PHC Chapter 22: Medicines used in palliative care

INTRODUCTION

Palliative care improves the quality of life of patients facing life-threatening illnesses and their family members, regardless of whether or not they also receive life-prolonging treatment. It requires a multidisciplinary approach, and aims to address physical, psychological, spiritual and social problems.

General principles of palliative care include:

» Treat the underlying causes of symptoms;
» Minimise medicine side effects; and
» Ensure that the patient and caregivers are informed of the nature of the disease, treatment, side-effects, and likely outcomes.

Palliative care patients who are down-referred from higher levels of care with a care plan should be managed according to that plan. Palliative care patients should be assessed by community-based palliative care teams where available.

The SPICT™-SA is a generic tool (https://www.spict.org.uk/the-spict/spict-sa/), designed for the South African setting, to help identify adults with advanced life-limiting illnesses when the best available and appropriate treatment has been given and their condition continues to deteriorate.

LoE:IVb[1]

Always refer to the latest National Department of Health Guidelines on Palliative Care.

Note: Please be advised that the recommendations in this chapter are directed at treating common symptoms alongside disease directed care and symptoms associated with end-of-life care.

22.1 GASTROINTESTINAL CONDITIONS

22.1.1 CONSTIPATION

K59.0 + (Z51.5)

See section 2.8: Constipation.

DESCRIPTION

The underlying cause of constipation in palliative care patients may be functional, disease, or treatment related. Developmental disorders with or without cognitive deficits, mood and situational circumstances can impact bowel habits in chronically ill children.

GENERAL MEASURES

Ensure privacy and comfort to allow a patient to defecate normally.
Increase fluid intake within the patient's limits.
Encourage activity and increased mobility within the patient's limits.
Anticipate the constipating effects of pharmacological agents, such as opioids, and provide laxatives prophylactically.

MEDICINE TREATMENT

Adults and children >15 years of age

- Sennosides A and B, oral, 13.5 mg, 1 tablet at night.
  - In resistant cases increase to 2 tablets. *LoE:IIb*[2]

AND/OR

- Lactulose, oral, 10 to 30 mL 12 to 24 hourly. *LoE:IIb*[3]

Children

- Lactulose, oral:
  - 1-11 months: 5 mL daily, adjusted according to response
  - 1-4 years: 10 mL daily, adjusted according to response
  - 5-14 years: 15 mL daily, adjusted according to response

Adjust dose as needed to achieve 2-3 soft stool per day, by:

- Increasing frequency of administration to 12 hourly, or
- Increasing volume by 2.5 - 5 mL per dose.

Note: Manual removal should only be undertaken if the patient has received adequate pain relief and, if necessary, sedation as well. *LoE:IVb*[4]

For management of opioid-induced constipation:
See adjuvant therapy in Section 20.4: Chronic cancer pain.

REFERRAL

» All patients with suspected bowel obstruction.
» Patients with severe constipation, not relieved with oral treatment, or who are unable to swallow.

22.1.2 DIARRHOEA

A09.0

See Section 2.9: Diarrhoea.

DESCRIPTION

The commonest cause of diarrhoea in palliative care is laxative use. Other causes include partial intestinal obstruction, HIV-associated diarrhoea, pancreatic insufficiency, *Clostridium difficile* infection, chemotherapeutics, and radiation enteritis.
Severe constipation and faecal impaction can also cause diarrhoea as backed-up, liquefied stool may be all that the patient can pass (“overflow diarrhoea").

GENERAL MEASURES

Refer to a dietician.
Consider faecal impaction and perform rectal examination if indicated.

MEDICINE TREATMENT

Rehydrate the patient as appropriate if necessary. See Sections 2.9.1: Diarrhoea, acute in children and Section 2.9.3: Diarrhoea, acute, without blood, in adults.

Adults:

- Loperamide, oral, 4 mg immediately and 2 mg as required after each loose stool up to 6 hourly.
  - Not more than 16 mg daily
  - Contraindicated in antibiotic-induced diarrhoea and overflow diarrhoea.

REFERRAL

Persistent diarrhoea (>2 weeks) in children.

22.1.3 NAUSEA AND VOMITING

R11 + (Z51.5)

See Section 2.4: Nausea and vomiting, non-specific.

DESCRIPTION

Nausea and vomiting may have many causes in palliative care patients e.g. medication, constipation, anxiety, infection, and raised intracranial pressure.

GENERAL MEASURES

Refer to a dietician if available.
Identify and manage reversible causes, which include medication, hypercalcemia, constipation, uraemia, gastritis, gastroenteritis, coughing, and infections.
Manage odours e.g. cooking smells and fungating wounds.

MEDICINE TREATMENT

Treat the underlying cause and rehydrate the patient if necessary.
Deliver medicines via an appropriate route and regularly.

Adults:

- Metoclopramide, oral, 10 mg, 8 hourly as needed.
  - In renal impairment start with a dose of 5 mg, 8 hourly. *LoE:IVb*[5]
  - Increase according to clinical response using alternate 5 mg and 10 mg doses if required. *LoE:IVb*[6]

Children:

- Metoclopramide, oral, 0.1 mg/kg/dose, 8 to 12 hourly.

Weight kg	**Dose** mg	**Syrup** 5 mg/5 mL	**Age** months/years
> 9–11 kg	1 mg	1 mL	> 12–18 months
> 11–14 kg	1.2 mg	1.2 mL	> 2–3 years
> 14–17.5 kg	1.6 mg	1.6 mL	>3–5 years
> 17.5–25 kg	2 mg	2 mL	>5–7 years
> 25–35 kg	3 mg	3 mL	>7–11 years
> 35–55 kg	4.5 mg	4.5 mL	>11–15 years

Use with caution as extrapyramidal side effects may occur (especially at higher doses).

LoE:IVb[7]

REFERRAL
» All patients with a diagnosed or suspected underlying cause that requires treatment at a higher level of care.
» Consult a palliative care trained doctor if nausea and vomiting persist despite treatment.

22.2 NEUROPSYCHIATRIC CONDITIONS

22.2.1 ANXIETY
F41.0-3/F41.8-9/ + (Z51.5)
See Section 16.3: Anxiety disorders.

DESCRIPTION
Some symptoms of anxiety in palliative care patients may be expected, given the concerns of living with a serious illness. However, if the symptoms are debilitating, they require treatment.

GENERAL MEASURES
Address any contributing factors such as pain and dyspnoea.
Consider other underlying conditions that may mimic anxiety e.g. electrolyte imbalance, hyperthyroidism, hypoxia, arrhythmias and many adverse drug reactions.
Assess for depression.
Offer referral for psychotherapy if available.

MEDICINE TREATMENT
Adult:
- Fluoxetine, oral.
  - Initiate at 20 mg alternate days for 2 weeks.
  - Increase to 20 mg daily after 2 to 4 weeks.
  - Delay dosage increase if increased agitation/panicky feelings occur.

LoE:IIb[8]

CAUTION FLUOXETINE
Fluoxetine is contraindicated if eGFR <10 mL/min

OR

LoE:IVb[9]

If fluoxetine is poorly tolerated:
- Alternative SSRI e.g.:
- Citalopram, oral.
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily.

LoE:IIb[10]

Note: Effects of SSRIs are only apparent after 2 to 3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

For acute anxiety reactions:

- Benzodiazepine, e.g.:
- Diazepam, oral, 2.5 to 5 mg. *LoE:IIb*[11]
  - For a maximum of 10 days.

Note: Benzodiazepines might cause sedation and confusion. Use with caution.

CAUTION - BENZODIAZEPINES

» Associated with cognitive impairment – reversible with short-term use and irreversible with long-term use.
» Elderly are at risk of over-sedation, falls and hip fractures.
» Dependence may occur after only a few weeks of treatment.
» Prescribe for as short a period of time as possible.
» Warn patient not to drive or operate machinery when used short-term.
» Avoid use in people at high risk of addiction – personality disorders and those with previous or other substance misuse. *LoE:IIIb*[12]

REFERRAL

All children.

22.2.2 DELIRIUM

F05.0-1/F05.8-9/R45.1/ + (Z51.5)

See Section 21.2.4: Delirium.

DESCRIPTION

Delirium (confusion) is common in the terminal stages of advanced disease, but is rarely seen in children. Supportive measures such as frequent re-orientation may be useful.

GENERAL MEASURES

Assess for underlying causes e.g. infection, electrolyte imbalance.
Remove factors that can agitate patient (full bladders, thirst, pain, constipation).
Reduce polypharmacy.
Monitor for sensory deficits e.g. hearing impairment.

MEDICINE TREATMENT

CAUTION

» Rapid tranquillisation may cause cardiovascular collapse, respiratory depression, neuroleptic malignant syndrome and acute dystonic reactions.
» The elderly, children, intellectually disabled and those with comorbid medical conditions and substance users are at highest risk.
» An emergency trolley, airway, bag, oxygen and intravenous line must be available.

Adults:

For hyperactive delirium and severe agitation:

- Benzodiazepine, e.g.:
- Diazepam, IV, 2.5 to 5 mg as a single dose LoE:IIIb[13]
  - If no response, give a second dose.
  - Do not administer at a rate over 5 mg/minute.

OR

- Midazolam, IM, 1 to 5 mg immediately.
  - Repeat after 30 to 60 minutes if needed.
  - Lower doses are indicated for patients with liver failure. LoE:IVb[14]

Switch to oral benzodiazepine if possible.

CAUTION - BENZODIAZEPINES

» Associated with cognitive impairment – reversible with short-term use and irreversible with long-term use.
» Elderly are at risk of over-sedation, falls and hip fractures.
» Dependence may occur after only a few weeks of treatment.
» Prescribe for as short a period of time as possible.
» Warn patient not to drive or operate machinery when used short-term.
» Avoid use in people at high risk of addiction – personality disorders and those with previous or other substance misuse. LoE:IIIb[15]

REFERRAL

All children.

22.2.3 DEPRESSION

F32.0-3/F32.8-9/F33.0-3/F33.8-9/F34.1 + (Z51.5)

See section 16.4.1: Depressive disorders.

DESCRIPTION

Depression might be difficult to diagnose in palliative care patients as some symptoms of depression are similar to disease manifestations such as anorexia and insomnia. The key indicators of depression in palliative care patients are persistent feelings of hopelessness and worthlessness and/or suicidal ideation. Young children may present with somatic complaints e.g. abdominal pain or headaches, or may have restlessness.

GENERAL MEASURES

Refer to a social worker to assist with concerns of future care of patient, family, and finances.

MEDICINE TREATMENT

Adults

- Fluoxetine, oral.
  - Initiate at 20 mg alternate days for 2 weeks.
  - Increase to 20 mg daily after 2 to 4 weeks.

- Delay dosage increase if increased agitation/panicky feelings occur. *LoE:IIb*[16]

CAUTION FLUOXETINE
Fluoxetine is contraindicated if eGFR <10 mL/min

OR

If fluoxetine is poorly tolerated:

- Alternative SSRI e.g.:
- Citalopram, oral.
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily. *LoE:Ib*[17]

OR

If a sedating antidepressant is required:

- Tricyclic antidepressants (Doctor prescribed), e.g.:
- Amitriptyline, oral, at bedtime.
  - Initial dose: 25 mg per day.
  - Increase by 25 mg per day at 3- to 5-day intervals.
  - Maximum dose: 150 mg per day.

Note: Tricyclic antidepressants may cause dry mouth, constipation, urinary retention, and confusion, which might be especially problematic in palliative care patients. Use the lowest dose possible, and titrate slowly. *LoE:IVb*[18]

Note: Effects of SSRIs are only apparent after 2 to 3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

REFERRAL

» All children and adolescents.
» All patients to a psychologist and social worker if available.

22.3 PAIN

See chapter 20: Pain.

22.3.1 CHRONIC CANCER PAIN

See Section 20.4: Chronic cancer pain.

22.4 RESPIRATORY CONDITIONS

For Coronavirus Disease-19. See Section 10.19.1: COVID-19.

22.4.1 DYSPNOEA

R06.0 + (Z51.5)

DESCRIPTION

Dyspnoea is the subjective, unpleasant sensation of being unable to breathe adequately (breathlessness). Dyspnoea is a complex symptom which can be caused or exacerbated by physical, psychological, and emotional factors. The intensity of dyspnoea is not related to the oxygen saturation. In the palliative care patient fluid overload is a potential cause of dyspnoea.

LoE:IIIb[19]

The aim should always be to address the underlying cause. However, in end stage disease it may not be possible to resolve dyspnoea. Therefore, symptomatic treatment is indicated in addition to treating the cause.
In children dyspnoea is often evidenced by difficulty talking or feeding, or restlessness.

GENERAL MEASURES

If available refer to a physiotherapist and occupational therapist for pulmonary rehabilitation, and to teach patients pursed lip breathing, pacing of activities, relaxation techniques and positioning.
A fan might reduce the sensation of dyspnoea.
Where possible treat the underlying cause e.g. antibiotics for underlying respiratory infection.

MEDICINE TREATMENT

Adults

LoE:IIIb[20]

- Morphine solution, oral. (Doctor prescribed.)
  - Starting dose: 2.5 to 5 mg, as required 4 hourly, titrating up slowly.
  - In renal failure: start at 1 to 2 mg and observe patient closely before titrating up as required.

LoE:IVb[21]

Children

- Morphine solution, oral. (Doctor prescribed.)
  - Starting dose:
    - 0–1 month of age: 0.05 mg/kg 6 hourly.
    - ≥ 1–12 months of age: 0.1 mg/kg/dose 4-6 hourly.
    - ≥ 12 months of age: 0.2–0.4 mg/kg/dose 4-6 hourly.

LoE:IVb[22]

REFERRAL

Dyspnoea associated with hypoxia for consideration of home-based oxygen.

22.5 PRESSURE ULCERS/SORES

See Section 5.19: Pressure ulcers/sores.

22.6 END OF LIFE CARE

Z51.5

The management of a patient who is imminently terminal (death suspected to occur within a few days or weeks), should include:

» Communicating honest, direct, compassionate, and culturally sensitive information regarding the prognosis, and symptoms that might develop.
» Relieving physical, spiritual and emotional distress in the patient and family.
» Treating easily manageable complications that cause suffering.
» Stopping all unnecessary medicines.
» Limiting hospital admissions, if possible.
» Ensuring that parents/caregivers are adequately counselled.
» Decision making as to the preferred place of death (home, hospice, hospital) and referral to community-based services where available (hospice, palliative, and home-based care services).

Indications for referral for in-patient hospital or hospice care:

» Hypoxia and respiratory distress where oxygen therapy provides relief. IV/ nasogastric fluid requirements or medication administration needed to relieve suffering.
» Carer/s unable to cope at home.

Feeds and fluids at the end of life:

» Anorexia and refusal of feeds/fluids in dying patients is a normal phenomenon.
» Encourage the family to feed for comfort only and reassure them that the dying patient is not hungry.

Investigations at the end of life:

» Investigations should be kept to a minimum and only done if it might contribute to the patient's comfort.

Antibiotics at the end of life:

» Oral antibiotic therapy might not be indicated. Refer to the patient's palliative care plan if available, or consult a palliative care trained doctor.

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SOUTH AFRICAN PRIMARY HEALTH CARE ESSENTIAL MEDICINES LIST
CHAPTER 22: MEDICINES USED IN PALLIATIVE CARE
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020-4)

The Primary Health Care (PHC) Level Medicines Used in Palliative Care chapter underwent detailed clinical editing and editorial changes for clarity.

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG) and supporting medicine reviews. All reviews and costing reports may be accessed at: https://www.health.gov.za/nhi-edp-stgs-eml/.

Review of the palliative care chapters is an ongoing process as aspects of the chapters continue to be prioritized for review as a long-term priority of NEMLC.

A: PROPOSED AMENDMENTS

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
INTRODUCTION	SPICT-SA Tool	SPICT-SA Tool added for identification of patients with palliative care needs
22.1.2 DIARRHOEA	Loperamide	Retained with amendment in maximum adult daily dose
22.1.3 NAUSEA AND VOMITING	Ondansetron, oral	Not Added
	Metoclopramide, oral	Retained with additional guidance provided for dosing in renal impairment
22.2.1 ANXIETY	Fluoxetine, oral	Retained with additional guidance provided for dosing in renal impairment
22.2.2 DELIRIUM	**For hyperactive delirium and severe agitation:** Diazepam, IV	Amended
	Elderly or frail patients, or those with liver impairment: Diazepam, IV	Amended
	Elderly or frail patients, or those with liver impairment: Midazolam, IM	Amended
22.2.3 DEPRESSION	Fluoxetine, oral	Retained with additional guidance provided for dosing in renal impairment
	Tricyclic Antidepressants	Aligned to Primary Health Care Mental Health Chapter (Doctor prescribed for Tricyclic Antidepressants)
22.4 RESPIRATORY CONDITIONS	Coronavirus Disease-19	Cross referenced to PHC Infections and related conditions Section 10.19.1: COVID-19: CORONAVIRUS DISEASE-19.
22.4.1 DYSPNOEA	Morphine, solution, oral	Retained with alignment of dosing frequency to AHL Palliative Care Chapter and chapter 23 paediatric dosing tables. Additional guidance provided for dosing in renal impairment

An external commentator raised the importance of palliative care of kidney failure, as an exceptionally common problem in the primary healthcare (PHC) setting and that it deserves its own standard treatment guideline (STG) in the palliative care chapter. Additionally, through external comment it was raised that dosage adjustments should be considered for certain drugs in the palliative care setting. A palliative care STG for kidney failure was not added to the PHC STGs as it is not feasible to have a palliative care STG for all conditions. However, the PHC and AHL kidney and nephrology chapters were shared with renal experts for input, in order to strengthen the renal recommendations in the STGs. Additionally, the PHC palliative care chapter was shared with renal experts for comment regarding dosage adjustments in renal impairment in the palliative care patient. For the medicines mentioned in the palliative care chapter, adjustment of dosages was recommended for metoclopramide, fluoxetine and morphine in renal impairment in the palliative care patient. These revisions are outlined in the appropriate STGs below.

INTRODUCTION

The Committee deliberated the addition of a note regarding the use of cannabinoids in the palliative care setting and the potential for drug-drug interactions. No note was added to the chapter regarding cannabinoids which are currently not registered; as other traditional and non-registered medicines may also be used by patients in this setting and are not specifically mentioned.

An editorial amendment was made to the introduction of the chapter to convey that when best available and appropriate treatment has been given in patients with advanced life limiting illnesses and a patient's condition continues to deteriorate a palliative care approach is recommended.

The SPICT-SA tool for earlier identification of patients with palliative care needs was included. SPICT™ "is used to help identify people with deteriorating health due to a new serious illness, and those with one or multiple advanced conditions so they benefit from holistic assessment, future care planning (advance/anticipatory care planning) and a palliative approach to care."[1]

The introduction to the STG was updated as follows:

Palliative care improves the quality of life of patients facing life-threatening illnesses and their family members, regardless of whether or not they also receive life-prolonging treatment. It requires a multidisciplinary approach, and aims to address physical, psychological, spiritual and social problems.
General principles of palliative care include:
Treat the underlying causes of symptoms;
Minimise medicine side effects; and
Ensure that the patient and caregivers are informed of the nature of the disease, treatment, side-effects, and likely outcomes.
Palliative care patients who are down-referred from higher levels of care with a care plan should be managed according to that plan.
Palliative care patients should be assessed by community-based palliative care teams where available.

The SPICT™-SA is a generic tool (https://www.spict.org.uk/the-spict/spict-sa/), designed for the South African setting, to help identify adults with advanced life-limiting illnesses when the best available and appropriate treatment has been given and their condition continues to deteriorate.

Always refer to the latest National Department of Health Guidelines on Palliative Care.

Note: Please be advised that the recommendations in this chapter are directed at treating common symptoms alongside disease directed care and symptoms associated with end-of-life care. ~~The recommendations in this chapter are primarily directed at end-of-life care, which is a component of palliative care.~~

22.1.1 CONSTIPATION

The dose of lactulose for adults and children > 15 years was adjusted to the South African Medicines Formulary[2] and the Palliative care Formulary[3].

With paediatrician input, the starting age for children (>12 months) for the use of lactulose for constipation was revised to apply to all children. This revision is in alignment with PHC Ch 20 Pain and the paediatric Hospital Level 2023 STG. Lactulose dosing was revised from milligram per kilogram dosing to dosing in millilitres as per the PHC Ch 21 Palliative Care paediatric Hospital Level 2023 STG.

The STG was updated as follows:

K59.0 + (Z51.5)
See section 2.8: Constipation.

DESCRIPTION
The underlying cause of constipation in palliative care patients may be functional, disease, or treatment related. Developmental disorders with or without cognitive deficits, mood and situational circumstances can impact bowel habits in chronically ill children.

[1] Palliative Care: SA Supportive and Palliative Care Indicators Tool (SPICTTM-SA). Available: file:///C:/Users/27798/Downloads/Version-2-SPICT-SA-Dec-2020%20(3).pdf.

[2] South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[3] Charlesworth, S. (Ed.). (2020). Palliative Care Formulary (7th ed.). Pharmaceutical Press.

GENERAL MEASURES
Ensure privacy and comfort to allow a patient to defecate normally.
Increase fluid intake within the patient's limits.
Encourage activity and increased mobility within the patient's limits.
Anticipate the constipating effects of pharmacological agents, such as opioids, and provide laxatives prophylactically.

MEDICINE TREATMENT

Adults and children > 15 years of age
- Sennosides A and B, oral, 13.5 mg, 1 tablet at night.
  In resistant cases increase to 2 tablets.

AND/OR
- Lactulose, oral, 10–~~20~~ 30 mL 12–24 hourly.

Children ~~> 12 months of age~~
- Lactulose, oral, 2.5–10 mL 12 hourly ~~0.5 mg/kg/dose once daily. See dosing tables, pg 23.6~~.
  If poor response, increase frequency to 12 hourly.

Note: Manual removal should only be undertaken if the patient has received adequate pain relief and, if necessary ~~need be~~ sedation as well.

For management of opioid-induced constipation:
See adjuvant therapy in Section 20.4: Chronic cancer pain.

22.1.3 DIARRHOEA

Loperamide, oral*: Retained with amendment in maximum adult daily dose*

The maximum allowable daily loperamide adult dose was aligned to the South African Medicines Formulary[4].

The STG was updated as follows:

MEDICINE TREATMENT
Rehydrate the patient as appropriate if necessary. See Section 2.9.1: Diarrhoea, acute in children and Section 2.9.3: Diarrhoea, acute, without blood, in adults.

Adults:
- Loperamide, oral, 4 mg immediately and 2 mg as required after each loose stool up to 6 hourly.
  - Not more than ~~12~~ 16 mg daily
  - Contraindicated in antibiotic-induced diarrhoea and overflow diarrhoea.

22.1.3 NAUSEA AND VOMITING

General Measures

An external comment to include the following detailed guidance on the causes of nausea and vomiting was not supported:

Identify the most likely cause of nausea and treat with the appropriate agent. Multiple agents are sometimes required
If the agent used is not effective within the first 24 hours, increase the dose or choose another agent
Always institute pharmacological and non-pharmacological measures
Indications for subcutaneous infusions for medications include:

- Persistent nausea and vomiting refractory to tablets
- Dysphagia
- Complete Intestinal obstruction
- Semi-comatose or comatose states
- Profound weakness
- Poor gastrointestinal absorption of medications

Instead, the general measures wording was aligned to the causes for nausea and vomiting in the AH Ch 24: Medicines used in palliative care chapter.

[4] South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

The STG was updated as follows:

GENERAL MEASURES
Refer to a dietician if available.
Identify and manage reversible causes, which include medication, hypercalcemia, constipation, uraemia, gastritis, gastroenteritis, coughing and infections.
Manage odours e.g. cooking smells and fungating wounds.

Medicine Treatment

Ondansetron, oral*: Not Added*

An external comment was received for the aetiology for nausea and vomiting to be considered for targeted pharmacological therapy. It was mentioned, through external comment without example, that non-pharmacological therapy is cost effective and should always be applied and that ideally, ondansetron would be useful as a second-line agent, but that it was understandable that this might not align with national pharmaceutical procurement budgets. The external comment to include ondansetron for nausea and vomiting was not supported for PHC level of care.

An external comment to include wording on contraindications for use of metoclopramide e.g., for mechanical causes except complete bowel obstruction was not supported. For the PHC level of care it is clearly articulated that a referral is indicated for all patients with a diagnosed or suspected underlying cause that requires treatment at a higher level of care. Additionally, advice is provided to consult a palliative care trained doctor if nausea and vomiting persist despite treatment.

Metoclopramide, oral: *Retained with additional guidance provided for dosing in renal impairment*[5]

An external suggestion to revise the dosing of metoclopramide from 8 hourly dosing to 6 hourly, in adults, was not supported as this dosing change would not be aligned to SAMF and palliative care formulary guidance.

Through expert input, dosing guidance for metoclopramide is now provided for the palliative care patient with renal impairment.[5] Renal experts suggested that if eGFR is 10-50 mL/min or < 10 mL/min then metoclopramide dosing should be adjusted to 75% or 50% of the usual dose respectively. Considering the difficulty of attaining a dose of metoclopramide of 7.5 mg using a 5mg tablet, the Committee recommended in renal impairment to start with a dose of 5mg, 8 hourly and if higher daily doses are required to alternate a dose of 5mg & 10mg to achieve a higher daily dose.

A suggestion to use metoclopramide as continuous subcutaneous infusion was not supported by the Committee for the PHC level of care.

The STG was updated as follows:

Treat the underlying cause and rehydrate the patient if necessary.
Deliver medicines via an appropriate route and regularly.
Adults:

- Metoclopramide, oral, 10 mg, 8 hourly as needed.
    - In renal impairment start with a dose of 5 mg, 8 hourly.
    - Increase according to clinical response using alternate 5 mg and 10 mg doses if required.

22.2.1 ANXIETY

Fluoxetine, oral: *Retained with additional guidance provided for dosing in renal impairment*

[5] South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

The Committee approved the addition of a contra-indication for the use of fluoxetine in renal impairment if eGFR is < 10 mL/min; based on expert input.[6]

In alignment with AHL Chapter a note was added that effects of SSRIs are only apparent after 2–3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

22.2.2 DELIRIUM

The indication "for acute agitation" was edited to "hyperactive delirium and severe agitation."

For hyperactive delirium and severe agitation:
Diazepam IV: *Amended*

Elderly or frail patients, or those with liver impairment:
Diazepam, IV: *Amended*
Midazolam, IM: *Amended*

The dose of midazolam and diazepam was conservatively decreased for palliative care use recommending a low starting dose and repeat dosing for clinical effect in line with stepwise guidance for primary level palliative care.[7,8,9]

The two sections: (1) hyperactive delirium and severe agitation and (2) elderly or frail patients, or those with liver impairment were merged because the same dose is now offered for all groups of patients.

Level of Evidence: Low - IIIb – Review and IVb - Guidelines

The STG may be aligned to the final Primary Health Care Emergencies and Injuries Chapter before publication. The Primary Health Care Emergencies and Injuries Chapter was out for external comment and currently comments are being reviewed and finalised by the Primary Health Care Expert Review Committee for tabling at a National Essential Medicines List Committee meeting for publication.

The STG was revised as follows

Adults:

For ~~acute agitation~~ hyperactive delirium and severe agitation**: ~~(including elderly or frail patients, or those with liver impairment):~~**

- Benzodiazepine, e.g.:
- Diazepam, IV, ~~10 mg~~ **2.5–5 mg as a single dose**
  - If no response, give a ~~2~~ second dose.
  - Do not administer at a rate over 5 mg/minute.

~~Elderly or frail patients, or those with liver impairment:~~

- ~~Diazepam, IV, 5 mg~~
  - ~~If no response, give a 2nd dose.~~
  - ~~Do not administer at a rate over 5 mg/minute.~~

OR

- Midazolam, IM, ~~7.5–15~~ **1–5** mg immediately.
  - Repeat after 30–60 minutes if needed.
  - Lower doses are indicated for patients with liver failure.

Switch to oral benzodiazepine if possible.

[6] Fluoxetine, oral (renal dosing): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.
7 Grassi L, Caraceni A, Mitchell AJ, Nanni MG, Berardi MA, Caruso R, Riba M. Management of delirium in palliative care: a review. Curr Psychiatry Rep. 2015 Mar;17(3):550. https://www.ncbi.nlm.nih.gov/pubmed/25663153

8 South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

9 Charlesworth, S. (Ed.). (2020). Palliative Care Formulary (7th ed.). Pharmaceutical Press

22.2.3 DEPRESSION

Medicine Treatment

Fluoxetine, oral: *Retained with additional guidance provided for dosing in renal impairment*

The contraindication for the use of fluoxetine was also added for the indication of depression in renal impairment if the eGFR is < 10 mL/min.[10]

The STG was updated as follows:

MEDICINE TREATMENT

Adults

- Fluoxetine, oral.
  Initiate at 20 mg alternate days for 2 weeks.
  Increase to 20 mg daily after 2–4 weeks.
  Delay dosage increase if increased agitation/panicky feelings occur.

CAUTION FLUOXETINE

Fluoxetine is contraindicated if eGFR < 10 mL/min

OR

If fluoxetine is poorly tolerated:

Alternative SSRI e.g.:

- Citalopram, oral.
  Initiate at 10 mg daily for 2 weeks.
  Then increase to 20 mg daily.

Alignment was ensured to the Primary Health Care Mental Health Chapter to include "Doctor prescribed" for all schedule 5 medicines as PHC nurses with section 56(6) permit are prohibited to prescribe schedule 5 medicines.

In alignment with AHL Chapter a note was added that effects of SSRIs are only apparent after 2–3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.
The STG was updated as follows:

If a sedating antidepressant is required:

- Tricyclic antidepressants (Doctor prescribed), e.g.:
- Amitriptyline, oral, at bedtime.
  - Initial dose: 25 mg per day.
  - Increase by 25 mg per day at 3–5 day intervals.
  - Maximum dose: 150 mg per day.

Note: Tricyclic antidepressants may cause dry mouth, constipation, urinary retention, and confusion, which might be especially problematic in palliative care patients. Use the lowest dose possible, and titrate slowly.

Note: Effects of SSRIs are only apparent after 2–3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

22.4 RESPIRATORY CONDITIONS

For COVID-19 management relevant cross-references to the infections chapter were ensured.

The STG was updated as follow

22.4 RESPIRATORY CONDITIONS

For Coronavirus Disease-19. See PHC Infections and related conditions Section 10.19.1: COVID-19: CORONAVIRUS DISEASE-19.

[10] Fluoxetine, oral (renal dosing): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

22.4.1 DYSPNOEA

Description

Through expert input, fluid overload was listed as a cause of dyspnoea.[11] Additionally, editorial amendments were made to provide further clarity on the management of fluid overload in the STG.

The STG was updated as follows:

Dyspnoea is the subjective, unpleasant sensation of being unable to breathe adequately (breathlessness). Dyspnoea is a complex symptom which can be caused or exacerbated by physical, psychological, and emotional factors. The intensity of dyspnoea is not related to the oxygen saturation. In the palliative care patient fluid overload is a potential cause of dyspnoea.

The aim should always be to address the underlying cause. However, in end stage disease it may not be possible to resolve dyspnoea. Therefore, symptomatic treatment is indicated in addition to treating the cause.
In children dyspnoea is often evidenced by difficulty talking or feeding, or restlessness.

Medicine Treatment

Morphine, solution, oral: *Retained with alignment of dosing frequency to the AHL Palliative Care Chapter and additional guidance provided for dosing in renal impairment*

Through expert input, a caution has been added to adjust the dose of morphine solution in patients with renal impairment by initiating doses at 1-2 mg as required as compared to the usual dosage range of 2.5–5 mg as required.

The STG was updated as follows:

Adults
- Morphine solution, oral (Doctor prescribed).
  Starting dose: 2.5–5 mg, 4 hourly as required, titrating up slowly.
  - In renal failure: start at 1-2 mg and observe patient closely before titrating up as required..

Paediatric dosing was aligned to chapter 23, standard paediatric dosing tables.

2026 Updates

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
22.1.1	Constipation	Standardisation of lactulose dosing to dosing by age for the indication of constipation

22.1.1 CONSTIPATION

Lactulose, oral: Amended

The PHC Ch 22: Medicines used in Palliative care has been aligned with PHC Ch 20: Pain as below:

An external commentator raised concerns regarding the presentation and lack of standardisation of lactulose dosing for children in the pain and palliative care standard treatment guidelines. Lactulose dosing was considered, and it was recommended that dosing by age be implemented in the STGs for children with guidance for dose escalation on volume and frequency while noting the aim is to achieve two to three loose stools per day.

The STG was updated from:

[11] Dyspnoea: Wearne, N., Davidson, B., Motsohi, T., McCulloch, M., & Krause, R. (2020). Radically Rethinking Renal Supportive and Palliative Care in South Africa. Kidney International Reports. doi:https://doi.org/10.1016/j.ekir.2020.11.024

Children

- Lactulose, oral, 0.5 mL/kg/dose once daily. See dosing table: Chapter 23.
  - If poor response, increase frequency to 12 hourly.

To

Children

- Lactulose, oral:
  - 1-11 months: 5 mL daily, adjusted according to response
  - 1-4 years: 10 mL daily, adjusted according to response
  - 5-14 years: 15 mL daily, adjusted according to response

Adjust dose as needed to achieve 2-3 soft stool per day, by:

- Increasing frequency of administration to 12 hourly, or
- Increasing volume by 2.5 - 5 mL per dose.

Level of Evidence: IV (Guidelines)[12,13]

The dosing will be applied to all pain and palliative care chapters for the indication of constipation in children.

[12] South African Health Product Regulatory Authority. Professional information – Duphalac.

[13] British National Formulary for children 2025. London: BMJ Group, Pharmaceutical Press and RCPCH Publications Ltd.