All Wales Guidance: Care Decisions for the Last Days of Life

Symptom Control Guidance

Introduction

This guideline is an aid to clinical decision-making in managing common symptoms which can occur in people in the last days of life.

- **Regular assessment of symptoms remains important.**
  - Assess the patient for symptoms likely to occur in the last days of life (including pain, breathlessness, nausea and vomiting, anxiety, delirium, agitation, and noisy respiratory secretions).
  - **Consider reversible causes of symptoms** e.g. pain or agitation caused by urinary retention or constipation.
- **Management requires an individualised approach to the patient.**
  - An individualised approach may suggest a different medication/dose/strategy being indicated to those listed as 1st line in the guidance.
  - There should also be **consideration of non-pharmacological strategies** in addition to medication to manage symptoms e.g. positioning, environment, reassurance.
- **Medication considerations:**
  - **Prescribe anticipatory (including injectable) medication** with individualised indications for use, dosage and route of administration. Such injectable subcutaneous (SC) medication should be available for use in anticipation of the common symptoms in the last days of life even if these symptoms are not yet present.
  - **Continuous subcutaneous infusion (CSCI)** using a syringe driver/pump is indicated if a patient requires regular symptom control medication but can no longer take this by mouth or if there are concerns about absorption from the oral route.
  - It is good practice to **indicate a maximum dose in 24 hours**. This aids timely clinical review if frequent as-required doses are needed. The maximum dose indicated should include both as-required and regular medication (e.g. medication via CSCI).
  - Where CSCI is required the diluent should be water for injection. Contact pharmacy for advice if drug compatibility is a problem.

Contact your local specialist palliative care team (SPCT) for more advice.

With the OOH service outlined below, support is available 24/7

Out of Hours Specialist Palliative Medicine Telephone Advice Line:

- **North Wales**: 01745 585221
- **South East Wales** (via UHW switchboard): 02920 747747
- **South East Powys** (Royal Glamorgan / Royal Gwent Hospitals): 01443 443443 / 01633 234234
- **South West Wales** & **South West Powys** (Morriston Hospital): 01792 703412 / 01792 702222
- **Mid Powys** (St Michael's Hospice): 01432 852080
- **North Powys** (Severn Hospice): 01743 236565

For more information see:

- Current version of the BNF
- Current version of the PCF (Palliative Care Formulary)
- Palliative Care (Adult) Network Guidelines - PANG. Max Watson, Peter Armstrong, Craig Gannon, Nigel Sykes, Ian Back. 2017 Palliative Care Guidelines Plus (pallcare.info)

Acknowledgements: This document has been developed in accordance with NICE guidance 'Care of dying adults in the last days of life' (NG31, 2015, Overview | Care of dying adults in the last days of life | Guidance | NICE, NG142, 2019, Overview | End of life care for adults: service delivery | Guidance | NICE) and e-Learning for Health EOLC module (HEE elfh Hub (e-lfh.org.uk)). It describes pragmatic practice.

The management of pain with morphine in the last days of life

Is the patient in pain?

No

Is the patient prescribed regular oral morphine?

No

Prescribe in anticipation of the symptom developing:

- Morphine 2.5mg SC PRN up to 2 hourly

Yes

If the patient can no longer take oral morphine, convert to morphine CSCI:

1. Divide regular 24 hour oral morphine dose by 2 and prescribe as morphine via CSCI over 24 hours
2. Prescribe PRN SC morphine at 1/6th of the 24 hour CSCI dose up to 2 hourly

Yes

Is the patient prescribed regular oral morphine?

No

If the patient can take oral morphine PRN, continue this. In addition, prescribe morphine 2.5mg SC PRN up to 2 hourly.

If two or more PRN doses are given with effect in 24 hours, consider using morphine via CSCI over 24 hours.

Yes

1. Convert oral morphine to morphine CSCI by dividing the regular 24 hour oral morphine dose by 2; then, increase by approximately 20 to 30% (i.e. the equivalent of 2 PRN doses), and prescribe as morphine via CSCI over 24 hours. Stop regular oral morphine!
2. Prescribe PRN SC morphine at 1/6th of the 24 hour CSCI dose up to 2 hourly.

Note: If the patient is on **another regular opioid**, please see page 3 of 8.

Note: Caution required in **renal and/or hepatic impairment** – alternative dosing or medication choice may be required – see page 8 of 8.

Is the patient still in pain 24 hours after commencing morphine via CSCI?

Yes

Consider another 30% increase in morphine via CSCI (if pain is opioid-responsive). *Contact the SPCT for advice.*

Other pain management considerations in the last days of life – V 12 update

Diamorphine

- Diamorphine can be useful where large doses of opioid is needed as smaller volume is required.
- To convert oral morphine to SC diamorphine divide by 3:
  E.g. 30mg oral morphine = 10mg SC diamorphine
- All the other prescribing principles remain the same as morphine.

Note:

PRN doses will generally be approximately 1/6th of the total equivalent regular daily opioid dose.

Oxycodone

- Oxycodone may be useful where morphine not tolerated or contraindicated.
- Oxycodone is often favoured over morphine in mild to moderate renal impairment but caution still required.
- Oxycodone is generally contraindicated in moderate to severe hepatic failure.

For converting oral oxycodone to SC oxycodone two different conversions are commonly used. Either:

- Reduce dose by 1/3:
  E.g. 30mg oral oxycodone = 20mg SC oxycodone OR
- Reduce dose by 1/2:
  E.g. 30mg oral oxycodone = 15mg SC oxycodone

Contact the SPCT for advice if needed.

Fentanyl/Buprenorphine patch(es)

- Leave the patch in situ when commencing a CSCI and continue to change at prescribed frequency.
- PRN dose should be roughly 1/6th of the 24 hour opioid dose including both equivalent patch and CSCI doses.
- See BNF "prescribing in palliative care" section for conversion details or *contact the SPCT for advice* if needed.

Alfentanil

- Alfentanil can be used in moderate to severe renal impairment, *but only under the direction of specialist palliative care team.*
- To convert oral morphine to SC alfentanil divide by 30:
  E.g. 30mg oral morphine = 1mg alfentanil

Renal impairment / renal failure

Seek advice from SPCT or renal specialists for patients with end stage renal failure (ESRF).

- *Drug elimination will be significantly slower.*
- *PRNs alone may be sufficient.*

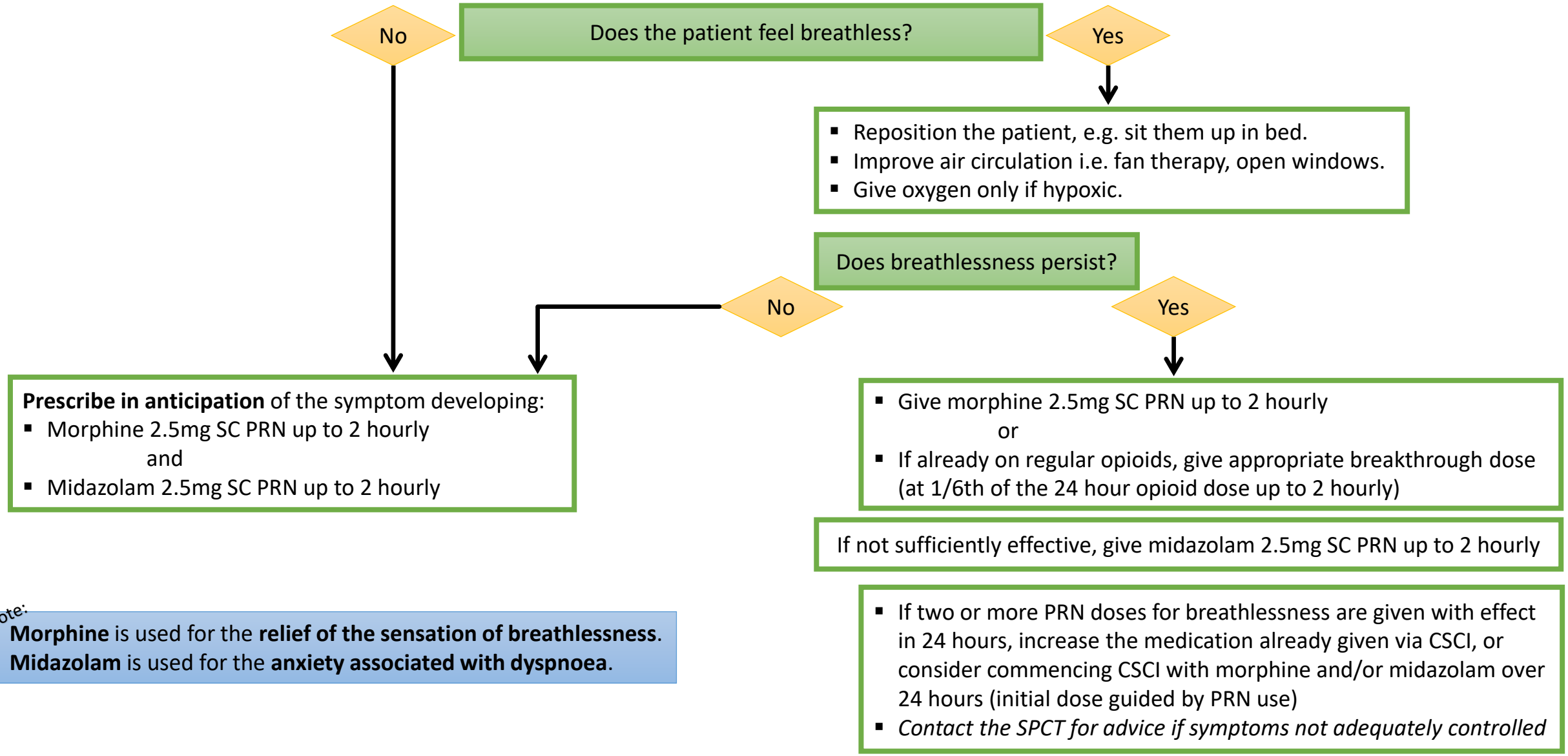
Pain:

- Oxycodone is an alternative to morphine in mild to moderate renal impairment (caution is still needed).
- Start with low doses: 1 or 2mg SC 4 hourly PRN and titrate slowly, monitoring the patient for toxicity. Seek SPCT advice if a CSCI is required for the safest analgesic.

Note:

Where **alfentanil** is used via CSCI the PRN dose will likely be morphine or oxycodone as alfentanil is too short-acting to be suitable for PRN use.

The management of breathlessness in the last days of life



Note:
Morphine is used for the **relief of the sensation of breathlessness**.
Midazolam is used for the **anxiety associated with dyspnoea**.

The management of agitation and restlessness in the last days of life

Is the patient restless or agitated?

No

Prescribe in anticipation of the symptom developing:

- For agitation (anxiety): Midazolam 2.5 or 5mg SC PRN up to 2 hourly
- For agitation (delirium): Haloperidol 2.5mg SC PRN up to 4 hourly

Yes

Consider and resolve where possible any underlying causes such as:

- Uncontrolled pain
- Full bladder
- Full rectum
- Breathlessness
- Anxiety and fear

If the patient's distress cannot be otherwise relieved:

1. If **delirium** and psychotic features are predominant (e.g. hallucinations, confusion, restlessness),
   - Give haloperidol 2.5mg SC PRN up to 4 hourly.
   - If two or more PRN doses of medication are given with effect in 24 hours, consider using the medication via CSCI over 24 hours.
   - Levomepromazine 6.25 or 12.5mg SC PRN up to 6 hourly is an alternative to haloperidol.

   If symptoms persist, contact the SPCT for advice. In certain circumstances, the SPCT may advise larger doses than the ones stated above.
2. Where **anguish and anxiety** are prominent,
   - Give midazolam 2.5 or 5mg SC PRN up to 2 hourly.
   - If two or more PRN doses of midazolam are given with effect in 24 hours, consider using midazolam 10mg via CSCI over 24 hours.
   - The CSCI dose of midazolam may need to be increased gradually up to 30mg over 24 hours.

   If symptoms persist, or if frequent PRN doses used, contact the SPCT for advice. In certain circumstances, the SPCT may advise larger or more frequent doses than the ones stated above.

Note:

Terminal agitation is often a feature of hyperactive delirium and therefore antipsychotics are commonly used first line, either alone or in combination with a benzodiazepine.

The management of noisy respiratory secretions ('rattle') in the last days of life

Does the patient have noisy respiratory secretions?

No

Prescribe in anticipation of the symptom developing:

- Hyoscine hydrobromide 400 micrograms SC PRN up to 4 hourly

or

- Glycopyrronium 200 microgram SC PRN up to 4 hourly

Yes

- Provide explanation and reassurance to those around the patient.
- Consider repositioning the patient
- Continue regular mouth care

Do noisy respiratory secretions persist?

No

Yes

Prescribe either hyoscine hydrobromide or glycopyrronium

1. Hyoscine hydrobromide
   - Give hyoscine hydrobromide 400 micrograms SC and repeat up to 4 hourly if needed.
   - If two or more PRN doses are given with effect in 24 hours, consider using hyoscine hydrobromide 1.2mg via CSCI over 24 hours.
   - If symptoms persist after 24 hours and there are no intolerable side effects, increase to a maximum of hyoscine hydrobromide 2.4mg via CSCI over 24 hours.
2. Glycopyrronium
   - Give glycopyrronium 200 micrograms SC and repeat up to 4 hourly.
   - If two or more PRN doses are given with effect in 24 hours, consider using glycopyrronium 600 microgram via CSCI over 24 hours.
   - If symptoms persist after 24 hours and there are no intolerable side effects, increase to a maximum of glycopyrronium 1.2mg via CSCI over 24 hours.

Note:

It may be helpful to explain to those present that noisy respiratory tract secretions can be a **normal part of dying** as fluid pools in the oropharynx. Consider whether this symptom need treating at all; most patients are unaware of secretions.

If the patient is distressed, follow breathlessness management guidelines.

The management of nausea and vomiting in the last days of life

Does the patient have nausea or vomiting?

No

Is the patient prescribed a regular oral anti-emetic?

No

Prescribe in anticipation of the symptom developing:

- Haloperidol 1mg - 1.5mg SC PRN 4 hourly and/or
- Cyclizine 50mg SC PRN 4 hourly (max 150mg/24 hours).

Yes

- Prescribe this anti-emetic via CSCI over 24 hours.
- Prescribe a PRN anti-emetic e.g. levomepromazine 6.25mg SC PRN 4 hourly (max 25mg/24 hours).

Note:

Considering the **likely cause** of nausea/vomiting to help decide the most appropriate 1st line anti-emetic:

- Toxic/ biochemical causes (e.g. renal failure, opioids, hypercalcaemia) – **haloperidol**
- Vestibular causes/ raised intracranial pressure – **cyclizine**
- Gastric stasis/ functional bowel obstruction – **metoclopramide**
- In **Parkinson's disease,** consider Ondansetron first line (see page 8 of 8)

Levomepromazine is a broad spectrum anti-emetic and is often used second or third line.

Yes

Is the patient prescribed a regular oral anti-emetic?

No

- Consider prescribing an anti-emetic via CSCI over 24 hours. (See examples of common regimes below.)
- Prescribe a PRN anti-emetic e.g. levomepromazine 6.25mg SC PRN 4 hourly (max 25mg/24 hours).
- *If symptoms persist, contact the SPCT for advice.*

Yes

- Prescribe this anti-emetic via CSCI over 24 hours.
- Prescribe levomepromazine 6.25mg SC PRN 4 hourly (max 25mg/24hours).
- If two or more PRN doses are given with effect in 24 hours, consider swapping to levomepromazine 12.5mg via CSCI over 24 hours.
- Prescribe a PRN SC anti-emetic.

Note:

Examples of common anti-emetic regimens for nausea/vomiting in the last days of life:

- Haloperidol via CSCI over 24 hours, Cyclizine or Levomepromazine PRN
- Cyclizine (+/- Haloperidol) via CSCI over 24 hours, Levomepromazine PRN
- Metoclopramide via CSCI over 24 hours, Levomepromazine PRN
- Levomepromazine via CSCI over 24 hours, Levomepromazine and/or Ondansetron PRN

Do not use Cyclizine and Metoclopramide together, as they counter-act each other.

Special considerations in the last days of life

Renal impairment / renal failure

Seek advice from SPCT or renal specialists for patients with end stage renal failure (ESRF). Drug elimination will be significantly slower. PRNs alone may be sufficient.

Pain: see page 3 for prescribing advice.

Other symptoms:

- Most symptom control medications can be used in renal impairment with caution.
- Glycopyrronium is preferred to hyoscine hydrobromide in ESRF.
- Consider starting with lower doses and/or longer dosing intervals, especially midazolam, haloperidol and levomepromazine.
- Refer to BNF for further information.

Seizures

- If there is a risk of seizures, prescribe buccal midazolam 10mg PRN.
- If on regular oral anti-epileptic medication(s) and unable to take these, *seek SPCT advice* regarding the best medicine to use via CSCI over 24 hours.

Heart failure

- Heart failure medications may offer significant symptom relief: So, where possible, do not abruptly stop these medications just because the patient is entering their last days of life.
- Opioids and midazolam can be helpful for breathlessness. Dose adjustment is needed if the patient has concurrent renal impairment.
- Avoid cyclizine.
- Diuretics can sometimes be given subcutaneously *– seek advice from the heart failure team or SPCT.*

Parkinson's disease

- Avoid anti-dopaminergic medications e.g. haloperidol, metoclopramide and levomepromazine.
- *Seek advice from Pharmacy, Care of the Elderly, Parkinson's CNS, or SPCT colleagues.*
- If unable to take oral Parkinson's medications consider using a rotigotine transdermal patch starting at 2mg/24 hours. *Please note that online dose conversion tables may be unreliable.*

Liver failure

Pain:

- Morphine is first-line strong opioid of choice
- Use lowest effective dose (reduced dosage and/or extended dose interval), titrate slowly and monitor for toxicity.
- e.g. morphine 2.5 mg SC PRN 2 hourly.
- Seek SPCT advice if concurrent renal impairment.

Other symptoms:

- Use lower doses of midazolam, haloperidol and levomepromazine.
- Use Glycopyrronium for secretions (avoid Hyoscine Hydrobromide).

Diabetes management

- For advice on diabetes management in the last days of life, see Supplementary document.
- *Seek advice from Diabetes team or SPCT if needed.*