Pharmacological Management of Symptoms for Adults in the Last Days of Life Clinical Guideline

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Disclaimer

This clinical guideline provides advice of a general nature. It has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this state-wide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to significantly depart from the guideline, the responsible clinician should document in the patient’s medical record, the decision made, by whom and detailed reasons for the departure from the guideline.

This state-wide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for:

> discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion; this includes the use of interpreter services where necessary.
> advising consumers of their choice and ensuring informed consent is obtained
> providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
> documenting all care in accordance with mandatory and local requirements.
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1. Introduction

The majority of people who die in Australia receive their end-of-life care in acute hospitals. In this setting, recognition of clinical deterioration that is irreversible may be delayed. Being aware that a patient is approaching the last days of life is critical to delivering appropriate and timely care, especially the management of distressing symptoms.

The Pharmacological Management of Symptoms for Adults in the Last Days of Life Clinical Guideline gives recommendations for initial prescribing practices for adult patients assessed as being in the last days of their lives and likely to die in a general hospital ward. The recommendations may also be useful in other care settings.

The Guideline addresses medication prescribing for common symptoms, medication administration, and considerations for ceasing medications. It provides guidance for the management of non-complex patients and specialist advice should be sought for the management of patients with complex needs. Medications are only one aspect of symptom management and should be combined with non-medication symptom management strategies.

2. Background

A Report by the Health Performance Council of SA in September 2013 (Improving End of Life Care for South Australians) indicated that almost 50% of South Australians die in an acute hospital. The large majority of these people are elderly, have advanced, chronic illness from which death is predictable, and are cared for by clinicians other than specialist palliative care clinicians. Specialist palliative care services are not growing, highlighting the importance of educating all clinicians to care for dying patients.

The National Consensus Statement: Essential Elements for Safe and High Quality End-of-Life Care 2015 recognises that care of patients who are at the end of life is the responsibility of every clinician and that all patients have a right to adequate symptom control at the end of life. A systems approach to clinician training, prescribing and medication access is recommended.

The Medical Board of Australia: Good Medical Practice: A Code of Conduct for Doctors in Australia, section 3.12.4, clearly states that medical practitioners have a professional duty to ensure that dying patients receive appropriate relief from distress.

3. Definitions

1. **Anticipatory prescribing**

   Anticipatory prescribing is prescribing done in advance of the development of the occurrence of symptoms. It is designed to enable prompt symptom relief at whatever time the patient develops distressing symptoms, and is based on the premise that although each patient has individual needs, many symptoms at the end of life are predictable, meaning management options can be made available in advance.
2. **Carers and Family**
Carers and family are those people closest to the patient in knowledge, care and affection. Carers and family may include the biological family, the family of acquisition (related by marriage or contract), and the family and friends of choice.

3. **Clinicians**
Clinicians are people who provide clinical care and/or medical treatments to patients. They include registered practitioners such as medical, nursing, pharmacy, allied health and other registered practitioners who provide health care. This includes Aboriginal and Torres Strait Islander health workers, ambulance officers and paramedics.

4. **Dying**
In this document the term ‘dying’ is used in reference to the terminal phase of life, where death is imminent and likely to occur within days or hours and occasionally weeks. This is sometimes referred to as ‘actively dying’.

5. **End-of-Life**
‘End-of-Life’ is the term used to describe the stage of life where a person is living with, and impaired by an eventually fatal (or terminal) condition, even if the prognosis is ambiguous or unknown.

6. **Health Practitioners**
See definition for clinicians

7. **Imprest Medications**
Restricted (Schedule 4) and controlled (Schedule 8) medications that are available on a hospital ward to be used as emergency stock.

8. **Opioid**
Opioids are a group of substances that resemble morphine in their physiological and/or pharmacological effects, especially in their pain-relieving properties.

9. **Opioid Naïve**
This term refers to an individual who has either never had an opioid or who has received occasional opioid doses for a two to three week period only.

10. **Palliative Care**
Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

11. **Renal Impairment**
Renal impairment is characterised by the kidney’s inability to filter wastes from the blood. It may be acute (occurring suddenly and usually reversible) or chronic (developing slowly over time as a result of permanent damage). Renal impairment renders some medications toxic unless an appropriate dose adjustment is made. When prescribing for the elderly, at least a mild degree of renal impairment may be assumed. The Australian Medicines Handbook describes three categories of impairment, based on creatinine clearance:
- severe impairment, CrCl < 10 mL/minute
- moderate impairment, CrCl 10-25 mL/minute
- mild impairment, CrCl 25-50 mL/minute
Anuria alone in the absence of recent renal biochemistry is enough to presume a degree of renal impairment.

12. **Resuscitation Plan - 7 Step Pathway**
The Resuscitation Plan - 7 Step Pathway provides a step-by-step process for developing a resuscitation and care plan and for clinical decision-making for patients
near the end of their lives. It is not a legal document but an extension of the medical notes. The form is used to document decisions (and the decision-making process used) about resuscitation and end-of-life clinical treatment and care.

13. **Specialist Palliative Care Services**

Services provided by clinicians who have advanced training in palliative care. The role of specialist palliative care services includes providing direct care to patients with complex palliative care needs, and providing consultation services to support, advise and educate non-specialist clinicians who are providing palliative care.

14. **Substitute Decision-Maker**

A Substitute Decision-Maker is an adult one can choose and appoint in an Advance Care Directive to make decisions about their future health care, living arrangements and other personal matters when the person giving the Advance Care Directive is unable to make their own decision(s).

An Enduring Guardian and a Medical Agent are considered to be Substitute Decision-Makers for the purposes of the *Advance Care Directive Act 2013*.

4. **Principles of the standards**

The following [National Safety and Quality Health Service Standards](#) (NSQHSS) apply:

- **Standard 1** – Clinical Governance
- **Standard 2** – Partnering with Consumers
- **Standard 4** – Medication Safety
- **Standard 5** – Comprehensive Care
- **Standard 6** – Communicating for Safety
- **Standard 8** – Recognising and Responding to Acute Deterioration

**Standard 1** aims to ensure:

- care provided by the clinical workforce is guided by current best practice and the clinical workforce have the right qualifications, skills and approach to provide safe, high quality health care
- patient rights are respected and their engagement in their care is supported.

**Standard 2** aims to improve quality and safety by partnering with consumers in service planning, designing care and evaluation.

**Standard 4** aims to ensure that competent clinicians safely prescribe, dispense and administer appropriate medicines and patients and/or carers are informed regarding treatment options, benefits and associated risks.

**Standard 5** ensures integrated screening assessment and risk identification processes for developing an individualised care plan to prevent and minimise the risks of harm in identified areas.

**Standard 6** aims to ensure timely, purpose-driven and effective communication and documentation that support continuous, coordinated and safe care for patients.

**Standard 8** aims to ensure a patient’s deterioration is recognised promptly, and appropriate action is taken and patients and/or carers are informed and can contribute to decisions about escalating care.

5. **General principles for prescribing in the last days of life**

The principles outlined in these prescribing guidelines are also applicable earlier in the end-of-life stage of illness.
Purpose:
This clinical guideline is an educational tool designed to promote clinicians’ general knowledge about medication in dying adult patients as well as to promote critical thinking about medication use in individual patients.

The guideline is intended to promote and systematise consistent, best practice medication use during the last days of life, in line with the following principles.

1. Patient-centred care
   > All other Guideline Principles arise from this principle.
   > Clinicians have a duty to ensure patients receive appropriate relief from distress. Therefore, individual, holistic patient assessment by a multi-disciplinary team is essential.
   > Patient-centred care involves ongoing communication and shared decision making with the patient and their nominated carers/family members to ensure care that is respectful and responsive to the needs, values and preferences of the person.

2. Timeliness
   > Symptoms during dying can often be anticipated. Therefore, regular or ‘as-needed’ anticipatory prescribing and administration of medications are encouraged in order to avoid distress.

3. Access
   > Appropriate medications need to be readily available and used appropriately, in all SA Health services.
   > A patient who is diagnosed as dying and requires rapid transfer to a community setting to die, will have access to the same medications as would have been used in the hospital setting, through providing the medication on discharge.
   > Medication orders should accompany the patient to ensure continuity of care.

4. Safety
   > Medication choices and dosages require consideration of individual patient factors.
   > Medication doses require titration according to patient need.
   > Frequent patient assessment and medication review is required.
   > Clinicians are encouraged to consider the clinical consequences and symptoms that may occur with cessation of regular medications in the last days of life, particularly when these are abruptly ceased due to the unavailability of the oral route.
   > Multidisciplinary assessment, decision-making and clinical handover processes are essential elements of prescribing medications for dying patients.

5. Effectiveness
   > Where two medications are equally efficacious, cost effectiveness is given consideration.
   > Medication administration occurs via the most appropriate route. This will generally be via the subcutaneous route of administration but may on occasion, be via other ‘non-oral’ routes, such as intravenous, rectal or via a Percutaneous Endoscopic Gastrostomy (PEG) tube.

6. Evidence-based
   > The limited evidence base for medications used in the last days of life is acknowledged. However, the highest available evidence base is utilised.
6. Detail

Dying patients are cared for in many settings. This guideline provides useful advice for
generalist clinicians treating adult patients assessed as being in the last days of their life,
and likely to die in a general hospital ward. The recommendations may also be useful in
other care settings. All patients have the right to adequate pain relief and symptom
control, in accordance with their wishes.

Anticipatory prescribing, or ordering medicines ahead of time, enables prompt
management when symptoms occur. Recognising symptoms enables timely treatment,
and continued review with the patient and nominated carers/family members ensures
further intervention if there is inadequate relief.

Prescribing guidelines for the pharmacological management of symptoms in
the last days of life

1. Before writing up medication orders:
   > Discuss the need for medications to support symptom management with the
     patient and/or substitute decision maker(s) and family.
   > Review the patient’s current medications and consider:
     > continuing any medications that are essential for symptom management
       via the subcutaneous route where possible
     > ceasing any non-beneficial or burdensome medications, and
     > the potential for the development of distressing withdrawal symptoms,
       rebound phenomena or recurrence of symptoms if specific medications are
       abruptly ceased (refer to Medication Cessation for Adults in the Last Days
       of Life fact sheet).
   > Be aware that the medications and doses outlined in these guidelines may be
     inadequate if the patient is already prescribed analgesics (particularly moderate to
     high dose opioids), anxiolytics, anti-emetics or anticonvulsants.
   > Check for allergies and for potential contraindications, interactions or side effects.

2. While writing up the medication orders:
   > Ensure that the reason for administering the medication is documented in the
     ‘indication’ box of each medication using terms consistent with those listed below
     under symptoms.

3. After medication orders are written up:
   > Ensure the patient is reviewed and commence medications in anticipation of, or as
     soon as, symptoms are identified.
   > Review treatment outcome for effectiveness and side effects.
   > Regularly review the management plan with the patient and/or substitute decision
     maker(s).
   > Ensure handover to all medical and nursing staff involved in the care of the
     patient; for example, at shift changes, on transfer of the patient to another ward or
     facility, or on discharge of the patient.

4. Common symptoms and treatment:
   4.1. Pain or dyspnoea
   Pain and dyspnoea can be distressing symptoms for the patient, family and carers
   and commonly occur in the terminally ill. They are considered together in this
   guideline because opioids are the preferred treatment for treating pain and dyspnoea.
   Assessing and managing pain in palliative care patients differs from pain management
   in the general population.14
Morphine is the opioid of choice.

> **Opioid-naïve patients:**
  > **Starting dose (pain):** morphine 2.5mg to 5mg by subcutaneous injection every hour as required.
  > **Starting dose (dyspnoea):** morphine 1mg to 2.5mg by subcutaneous injection every hour as required.

> **Patients already prescribed opioids:**
  > Convert regular oral opioid dose to the appropriate 24 hour subcutaneous dose and administer by a continuous subcutaneous infusion.

> **For patients with a contra-indication to morphine, such as known or suspected renal impairment, or an allergy to morphine:**
  > **Starting dose:** fentanyl 25 microgram to 50 microgram by subcutaneous injection every hour as required, or
  > **Starting dose:** HYDROmorphone 0.5mg to 1mg by subcutaneous injection every hour as required.

> **Practice Points:**
  > HYDROmorphone is approximately **FIVE** times more potent than morphine.
  > Commence on lowest dose and titrate up if required.
  > Whilst routine sedation monitoring and scores are not indicated in this setting, clinical observation using critical thinking and knowledge of opioids is still needed.

### 4.2. Anxiety or terminal restlessness
Prompt recognition and treatment of terminal restlessness and anxiety provides relief for the patient and their family and carers. Benzodiazepines are the preferred treatment in the following doses:

> **Starting dose:** clonazepam 0.25mg to 0.5mg by subcutaneous injection every 12 hours as required, or
> **Starting dose:** midazolam 2.5mg by subcutaneous injection every hour as required.

> **Practice points:**
  > Clonazepam has a long duration of action and is prone to accumulate and lead to over sedation.
  > Midazolam has a very rapid onset and short duration of action. It is preferred if amnesia and sedation are required. A continuous subcutaneous infusion is required to achieve a sustained effect.

### 4.3. Delirium or agitation
The primary aim of treatment is to reduce the patient’s distress by targeting the agitation or hallucinations.

The use of non-pharmacological strategies remains a critical strategy for the prevention and treatment of delirium\(^\text{15}\). Treatment of the underlying cause, for example sepsis or polypharmacy, should also be considered; however it may be inappropriate or impractical, such as in the last days of life. There is growing evidence of the lack of benefit, and potential harms of antipsychotics and benzodiazepines\(^\text{16}\). Findings from a recent study by AGAR et al\(^\text{17}\) suggest that antipsychotic medications may be harmful in treating mild to moderate delirium in palliative care patients with an estimated prognosis greater than one week. Given these findings, pharmacological treatment should be reserved for patients with distressing symptoms refractory to non-pharmacological measures, using the lowest dose possible.
> **Starting dose**: clonazepam 0.25mg to 0.5mg by subcutaneous injection, every 12 hours as required, or
> **Starting dose**: midazolam 2.5mg by subcutaneous injection every hour as required, or
> **Starting dose**: haloperidol 0.5mg to 1mg by subcutaneous injection, every two hours as required, to a suggested maximum of 5mg in 24 hours in moderate to severe delirium.

> **Practice points:**
> - An antipsychotic may be used as an alternative to or in addition to a benzodiazepine.
> - Avoid haloperidol in patients with Parkinson’s disease or if extrapyramidal side effects are distressing; olanzapine is preferred. Seek specialist palliative care clinician advice.

4.4. Nausea

The medication most commonly used for the treatment of nausea and vomiting in the dying patient is metoclopramide.

> **Starting dose**: metoclopramide 10mg by subcutaneous injection every four hours as required, to a suggested maximum of 30mg in 24 hours, or
> **Starting dose**: haloperidol 0.5mg to 1mg by subcutaneous injection every four hours as required; suggested maximum 5mg in 24 hours.

> **Practice points:**
> - Combining haloperidol and metoclopramide adds to side effect risk due to their additive anti-dopaminergic effects.
> - Metoclopramide is contra-indicated in suspected bowel obstruction
> - Avoid using metoclopramide or haloperidol in patients with Parkinson’s disease or if extrapyramidal side effects are distressing; ondansetron is preferred. Seek specialist palliative care clinician advice.

4.5. Gurgly / noisy breathing

Dying patients are often unable to clear their respiratory tract secretions by coughing and swallowing. This results in gurgly or noisy breathing. The level of evidence to support the use of anticholinergics in drying terminal secretions is poor, and palliative care practice relies on re-positioning the patient. However, if a medicine is deemed necessary use hyoscine butylbromide and review for effect.

> **Starting dose**: hyoscine butylbromide 20mg by subcutaneous injection every two to four hours as required.

> **Practice point:**
> - Commence treatment early and evaluate the response. Cease therapy if ineffective after three consecutive doses.

5. Clinical review

**Urgent clinical review is required if:**

> - there is inadequate relief of a symptom despite three maximum doses administered in succession at the shortest specified time interval, or
> - there is any other clinical concern.

6. Assistance

Further information about symptom management, prescribing or administering medications, or other related issues may be obtained from:

> **Therapeutic Guidelines: Palliative Care**
Urgent phone advice can be obtained from Specialist Palliative Services; contact via the hospital switchboard.

**Two-page prescribing reference guide**

A quick two-page prescribing reference guide is available for clinicians (Appendix One): *Prescribing Guidelines for the Pharmacological Management of Symptoms for Adults in the Last Days of Life*.

The guide includes built-in prompts and recommends when specialist palliative care support is indicated. There are links to the following fact sheet:

> Medication Cessation for Adults in the Last Days of Life

**Practice Points**

The prescribing principles outlined in this guideline may also be applicable in an earlier phase of a terminal illness, when patients are recognised as being at risk of acute deterioration and dying. Prescribing in anticipation of distressing symptoms accompanying acute deterioration should therefore be considered for patients with a **valid Resuscitation Plan - 7 Step Pathway (MR-Resus)** stating that the patient:

> is no longer for any treatment aimed at prolonging life, or
> is not for resuscitation and a limited trial of treatment has failed, or has a significant chance of failure, and no other treatment option is being considered.

This particularly applies if the patient is also documented to be 'MER Call No' or 'NOT FOR TRANSFER TO HOSPITAL'.

1. **Starting doses:**
   > Commence dosing with the lower dose in any given range.

2. **Opioid dose conversion:**

   Opioid doses require adjustment when:
   > changing the administration route, using the same opioid, or
   > changing the opioid.

   Refer to your local hospital protocol, Therapeutic Guidelines: Palliative Care, the Australian Medicines Handbook or SA Health website when calculating opioid dose conversion.

3. **Continuous Subcutaneous infusions:**

   Refer to your local hospital protocol when setting up and maintaining a syringe driver for administering medications by continuous subcutaneous infusion.

**7. Roles and Responsibilities**

1. **Chief Executive SA Health is responsible for:**
   > ensuring SA Health services are aware of this clinical guideline.

2. **Director of Medicines and Technology Programs will:**
   > establish, maintain and periodically review the Pharmacological Management of Symptoms for Adults in the Last Days of Life Clinical Guideline to ensure their consistency with current evidence and nationally agreed best practice.

3. **Chief Executives of Local Health Networks will:**
   > ensure the health services within their area of control have systems in place to ensure that clinical practice is in accord with this Clinical Guideline and accompanying education framework.
> ensure sufficient resources are in place to enable effective clinical practice, appropriate education and training for employees, and on-going evaluation of the effectiveness of pharmacological management of symptoms for adults in the last days of life
> delegate the day-to-day responsibility for establishing and monitoring the implementation of the guideline to the relevant senior managers.

4. **General Managers, Executive Directors, Heads of Service/Department/Streams and other Senior Managers will:**
> ensure that all clinical staff are aware of this Clinical Guideline
> provide organisational governance and leadership in relation to the pharmacological management of symptoms for adults in the last days of life processes and practice
> develop, implement and monitor local processes that support employees to effectively manage common symptoms occurring in the last days of life
> ensure that an education program in recognition and response to pharmacological management of symptoms for adults in the last days of life, is available
> ensure that incidents involving inappropriate management of symptoms for adults in the last days of life, are reported, investigated and action is taken in accordance with the SA Health Incident Management Policy Directive and Incident Management Guideline.

5. **Health care professionals will:**
> ensure they are familiar with the requirements of the Clinical Guideline
> adhere to the principles and aims of this guideline and ensure they operate in accordance with them
> participate in clinical teamwork that underpins effective recognition and response to the dying patient
> ensure timely, sensitive and respectful communication with patients, family and carers about recognising and treating common symptoms that occur in the last days of life
> ensure that any incidents relating to the pharmacological management of symptoms occurring for adults in the last days of life are reported via the appropriate process
> participate in education and training to ensure they have knowledge and skills relevant to their role in managing patients in the last days of life.

6. **Medical practitioners will, in addition to the responsibilities for health professionals:**
> ensure appropriate and timely prescribing of medications, including anticipatory prescribing, in anticipation of or in response to an adult patient suffering from distressing symptoms in the last days of life
> review treatment outcome for effectiveness and side effects
> ensure handover to all health professionals involved in the care of the patient; for example, at shift changes or transfer to another ward or facility.

7. **Nursing/Midwifery staff will, in addition to the responsibilities for health professionals:**
> ensure patients are monitored and commence medications as soon as symptoms are identified
> ensure handover to all health professionals involved in the care of the patient; for example, at shift changes or transfer to another ward or facility.
8. Pharmacists will, in addition to the responsibilities for health professionals:
   > review appropriateness of medication and doses
   > review treatment outcome for effectiveness and side effects and seek help if required
   > ensure medications are available when required.

8. Safety, quality and risk management

National Safety and Quality Health Service Standards

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9. Eligibility criteria

Inclusion
All SA Health clinical staff working within SA Health facilities.

Exclusion
All SA Health non-clinical staff working within SA Health facilities.

10. Administration

Consultation
1. End of Life Prescribing Working Group:
   > Dr Christine Drummond, Senior Consultant, Central Adelaide Palliative Care Service, Chair
   > Dr Chris Moy, General Practitioner
   > Mr Paul Tait, Lead Palliative Care Pharmacist, Southern Adelaide Palliative Service
   > Ms Josephine To, Senior Pharmacist, Aged Care, Rehabilitation and Palliative Care Services, Northern Adelaide Local Health Network
   > Dr Tim To, Palliative Care Consultant, Southern Adelaide Palliative Service
   > Dr Linda Foreman, Palliative Care Consultant, Central Adelaide Palliative Care Service
   > Mr David Stephenson, Renal Supportive Care Nurse Practitioner, Central Northern Adelaide Renal and Transplantation Service
   > Dr Holly Deer, General Practitioner, Country Health SA Local Health Network
> Ms Naomi Burgess, Director, Medicines and Technology Programs and Out of Hospital Pharmacy Services, SA Pharmacy
> Ms Kaye Barratt, Senior Pharmacist, Medicines and Technology Programs, SA Health
> Ms Jenny Pink, Director of Pharmacy, Country Health SA Local Health Network
> Ms Michaela del Campo, Senior Pharmacist, Central Adelaide Palliative Care Service
> Ms Laura Lunardi, Renal Supportive Care Nurse Practitioner, Central Adelaide Local Health Network

2. Local Health Network Drug and Therapeutics Committees; CALHN, CHSA LHN, NALHN, SALHN

3. SA Health Specialist Palliative Medicine Consultants from CAPS, NAPS & SAPS

4. SA Palliative Care Clinical Network

5. South Australian Medicines Advisory Committee (SAMAC)

Relevant Legislation

> Advance Care Directives Act 2013
> Consent to Medical Treatment and Palliative Care Act 1995
> Mental Health Act 2009
> Guardianship and Administration Act 1993
> Health Care Act 2008
> SA Controlled Substances (Poisons) Regulations 2011

Relevant SA Health Policies and Guidelines:

> Advance Care Directives Policy Directive (D0319)
> Resuscitation Planning – 7 Step Pathway Policy Directive (D0432)
> Recognising and Responding to Clinical Deterioration Clinical Directive (CD068)
> Recognising and Responding to Clinical Deterioration Clinical Guideline (CD 069)
> Consent to Medical Treatment and Health Care Policy Guideline (G0144)
> Providing Medical Assessment and/or Treatment where Patient Consent cannot be Obtained Policy Directive (D0265)
> SA Health Clinical Handover Policy Directive (D0211)
> SA Health Clinical Handover Guideline (G0099)
> Framework for Active Partnership with Consumers and the Community (D0306)
> Guide for Engaging with Consumers and the Community (G0126)
> Patient Incident Management and Open Disclosure Policy Directive

Other Relevant Policies and Standards

> The National Palliative Care Standards: [link]
11. Appendices

1. Prescribing Guidelines for the Pharmacological Management of Symptoms for Adults in the Last Days of Life

2. Fact sheet - Medication Cessation for Adults in the Last Days of Life

12. References


References for two-page Prescribing Guideline (Appendix One):


13. Document Ownership & History

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