, it is suggested that potentially reversible causes are treated, for example, constipation should be treated with laxatives and anxiety should be treated with benzodiazepines.

Non-Pharmacological Management

- Dietary Adjustments:
  - Frequent, Small Meals:
  - Bland and low foods food
  - Maintain hydration
  - Take Ginger and Peppermint

- Complimentary and traditional therapy:
  - Acupressure on the P6 point
  - Aromatherapy (e.g. lavender, lemon, and peppermint essential oils)
  - Relaxation Techniques

Pharmacological management[5]

There are two main brainstem centres which receive and integrate neurotransmitters responsible for nausea and vomiting: the vomiting centre (VC) and the chemoreceptor trigger zone (CTZ). The VC is not a specific anatomical structure, but is a collection of nuclei, which receives input from the cerebral cortex, the vestibular system and the GI tract, as well as integrating input from the CTZ. The CTZ is in the floor of the fourth ventricle, the CTZ sits outside of the blood-brain barrier, rendering it sensitive to toxins, medications and biochemical derangements. Concomitant use of medications with similar receptor profiles is not recommended. Parenteral administration is recommended in cases of vomiting, poor GI absorption or significant gastric stasis. For maximum effect, antiemetic should be prescribed on a regular basis, titrated according to response, and reviewed frequently for effectiveness and adverse effects.

The routine use of selective serotonin receptor (5HT3) antagonists and neurokinin 1 receptor antagonists is not recommended in patients receiving palliative care but may be useful in chemotherapy-related nausea and vomiting.

Medication	Recommended Dosage	Side Effects	Remarks
Antipsychotics			
Haloperidol# Effective for opioid-induced nausea and	**SC:** 0.5 mg as needed (usually do not exceed 3 mg/day)	• Extrapyramidal effects • Altered Liver Function Tests • Dizziness	• Contraindicated in Parkinson's disease, prolonged QT-interval (gastrointestinal

Medication	Recommended Dosage	Side Effects	Remarks
vomiting, nausea as a result of end stage renal disease or hypercalcaemia.	**CSCI:** 1 – 3 mg/ day **PO:** 0.75 – 1.5 mg ON/BD as needed	• Sedation • Depression • Visual Disturbance • Hypotension	obstruction is a relative contraindication in the last days of life). • Avoid in patients with Lewy body dementia due to an increased risk of neuroleptic malignant syndrome.
Levomepromazine # Broad spectrum antiemetic, second-line for refractory nausea and vomiting	**SC:** 3.125 – 12.5 mg, as needed **CSCI:** 25 mg/day	• Dry mouth • Sedation • Hypotension • QT alterations	• Monitor for postural hypotension and excessive sedation • Use under guidance of palliative care specialist
Prokinetics			
Metoclopramide* Nausea and vomiting caused by gastroparesis, functional bowel obstruction (due to opioid use) and gastro-oesophageal reflux disease[3].	**PO:** 10mg TDS, if necessary, titrate to a maximum dose of 20mg QID **SC:** 10 - 20 mg TDS-QID **CSCI:** 30 – 60 mg/ day Higher doses of metoclopramide, e.g. 100 mg over a 24-hour period, should be reserved for managing	• GI side effects • Somnolence/ Drowsiness • Headache • Nausea/Vomiting • Asthenia • Altered taste sense • Fluid retention • Extrapyramidal Symptoms • Neuroleptic Malignant Syndrome	• Contraindicated in Parkinson's disease, prolonged QT-interval, or if complete bowel obstruction. • Monitor for extrapyramidal adverse effects e.g. tardive dyskinesia (more common at doses greater than 30mg/day) • May worsen abdominal cramps in some patients • Do not co-prescribe with anticholinergics e.g. cyclizine, hyoscine

Medication	Recommended Dosage	Side Effects	Remarks
	nausea and vomiting that is likely caused by delayed gastric emptying (without obstruction).		butylbromide if delayed gastric emptying is the clear cause of nausea and vomiting.
Antihistamine Antimuscarinic Nausea and Vomiting resulting from raised intracranial pressure, motion sickness, vertigo and labyrinthine, bowel obstruction and vestibular disease			
Promethazine	**PO:** 12.5-25 mg TDS, as needed	• Sedation/ somnolence • Dizziness • Xerostomia • Nausea/Vomiting • Depression • Urticaria • Dermatitis/Photot oxicity • Extrapyramidal disease • Lowered convulsive threshold	• Do not co-prescribe with metoclopramide if the likely cause of nausea and vomiting is delayed gastric emptying (without obstruction) • Not recommended to be given as a subcutaneous bolus due to injection site reactions
Prochlorperazine	**PO:** 25 mg BD, as needed	• Drowsiness • Dizziness • Light-headedness • Constipation • Dry Mouth • Blurred vision • Prolonged QT Interval	

Medication	Recommended Dosage	Side Effects	Remarks
Meclozine 25mg/ Pyridoxine 50mg (Veloxin)	**PO:** 1 – 2 tab as needed, max 4 tabs/ day	• Dizziness • Headache • Nausea • Vomiting • Diarrhoea • Constipation • Change in taste	
Corticosteroids			
Dexamethasone Nausea and vomiting due to raised intracranial pressure or cerebral oedema due to metastases[4]. Corticosteroids are also used to manage chemotherapy-induced nausea and vomiting and malignant bowel obstruction (MBO).	**PO/SC:** 4-8 mg/day Max: 16 mg daily in severe symptoms	• Body fluid retention • Hypertension • Skin irritation • Cushing's syndrome • Decreased body growth • Depression • Euphoria	• Dexamethasone increases risk of bleeding and must be used with caution. • Proton pump inhibitors must be started in Dexamethasone doses higher than 4mg/day. • Response should be reviewed within 5 days for reduction to maintenance dose or off[5].

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

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1. Stephenson J, Davies A. An Assessment of Aetiology-Based guidelines for the Management of Nausea and Vomiting in Patients with Advanced Cancer. Support Care Cancer. 2006;14(4):348–53.
2. Solano J, Gomes B, Higginson I. A Comparison of Symptom Prevalence in Far Advanced Cancer, AIDS, Heart Disease, Chronic Obstructive Pulmonary Disease and Renal Disease. J Pain Symptom Manage. 2006;31(1):58–69.
3. Moorthy GS, Letizia M. The Management of Nausea at the End of Life. J Hosp Palliat Nurs. 2018;20(5):442–9.
4. Ryken T, McDermott M, Robinson P, et al. The Role of Steroids in the Management of Brain Metastases: A Systematic Review and Evidence-Based Clinical Practice Guideline. J Neurooncol. 2009;96(1):103–14.
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8.4 NEUROLOGICAL SYMPTOMS

8.4.1 DELIRIUM

It is the most common neuropsychiatric disorder in patients with advanced illnesses. Acute onset of symptoms such as disturbances in attention and awareness, cognitive changes and altered psychomotor behaviour, mood and sleep-wake cycle. It may be a sign of imminent death if the symptoms are not reversible.

Possible Causes

- Fluid/ metabolic imbalance (hypercalcemia, hypo- or hypernatremia, hypo- or hyperglycaemia)
- Medications (e.g. opioids, benzodiazepines, steroids, anticholinergics)
- Infections
- Hepatic and renal failure
- Hypoxia
- Anaemia
- Constipation
- Urinary retention
- Brain metastases
- Ischemia

Management

Correct the underlying causes if they are identifiable and treatable.

Non-Pharmacological Management

- Reduce polypharmacy (e.g. deprescribe anticholinergic medications)
- Reassurance
- Optimise hydration and nutrition
- Minimise sensory deficits (e.g. use of visual aids and adaptive equipment, portable amplifying devices and special communication devices)
- Used of orientating aids (e.g. clocks, pictures and objects)
- Encourage early mobilization (minimise the use of immobilizing catheters, intravenous lines and physical restrains)
- Sleep hygiene
- Encourage cognitive stimulating activities

Pharmacological treatment[1,2,3,4,5]

Medication	Recommended Dosage	Side Effects	Remarks
Antipsychotics			
Haloperidol#	**Delirium** **PO**: start with 0.75mg/day at bedtime and PRN; if necessary, increase in 0.75mg-1.5mg increments. **SC/CSCI:** start with 0.5mg/day at bedtime and PRN; if necessary, increase in 0.5-1mg increments. **Terminal agitation:** **CSCI: s**tart with 1.5-5mg and PRN	• Extrapyramidal effects • Altered Liver Function Tests • Dizziness • Sedation • Depression • Visual Disturbance • Hypotension	• Contraindicated in Parkinson's disease, prolonged QT-interval • Relative contraindication :GI obstruction (in the last days of life). • Avoid in patients with Lewy body dementia due to an increased risk of neuroleptic malignant syndrome.
Levomepromazine #†	**Terminal agitation:** **SC:** start with 25mg STAT and q1h PRN (12.5mg in elderly); if necessary, titrate dose according to response, maintain with 50-200 mg/day CSCI SC dose can be given ON/BD and PRN		• Monitor for postural hypotension and excessive sedation
Olanzapine	**Delirium:** **PO:** start with 2.5mg at bedtime and PRN; titrate if necessary, mean effective dose: 5mg/day		• Contraindicated in narrow angle glaucoma • Incidence of extrapyramidal symptoms are lesser than

Medication	Recommended Dosage	Side Effects	Remarks
			haloperidol.
Benzodiazepines			
Midazolam#	**SC**: 2-5mg 1-2hourly, if increased sedation needed, can titrate midazolam from 10mg-60mg over 24 hours	• Drowsiness • Sedation • Dizziness • Muscle weakness • Memory impairment • Hypotension (more common in midazolam) • Paradoxical arousal/ agitation • Respiratory depression	• Lower starting dose for benzodiazepines which have long half-life (e.g. lorazepam) • Contraindicated in severe hepatic impairment unless patient is imminently dying
Lorazepam	**PO:** 0.5mg-1mg BD and PRN (Sublingual)		

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*Consider dose reduction in renal impairment.
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1. Cherny, NI, Fallon MT, Kaasa S., Portenoy RK, Currow, DC, editors. Oxford Textbook of Palliative Medicine. 6th ed. Oxford: Oxford University Press; 2021.
2. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.
3. Wilcock A, Howard P, Charlesworth S, editors. Palliative Care Formulary. Eighth Edition. London: Pharmaceutical Press; 2022.
4. David H et.al. Pharmacologic Management of End-of-life Delirium: Translating Evidence into Practice. Cancers. 2024;16:2045.
5. Scottish Palliative Care Guidelines.

8.4.2 INSOMNIA

It is the most common prevalence of sleep disorder and can become a persistent problem for patients with serious illness or life-threatening illnesses.

Patient's subjective report of difficulty initiating or maintaining sleep, despite adequate opportunity and circumstance to sleep specifically in dissatisfaction with sleep quality or quantity. Insomnia can lead to irritability, anxiety, depression, fatigue and eventually impair a patient's quality of life.

Possible Causes

- **Physical symptoms:** uncontrolled pain, uncontrolled dyspnoea, cough, nausea and vomiting, uncontrolled bowel and bladder symptoms
- **Psycho-spiritual issues:** depression, anxiety, various factors of fears
- **Medications:** corticosteroids, methylphenidates, beta blockers, diuretics
- **Caffeine and alcohol**
- **Substance withdrawal:** benzodiazepine, alcohol, nicotine

Management

Address symptoms of pain, dyspnoea, cough etc.

Non-Pharmacological Management

- Establish good sleep hygiene
    - Regular bedtimes and wake up time
    - Make sure peaceful mind in the evening prior to bedtime
    - Minimise daytime napping
    - Reduce evening stimulants such as corticosteroids/ coffee
    - Conducive sleep environment (room, bedding, surrounding sound, room temperature)
- Consider earplugs
- Practice relaxing techniques such as music, meditation, massage, aromatherapy, mindfulness therapy

Pharmacological Management[1,2,3,4]

Medication	Recommended Dosage	Side Effects	Remarks
Benzodiazepines			
Lorazepam	**PO:** 0.5mg-1mg BD and PRN (Sublingual)	• Drowsiness • Sedation • Dizziness • Muscle weakness • Memory impairment • Paradoxical arousal/ agitation • Respiratory depression	• Lower starting dose for benzodiazepines which have long half-life (e.g. lorazepam) • Contraindicated in severe hepatic impairment unless patient is imminently dying
Non-Benzodiazepines			
Zolpidem	**PO:** 5-10mg ON	• Dizziness • Headache • Somnolence	• Use with caution in older adult patients; dose adjustment recommended
Antidepressants **For insomnia with depressive symptoms**			
Amitriptyline	**PO:** 25-100mg ON	• Restlessness • Dizziness • Sedation • Fatigue • Dry Mouth	• Contraindication with concurrent use of monoamine oxidase inhibitors (MAOI) or within 2 weeks of its cessation, chronic heart failure, coronary artery insufficiency, recent myocardial infarction and arrhythmias.

Medication	Recommended Dosage	Side Effects	Remarks
Mirtazapine#*	**PO:** 15-45mg ON	• Somnolence • Constipation • Increase appetite • Weight gain	• Contraindication with concurrent use of MAOIs or within 2 weeks of its cessation. • Maximum dose of 30mg in elderly patients and those with hepatic impairment or renal impairment (CrCl <40mL/min)

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

References:

1. Cherny, NI, Fallon MT, Kaasa S., Portenoy RK, Currow, DC, editors. Oxford Textbook of Palliative Medicine. 6th ed. Oxford: Oxford University Press; 2021.
2. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.
3. Wilcock A, Howard P, Charlesworth S, editors. Palliative Care Formulary. Eighth Edition. London: Pharmaceutical Press; 2022.
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9.0 PALLIATIVE EMERGENCIES

Palliative emergencies are acute, life-threatening conditions requiring prompt recognition and management to relieve distress and maintain comfort. These may include severe pain crises, massive haemorrhage, acute dyspnoea, spinal cord compression, or hypercalcemia of malignancy. While palliative care prioritises quality of life, addressing emergencies prevents suffering and upholds patient dignity through tailored, goal-directed approaches.

9.1 MALIGNANT HYPERCALCAEMIA

Hypercalcaemia occurs in 20–30% of patients with cancer as a result of increased osteoclastic activity leading to release of calcium from bone and decreased excretion of urinary calcium. It is commonly associated with breast and prostate carcinomas, renal cell carcinoma, multiple myeloma, lymphoma and squamous cell cancers.[1]

The formula for **total serum calcium, corrected for albumin** (mmol/L) = measured serum calcium (mmol/L) + [40 – measured serum albumin (g/dL)] x 0.02

Clinical presentation is usually mild unless serum calcium is elevated beyond 3.0mmol/L. Symptoms roughly correlate with the degree of hypercalcemia (corrected) and the rapidity of rise:[1,2]

- Cognitive: sedation, delirium, coma
- Gastrointestinal: anorexia, nausea, vomiting
- Renal: dehydration, polyuria, polydipsia

The supportive measures include the treatment of the underlying malignancy with systemic therapy (e.g. chemotherapy) for long-term management. In cases where further anticancer therapy is not feasible, the decision to treat or not treat hypercalcemia is based on severity of symptoms, prognosis and careful exploration of the patient's goals of care. Additionally, all medications that can increase serum calcium (e.g. thiazides, supplements containing calcitriol and calcium) shall be reviewed and discontinued. Fluid replacement is considered if clinical signs of dehydration are present. Intravenous hydration with Normal Saline of up to 3 litres/day is calciuretic, but exercise caution in the elderly and populations at risk of fluid overload. Renal dialysis can be used in cases of acute/chronic renal failure.[1,2,3]

Possible Causes:[2]

- Parathyroid hormone-related protein secretion by tumours
- Bone metastases inducing local osteolysis through release of cytokines
- Production of 1,25-dihydroxyvitamin D (calcitriol) by tumours

Management

Pharmacological Management[1,2,3]

Medication	Recommended Dosage	Side Effects	Remarks
Bisphosphonates			
Zoledronic Acid*	**IV Infusion:** 4 mg in 100ml Normal Saline (over 15–30 minutes)	• Flu-like symptoms • Hypocalcaemia • Hypophosphatemia • Osteonecrosis of the jaw	• Drug class of choice for most patients • Ensure that the patient is hydrated adequately before starting bisphosphonates • Pamidronate and zoledronic acid are noted to have full efficacy 2-4 days after administration; responses usually last 1-3 weeks • May lead to hypocalcaemia or azotemia; use with caution in renal dysfunction, and consider reduced doses. • Repeated doses of bisphosphonates can only be given after 7 days has elapsed from the 1st dose
Pamidronate*	**IV Infusion:** 30-90mg in 500ml Normal Saline (over 2 to 4 hours)		

Medication	Recommended Dosage	Side Effects	Remarks
Others			
Denosumab	**SC:** 120mg (may be repeated after 4 weeks)	• Hypocalcaemia • Hypophosphatemia • Osteonecrosis of the jaw	• Durable responses in over 60% of patients with hypercalcemia refractory to bisphosphonates • Cost may be prohibitive in palliative settings
Calcitonin	**SC:** 4-8 IU/kg every 6-12 hours for 2 days	• Nausea	• May lead to transient reductions in serum calcium (within 12-24 hours) • Limited role in severe hypercalcemia; administration should be limited to 48 to 72 hours due to risk of tachyphylaxis
Glucocorticoids			
Hydrocortisone	**IV:** 200mg OD for 3 days	• Hyperglycaemia	• Useful in lymphoid malignancies that secrete 11,25-dihydroxyvitamin D

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

References:

1. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.
2. Fast Fact Number 151. Palliative Care Network of Wisconsin. Gary Hsin and James Hallenbeck. 2019. https://www.mypcnow.org/fast-fact/hypercalcemia-of-malignancy/
3. Carroll MF, Schade DS. A Practical Approach to Hypercalcemia. Am Fam Physician. 2003 May 1;67(9):1959-66

9.2 SUPERIOR VENA CAVA OBSTRUCTION (SVCO)

Superior Vena Cava Obstruction (SVCO) is a medical emergency which occurs due to the obstruction of blood flow through the superior vena cava, leading to venous congestion. Most patients presenting with SVCO have thoracic malignancies, predominantly lung cancer.

The clinical presentations of SVCO include facial swelling, cough, dyspnoea and swelling of the neck, trunk and upper extremities.

Possible Causes

- Malignant tumours within the mediastinum
- Intraluminal thrombosis
- Aortic aneurysm

Management

SVCO can lead to serious complications like cerebral oedema or airway obstruction if untreated, necessitating prompt recognition and management. Management requires both alleviation of symptoms and shrinkage of intrathoracic tumour to relieve the obstruction. Non-pharmacological strategies include radiotherapy, stenting of the superior vena cava or postural maneuvers to reduce congestion.

Pharmacological management includes anticancer therapy to shrink the tumour. Cough and dyspnoea is managed in the same way as mentioned in Chapter 9 on dyspnoea.

Pharmacological Management[1]

Medication	Recommended Dose	Side effects	Remarks
Corticosteroids			
Dexamethasone	**IV:** 10-16mg/day with gradual tapering over several weeks	• CNS: Agitation, Insomnia, Irritability • GI: Peptic ulcer, Gastritis, Dyspepsia • Cushing syndrome • Hyperglycaemia	Administer dexamethasone before evening to avoid insomnia.

References:

1. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.

9.3 MALIGNANT SPINAL CORD COMPRESSION (MSCC)

MSCC occurs in 2.5-5% of patients with cancer in the last 5 years of life. It occurs when the dural sac and its contents are compressed at the level of the cord or cauda equina as a result of direct pressure, vertebral collapse or instability caused by metastatic spread or by direct extension of malignancy.

Patients with MSCC can present with the signs and symptoms such as muscle weakness, shock-like sensation in the back, arms and legs when the neck flexes, changes in bowel and bladder function as well as back pain.

Possible Causes[1,2]

Cancers commonly associated with spinal cord compression:

Accounts for 15-25% of those presenting with MSCC	• Prostate cancer • Breast cancer • Lung cancer
Accounts for 5-10% of those presenting with MSCC	• Kidney or renal cancer • Lymphoma • Myeloma
Accounts for less than 5% of those presenting with MSCC	• Colorectal cancer • Tumours of unknown primary • Melanoma • Sarcoma

Management

MSCC warrants rapid treatment and immediate hospital care. Non-pharmacological management includes modalities such as single fraction radiotherapy for patients with a short prognosis or surgical decompression.

Other symptoms management include the alleviation of pain (Refer Chapter 8.1 Pain), constipation (Refer Chapter 8.3,2 Constipation) and the use of corticosteroids to reduce the swelling around the spinal cord and hence reducing the numbness and muscle weakness.

Pharmacological Management[1,2]

Medication	Recommended Dose	Side effects	Remarks
Corticosteroids			
Dexamethasone	**IV:** 10-16mg/day with gradual tapering over several weeks	• CNS: Agitation, Insomnia, Irritability, Restlessness • GI: Peptic ulcer, Gastritis, Dyspepsia • Cushing syndrome • Hyperglycaemia	Administer dexamethasone before evening to avoid insomnia.

References:

1. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.
2. Stephanie BK, Christine SR. What are the Signs, Symptoms, and Treatments of Spinal Cord Compression. Evidence-Based Practice of Palliative Medicine. 2nd ed. Elsevier Inc. 2023.

9.4 HAEMORRHAGE

Haemorrhage can present in a variety of ways, from occult bleeds causing anaemia over weeks to months, to overt external bleeding from particular anatomical sites, e.g. haemoptysis, haematuria etc.

Massive haemorrhage is an emergency in palliative care. The management of haemorrhage will vary based on anatomic location, the extent of the injury and patient presentation.

Possible Causes[1,2]

- Tumour-related: head and neck cancers: malignant neck ulceration leading to erosion of a major artery, lung cancers: haemoptysis, gastrointestinal: hematemesis, malaena, urological: haematuria, clot retention
- Treatment-related: mucosal damage; NSAIDs and steroids, chemotherapy induced thrombocytopenia
- Coagulopathy related: marrow failure.
- Thrombo-embolic phenomena including disseminated intravascular coagulopathy (DIC)
- Complications of anticoagulation.

Management[3]

1	**Anticipate and identify those at risk**	• Consider risk factors for terminal haemorrhage

2	**Provide anticipatory guidance and prepare the care team**	• Provide local compression with dark towels
		• Follow the "ABCs":
		  ○ A (assure the patient)
		  ○ B (be there; stay with the patient)
		  ○ C (comfort and calm)

3	**Implement preventive measures**	• Weigh benefits of medications that has higher risk of bleeding, such as NSAIDs, steroids and anticoagulants • Consider continuing antihypertensive medications to reduce intraarterial pressure and reduce risk of bleeding • Can consider Vitamin K and antifibrinolytic agent (tranexamic acid)

4	**Actively manage**	• Mainstay is not medication treatment, but to apply "ABC" • Patient positioning • Dark linens and dark towels
5	**Escalate care**	• Palliative sedation can be considered otherwise administer midazolam 5-10mg IV/SC
6	**Follow up**	• Debrief health care workers and provide bereavement care to family members who witnessed terminal haemorrhage

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9.5 SEIZURE

Seizures can occur in about 13% of cases in palliative care[1,2]. About 25% to 50% of palliative patients who develop seizure activity have brain metastases[2,3]. Of patients with primary brain tumours, 20% to 45% will present at diagnosis with convulsions[3] and more will develop seizures as their cancer progresses. It is interesting to note that slow-growing primary brain cancers such as oligodendroglioma and low-grade astrocytoma tend to present more often with seizures, with a prevalence of 70% to 100%, unlike the more aggressive glioblastoma, with a prevalence of 10% to 20%[3,4]. It was also noticed that being female could double the risk of developing seizures[4], and that children with cancer have a higher incidence of seizure activity[2] than adults with cancer do.

Possible Causes

- Seizures can be caused by structural damage to the brain or by a systemic insult to the brain. Structural damage can be due to primary tumours, metastases, abscesses, reversible posterior leukoencephalopathy syndrome, paraneoplastic limbic encephalitis, hemorrhage, or radiation necrosis.
- Systemic causes include hypoxia, hypoglycemia, hyperglycemia, hyponatremia (e.g., in the syndrome of inappropriate antidiuretic hormone secretion), hypernatremia, low levels of magnesium, hypocalcemia, hypercalcemia, uremia, and hepatic failure
- Medications such as tramadol, ondansetron, antipsychotics, and chemotherapeutic agents[1,2], either through their proconvulsant effect or by lowering the seizure threshold.

Management

<u>Pharmacological Management</u>[5]

- Prophylaxis

Anticonvulsant prophylaxis is not recommended in patients with brain tumours, whether primary or metastatic, if the patient has never had any seizures. This is because of the relatively low risk of developing convulsions for most tumours, and the considerable potential burden of antiseizure side effects (drug-drug interactions, sedation, cognitive impairment, etc). Patients can be on dexamethasone to prevent the brain oedema, which could otherwise provoke seizures.[1]

- Treatment (anti-convulsant)

The treatment of seizures will vary according to the frequency of the convulsive episodes, the duration of each episode, and whether there is a reversible cause. Indeed, a first-time seizure with a reversible cause does not require long-term anticonvulsants. On the other hand, a first episode of seizure in a patient with a brain lesion should warrant the institution of long-term anticonvulsants. When this lesion is a known brain tumour (primary or metastatic) and no other reversible cause of seizure activity has been identified, the institution or increase in dosage of a steroid, such as dexamethasone, could be considered as the first-line treatment alongside long-term treatment. If patients require long-term anticonvulsants but are candidates for further chemotherapy, then institution of antiseizure medications with little risk of interaction with the chemotherapeutic agents should be considered. These include levetiracetam, gabapentin, lamotrigine, topiramate, and pregabalin, as they do not induce cytochrome P450 activity.

Medication	Recommended Dosage	Side effects	Remarks
Anticonvulsants			
Phenytoin	**PO:** 200–500 mg/day in single or divided doses **Slow IV**: 10–15mg/kg Oral to IV conversion 1:1 Titrate dose according to TDM result	• CNS: ataxia, restlessness, vertigo • Hepatotoxicity • GI: nausea, vomiting, diarrhoea, constipation • Dermatologic: Purpuric rash, Toxic epidermal necrolysis • Hirsutism • Anaemia • Osteoporosis	• High risk of drug-drug interactions including dexamethasone • Associated with an increased risk of serious skin reactions. Decreased bone mineral density and increased risk of osteomalacia. Impair hormonal contraceptives
Carbamazepine	**PO:** 200 mg/day; increase by 200 mg/week. 300–1600 mg/day in 3–4 divided doses or 2 divided doses if long-acting	• SIADH • CNS: sedation, vertigo, ataxia, diplopia • Myelotoxicity	• Associated with an increased risk of serious skin reactions. • Decreased bone mineral density

Medication	Recommended Dosage	Side effects	Remarks
			and increased risk of osteomalacia. • Impair hormonal contraceptives
Valproic acid	Oral:IV:SC conversion 1:1:1 Dose: 15 mg/kg daily; 250–500 mg/day, increased weekly by 250 mg/week 1000–3000 mg/day, up to 60 mg/kg daily (check serum levels) in 3 divided doses or 2 divided doses if long-acting or infusion; decrease dose if hepatic failure occurs Titrate dose according to TDM result	• Drug-drug interactions • CNS (ataxia, tremors, sedation) • Weight gain • Hair loss • Gastrointestinal: abdominal pain, diarrhea, dyspepsia, gingival disorder, nausea, vomiting • Thrombocytopenia • Liver toxicity	• Decreased bone mineral density and increased risk of osteomalacia. Not safe for pregnancy
Phenobarbital	Oral:IV conversion 1:1 Dose: 60–250mg/day, maximum 600mg/day (1–5 mg/kg in adults) in single or divided doses	• Drug-drug interactions • CNS depressor • Respiratory depression • Somnolence • Rash	• Confusion, worsening of depression, hallucinations, and unusual excitement, nervousness, or irritability. • Serious allergic reactions, including anaphylaxis and angioedema and eosinophilia and systemic symptoms (DRESS) (fever, dark urine,

Medication	Recommended Dosage	Side effects	Remarks
			headache, rash, stomach pain, swollen, painful, or tender lymph glands in the neck, armpit, or groin, unusual tiredness, or yellow eyes or skin). QT prolongation.
Gabapentin*	**PO:** 300–3600mg/day as monotherapy; up to 1800 mg/day as adjuvant therapy, in 3–4 divided doses	• Drowsiness • Dizziness • Ataxia • Weight Gain • Oedema • Cognitive Impairment • Drug Abuse/ Dependance • Withdrawal Symptoms • Suicidal ideation • Angioedema/ Anaphylaxis	• Interaction with antacids
Levetiracetam*	Oral:IV:SC conversion 1:1:1 Dose: 750–1000mg/day. 1000–3000mg/day in 2 divided doses or infusion	• Anxiety • Aggressivity • Somnolence • Asthenia • Dizziness	• Can be given IV or SC • Can be used in patients with hepatic and cardiac comorbidities
Benzodiazepines			
Clonazepam	**PO:** 1–6 mg/day in 2–3 divided doses. Maximum dose: 20mg/day	Same as for benzodiazepines; paradoxical excitation	• Long half-life (20-60h), longer sedation and side effect duration.

Medication	Recommended Dosage	Side effects	Remarks
			• Increased risk of fall
Midazolam#	**CSCI:** 20-60mg/day. No maximum titrate accordingly	Same as for benzodiazepines; paradoxical excitation	• Short half-life (1-4h) • Increased risk of fall

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

Breakthrough seizure treatment

Status epilepticus has traditionally been defined as either seizure activity, convulsive or non-convulsive, lasting longer than 30 minutes, or 3 episodes without return of consciousness within a 30-minute span[6,7].

It carries a mortality risk of 11% to 34%[3]. As the probability of spontaneous resolution of the seizure decreases with time, treatment of status epilepticus should be instituted when a convulsion lasts 5 minutes or more. The treatment might vary according to the patient's location: home care, hospice, or hospital and availability of the medication.

Medication	Recommended Dosage	Side effects	Remarks
Benzodiazepines			
Midazolam#	**SC:** 5mg **Buccal:** 5mg Can be repeated every 10-15 mins	Sedation of up to 1-3 hours	Can be given via subcutaneous port or buccal access
Lorazepam	**Buccal**: 1-2mg Can be repeated every 10-15 mins	Sedation of up 6-8 hours	Slower acting compared to Midazolam. Can be given via buccal access
Diazepam	**Rectal**: 5mg Can be repeated every 10-15 mins	Sedation of up to 4-10 hours	Issue with repositioning patients for administration,

Medication	Recommended Dosage	Side effects	Remarks
Benzodiazepines			
			individual's dignity, harder to administer.

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

References:

1. Grewal J, Grewal HK, Forman AD. Seizures and Epilepsy in Cancer: Etiologies, Evaluation, and Management. Curr Oncol Rep. 2008;10(1):63–9.
2. Singh G, Rees JH, Sander JW. Seizures and Epilepsy in Oncological Practice: Causes, Course, Mechanisms and Treatment. J Neurol Neurosurg Psychiatry. 2007;78(4):342–9.
3. Beaulieu I, Nadeau C. Myoclonies et convulsions. In: Beausoleil M, Association des Pharmaciens des Etablissements de Santé du Québec, editor. *Guide Pratique des Soins Palliatifs: Gestion de la Douleur et Autres Symptômes*. 4th ed. Montreal, QC: Association des Pharmaciens des Etablissements de Santé du Québec; 2008. p. 287–98.
4. Forsyth PA, Weaver S, Fulton D, Brasher PM, Sutherland G, Stewart D, et al. Prophylactic Anticonvulsants in Patients with Brain Tumour. Can J Neurol Sci. 2003;30(2):106–12.
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9.6 PAIN CRISIS

Pain crisis is a palliative care emergency when there is a severe, uncontrolled pain and causes distress for the patient [1].

Assessment [1,2]

During a pain crisis, assessment needs to be focused and it usually occurs simultaneously with management. Important aspects of assessment include:

- Etiology and nature of the pain
- Intensity of pain
- Elicit if this is a new pain or an exacerbation of an existing pain
- Exclude reversible factors (e.g. acute retention of urine)

Management [1,2]

- Respond promptly in a calm and reassuring manner
- Seek help from senior members in the team, and/or a specialist palliative care team
- Use strong opioids for rapid titration
    - Opioid selection is based on pain assessment, patient's response to opioids, and if there is renal/liver impairment.
    - Use parenteral route for rapid onset of analgesia.
- Aim to achieve 'acceptable subjective analgesia', or reduction of pain severity by 50% or a reduction of pain score by 2 points
- Monitor for signs of opioid toxicity (e.g. low respiratory rate, excessive sedation, myoclonic jerks and hallucinations).
- Initiate Rapid Opioid Titration

Rapid Opioid Titration (Refer flow chart below):

For opioid-naïve patients:

- IV Morphine 1-2mg every 5-10min or SC morphine 2.5-5mg every 15-30min, or

For patients already on regular opioids, including parenteral opioid infusions:

- Convert to the equivalent parenteral daily dose using conversion ratios
- Administer at 1/10th of the total daily dose every 5-10min (if IV route) or every 15-30min (if SC route) till analgesia is achieved.
- For elderly, frail or renally impaired patient use a lower dose
- If ineffective after 3 doses, please call for help.

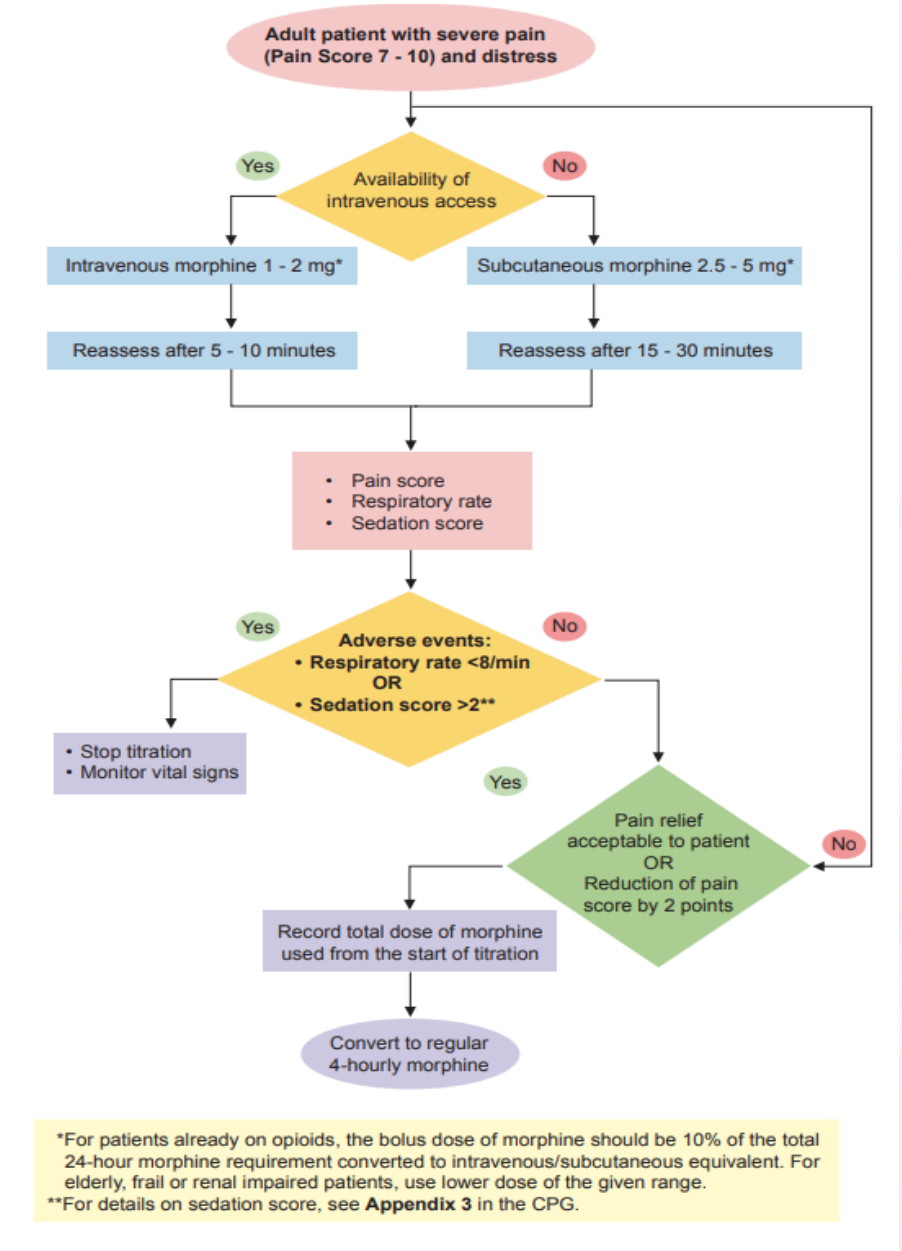
After rapid opioid titration:

- Once analgesia is achieved, start a continuous infusion of the opioid, or increase the baseline opioid infusion to maintain analgesia.
- The total effective dose of Morphine is assumed to last for 4 hours; hence the total daily dose of morphine is times by 6 for patients that are no renally impaired.
- Breakthrough doses should be available for breakthrough pain.
- Revisit the pain history in greater detail when the patient is more comfortable.
- Titrate the opioid infusion over a period of time (usually a few days) until pain is well-controlled, then consider converting to a non-parenteral route.

Other Considerations:

- Optimise adjuvant agents.
- Consider interventional techniques, if appropriate.

Algorithm 1. Titration of Morphine for Rapid Pain Relief in Adults with Severe Pain and Distress[1]



References:

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9.7 MALIGNANT BOWEL OBSTRUCTION

Malignant bowel obstruction (MBO) most frequently occurs in patients with advanced cancer that originate from abdominal or pelvis. It is a severe complication in advanced cancer. It is estimated to occur in 10–28% of patients with gastrointestinal cancers and up to 51% of patients with advanced ovarian cancer.

According to International Conference on MBO and Clinical Protocol Committee, MBO is defined as:

i. Clinical evidence of bowel obstruction (via history, physical, and/ or radiological examination)
ii. Bowel obstruction beyond the ligament of Treitz
iii. Diagnosis of intra-abdominal cancer with an incurable disease, or a non-intra-abdominal primary cancer with the clear intraperitoneal disease

Possible Causes

- Mechanical bowel obstruction (intraluminal, intramural, extrinsic obstruction of the lumen)
- Functional bowel obstruction (tumor infiltration of mesentery, nerves and/or celiac and enteric plexus, and paraneoplastic syndromes)

Management

Non-pharmacological Management

- Consider stenting to relieve proximal small bowel or colonic obstruction

Pharmacological Management

Medication	Recommended Dosage	Side effects	Remarks
Antisecretory agent			
Octreotide#*†	**SC:** 50 - 100 mcg q8h **CSCI:** start at 10-20 mcg/h and titrate q24h to achieve symptom relief	• Pain at injection site • Localised skin reaction • Impaired glucose tolerance	Octreotide is painful if given as SC bolus injection

Medication	Recommended Dosage	Side effects	Remarks
Antisecretory agent			
		• Biliary sludging with long term use	
Ranitidine#*†	**IV/SC:** 50mg TDS-QID	• Constipation • Diarrhoea • Nausea • Vomiting	H_2 antagonists increase gastric pH, and this reduces the absorption of some drugs and formulations

#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.
†The use of medications not registered with Drug Control Authority (DCA), medications for off-label indications and medications not listed in the MOH Medicines Formulary (MOHMF) requires prior submission of a Special Approval Medicine (SAM) application to the Pharmacy Practice and Development Division, Ministry of Health (MOH). This requirement does not apply to medications that have been granted exemption from SAM application by the MOHMF Panel.

References:

1. Ainhoa M, Jenny L et.al. MASCC Multidisciplinary Evidence-based Recommendations for the Management of Malignant Bowel Obstruction in Advanced Cancer. Supportive Care in Cancer. 2002; 30:4711–4728
2. Cousins SE, Tempest E, Feuer DJ (2016) Surgery for the Resolution of Symptoms in Malignant Bowel Obstruction in Advanced Gynaecological and Gastrointestinal Cancer. Cochrane Database Syst Rev 2016(1):CD002764.
3. Christopher PS, Pasithorn AS. What Interventions are Effective for Relieving Acute Bowel Obstruction in Cancer and Other Conditions? Evidence-based Practice of Palliative Medicine. 2023. 171-178

10.0 END OF LIFE CARE

10.1 MANAGEMENT IN THE LAST DAYS OF LIFE

The last days of life are an important period for both the patient and the loved one. It mainly focused on ensuring comfort, dignity and respect while alleviating suffering. The last days of life are associated with end-of-life care, active phase of dying and terminal phase. Thus, the signs of dying should be recognised and manage the symptoms.

Common Signs of Dying

- Diminished intake of food and fluids
- Difficulty swallowing medications
- Decreased level of consciousness
- Weakness and lethargy
- Changes in respiration pattern such as intermittent apnoea, Cheyne-stokes respirators, mandibular movement on respiration (gasping)
- Audible respiratory secretions (death rattles)
- Signs of hypo-perfusion: cold peripheries, impalpable radial pulse and oliguria

Management[1,2]

Symptom management at the last days of life is one of the important management in palliative care. It is crucial to manage patients' symptoms which may change as they approach death. End-of-life patients might require regular symptoms management medications to be delivered in a syringe driver in hospital or elastomeric pump in home setting. They would also require anticipatory medications to be given when there are new or worsening symptoms. The symptoms and medications are as follow:

Symptoms	Medication	Recommended Doses
Pain and dyspnoea	Morphine	**Opioid naïve:** S/C Morphine 1mg PRN **Opioid tolerant:** S/C Morphine (1/6th of 24 hour dose)
Nausea and vomiting	Haloperidol	S/C Haloperidol 0.5-1mg PRN
Terminal delirium	Midazolam Haloperidol	S/C Midazolam 2.5mg PRN S/C Haloperidol 0.5-1mg PRN
Terminal secretions ('death rattle')	Hyoscine butylbromide	S/C Hyoscine Butylbromide 20mg PRN

Apart from specific symptom management, few issues have to be addressed such as artificial nutrition and hydration, oral care and skin care.

The management of last days of life in palliative care patients is a multidimensional process that involves not only medical interventions but also psychological, spiritual and social support. Eventually, end-of-life care patients can be managed in a holistic manner.

References:

1. Cherny, NI, Fallon MT, Kaasa S., Portenoy RK, Currow, DC, editors. Oxford Textbook of Palliative Medicine. 6th ed. Oxford: Oxford University Press; 2021.
2. Katiman D, Lim RBL, editors. Handbook of palliative medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.

10.2 PROCEDURES IN TERMINAL DISCHARGE DISPENSING

Terminal discharge is the rapid discharge of a patient from hospital to home when death is anticipated and imminent.[1] Fulfilling patients and caregivers' preferences for the dying process, including the place of death, are indicators of a good death. Dying at home is associated with 'good death', preferred by the majority of Malaysians and may also have additional religious and cultural significance.

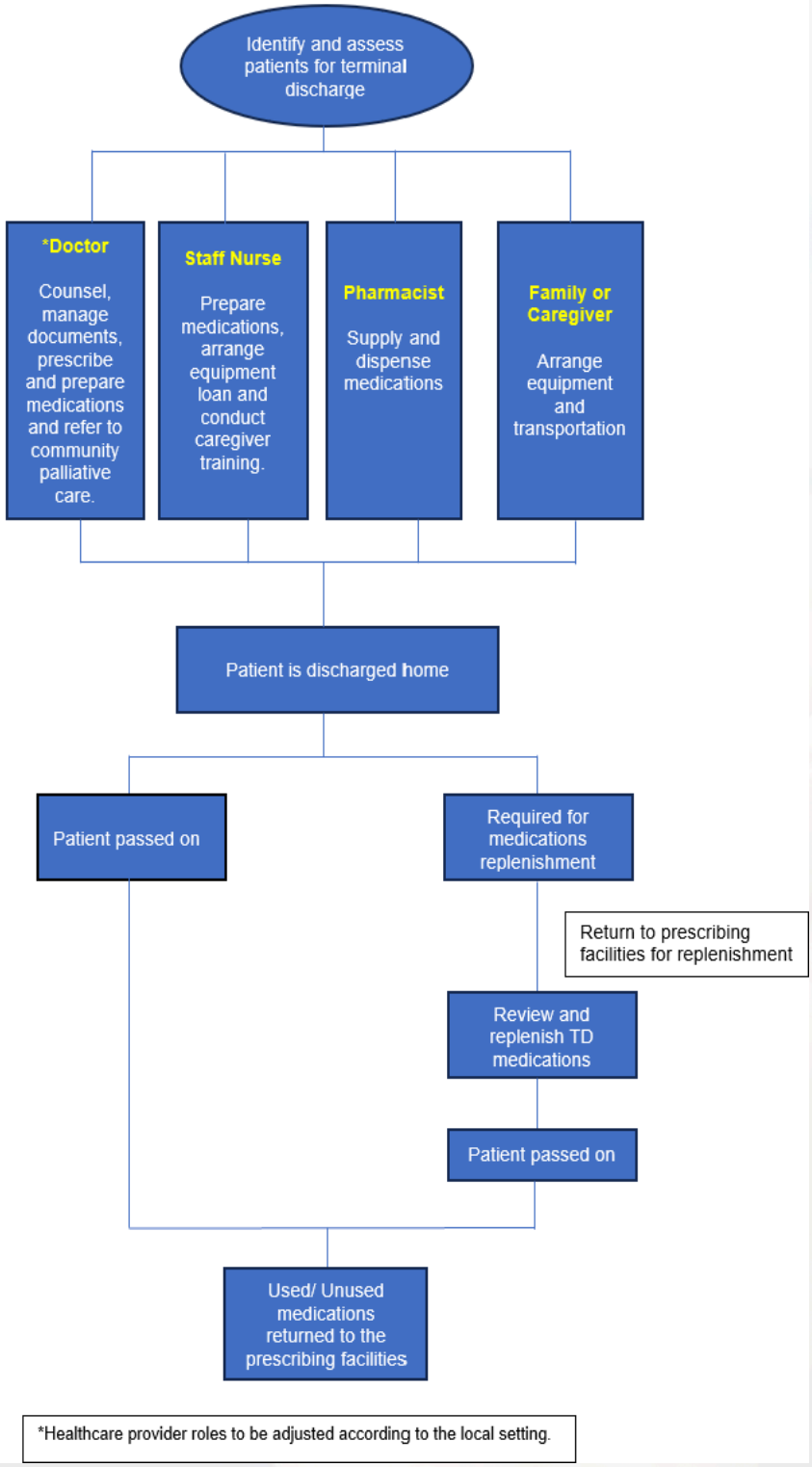
Recognising that terminal discharge can be stressful and complex as it happens over a limited period of time, thus, it is necessary to develop a terminal discharge framework in Malaysia.

Each member of the interdisciplinary team plays an integral role in facilitating terminal discharge. Doctors are the primary healthcare providers who are responsible for the terminal discharge discussion with family members of end-of-life patients. The discussion should be navigated based on the patient's goals of care in terms of symptoms management and preference for discharge destination. Pharmacists are important in reviewing discharge prescriptions and supply of the medications. They are also responsible for education and counselling of medications to the family members.

Nurses are responsible for caregiver training to family or caregivers which include nursing care (repositioning for respiratory secretions, stoma care, wound care and handling tubes e.g. nasogastric tube and urinary tube catheter). Besides that, they also guide family members and caregivers regarding equipment and the transport back to the preferred destination. Everyone in the interdisciplinary team is responsible for the preparation of terminal discharge medications, be it in elastomeric pumps or syringes.

Lastly, patients can be discharged for the last miles of life with the support of family members, caregivers or community teams such as hospices or domiciliary teams.

Algorithm 3. Overview of terminal discharge process



Roles and responsibilities of pharmacist in Terminal Discharge

- Review discharge prescriptions in accordance with the patient's clinical notes to ensure medication safety, accuracy and appropriateness prior to discharge.
- Train caregivers on common symptoms and their management including medications dosages, timing and side effects.
- Educate caregivers about the patient's current condition, expected disease trajectory and potential complications.
- Address myths and misconceptions surrounding medications for symptom control in end-of-life care.
- Facilitate seamless medication reconciliation and supply continuity during transition of care.

Medications List in Terminal Discharge

Medications used in terminal discharge should be individualised and tailored to the patient's end of life symptoms. The preferred route of administration is via subcutaneous using needleless subcutaneous port; however, other routes of administration can be considered for patients with functioning PEG tubes.

MEDICATION GROUP	MEDICATIONS
Opioids	• Parenteral Morphine • Parenteral Fentanyl • Parenteral Oxycodone • Transdermal Fentanyl
Benzodiazepines	• Parenteral Midazolam • Sublingual Lorazepam
Antipsychotics	• Parenteral Haloperidol
Anti-cholinergic	• Parenteral Hyoscine Butylbromide

The examples of documents used by the Palliative Care Unit (PCU) to ensure proper handling of terminal discharge medications are as in **Appendix 3** Example of the Checklist for Terminal Discharge, **Appendix 4** Example of the Terminal Discharge Medication Information Sheet, **Appendix 5** Example of the Letter for Terminal Discharge and **Appendix 6** Example of the Declaration Letter for Care.

References:

1. Tan YY, Blackford J. 'Rapid Discharge': Issues for Hospital-Based Nurses in Discharging Cancer Patients Home to Die. Journal of Clinical Nursing. 2015 Sep;24(17-18):2601-10.
2. Hospital Kuala Lumpur. Terminal Discharge Guideline. 1st ed. Kuala Lumpur: Hospital Kuala Lumpur; 2023.
3. Katiman D, Lim RBL, editors. Handbook of Palliative Medicine in Malaysia. 2nd ed. Kuala Lumpur: Malaysian Hospice Council; 2023.

11.0 RETURN OF UNUSED AND DISPOSAL OF USED *PARENTERAL MEDICATIONS

Opioids have significant potential for misuse and abuse. Many of these medications carry the risk of non-medical use (e.g. diversion and self-harm). Therefore, regular review should be conducted throughout the prescribing and medication ordering process to ensure appropriate use.

In Malaysia, opioids are regulated under multiple legislative frameworks, including the Poisons Act, 1952[1], Poisons (Psychotropic Substances) Regulations 1989[2], Dangerous Drugs Act, 1952[3], Dangerous Drugs Regulations, 1952[4] and Sale of Drugs Act, 1952[5]. All opioids intended for medicinal use must comply with the relevant legislation, including issued guidelines that outline specific requirements for storage, record-keeping, and disposal.

Storage

Most opioids should be stored at room temperature, away from heat, moisture and direct sunlight. The patient and the carer should be advised on safe storage of medications within the home (e.g. out of reach and sight of children) and to ensure easy access of PRN medications. Keep opioids in its original container or packaging. For patients storing opioids at home, storage should follow the instructions stated on the product packaging,

Disposal

Patients and carers should be educated on the importance of proper disposal of unused or expired opioids to prevent its misuse by others or accidental ingestion, particularly by children.

In the context of opioids disposal in Ministry of Health (MOH) healthcare facilities, disposal must comply with regulation 25 of the Poisons (Psychotropic Substances) Regulations 1989. For disposal by patients at home, patients or their next of kin are advised to return unused or expired opioids to MOH healthcare facilities, preferably hospital/ dispensing facility for proper and safe disposal.

References:

1. Poisons Act 1952 [*Act 366*]
2. Poisons (Pschotropic Substances) Regulations 1989
3. Dangerous Drugs Act 1952 [*Act 234*]
4. Dangerous Drugs Regulations 1952 (Malaysia)

12.0 APPENDICES

PEDIATRIC DOSING RECOMMENDATIONS

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
1	Atropine	● Reduction of death rattle ● Hypersalivation/ Hypersecretion	**SL:** ● Neonates: (Injection solution) 20-40 mcg/kg/dose BD/TDS ● Child 10-19kg: (Eye drop solution 0.5%) 1 drop TDS at 6 hourly intervals. ● Child 5-18 years (>20 kg): (Eye drop solution 0.5-1%) 1-2 drops 4-6 hourly	● Very dry mouth and throat ● Blurred vision ● Palpitations ● Constipation ● Urinary retention	1. Used as third line if glycopyrronium or hyoscine are not available or effective. 2. Concurrent treatment with 2 or more antimuscarinic drugs increases risk of side effects and central toxicity.
2	Baclofen*	● Chronic severe spasticity or spasms of voluntary muscle ● Considered as third line neuropathic agent ● Hiccup (strong evidence in adults but none in children)	**PO:** ● Child < 18 years: Start with 300 mcg/kg/day in 4 divided doses, increase gradually at weekly intervals to a usual maintenance dose of 0.75-2 mg/kg/day in divided doses. Maximum daily doses ● Child 1 month-7 years: max 40 mg/day ● Child 8-18 years: max 60 mg/day IT: ● By specialist teams only. ● Maintenance 25-200mcg/day via intrathecal pump.	• Drowsiness • Nausea	1. Review treatment for spasticity if no benefit within 6 weeks of achieving maximum dose, and withdraw over 1-2 weeks if ineffective. 2. Likely onset of action for hiccups 4-8 hours, for muscle spasm in 1-2 days, for spasticity 3-4 days. 3. For severe intractable hiccups, lower dose range to be used. May have direct effect on diaphragm. 4. Monitor and review reduction in muscle tone and potential adverse effects on swallow,

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
					airway protection, posture and function. 5. Impact of undesirable hypotonia may be minimised by reducing daytime and increasing evening doses. 6. Abrupt withdrawal can precipitate serious psychiatric reactions and (especially after intrathecal use), life-threatening withdrawal syndrome including hyperactivity, increased spasticity, autonomic dysfunction. 7. Baclofen CSCI (using intrathecal preparation) may be used short term (after a test dose) to avoid sudden withdrawal when enteral and/or intrathecal routes become impossible. 8. Contraindicated if there is a history of active peptic ulceration.
3.	Bisacodyl	● Constipation	**PO:** ● Child 4–17 years: 5-20 mg OD (recommended to be taken at night) adjust according to response. **PR (Supp):** ● Child 2–17 years: 5-10 mg OD; adjust according to response.	● Abdominal pain ● Diarrhoea ● Flatulence	Tablets should not be crushed and are not suitable for enteral tube administration.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
4	Carbamazepine	● Neuropathic pain ● Some movement disorders ● Anticonvulsant	**PO:** ● Neonates: Experience is limited. Initial dose 5 mg/kg BD ● Child 1 month–11 years: Initial dose 5 mg/kg ON or 2.5 mg/kg BD, increased as necessary by 2.5-5 mg/kg every 3–7 days; usual maintenance dose 5 mg/kg BD/TDS. Doses up to 20 mg/kg/day in divided doses have been used. ● Child 12–17 years: Initial dose 100–200 mg OD/BD; increased slowly to usual maintenance of 200-400 mg BD/TDS. Max 1.8 g/day in divided doses. **PR:** ● Child 1 month–17 years: Use approximately 25% more than the oral dose (max single dose 250 mg) up to QID.	● SIADH ● CNS (sedation, vertigo, ataxia, diplopia) ● Myelotoxicity	1. Can cause serious blood, hepatic, and skin disorders. Parents should be taught how to recognise signs of these conditions, particularly leucopenia. 2. Numerous interactions with other drugs, etc. chemotherapy drugs and opioids. 3. May cause hyperalgesia on abrupt withdrawal.
5	Celecoxib*	● Not used as first line: Pain, inflammatory pain, bone pain, stiffness ● Dose based on management of juvenile rheumatoid arthritis.	**PO:** ● Child ≥ 2 years: o 10-25 kg: 2-3 mg/kg/dose BD (Max 50 mg BD/ 100mg daily) o 25 kg: 100 mg BD ● ≥ 16 years: Adult dose of 100 mg BD. Can be doubled in severe pain to 200 mg BD	● Hypertension ● Renal impairment ● Cardiac events	Numerous interactions with other drugs, etc. Reduce dose of celecoxib by 50% if using fluconazole.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
6	Clonazepam	●Tonic-clonic seizures ●Partial seizures ●Cluster seizures ●Myoclonus ●Status epilepticus (3rd line, particularly in neonates) ●Neuropathic pain ●Restless legs ●Gasping ●Anxiety and panic ●Oral dysaesthesia in the adolescent ●Has been used in Neonatal units to control severe continuous seizures resistant to other anticonvulsants	Anticonvulsant: **PO** ●Child 1 –11 months: Initially 0.25 mg ON for 4 nights, increased over 2–4 weeks to usual maintenance dose of 0.5–1 mg ON (may be given in 3 divided doses if necessary). ●Child 1–4 years: Initially 0.25 mg ON for 4 nights, increased over 2–4 weeks to usual maintenance of 1–3 mg at night (may be given in 3 divided doses if necessary) ●Child 5–11 years: Initially 0.5 mg ON for 4 nights, increased over 2–4 weeks to usual maintenance dose of 3–6 mg at night (may be given in 3 divided doses if necessary) ●Child 12–17 years: Initially 1 mg ON for 4 nights, increased over 2–4 weeks to usual maintenance of 4–8 mg at night (may be given in 3 divided doses if necessary). Reduce oral dose for other indications. Oral dysaesthesia [burning mouth syndrome]: Rinse with 0.1mg/ml solution For status epilepticus: (SR) **CSCI:** ●Child 1 month–17 years: Starting dose 20-25 mcg/kg/24 hours	Same as for benzodiazepines; paradoxical excitation	1. Very effective anticonvulsant, usually used as 3rd line due to side effects and development of tolerance. 2. Do not use in acute or severe respiratory insufficiency unless imminently dying. Be cautious in those with chronic respiratory disease. 3. As an anxiolytic/sedative, clonazepam orally is approximately 20 times as potent as diazepam (i.e. 250 mcg clonazepam equivalent to 5 mg diazepam orally) 4. Many children with complex seizure disorders are on twice daily doses and on higher than recommended dosages. 5. Tolerance in longer term use may be managed by 'switching/rotating' benzodiazepines. 6. The dose may be increased for short periods of 3-5 days during times of increased seizures e.g. from viral illness 7. Avoid abrupt withdrawal. 8. Associated with salivary hypersecretion and drooling.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			● Maximum starting doses: 1-5 years: 250 mcg/24 hours; 5-12 years: 500 mcg/24 hours. ● Increase at intervals of not less than 12 hours to 200 mcg/kg/24hours (maximum 8 mg/24 hours) ● Doses of up to 1.4 mg/kg/24 hours have been used in status epilepticus in PICU environment. **By IV injection over at least 2 minutes, or infusion:** ● Neonate: 100 mcg/kg intravenous over at least 2 minutes, repeated after 24 hours if necessary (avoid unless no safer alternative). Used for seizures not controlled with phenobarbital or phenytoin. ● Child 1 month-11 years: Loading dose 50 mcg/kg (max 1 mg) by IV injection followed by IV infusion of 10 mcg/kg/hour adjusted according to response; max 60 mcg/kg/hour. ● Child 12-17 years: Loading dose 1 mg by IV injection followed by IV infusion of 10 mcg/kg/hour adjusted according to response; max 60 mcg/kg/hour		
7	Dexamethasone	Dexamethasone has a wide range of potential uses associated with its capacity to reduce inflammation. They include: ● Headache associated with	Headache associated with raised intracranial pressure **PO/ IV:** Child 1 month–12 years: 250 mcg/kg BD for 5 days; then reduce or stop. To relieve symptoms of brain or other tumour Numerous other indications in cancer management such as spinal cordand/or nerve compression, some causes of dyspnoea, bone pain, superior vena caval obstruction etc, only in discussion with specialist palliative medicine team.	Main concern in children: ● Problems of weight gain ● Cushingoid appearance Others:	1. Dexamethasone can be stopped abruptly if it has been given for less than two weeks, but otherwise should be weaned down over a number of weeks to allow recovery of the hypo-pituitary axis and avoid an Addisonian crisis.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		raised intracranial pressure caused by a tumour. ● Anti-inflammatory in brain and other tumours which cause pressure on nerves or bone or obstruction of hollow viscus. ● Analgesic role in nerve compression, spinal cord compression and bone pain. ● Antiemetic either as an adjuvant or in highly emetogenic cytotoxic therapies.	High doses < 16 mg/24 hrs may be advised. Antiemetic **PO/ IV:** ● Child < 1 year: Initial dose 250 mcg TDS, may increase up to 1mg TDS ● Child 1–5 years: Initial dose 1 mgTDS. may increase up to 2 mg TDS ● Child 6–11 years: Initial dose 2 mg TDS. may increase up to 4 mg TDS ● Child 12–17 years: 4 mg TDS	● Diabetes ● Osteoporosis ● Muscle wasting ● Peptic ulceration ● Behavioural problems and agitation ● Extreme exacerbation of and lability of mood (tearfulness, physical aggression)	2. Dexamethasone can be given in a single daily dose each morning for most indications. Whether in a single dose or two divided doses, giving the total daily dose of dexamethasone before midday reduces the likelihood of corticosteroid induced insomnia and agitation. 3. Dexamethasone 1 mg = 7 mg prednisolone (anti-inflammatory equivalence).
8	Diazepam#	● Short term anxiety relief ● Agitation ● Panic attacks ● Relief of muscle spasm ● Treatment of status epilepticus.	Short term anxiety relief, panic attacks and agitation **PO:** • Child 2–11 years: 0.5-2 mg TDS • Child 12–18 years: Initial dose of 2 mg TDS, may up to 10 mg TDS Relief of muscle spasm **PO:** • Child 1–11 months: Initial dose of 250 mcg/kg BD • Child 1–4 years: Initial dose of 2.5 mg BD • Child 5–11 years: Initial dose of 5 mg BD	● Dose-dependent drowsiness ● Impaired psychomotor and cognitive skills	1. Do not use in acute or severe respiratory insufficiency unless imminently dying. 2. Use with caution in mild-moderate hepatic disease and children with muscle weakness, respiratory depression or sleep apnoea. 3. Metabolised via the cytochrome P450 group of liver enzymes: – potential for interaction with any

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			• Child 12–17 years: Initial dose of 10 mg BD; max 40mg/day. Status epilepticus (IV/ PR Doses may repeated once after 10 minutes if necessary) **<u>IV injection over 3–5minutes:</u>** • Neonate: 300-400 mcg/kg as a single dose • Child 1 month–11 years: 300-400 mcg/kg (max 10 mg) as a single dose • Child 12–17 years: 10 mg as a single dose **<u>PR (rectal solution):</u>** • Neonate: 1.25–2.5 mg as a single dose • Child 1 month–1 year: 5 mg as a single dose • Child 2–11 years: 5–10 mg as a single dose • Child 12–17 years: 10-20 mg as a single dose		concurrent medicine that induces or inhibits this group of enzymes. 4. Enhancement of the central depressive effect may occur if diazepam is combined with drugs such as neuroleptics, antipsychotics, tranquillisers, antidepressants, hypnotics, analgesics, anaesthetics, barbiturates or sedative antihistamines.
9	Dihydrocodeine#*	Alternative to low dose morphine on WHO pain ladder, mild to moderate pain in patients known to be able to benefit. Step 2 pain (i.e. moderate and/or intermittent) that is opioid sensitive.	**<u>PO or deep SC/ IM injection:</u>** ● Child 1-3 years: 500 mcg/kg every 4-6 hours ● Child 4-11 years: Initial dose of 500 mcg/kg (max 30 mg/dose) every 4-6 hours. Dose may be increased if necessary to 1 mg/kg every 4-6 hours (max 30 mg/dose) ● Child 12-17 years: 30 mg (max 50 mg by IM/deep SC injection) every 4-6 hours. Oral doses up to 40-80 mg TDS can be given (max 240 mg/day). **<u>Modified release tablets</u>** used 12 hourly (use ½ of previous total daily dose for each modified release dose). ● Children 12-18 years: Doses up to 60-120 mg BD can be given.	• Drowsiness • Nausea • Vomiting • Constipation • Paralytic ileus • Abdominal pain • Paraesthesia	1. Potency around one fifth of oral morphine (OME 0.2). 2. Relatively constipating compared with morphine/diamorphine.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
10	Fentanyl*#	Step 2 WHO pain ladder (moderate to severe pain)	Normally convert using oral morphine equivalent (OME) from previous analgesia. Use the following starting doses in the opioid naive patient. The maximum dose stated applies to starting dose only. **By transdermal patch or continuous infusion:** Based on oral morphine dose equivalent (given as 24-hour totals). 72-hour Fentanyl patches are approximately equivalent to the following 24-hour doses of oral morphine: o morphine salt 30 mg daily = fentanyl '12' patch o morphine salt 60 mg daily = fentanyl '25' patch o morphine salt 120 mg daily = fentanyl '50' patch o morphine salt 180 mg daily = fentanyl '75' patch o morphine salt 240 mg daily = fentanyl '100' patch **By oromucosal application** (lozenge with oromucosal applicator) ● Child 2-18 years and greater than 10 kg: 15 mcg/kg as a single dose, titrated to a maximum dose 400 mcg (higher doses under specialist supervision). **By intranasal** (starting doses for opioid naïve patients and acute pain) ● Neonate - Child<2 years: 1 mcg/kg as a single dose ● Child 2-18 years: 1-2 mcg/kg as a single dose, with initial maximum single dose of 50 mcg **By continuous IV or SC infusion:** ● Neonate or infant: 0.15-0.5 mcg/kg/hour ● Child: 0.25-1 mcg/kg/hour	• Drowsiness • Dizziness • Nausea • Vomiting • Constipation	1. Consider reducing starting doses in obese children – to use ideal body weight rather than actual body weight. 2. 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. 3. For breakthrough pain, fentanyl effect is idiosyncratic: start at significantly lower doses than the equivalent for oral morphine. Always start at lower doses then titrate up. 4. The patch formulation is not usually suitable for the initiation or titration phases of opioid management in palliative care since the patches represent large dose increments and because of the time lag to achieve steady state. 5. Fentanyl patches take up to 17 hours to reach steady state. Commence fentanyl patch with last dose of slow release morphine.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			By IV/ SC injection (lower doses are required in non-ventilated neonates and opioid naïve patients) ● Neonate or infant: o Non-ventilated: 0.15-0.25 mcg/kg per dose slowly over 3-5 minutes; repeated 30-60 minutes o Ventilated: 0.25-0.5 mcg/kg per dose slowly over 3-5 minutes; repeated every 30-60 minutes ● Child over 1 year: 0.25–0.5 mcg/kg per dose, slowly over 3-5 minutes, repeated every 30-60 minutes		6. Fentanyl patches should be changed every 72 hours and the site of application rotated. In some children who are rapid metabolisers the patch may not last for 72 hours and the patches may need to be changed every 36-48 hours. 7. Conversion ratio is 1:1 for transdermal fentanyl to intravenous/ subcutaneous routes. 8. For rapidly escalating symptoms in the last few hours and days of life, continue transdermal fentanyl and give additional SC morphine PRN. If >2 PRN doses are required in 24 hours, give morphine by continuous subcutaneous infusion, while continuing transdermal fentanyl, starting with a dose equal to the sum of the PRN doses over the preceding 24 hours. If necessary, adjust the PRN dose considering the total opioid dose (i.e. transdermal fentanyl + continuous subcutaneous morphine)

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
11	Gabapentin*	● Adjuvant in neuropathic pain ● Neuroirritability ● Visceral hyperalgesia ● Third line management of abnormal tone and movement disorders in cerebral palsy ● Epilepsy	Epilepsy Consult BNFc or local neurology protocols Neuropathic pain **PO:** ●Neonate-Child 1 year: 5 mg/kg given as below ●Child 2 -11 years: 5-10 mg/kg given as below o Day 1 – give 5-10 mg/kg as a single dose (maximum single dose 300 mg), o Day 2 – give 5-10 mg/kg twice daily (maximum single dose 300 mg), o Day 3 onwards, give 5-10 mg/kg three times daily (maximum single dose 300 mg), o Increase further if necessary to a maximum of 20 mg/kg/dose (maximum single dose 600 mg). See notes for day 3 onward titration regimes. ●≥ 12 years: Initially 300 mg OD for day 1, then 300 mg BD for day 2, then 300 mg TDS for day 3, then increase in steps of 300 mg every 3-7 days given in 3 divided doses daily.The maximum daily dose can be increased according to response to a maximum of 3600 mg/day	• Somnolence • Dizziness • Ataxia • Viral infection • Fatigue • Fever	1. Speed of titration after first 3 days of initiation varies between: ●fast regime, increase every 3 days ●slow regime (for debilitated children or when taking other CNS depressants), to increase every one to two weeks. 2. Food does not affect gabapentin bioavailability. However co-administration with antacids containing aluminium and magnesium can reduce bioavailability by up to 24%. Manufacturers recommend giving gabapentin two hours after antacids. 3. Patients who use gabapentin and morphine concomitantly may experience increases in gabapentin concentrations. The dose of gabapentin or opioids should be reduced as clinically appropriate.
12	Glycopyrronium bromide	Control of upper airways secretion and hypersalivation.	**PO:** ● Child 1 month-17 years: Initial dose of 40 mcg/kg TDS/ QID, may be increased to 100 mcg/kg TDS/ QID. Max 2 mg/dose TDS/ QID.	● Drowsiness ● Blurred vision ● Constipation ● Intestinal pseudo-obstruction	Glycopyrronium 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.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			SC/ IV injection: ● Child 1 month-11 years: Initial dose of 4 mcg/kg TDS/ QID, may be increased to 10 mcg/kg TDS/ QID. Max 200 mcg/dose QID ● Child 12-17 years: 200 mcg every 4 hours when required **Continuous IV or SC infusion:** ● Child 1 month-11 years: Initial dose of 12 mcg/kg/24 hours, may be increased to 40 mcg/kg/24 hours (max 1.2 mg/24 hours) ● Child 12-17 years: Initial dose of 600 mcg/24 hours, may be increased to 1.2 mg/24 hours. Max 2.4 mg/ 24 hours.	● Heat prostration ● Diarrhoea ● Incomplete intestinal obstruction ● Urinary retention ● Bronchospasm ● Hypersensitivity reactions	
13	Haloperidol#	● Nausea and vomiting where the cause is metabolic, or in difficult to manage cases such as end stage renal failure. ● Restlessness and confusion / terminal agitation. ● Persistent severe aggression in autism or pervasive	Nausea and vomiting **PO:** ● Child 1 month–11 years: 10-20 mcg/dose BD/TDS, max 50-60 mcg/kg/dose BD/TDS ● Child 12–17 years: 1.5 mg ON, increased as necessary to 1.5 mg BD; max 5 mg BD. Restlessness and confusion **PO:** ● Child 1 month–17 years: 10–20 mcg/kg BD/TDS; maximum 5 mg BD Intractable hiccups **PO:** ●Child 1 month–11 years: Initial dose of 50 mcg/kg/24 hours (max initial dose: 3 mg/24 hrs) in divided doses. Dose may be increased to max 170 mcg/kg/24 hours in divided doses	●Behavioural problems	1. Haloperidol can cause potentially fatal prolongation of the QT interval and Torsades de Pointes, particularly if given IV (off-label route) or at higher than recommended doses. 2. Caution is required if any formulation of haloperidol is given to patients with an underlying predisposition e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT interval.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		developmental disorders. ● Intractable hiccups. ● Psychosis (including steroid induced), hallucinations.	● Child 12–17 years: 1.5 mg TDS **<u>Continuous IV or SC infusion (for any indication):</u>** ● Child 1 month–11 years: Initial dose of 25 mcg/kg/24 hours (max initial dose: 1.5 mg/24hrs). Dose may be increased to max 85 mcg/kg/24 hours ● Child 12–17 years: Initial dose of 1.5 mg/24 hours. Dose may be increased to max 5 mg/24 hours though higher doses may be used under specialist advice.		3. If IV haloperidol is essential, ECG monitoring during drug administration is recommended.
14	Hyoscine Butylbromide*	● Adjuvant for pain caused by spasm of the GI or genitourinary tract (smooth muscle spasm) ● 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	**<u>PO/ IM/ IV injection:</u>** ● Child 1 month-4 years: 300–500 mcg/kg (max 5 mg/dose) TDS/ QID ● Child 5-11 years: 5-10 mg TDS/ QID ● Child 12-17 years: 10–20 mg TDS/ QID **<u>CSCI:</u>** ● Child 1 month-4 years: 1.5 mg/kg/day (max 15 mg/day) ● Child 5-11 years: 30 mg/day ● Child 12-17 years: Up to 60-80 mg/day ● Higher doses may be needed; doses used in adults range from 20-120 mg/day (max 300 mg/day).	● Anticholinergic side-effects (e.g. dry mouth, urinary retention) ● Over-drying, which may cause overly thick mucus and mucus plugging	1. Does not cross the blood brain barrier (unlike hyoscine hydrobromide), hence no central antiemetic effect and doesn't cause drowsiness. 2. Increased risk of cardiac arrhythmia and anaphylaxis in patients with underlying cardiac disease. 3. Hyoscine butylbromide injection is contraindicated in patients with tachycardia and should be used with caution in patients with cardiac disease. 4. Likely to exacerbate acid reflux.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		effective if started early)			
15	Lactulose	●Constipation, faecal incontinence related to constipation. ●Hepatic encephalopathy (portal systemic encephalopathy) and coma.	Constipation **PO:** Initial dose BD, then adjusted to suit patient • Neonate: 2.5 mL/dose BD • Child 1 month-11 months: 2.5 mL/dose OD-TDS • Child 1-4 years: 5 mL/dose OD-TDS • Child 5-9 years: 10 mL/dose OD-TDS • Child 10-17 years: 15 mL/dose OD-TDS Hepatic encephalopathy **PO:** Child 12-17 years: use 30-50mL TDS as initial dose. Adjust dose to produce 2-3 soft stools/ day.	●Electrolyte imbalance, abdominal cramps, nausea & vomiting, flatulence, with colic especially at high doses ●Hyperphosphatemia & Hypokalemia	1. Increases colonic bacterial flora (macrogols do not). 2. Precautions and contraindications; Galactosaemia, intestinal obstruction. Caution in lactose intolerance. 3. Use is limited as macrogols are often better in palliative care. However, the volume per dose of macrogols is 5-10 times greater than lactulose and may not be tolerated in some patients. 4. Lactulose is less effective than macrogols or sodium picosulfate for opioid induced constipation in ambulatory palliative care patients.
16	Levetiracetam*	Epileptic seizures	Background seizure management **PO:** ● Child 1-5 months: Initially 7 mg/kg OD, then increase in steps of up to 7 mg/kg BD (max 21 mg/kg BD). Dose to be increased every 2 weeks ● Child 6 months–17 years (body weight < 50 kg): Initially 10 mg/kg OD, then increase in steps of up to 10 mg/kg BD (max 30 mg/kg BD). Dose to be increased every 2 weeks	• Anxiety • Aggressivity • Somnolence • Asthenia • Dizziness	Benefits of levetiracetam over phenobarbitone or phenytoin for breakthrough seizure management include fewer side effects and lower volume enteral dose availability.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			● 18 years and over or body weight ≥ 50 kg: 250 mg BD then increase in steps of 500 mg BD (max 1.5 g BD). Dose to be increased every 2-4 weeks **<u>IV:</u>** ● Body weight < 50kg: 10 mg/kg OD then increase in steps of up to 10mg/kg BD (max 30mg/kg BD). Dose to be increased every 2 weeks ● Body weight ≥ 50 kg: 250 mg BD then increases in steps of 500 mg BD (max 1.5 g BD). Dose to be increased every 2-4 weeks **<u>Continuous IV or SC infusion:</u>** ● Dose conversion for PO:IV:SC is 1:1:1 ● Take total daily PO or IV dose and give as SC or IV infusion over 24hours Management of breakthrough seizures ● Can be used for breakthrough seizure management in prolonged seizures, usually after other first line medications have been tried (e.g. midazolam, paraldehyde). ● No need to measure levels **<u>By enteral, SC or IV</u>** ● Neonate: 10-20 mg/kg, then top up after 2-12 hours if required, with 10–20mg/kg, aiming not to give more than 40mg/kg/day (including any routine dose in this calculation) ● Child over 1 month: 20 mg/kg then top up after 2-12 hours if required, with 10–20mg/kg, aiming not to give more than		

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			60 mg/kg/day (including any routine dose in this calculation)		
17	Levomepromazine #	● Broad spectrum antiemetic where the cause is unclear, or where probably multifactorial. ● Second line if a specific antiemetic fails. ● Antipsychotic and anxiolytic ● Sedation for terminal agitation	Antiemetic **PO:** ● Child 2–11 years: Initial dose 50-100 mcg/kg OD/BD. Dose may be increased as necessary. Not to exceed 1mg/kg/dose (or max 25 mg/dose) OD/ BD. ● Child 12-17 years: Initial dose 3 mg OD/BD. Dose may be increased as necessary. Max dose 25 mg OD/BD. **Continuous IV or SC infusion over 24hours:** ● Child 1 month–11 years: Initial dose of 100mcg/kg/day increasing as necessary to max 400mcg/kg/day. Max 25mg/day ● Child 12–17 years: Initial dose of 5 mg/day increasing as necessary to max 25 mg/day **SC/ IV Injection** ● Child 12–17 years: Initial dose 2.5 mg OD/BD Sedation and confusion **Continuous IV or SC infusion over 24hours:** ● Child 1–11 years: Initial dose of 350 mcg/kg/day (max initial dose 12.5 mg), increasing as necessary up to 3 mg/kg/day ● Child 12–17 years: Initial dose of 12.5mg/day increasing as necessary up to 200 mg/day **SC/ IV Injection:** Child 12–17 years: Initial dose according to body weight <35 kg: 2.5 mg OD/BD >35 kg: 5mg OD/BD	• Somnolence • Asthenia High dose: hypotension	1. If the child is not stable on high dosage for nausea and vomiting, reconsider cause and combine with other agents e.g. dexamethasone. 2. Levomepromazine and its non-hydroxylated metabolites are reported to be potent inhibitors of cytochrome P450 2D6. Co-administration of levomepromazine and drugs primarily metabolised by the cytochrome P450 2D6 enzyme system may result in increased plasma concentrations of these drugs. 3. May lower seizure threshold. 4. Avoid, or use with caution, in patients with liver dysfunction or cardiac disease. Start at low dose in patients with severe renal impairment and give once daily, titrating according to response.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
18	Lorazepam#*	●Background anxiety. ●Agitation and distress. ●Adjuvant in cerebral irritation. ●Background management of dyspnoea. ●Muscle spasm. ●Status epilepticus	**PO:** • Child < 2 years: 25 mcg/kg BD/TDS • Child 2–5 years: 0.5mg BD/TDS • Child 6–10 years: 0.75 mg TDS • Child 11–14 years: 1 mg TDS • Child 15–18 years: 1–2 mg TDS **SL:** ● Children of all ages: 25 mcg/kg as a single dose. Increase to 50 mcg/kg (max 1 mg/dose) if necessary. Status epilepticus **Slow IV injection:** ● Neonate: 100 mcg/kg for a single dose then 100 mcg/kg after 10 minutes if required ● Child 1 month–11 years: As above with a maximum single dose of 4mg ● Child 12-17years: 4 mg for a single dose then a further 4 mg after 10 minutes if required	High dose: ● Drowsiness ● Respiratory depression	Potency in the order of 10 times that of diazepam per mg as anxiolytic/sedative.
19	Macrogol	●Constipation. ●Faecal impaction. ●Suitable for opioid-induced constipation	Constipation/ Prevention of faecal impaction: **PO:** ●Child under 1 year: ½-1 paediatric sachet daily ●Child 1–5 years: 1 paediatric sachet daily (adjust dose according to response; max 4 sachets daily) ●Child 6–11 years: 2 paediatric sachets daily (adjust dose according to response; max 4 sachets daily) ●Child 12–17 years: 1–3 adult sachets daily. Faecal impaction: **PO:** ● Child under 1 year: ½-1 paediatric sachet daily	● Electrolyte imbalance, abdominal cramps, nausea & vomiting, flatulence, with colic especially at high doses ● Hyperphosphatemia & Hypokalemia	1. Need to maintain hydration. Caution if fluid or electrolyte disturbance. 2. Caution with high doses (volumes) in those with impaired gag reflex, reflux oesophagitis or impaired consciousness.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			● Child 1–4 years: 2 paediatric sachets on first day and increase by 2 sachets every 2 days (max 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 (max 12 sachets daily). Treat until impaction resolved then switch to maintenance laxative therapy. ● Child 12–17 years: 4 sachets daily of adult preparation, then increase by 2 sachets daily (max 8 adult sachets daily). Total daily dose should be drunk within a 6-hour period. After disimpaction switch to maintenance laxative therapy.		
20	Metoclopramide# *	To minimise the risk of neurological side effects associated with metoclopramide, the EMA in 2013 issued the following recommendations: (NB use of metoclopramide in palliative care was excluded from these recommendations HOWEVER caution should be exercised nevertheless).	Metoclopramide should only be prescribed for short term use (up to 5 days). **<u>PO, IM, SC or IV (over ≥ 3 mins):</u>** ●Neonate: 100 mcg/kg every 6–8hours (PO/ IV only). ●Child 1 month–11 months and body weight up to 10 kg: 100 mcg/kg (max 1 mg/dose) BD ●Child 1–18 years: 100-150 mcg/kg up to TDS. Max 500 mcg/kg/day (max 10 mg/dose; 30 mg/day). If preferred the appropriate total daily dose may be administered as a continuous SC or IV infusion over 24 hours	● Gastrointestinal side effects ● Headache ● Somnolence ● Tardive dyskinesia	1. Metoclopramide can induce acute dystonic reactions such as facial and skeletal muscle spasms and oculogyric crises; children (especially girls, young women, and those under 10 kg) are particularly susceptible. With metoclopramide, dystonic effects usually occur shortly after starting treatment and subside within 24 hours after stopping it. 2. Use of metoclopramide is contraindicated in children younger than 1 year. In children aged 1-18 years, metoclopramide should only be used as a second-line option for prevention

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		Use ● Antiemetic if vomiting caused by gastric compression or hepatic disease. ● Prokinetic for slow transit time (not in complete obstruction or with anticholinergics). ● Hiccups			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.
21	Midazolam#	● Status epilepticus and terminal seizure control ● Management of anxiety/agitation associated with symptoms at the end of life ● Anxiety associated with dyspnoea ● Adjuvant for pain of cerebral irritation	Drug doses are quite different depending on underlying disease (i.e. children with cancer or organ failure) and children with severe neurological impairment (SNI). Use lower doses for children with cancer or organ failure and higher doses for children with SNI. Seizure control at end of life **By SC or IV infusion over 24 hours** ● Neonate - Child 18 years: Initial dose 1-3 mg/kg/24 hours increasing up to 7 mg/kg/24 hours (max 60 mg/24 hours or 150 mg/24 hours in specialist units for patients with refractory epilepsy). Seek specialist advice, and consider addition of other agents such as phenobarbital if midazolam is not effective.	● Drowsiness ● Falls ● Memory and cognitive impairment ● Paradoxical arousal ● Agitation ● Aggression	1. Onset of action by buccal and intranasal route 5-15 minutes. Time to peak concentration is 30 mins. Half-life 2-5 hours. For buccal administration, if possible, divide the dose so half is given into one cheek and the remaining half into the other cheek. 2. Both high and low doses can lead to paradoxical agitation. 3. Caution in known hypersensitivity; renal failure; hepatic or cardiac impairment; neuromuscular respiratory weakness; pulmonary insufficiency.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			Status epilepticus **<u>Buccal or Intranasal</u>** ● Neonate: 300 mcg/kg as a single dose, repeated once if necessary. ● Child 1–2 months: 300 mcg/kg (max initial dose 2.5mg), repeated once if necessary. ● Child 3 months–11 months: 2.5mg, repeated once if necessary. ● Child 1–4 years: 5mg, repeated once if necessary. ● Child 5–9 years: 7.5mg, repeated once if necessary. ● Child 10–17 years: 10mg, repeated once if necessary. By buccal or intranasal administration for status epilepticus, wait 10 minutes before repeating the dose. NB -In single dose for seizures, midazolam is twice as potent as rectal diazepam. For patients who usually receive rectal diazepam for management of status epilepticus, consider an initial dose of buccal midazolam that is 50% of their usual rectal diazepam dose to minimise the risk of respiratory depression. Conscious sedation (to be administered 30-60 minutes before a procedure; or to be administered for terminal haemorrhage in conjunction with an opiate): **<u>PO:</u>** ● Child: 500 mcg/kg (max 20 mg) as a single dose **<u>By buccal or intranasal administration</u>** ● Child 6 months-9 years: 200-300 mcg/kg (max 5 mg) as a single dose ● Child 10-17 years: 6-7 mg as a single dose		4. Important drug interactions: Midazolam is a major substrate of CYP3A4. Please refer to current edition of BNF for significant drug interactions. Fatalities have occurred after concurrent administration with higher than approved doses of olanzapine.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			PR: ● Child 6 months–11 years: 300–500 mcg/kg (max 20 mg) as a single dose **IV/ SC injection:** The dosages below are based on the BNF. However research evidence and adult formularies suggests that buccal/intranasal and subcutaneous injections have very similar bioavailability. Many units therefore will use doses of 100 mcg/kg. ● Child 1 month–5 years: Initially 25–50 mcg/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 6 mg per course. ● Child 6–11 years: Initially 25–50 mcg/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 7.5 mg per course. ● Child 12–17 years: Initially 25–50 mcg/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 10 mg per course. Anxiety/ agitation/ dyspnoea Use 25-50% of the conscious sedation dose		

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
22	Morphine#*	● Major opioid ● First line opioid for pain ● Dyspnoea ● Cough suppressant	Opioid naive patient: Use the following starting doses. (The maximum dose stated applies to starting dose only). Opioid conversion: Convert using OME (Oral Morphine Equivalent) from the previous opioid. **PO/ PR:** ●Neonate: Initially 25-50 mcg/kg every 6-8 hours adjusted to response ●Child 1–2 months: Initially 50 mcg/kg every 4 hours, adjusted according to response ●Child 3–5 months: Initially 50-100 mcg/kg every 4 hours, adjusted according to response ●Child 6–11 months: Initially 100-200 mcg/kg every 4 hours, adjusted according to response ●Child 1–11 years: Initially 200–300 mcg/kg (initial maximum 5-10 mg) every 4 hours, adjusted according to response ●Child 12–17 years: Initially 5–10 mg every 4 hours, adjusted according to response **SC/ IV injection (over ≥ 5 minutes):** ● Neonate: Initially 25 mcg/kg every 6-8 hours adjusted according to response. ● Child 1-5 months: Initially 50-100 mcg/kg every 6 hours adjusted according to response. ● Child 6 months-1 year: Initially 50-100 mcg/kg every 4 hours adjusted according to response. ● Child 2-11 years: Initially 100 mcg/kg every 4 hours adjusted according to response, maximum initial dose of 2.5 mg.	• Urinary retention • Pruritus • Constipation • Nausea • Vomiting	1. Where opioid substitution or rotation is to morphine: use oral morphine equivalency (OME). 2. Morphine toxicity often presents as myoclonic twitching. 3. Rectal route should be avoided if possible, and usually contraindicated in children with low platelets and/or neutropenia.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			● Child 12-17 years: Initially 2.5-5 mg every 4 hours adjusted according to response (maximum initial dose of 20 mg/day). **<u>Continuous IV or SC infusion:</u>** ● Neonate: 120 mcg/kg/day adjusted according to response ● Child 1-2 months: 240 mcg/kg/day adjusted according to response ● Child 3 months–17 years: 480 mcg/kg/day (maximum initial dose of 20 mg/day) adjusted according to response. Breakthrough pain ● For breakthrough pain use 10-16% of total daily morphine dose every 1-4 hours as needed. ● Contact the medical palliative team if someone has needed three doses consecutively as they will need a review of their pain control. Dyspnoea 30-50% of the dose used for pain.		
23	Octreotide#*	●Bleeding from oesophageal or gastric varices. ●Nausea and vomiting. ●Intestinal obstruction. ●Intractable diarrhoea. ●Hormone secreting tumours,	**<u>SC Injection</u>** ● Neonate: Initially 2–5 mcg/kg every 6–8 hours, adjusted according to response; increased if necessary up to 7 mcg/kg every 4 hours, dosing up to 7 mcg/kg may rarely be required. ● Child 1 month-17 years: Initially 1–2 mcg/kg every 4–6 hours, adjusted according to response; increased if necessary up to 7 mcg/kg every 4 hours, dosing up to 7 mcg/kg may rarely be required.	●Sinus bradycardia ●Hyperglycaemia ●Abdominal distress	Avoid abrupt withdrawal (associated with biliary colic and pancreatitis).

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		ascites, bronchorrhea	**<u>Continuous IV or SC infusion:</u>** ● Child 1 month-17 years: 1 mcg/kg/hour. Higher doses may be required initially. When there is no active bleeding, reduce the dose over 24 hours. Usual maximum dose is 50 mcg/hour		
24	Olanzapine#*	● Psychoses; delirium; agitation; anorexia when all other treatments have failed. ● Nausea and vomiting	Psychoses/mania **<u>PO:</u>** ● Child <12 years and <25 kg: Initial dose 2.5 mg ON ● Child <12 years and >25 kg: Initial dose 2.5-5 mg ON ● Child 12-17 years: Initial dose 5 mg at bedtime. Increase gradually as necessary and as tolerated to a maximum of 20mg/day given usually as ON. Can be given BD if needed. Agitation/delirium **<u>PO:</u>** ● Child <12 years: Initial dose 1.25 mg ON and PRN ● Child 12-17 years: Initial dose 2.5 mg ON and PRN Increase gradually as necessary and as tolerated to max 10mg/day. Nausea and vomiting/ Anorexia **<u>PO:</u>** ● Child <12 years: Initial dose 1.25 mg (or 0.625 mg if 2.5 mg tablets can be cut into quarters) ON and PRN ● Child 12-17 years: Initial dose 1.25-2.5 mg ON and PRN	● Weight gain ● Elevated triglyceride levels ● Increased appetite ● Sedation ● Increased ALT and AST levels ● Decreased bilirubin ● Increased GGT and plasma prolactin levels ● Elevated cholesterol levels ● Dry mouth	1. Use with caution in those with cardiovascular disease or epilepsy (and conditions predisposing to seizures as lowers seizure threshold). 2. Dose titration should be slow to minimise sedation. 3. A greater magnitude of weight gain and lipid and prolactin alterations have been reported in adolescents compared to adults. If prolonged use is likely, consider the monitoring of blood lipids, weight, fasting blood glucose and prolactin. Consider an ECG and BP measurement before initiation. 4. Consider lower starting dose (maximum 5mg in adults) in patients with renal and/or hepatic impairment. 5. Olanzapine does not inhibit or induce the main CYP450 isoenzymes. Olanzapine is metabolised by CYP1A2 therefore

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			Dose may be increased as necessary and as tolerated to a suggested maximum of 7.5 mg/day.		drugs/substances that specifically induce or inhibit this isoenzyme may affect the pharmacokinetics of olanzapine e.g. carbamazepine, fluvoxamine, nicotine.
25	Oxycodone#*	● Alternative opioid for severe pain ● Pain of all types unless opioid insensitive	Opioid switch: Convert using OME (Oral Morphine Equivalent) from the previous opioid. Use the following starting doses in the opioid naive patient. The maximum dose stated applies to the starting dose only. Conversion • Oral Morphine 1.5: Oral Oxycodone 1 • i.e. 15 mg Morphine: 10 mg Oxycodone **PO:** ●Child 1 month–11 years: Initial dose 200 mcg/kg (max single dose 5 mg) every 4 -6 hours. ●Child 12-17 years: Initial dose 5 mg every 4-6 hours. Titrate as for morphine: Increase dose if necessary according to severity of pain. **M/R tablets** ● Child 8-11 years: Initial dose 5 mg every 12 hours, increased if necessary ● Child 12-17 years: Initial dose 10 mg every 12 hours, increased if necessary.	• Drowsiness • Dizziness • Nausea • Vomiting • Constipation	1. Associated with dose dependent QTc prolongation. 2. It is important to prescribe breakthrough analgesia which is 5-10% of the total 24-hour dose, given every 1 to 4 hours.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			By IV injection, SC injection or CSCI: Conversion: ● Oral to IV or SC Oxycodone single bolus dose injection: Divide the oral Oxycodone dose by 1.5(some texts suggest divide by 2 but clinically 1.5 used). ● Oral to a continuous subcutaneous infusion of Oxycodone over 24 hours: Divide the total daily dose of oral Oxycodone by 1.5 (some texts suggest divide by 2 but clinically 1.5 used). ● SC/IV Morphine to SC/IV Oxycodone ratio is approximately 1:1. i.e. use the same dose. ● The reason behind the odd conversion ratio is bioavailability and rounding factors for safety.		
26	Pamidronate	● Adjuvant for bone pain caused by metastatic disease. ● Adjuvant for bone pain due to osteopenia or osteoporosis associated with neuromuscular conditions. ● Tumour-induced hypercalcaemia. ● Treatment of secondary	For bone pain (metastatic bone disease or osteopenia); secondary osteoporosis: An effect on pain can be seen within 2 weeks, but may need a year before definitive assessment. Continue dosing for as long as effective and tolerated or until substantial decline in performance status. **IV infusion** ● 1 mg/kg as a single dose infused over 4-6 hours repeated monthly as required; concentration not exceeding 90 mg in 250 mL. **OR** ● 1 mg/kg infused over 4-6 hours on 3 consecutive days and repeated every 3 months as required; concentration not exceeding 90 mg in 250 mL.	● Transient pyrexia ● Flu-like symptoms ● Fatigue ● Nausea	1. Caution: monitor renal function and electrolytes; ensure adequate hydration. 2. Prolonged hypocalcaemia and hypomagnesaemia may occur with concurrent use of aminoglycoside and a bisphosphonate. 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)

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		osteoporosis to reduce fracture risk. ● Osteogenesis imperfecta	Malignant hypercalcaemia: (Seek specialist advice) **IV infusion** ● 1 mg/kg infused over 6 hours; concentration not exceeding 90 mg in 250 mL. Then repeated as indicated by corrected serum calcium. Osteogenesis imperfecta **IV infusion** In total all patients receive 12 mg/kg over the course of 1 year as: ● 1 day regimen: 1 mg/kg/day on a single day repeated monthly ● 2 day regimen: 1.5 mg/kg/day on 2 consecutive days, repeated every 3 months ● 3 day regimen: 1mg /kg/day on 3 consecutive days, repeated every 3 months ● Usual maximum 90 mg/dose (although occasionally higher doses are seen) ● If there is any concern about the starting dose, 0.5 mg/kg may be considered as the first dose for the first cycle		3. Risk of renal impairment is increased by concurrent use with other nephrotoxic drugs. 4. Risk in adults of atypical femoral fractures, and of osteonecrosis especially of the jaw and the external auditory canal. Not widely reported in children but suggest dental treatment before treatment and good dental hygiene advised. Patient/ family education.
27	Paracetamol#*	● Mild to moderate pain (step 1 of WHO pain ladder). ● Pyrexia	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 75-150 mg/kg/day (ingestion of over 150 mg/kg/day is regarded as a definite risk of toxicity). **PO:** ● Neonate 28–32 weeks corrected gestational age: 20 mg/kg as a single dose then 10-15 mg/kg every 8 - 12 hours as necessary (maximum 30 mg/kg/day in divided doses).	Rare	1. Many children and young people with life limiting illness have low weight for their age. The doses above are therefore quoted mainly by weight rather than age (unlike most of the entries in the BNF and BNFc), in order to minimise risk of over-dosing in this patient group.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			• Neonates over 32 weeks corrected gestational age: 20 mg/kg as a single dose then 10-15 mg/kg every 6 - 8 hours as necessary (maximum 60 mg/kg/day in divided doses). • Child 1 month–5 years: 20-30 mg/kg as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 75 mg/kg/day in divided doses). • Child 6-11 years: 20-30 mg/kg (max 1 g) as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 75 mg/kg/day or 4 g/day in divided doses). • Over 12 years: 15-20 mg/kg (maximum 500 mg -1 g) every 4-6 hours as necessary (maximum 4 g /day in divided doses). **PR:** • Neonate 28–32 weeks corrected gestational age: 20 mg/kg as a single dose then 10-15 mg/kg every 12 hours as necessary (maximum 30 mg/kg/day in divided doses). • Neonates over 32 weeks corrected gestational age: 30 mg/kg as a single dose then 15-20 mg/kg every 8 hours as necessary (maximum 60 mg/kg/day in divided doses). • Child 1–2 months: 30 mg/kg as a single dose, then 15-20 mg/kg every 4-6 hours as necessary (maximum 75 mg/kg/day in divided doses). • Child 3 months-11years: 30 mg/kg as a single dose (maximum 1 g) then 15-20 mg/kg every 4-6 hours as necessary (maximum75 mg/kg/day or 4 g/day in divided doses). • Over 12 years: 15-20 mg/kg (maximum 500 mg -1 g) every 4-6 hours as necessary (maximum 4 g/day in divided doses).		2. Hepatotoxic in overdose or prolonged high doses.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			IV: (as infusion over 15 minutes) ● Preterm neonates over 32 weeks corrected gestational age: 7.5 mg/kg every 8 hours, maximum 25 mg/kg/day. ● Neonate: 10 mg/kg every 4-6 hours (maximum 30 mg/kg/day). ● Infant and child bodyweight <10 kg: 10 mg/kg every 4-6 hours (maximum 30 mg/kg/day) ● Child body weight 10-50 kg: 15 mg/kg every 4-6 hours (maximum 60mg/kg/day). ● Child body weight > 50 kg: 1 g every 4-6 hours (maximum 4 g/day)		
28	Phenobarbital	● Adjuvant in pain of cerebral irritation. ● Control of terminal seizures. ● Sedation (soporific and anxiolytic). ● Epilepsy including status epilepticus. Commonly used first line for seizures in neonates (phenytoin or benzodiazepine are the main alternatives). ● Agitation refractory to	Status epilepticus / terminal seizures / agitation Loading doses are not usually necessary unless it is for rapid control of terminal seizures in someone not already on anticonvulsants. This is because in paediatric palliative care it is not often used for emergency seizure control, but for cerebral irritation. Where it is for seizures, it is normally used for prophylaxis or adding it to other anticonvulsants. In those cases, there is usually no hurry to get to an effective serum concentration. Loading dose if required **PO, IV or SC injection:** All ages: 20 mg/kg/dose (max 1 g) administered over 20 mins if by IV or SC injection. **SC or IV injection or infusion:** ● Neonates for control of ongoing seizures: 2.5-5 mg/kg OD/BD as maintenance.	● CNS side effects (Confusion, worsening of depression, hallucinations) ● Respiratory depression ● Somnolence ● Rash	1. 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. 2. Phenobarbital induces various enzymes of the CYP450 system and thus may reduce the plasma concentrations of concomitant drugs that are metabolised by this system. 3. Consider vitamin D supplementation in patients who are immobilised for long periods or who have inadequate sun exposure or dietary intake of calcium.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
		midazolam in end of life care	● Child 1 month-11 years: 2.5-5 mg/kg (max single dose 300 mg) OD/BD or may be given as a continuous infusion over 24 hours. ● Child 12-17 years: 300 mg BD or may be given as a continuous infusion over 24 hours. Epilepsy: **PO:** ● Neonates for control of ongoing seizures: 2.5-5 mg/kg OD/BD as maintenance. ● Child 1 month–11 years: 1–1.5 mg/kg BD, increased by 2 mg/kg daily as required (usual maintenance dose 2.5–4 mg/kg OD/BD). ● Child 12–17 years: 60–180 mg OD		
29	Phenytoin	●Epilepsy (3rd or 4th line oral antiepileptic) including for status epilepticus ●Neuropathic pain (effective, at least short term, but not used first line)	All forms of epilepsy (including tonic-clonic, focal and neonatal seizures) except absence seizures. Neuropathic pain. **Oral or slow IV injection:** ● Neonate: Initial loading dose by slow IV injection 18 mg/kg THEN by mouth 2.5-5 mg/kg BD adjusted according to response and plasma phenytoin levels. Usual maximum 7.5 mg/kg BD. ● 1 month -11 years: Initial dose of 1.5-2.5 mg/kg twice daily then adjust according to response and plasma phenytoin levels to 2.5-5 mg/kg BD as a usual target maintenance dose. Usual maximum dose of 7.5 mg/kg BD or 300 mg daily. ● 12 -17 years: initial dose of 75-150 mg BD then adjusted according to response and plasma phenytoin levels to	● CNS (ataxia) ● Liver ● GI ● Dermatologic ● Hirsutism ● Anaemia ● Osteoporosis	1. Phenytoin has numerous interactions with other drugs due to hepatic enzyme induction. Long term use is associated with significant side effects. It is no more effective than other anti-epileptics and hence not usually used in the first line, although it does enable rapid titration. 2. Continuous ECG and BP monitoring required during IV administration. 3. Reduce dose in hepatic impairment. Monitor carefully if

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			150-200 mg BD as a usual target maintenance dose. Usual maximum dose of 300 mg BD. Status epilepticus, acute symptomatic seizures: **<u>Slow IV injection or infusion:</u>** ● Neonate: 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg/dose (over 30 minutes) every 12 hours as a usual maintenance dose in the first week of life. Adjust according to response and older babies may need the higher doses. After the first dose, PO doses are usually as effective as IV in babies over 2 weeks old. ● 1 month – 11 years: 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg BD as usual maintenance dose. ● 12 -17 years: 20 mg/kg loading dose over at least 20 minutes, then up to 100 mg (over 30 minutes) TDS/QID as usual maintenance dose.		reduced albumin or protein binding e.g. in renal failure. 4. Caution: cross-sensitivity is reported with carbamazepine. 5. Avoid abrupt withdrawal. 6. Consider vitamin D supplementation in patients who are immobilised for long periods or who have inadequate sun exposure or dietary intake of calcium.
30	Pregabalin*	● Epilepsy (focal seizures with or without secondary generalisation) ● Peripheral and central neuropathic pain ● Generalised anxiety disorder	Epilepsy (adjunctive therapy for partial seizures) ● Child: suggested maintenance dose of 5-10 mg/kg/day. Start at low dose and increase gradually every 3-7 days as tolerated. Maximum 600 mg/day given in 2-3 divided doses. Younger children less than 6 years old may need up to 15 mg/kg/day. Neuropathic Pain ● Child: o Day 1-3: 1 mg/kg OD o Day 4-6: 1 mg/kg BD o Day 7: Increase every 3-7 days by 1 mg/kg until ▪ Effective analgesia reached, or ▪ Side effects experienced, or	• Dizziness • Somnolence • Headache Note: Side effects are transient and mild to moderate in nature. May be minimised by a gradual increase to therapeutic dose.	1. Risk of pregabalin abuse and dependence. 2. Be aware of potential serious risks of interaction between pregabalin and other medicines that can cause CNS depression, particularly opioids. 3. Pregabalin has a binding affinity 6x greater than that of gabapentin.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			▪ Max total daily dose of 6mg/kg/day (although higher doses of 12 mg/kg have been used).		
31	Ranitidine	● Gastro-oesophageal reflux oesophagitis, dyspepsia. ● Treatment of gastritis, benign gastric and duodenal ulcers. ● Gastro-protection (e.g. with combination NSAID/ steroids or anticipating stress ulceration). ● Other conditions requiring reduction in gastric acid.	**PO:** ● Neonate: 2 mg/kg TDS, increasing if necessary to maximum 3 mg/kg TDS (absorption unreliable). ● Child 1–5 months: 1 mg/kg TDS increasing if necessary to maximum 3mg/kg TDS ● Child 6 months–2 years: 2–4 mg/kg BD ● Child 3–11 years: 2–4 mg/kg (maximum single dose 150 mg) BD. Dose may be increased up to 5 mg/kg (maximum 300 mg/dose) BD in severe gastro-oesophageal reflux disease, ● Child 12–18 years: 150 mg BD or 300 mg ON. May be increased if necessary in moderate to severe gastro-oesophageal reflux disease to 300 mg BD or 150 mg QID for up to 12 weeks. By **slow IV injection**, diluted to 2.5 mg/ml and given over at least minutes [some adult centres give as SC injection (unlicensed route)]: ● Neonate: 0.5–1 mg/kg every 6–8 hours (may need 2 mg/kg TDS as variable first pass metabolism affects uptake). ● Child 1 month–17 years: 1 mg/kg (max. 50 mg) TDS/ QID (may be given as an intermittent infusion at a rate of 25 mg/hour).	●Elevated ALT levels (particularly with high doses or prolonged IV use) ●Reduced absorption of Vitamin B12 (prolonged use) ●Increased risk of community-acquired pneumonia	1. Ranitidine may increase plasma concentration of midazolam. 2. May cause rebound hyperacidity at night.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
32	Tramadol	Minor opioid with additional non-opioid analgesic actions.	**PO:** ● Child 5-11 years: 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum of 4 doses in 24 hours). Increase if necessary to a maximum dose of 2 mg/kg (maximum single dose 100 mg) every 6 hours, ● Child 12–17 years: Initial dose of 50 mg every 4–6hours. Increase if necessary to a maximum of 400 mg/day given in divided doses every 4-6 hours. **IM or IV injection or infusion:** ● Child 5-11 years: 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum 4 doses in 24 hours). Increase if necessary to a maximum dose of 2 mg/kg (maximum single dose 100 mg) every 6 hours, ● Child 12-17 years: Initial dose of 50 mg every 4-6 hours. Dose may be increased if necessary to 100 mg every 4-6 hours. Maximum 600 mg/day in divided doses	• Diarrhoea • Retching • Fatigue • Paraesthesia	1. By mouth tramadol is about 1/10 as potent as morphine. 2. Causes less constipation and respiratory depression than the equivalent morphine dose. 3. Analgesic effect is reduced by ondansetron.
33	Tranexemic acid*	● Oozing of blood (e.g. from mucous membranes / capillaries), particularly when due to low or dysfunctional platelets. ● Menorrhagia	Inhibition of fibrinolysis **PO:** • Child 1 month–17 years: 15–25 mg/kg (maximum 1.5 g) BD/TDS Menorrhagia **PO:** ● Child 12-17 years: 1 g 3 times daily for up to 4 days. If very heavy bleeding a maximum daily dose of 4 g (in divided doses) may be used. Treatment should not be initiated until menstruation has started. Inhibition of fibrinolysis **IV injection over at least 10 minutes:**	● Visual defects ● Retinal venous and arterial occlusions ● Ligneous conjunctivitis ● Convulsions ● Severe hypersensitivity reactions ● Venous and arterial thrombosis or	1. Can cause clot ‘colic’ if used in presence of haematuria.

Bil	Medication Name	Indication	Paediatric Dosing	Side Effects	Remarks
			• Child 1 month -17 years: 10 mg/kg (maximum 1 g) BD/TDS. **Continuous intravenous infusion:** •Child 1 month-17 years: 45 mg/kg over 24 hours. **Other routes** **Mouthwash 5% solution:** • Child 6-17 years: 5-10 mL 4 times a day for 2 days. Not to be swallowed. **Topical treatment:** • Apply gauze soaked in 100mg/mL injection solution to the affected area.	thromboembolism • Cerebral oedema and infarction • Dizziness	

Note:
#Consider dose reduction in hepatic impairment.
*Consider dose reduction in renal impairment.

References:
The Association for Paediatric Palliative Medicine Formulary 6th Edition (2024)

Appendix 2

Suggested Dose Conversion Ratio in The Direction Specified

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

MULTIPLY DIVIDE

Source: Ministry of Health, Malaysia. CPG Management of Cancer Pain (Second Edition). Putrajaya: MoH; 2023.

Appendix 3

Example of Checklist for Terminal Discharge

PHARMACIST OR DOCTOR		
No	**Checklist for Terminal Discharge**	**Tick if done**
1.	**Check Medication Prescription** • Verify the prescription with clinical notes provided in the discharge summary • Identify patient details, including name, NRIC Number and MRN Number • Double-check medication details: Medication name, dose, frequency, quantity and expiry date	
2.	**Medication counselling for family and/ or caregiver** • Explain regarding medication prescribed by the doctor • Medication name, dose, frequency, quantity prescribed (syringes) and expiry date • Potential side effects and managements	
3.	**Refill of Medication** • Follow up either by hospice or domiciliary or primary team or palliative care doctor • During office hours, only authorised medication collectors may collect refill medications in the hospital by appointment after discussing with the doctor.	
4.	**Return of Medication** • Return all used syringes and unused medications to the ward, the hospice in charge or any healthcare facilities under the Ministry of Health Malaysia.	

Appendix 4A

Example of Terminal Discharge Medication Information Sheet (EN)

Medication for Terminal Discharge

1. Morphine
- For pain, shortness of breath or cough - Expect to see effect after 15 minutes - Can repeat every 1 (One) hour if symptoms persist
2. Midazolam
- For anxiety, shortness of breath or seizures - Expect to see effect after 5-10 minutes through subcutaneous (SC) route - Can repeat every 1 (One) hour if symptoms persist
3. Haloperidol
- For nausea and vomiting or agitation - Expect to see effect after 20 minutes - Can repeat every 1 (One) hour if symptoms persist
4. Hyoscine
- For severe respiratory secretions - Expect to see effect in less than 10 minutes - Can repeat every 1 (One) hour if symptoms persist
5. Diazepam (Rectal)
- For seizure - Expect to see effect in less than 15 minutes - Can repeat every 15 mins if seizure persist

Reference: Palliative Care Formulary Seventh Edition

Medication/s	Indication/s	Dose/ Frequency	As Needed	Remarks
Morphine	( ) Pain ( ) Dyspnea (Shortness of Breath) ( ) Cough ( ) Others:	( ) mg ( ) Frequency:		S/C: ( ) syringes provided
Midazolam	( ) Confusion ( ) Restlessness ( ) Seizure ( ) Anxiety ( ) Others:	( ) mg ( ) Frequency:		S/C: ( ) syringes provided
Haloperidol	( ) Agitation ( ) Nausea and Vomiting ( ) Others:	( ) mg ( ) Frequency:		S/C: ( ) syringes provided
Others				
Transdermal Fentanyl	( ) Pain ( ) Dyspnea (Shortness of Breath)	( ) mcg/h for every 72 hours		( ) patches provided

Medication/s	Indication/s	Dose/ Frequency	As Needed	Remarks
Rectal Diazepam	( ) Seizure	( ) mg ( ) Frequency:		( ) supp provided

Medication Diary

Medication/s	Date	Time	Quantity
Morphine			
Midazolam			
Haloperidol			
Hyoscine			

Storage, Disposal, Return or Refill of Medications

1. Store medications in a cool, dry place and keep out of reach of children.
2. Store the used syringes in a separate container to avoid confusion.
3. Return the used and unused syringes to the nearest MOH healthcare facilities, preferably hospital/ dispensing facility for proper disposal. The number of syringes will be accounted for upon return.
4. Regardless of the dosage form, return all the medications supplied, to the nearest MOH healthcare facilities, preferably hospital/ dispensing facility for proper disposal.
5. Each MOH healthcare facility should have procedures for receiving, recording and disposing of medications returned by patients or caregivers to prevent misuse.
6. Disposal of returned medications containing psychotropic substances or dangerous drugs by MOH healthcare facilities should be carried out in accordance with legal requirements and in the presence of an authorised enforcement officer.
7. Refill medications can only be collected by an authorised caregiver after contacting respective dispensing facilities during office hours.

Example of Terminal Discharge Medication Information Sheet (BM)

UBat-Ubatan Discaj Terminal

1. Morphine
- Untuk sakit, sesak nafas,atau batuk - Jangkamasa untuk melihat kesan tindakan adalah selepas 15 minit - Boleh diulang setiap satu (1) jam sekiranya simptom berterusan
2. Midazolam
- Untuk kecelaruan, kegelisahan yang serius dan sawan - Jangkamasa untuk melihat kesan tindakan adalah 15 minit selepas suntikan di bawah kulit diberikan - Boleh diulang setiap satu (1) jam sekiranya simptom berterusan
3. Haloperidol
- Untuk loya dan muntah atau kecelaruan dan kegelisahan serius - Jangkamasa untuk melihat kesan tindakan adalah selepas 15 minit - Boleh diulang setiap satu (1) jam sekiranya simptom berterusan
4. Hyoscine
- Untuk bendalir pernafasan yang teruk (kahak) - Jangkamasa untuk melihat kesan tindakan adalah dalam masa kurang 15 minit - Boleh diulang setiap satu (1) jam sekiranya simptom berterusan
5. Diazepam (Rectum/ Salur Punggung)
- Untuk sawan - Jangkamasa untuk melihat kesan tindakan adalah dalam masa kurang 15 minit - Boleh diulang setiap 15 minit sekiranya sawan berterusan

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Ubat	Kegunaan	Dos/ Kekerapan	Bila Perlu	Catatan
Morphine	( ) Sakit ( ) Sesak Nafas ( ) Batuk ( ) Lain-lain:	( ) mg ( ) kekerapan:		S/C: ( ) picagari dibekalkan
Midazolam	( ) Kecelaruan ( ) Kegelisahan ( ) Sawan ( ) Lain-lain:	( ) mg ( ) kekerapan:		S/C: ( ) picagari dibekalkan
Haloperidol	( ) Kecelaruan ( ) Loya dan Muntah ( ) Lain-lain:	( ) mg ( ) kekerapan:		S/C: ( ) picagari dibekalkan
Ubat-Ubatan Lain				
Transdermal Fentanyl	( ) Sakit ( ) Sesak Nafas	( ) mcg/h for setiap 72 jam		( ) keping dibekalkan

Ubat	Kegunaan	Dos/ Kekerapan	Bila Perlu	Catatan
Rectal Diazepam	( ) Sawan	( ) mg ( ) kekerapan:		( ) unit dibekalkan

Diari Ubat

Ubat	Tarikh	Masa	Kuantiti
Morphine			
Midazolam			
Haloperidol			
Hyoscine			

Penyimpanan, Pelupusan, Pemulangan atau Pengisian Semula Ubat-ubatan

1. Simpan ubat-ubatan di tempat yang sejuk dan kering serta jauh daripada capaian kanak-kanak.
2. Simpan picagari yang telah digunakan di dalam bekas berasingan bagi mengelakkan kekeliruan.
3. Pulangkan picagari yang telah digunakan dan yang tidak digunakan ke fasiliti kesihatan KKM yang terdekat, sebaiknya hospital atau fasiliti pendispensan, untuk pelupusan yang betul. Bilangan picagari akan direkodkan semasa pemulangan.
4. Tanpa mengira bentuk dos, pulangkan semua ubat yang dibekalkan ke fasiliti kesihatan KKM yang terdekat, sebaiknya hospital atau fasiliti pendispensan, untuk pelupusan yang betul.
5. Setiap fasiliti kesihatan KKM hendaklah mempunyai prosedur untuk menerima, merekod dan melupuskan ubat yang dipulangkan oleh pesakit atau penjaga bagi mengelakkan penyalahgunaan.
6. Pelupusan ubat yang dipulangkan yang mengandungi bahan psikotropik atau ubat berbahaya oleh fasiliti kesihatan KKM hendaklah dijalankan mengikut keperluan undang-undang dan disaksikan oleh pegawai penguat kuasa yang diberi kuasa.
7. Ubat ulangan hanya boleh diambil oleh penjaga yang diberi kuasa selepas menghubungi fasiliti pendispensan berkenaan pada waktu pejabat.

Appendix 5A

Example of Letter for Terminal Discharge (EN)

Hospital Name
Address of Hospital

Our Reference:
Date :

Dear Healthcare Professional/ Police officer concerned,

RE: DISCHARGE

This letter is to inform that

Patient's Name : _____
NRIC Number : _____

Is under the care of _____ department in Hospital ..... He/ She is critically ill and wishes to spend this period at home. Therefore, the patient will discharge with the following medication.

Medication:

The medication will be collected by the patient's caregiver.

Caregiver's Name : _____
NRIC Number : _____

If you have any queries, please do not hesitate to contact us at .....(Tel. No.).....

Thank you.

Best Regards,
_____
Dr. _____
Medical Officer
Department _____
Hospital _____

Appendix 5B

Contoh Surat untuk Terminal Discharge (BM)

Nama Hospital
Alamat Hospital

Rujukan kami:
Tarikh:

Kepada Pegawai Kesihatan/ Pegawai Polis yang berkenaan,

PER: DISCAJ

Adalah dimaklumkan bahawa

Nama Pesakit : _____
No. Kad Pengenalan : _____

Disahkan mendapatkan rawatan di Jabatan _____ Hospita.....Beliau adalah pada fasa yang amat kritikal dan ingin meluangkan masa ini di rumah. Pesakit memerlukan ubat peskripsi yang berkenaan bagi tujuan melegakan gejala fizikal di rumah:

Ubat-ubatan:

Ubat-ubatan ini akan diambil oleh wakil pesakit seperti yang berikut:

Nama Penjaga : _____
No. Kad Pengenalan : _____

Sekiranya terdapat sebarang pertanyaan, anda boleh menghubungi kami di .....(No. Tel).....

Sekian, terima kasih.

Yang Benar,
_____
Dr. _____
Pegawai Perubatan
Jabatan _____
Hospital _____

Appendix 6A

Example of Declaration Letter for Care (EN)

I, _____(Name),
_____(I/C number), the appointed caregiver of
_____(patient's name)
who live in_____
_____(Address),
understand that I have the responsibilities as below:

I) I will administer injectable medications only at the dosages and frequencies as advised by palliative care doctors, pharmacists or nurses.

II) If I am unsure with any medication related issues such as indication, dosage and frequency, I will read the medication information sheet provided or contact designated hospices, domiciliary care teams or the hospital Palliative Care Unit (PCU).

III) I will document the date and timing of medications administered in the medication diary provided.

IV) I will store medications in a safe and cool place out of reach from children.

V) I or an alternative authorised caregiver will replenish medication syringes if the supply is running low especially before weekends or public holidays. The alternative authorised caregiver will be given a letter of authorization and a photocopy of my identification card.

VI) I will return all used or unused medication syringes after the death of the patient to the nearest MOH healthcare facilities, preferably …….. (Facility Name)…….. along with the medication diary and terminal discharge letter provided.

VII) I agree to receive phone advice regarding the care of the patient from doctors and nurses from the hospital PCU if my area of stay is not covered by hospices or domiciliary care teams. I understand that the advice given is based on what is best understood over the phone.

VIII) I am aware that healthcare staff from the hospital PCU may call me after the death of the patient to enquire about the terminal discharge experience and obtain feedback for service improvement.

Signature : _____
Name : _____
I/C No. : _____
Relationship : _____
Date : _____

Appendix 6B

Contoh Surat Aku Janji Penjagaan (BM)

Saya, _____(Nama),
_____(Nombor Kad Pengenalan), penjaga kepada
_____(Nama Pesakit)
beralamat_____
_____(Alamat),
faham bahawa berikut adalah tanggungjawab saya:-

I) Saya akan memberi ubat mengikut dos dan kekerapan seperti yang diarahkan oleh doktor, pegawai farmasi atau jururawat.

II) Saya akan merujuk kepada kertas maklumat ubat-ubatan yang telah diberikan atau menghubungi pihak Unit Penjagaan Paliatif (PCU) hospital, hospis atau pasukan domisiliari berkaitan sekiranya saya tidak pasti mengenai kegunaan, dos dan kekerapan ubat–ubatan.

III) Saya akan menggunakan diari ubat yang disediakan untuk merekodkan tarikh dan masa pemberian ubat.

IV) Saya akan menyimpan ubat di tempat yang selamat supaya tidak diambil oleh kanak- kanak.

V) Saya atau wakil saya akan membuat penambahan semula ubat sebelum hari cuti hujung minggu atau cuti umum sekiranya bekalan tidak mencukupi. Wakil saya akan diberikan surat kebenaran dan salinan kad pengenalan saya.

VI) Saya akan memulangkan semua ubat yang digunakan dan tidak digunakan kepada fasiliti Kementerian Kesihatan Malaysia terdekat, sebaiknya .....(Nama Fasiliti)..... bersama diari ubat dan surat discaj.

VII) Saya bersetuju untuk menerima nasihat melalui panggilan telefon daripada doktor dan jururawat PCU hospital sekiranya kawasan saya tidak diliputi oleh hospis atau penjagaan domisiliari. Nasihat yang diberikan adalah berdasarkan pemahaman sebaik mungkin yang diterima melalui perbualan telefon.

VIII) Saya mengambil maklum bahawa kakitangan kesihatan daripada PCU hospital mungkin akan menghubungi saya selepas kematian pesakit untuk mengetahui pengalaman serta mendapatkan maklum balas mengenai perkhidmatan ini bagi tujuan penambahbaikan perkhidmatan

Tandatangan : _____
Nama : _____
No. K/P : _____
Hubungan : _____
Tarikh : _____