Greater Manchester Integrated Care Partnership

Palliative Care pain & symptom control guidelines for adults

For staff providing generalist palliative care

Greater Manchester and Eastern Cheshire Strategic Clinical Networks

Sixth edition

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GMMMG Greater Manchester Medicines Management Group

Contents

Introduction

This is the sixth edition of the Greater Manchester and Eastern Cheshire Strategic Clinical Networks Palliative Care Pain and Symptom Control Guidelines. The level of detail provided is designed to meet the needs of generalist staff caring for individuals with palliative care needs in all settings i.e. hospital, community and care homes. Those working in Specialist Palliative Care are advised to consult the latest Palliative Care Formulary (Currently 8th Edition - PCF8) and local specialist guidelines for more detailed symptom management information.

The guidelines cover the management of particular symptoms and situations which individuals with palliative care needs may experience, as well as end of life care for Individuals with an advanced progressive illness. They should be used in conjunction with other national and regional formularies and guidelines, for example:

- British National Formulary (BNF).
- Greater Manchester Medicines Management Group Formulary or Central and Eastern Cheshire Medicines Management Team Formulary.
- Relevant National Institute for Health and Care Excellence (NICE) guidance.

General principles of symptom management in palliative care

Good palliative care is not just about supporting someone in the last months, days and hours of life, but about enhancing the quality of life for individuals and those close to them at every stage of the disease process from diagnosis onwards. A palliative care approach should be considered alongside active disease management from an earlystage in the disease process. Palliative care focuses on the person, not the disease, and applies a holistic approach to meeting the physical, practical, functional, social, emotional and spiritual needs of individuals and carers facing progressive illness and bereavement.

The guidelines provide information about the general approach to managing a symptom or situation. **However, management must be individualised according to the needs of the particular individual.**

Effective symptom management includes:

- **Evaluation –** e.g. the cause of the symptom, its impact on the individual's life and the treatments tried already.
- **Explanation –** to the individual and those close to them about the cause of the symptom and options for treating it.
- **Management –** individualised to the particular patient. Treat any reversible causes, use non-drug treatments where available, keep drug treatment as simple as possible, seek advice when necessary.
- **Monitoring –** review the impact of treatment regularly, paying attention to detail.

(Ref: Scottish Palliative Care Guidelines, Symptom Management in Advanced Cancer)

Seeking Specialist Advice

Throughout the guidelines there are numerous recommendations to seek specialist advice. For advice or further information, please contact your local hospice or Specialist Palliative Care Team.

Use of medications outside their marketing authorisation (formerly known as product licence).

Many drugs are used in palliative care outside their marketing authorisation at the prescriber's discretion. The inclusion of a drug, dose or treatment in these guidelines does not absolve the prescriber of their personal responsibility in providing treatment that they are confident with, can justify and that is tailored to the individual. For details of authorised indications see the current BNF/PCF8.

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Section 1

Specific Symptoms

Pain

1. Pain assessment

- Good assessment is vital for effective management.
- Many individuals with palliative care needs have more than one pain.
- Assess each pain separately and if possible identify the likely cause of the pain.
- Pain may be constant or intermittent (breakthrough pain).
- Discuss with the individual directly if possible.
- Assess regularly.

Ask about:

- Site and radiation - a body diagram can help.
- Character - a list of descriptive words may help.
- Onset, intensity and severity - a rating scale can help e.g. a numerical score where 0 = no pain and 10 = severe/overwhelming. **OR**
- A simple verbal rating scale – none/mild/moderate/severe.
- Timing and duration.
- Exacerbating factors.
- Relieving factors, including medication.
- Effect on function, sleep and mood.
- Response to previous medication and treatment.
- Associated symptoms.

- Consider using a structured pain assessment tool to record the individual's pain.
- Examine the individual to try and determine the cause of the pain(s), and any associated features e.g. abnormal sensation, tender hepatomegaly etc.
- Assess the impact of the pain on the individual and those closest to them. Consider if other factors, such as emotional, psychological or spiritual distress, are having an effect on pain perception (concept of total pain).
- Consider appropriate investigations to try and determine the cause of the pain.

Common causes of pain

- **Disease related:** direct invasion by cancer, distension of an organ, pressure on surrounding structures:
  - Bone pain: worse on pressure or stressing bone or weight bearing.
  - Nerve pain: burning, shooting, tingling, jagging, altered sensation, dermatomal distribution.
  - Spinal cord compression: back or spinal pain in a radicular "band-like" pattern.
  - Liver pain: hepatomegaly, right upper quadrant tenderness, referred pain in shoulder tip.
  - Raised intracranial pressure: headache, nausea or both, often worse in the morning or with lying down.
  - Colic: intermittent cramping pain. Consider bowel obstruction, bladder spasm.
- **Treatment-related:** chemotherapy neuropathy, constipation due to opioids, radiation-induced mucositis, arthralgia and myalgia (e.g. due to immunotherapy).
- **Debility:** pressure sores, severe cachexia, oral candidiasis.
- **Other unrelated illnesses:** arthritis, osteoporosis, vascular disease, gastritis.

(Ref: Scottish Palliative Care Guidelines)

Table 1: Common types of pain in palliative care patients and suggested management

Pain	Examples	Character	Initial management	Adjuvants	Consider
Deep somatic	Bone metastases	Gnawing, aching. Worse on moving or weight bearing	WHO Ladder	NSAIDs gabapentin/ pregabalin	Radiotherapy surgery; bisphosphonate
Visceral	Liver, lung, bowel	Sharp ache or deep, throbbing. Worse on bending or breathing.	WHO Ladder	Corticosteroid NSAIDs	Nerve Block; Surgery
Neuro-pathic	Nerve compression; Nerve damage; Bone metastases	Burning, shooting; sensory disturbance in affected area	WHO Ladder	Tricyclic antidepressant e.g. amitriptyline; anti-epileptic e.g. gabapentin/ pregabalin; SNRI e.g. duloxetine; Corticosteroid	Radiotherapy; TENS/PENS; Nerve block; Topical capsaicin
Smooth muscle spasm	Bowel obstruction; Bladder spasm	Deep, twisting, colicky (waves)	May be sensitive to opioid - variable	Anticholinergic - e.g. hyoscine butylbromide for bowel colic	Surgical relief of obstruction Non pharmacological interventions eg psychological or physical therapy and complementary therapies Consider patient allergies and preferences

2. Pain management – general points

- When feasible, useoralroute ('by the mouth').
- Set realistic goals, e.g. pain-free overnight/at rest/on movement.
- Give the individual and those close to them information and instructions about the pain and its management. Encourage them to take an active role in managing the pain.
- Review pain control regularly to monitor benefits of analgesia, titrate as appropriate and treat undesirable side effects.
- Manage the individuals' expectations regarding optimal pain management, as it may not be achievable for them to be pain-free at all times.
- Consider checking renal and liver function before initiating analgesics, if no recent blood results are available and monitor bloods in line with the individual's condition and titration of analgesia, as appropriate.

3. Pain management - the WHO Analgesic Ladder

(Ref: WHO Guidelines for the Pharmacological and Radiotherapeutic Management of Cancer Pain In Adults and Adolescents, 2018)

- The WHO analgesic ladder provides a **general guide** to pain management based on pain severity. However, it does not replace the need for individualised management based on careful assessment of an individual patient's pain.

Figure 1: The WHO three-step analgesic ladder with examples

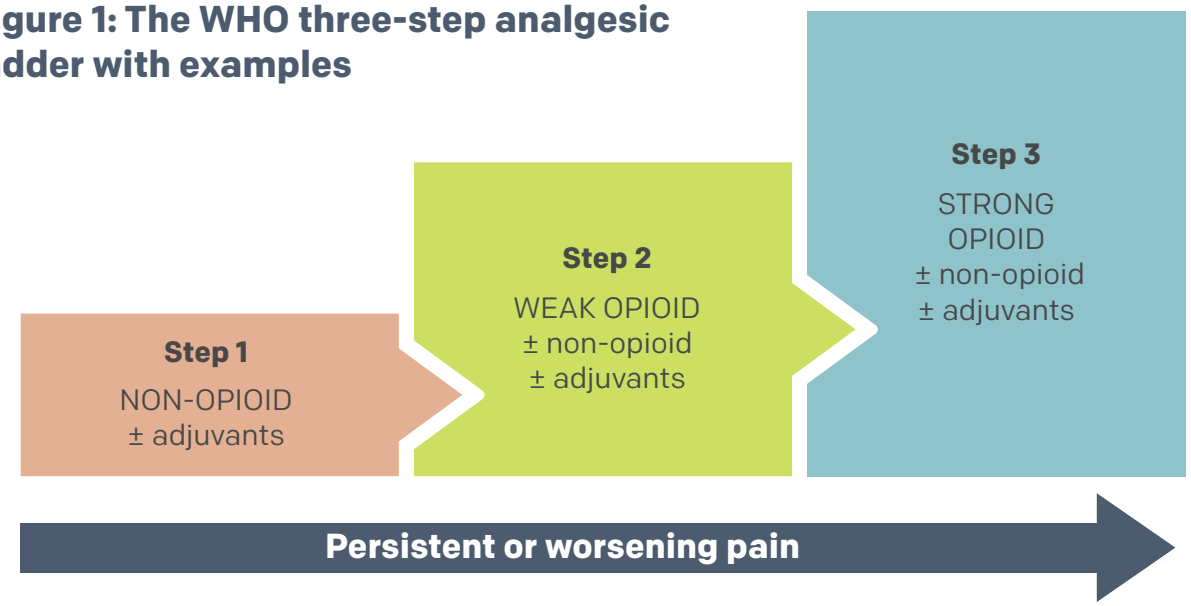


Table 2: Example of use of the WHO analgesic ladder

Patient on no analgesics - mild pain

Example - Step 1	Example - Step 2	Example - Step 3
Start **regular** paracetamol ■ usual dose 1g four times a day, but dose reduction is advisable in many palliative care patients *(see details below)* **and/or** NSAID e.g. celecoxib (PCF NSAID of choice), ibuprofen or naproxen	If pain is persistent or worsening ■ stop paracetamol if not helping pain ■ start codeine 30-60mg four times a day **regularly** *(Step 2 may be omitted – see details below)*	On maximum paracetamol and codeine, persistent or worsening pain ■ stop paracetamol if not helping pain ■ stop codeine ■ commence strong opioid e.g. oral morphine *(see details below)*

Choice of initial analgesic should take into account the cause and severity of pain

- For mild pain start at step 1.
- For moderate pain start at step 2 or step 3 (See section below re weak opioids).
- For severe pain, start at step 3.

Table 3: Principles of analgesic use

By mouth	Whenever possible, analgesics should be given by mouth.
By the clock	Doses of analgesic should be given at the appropriate regular time intervals, depending on the preparation and its duration of action.
For the individual	Management of an individual's pain requires careful assessment and a decision about appropriate treatment options.
With attention to detail	The first and last doses of the day should be linked to the individuals waking time and bedtime. Ideally, the individuals analgesic medicine regimen should be written out in full for the individual and those closest to them to work from and should include the names of the medicines, reasons for use, dosage and dosing intervals. The individual should be warned about possible adverse effects of each of the medicines they are being given.

WHO Analgesic Ladder Step 1 – Non-opioids

(i) Paracetamol *(Ref PCF8)*

- **Usual dosing –** For patients without risk factors for paracetamol hepatotoxicity, the standard regimen is 1g four times a day.
- **For patients with more than one hepatic risk factor (old age, weight less than 50kg, poor nutritional status, fasting/ anorexia, cachexia, chronic illness or chronic alcohol use) –** a reduced dose of 500mg oral four times a day, increased if necessary to a maximum of 3g per day in divided doses, is advisable.
- **Dispersible and effervescent paracetamol-containing tablets should be avoided in patients on a salt-restricted diet.**
- **For patients with severe renal impairment (eGFR<30ml/min) –** reduce dose (start 500mg oral 6 hourly with maximum 3g/24hrs) (Ref PCF8). For further guidance see section on **Symptom Management in patients with Renal Impairment**
- **For patients with severe hepatic impairment and no additional risk factors for paracetamol hepatotoxicity,** start with 500mg oral 8 hourly with maximum 3g/24 hrs *(Ref PCF8)*.

(ii) NSAIDs

NSAIDs are particularly useful when there is an inflammatory component to the pain. Options include:

- Celecoxib 100mg twice daily, increased if necessary to 200mg twice daily.
- Ibuprofen 200-400mg three times a day.
- Naproxen 250-500mg twice daily may also be used *(Ref: PCF8)*.

For further guidance see section on **Adjuvant Analgesics**

WHO Analgesic Ladder Step 2 - Weak Opioids *(Ref PCF8)*

There is no pharmacological need for weak opioids in cancer pain and moving directly from a non-opioid to a strong opioid is increasingly preferred in palliative care. Morphine (or an alternative strong opioid) at low doses generally provides quicker and better relief from cancer pain than weak opioids.

If considering prescribing a weak opioid, be aware that:

- Codeine has to be converted to morphine in the body to achieve an analgesic effect. Poor metabolisers of codeine may not experience analgesia. Ultrarapid metabolisers may experience toxicity.

Also see Table 42 - Dose conversions of weak opioids to oral morphine

WHO Analgesic Ladder Step 3 – Strong Opioids

Morphine is the strong opioid of choice for management of moderate to severe pain in palliative care patients, based on familiarity, availability and cost. The oral route is preferred as long as the patient has no problems with swallowing or absorption.

Other strong opioids are used mostly when:

- Morphine is not readily available.
- The patient has unacceptable side effects with morphine.
- The transdermal route is preferable.
- **The patient has severe renal impairment**

(Ref: NICE Guideline CG140 Palliative care for adults: strong opioids for pain relief, last updated August 2016 online **https://www.nice.org.uk/guidance/cg140** *PCF8)*

Factors to consider before prescribing strong opioids *(Ref: PCF8)*

There are generally no absolute contra-indications to the use of strong opioids for palliative care individuals with advanced progressive disease, provided the dose is titrated carefully against the individuals pain. However, for individuals who have palliative care needs with a longer prognosis, the potential side effects of long-term opioids and their limited effectiveness in chronic pain should be taken into consideration when deciding whether a strong opioid is the best treatment option. **See Box 2 - Management of long-term pain in palliative care patients**

Due to reports of serious incidents and the potential for toxicity with strong opioids, diligent prescribing, dispensing, administration, monitoring and counselling is required to reduce the risk of error and/or confusion, particularly between:

- Immediate-release and modified-release products.
- Products with different durations of action, e.g. 12 hourly versus 24 hourly modified-release products, 7-day versus 3- or 4- day transdermal patches.
- Products with both low and high strength concentrations, e.g. oral solutions, injections.
- Products with different bio-availabilities that are not interchangeable.

Information to be given to patients and carers

- When considering starting strong opioids, ask the individual and their carers about any concerns they may have about opioids e.g. addiction, tolerance, side effects, or fears that treatment implies the final stages of life.

Provide verbal and written information including:

- When and why strong opioids are used to treat pain.
- How effective they are likely to be.
- Taking strong opioids for background and breakthrough pain, addressing:
  - how, when and how often to take strong opioids
  - how long pain relief should last.
- Side effects and signs of toxicity.
- Safe storage.
- Follow-up and further prescribing.
- Information about who to contact out of hours, particularly during initiation of treatment.
- Information on strong opioids and driving *(see Box 1 below).*

Box 1 - Driving whilst taking strong opioids - The law on drugs and driving in the UK changed in 2015:

- Drivers are liable to prosecution if driving when impaired by drugs such as strong opioids, whether prescribed or illicit.
- Warn patients not to drive when starting or titrating strong opioids and other potentially sedating medications, or after taking a dose of strong opioid for breakthrough pain.
- Patients may drive when taking these medications once a stable dose is achieved, as long as they are not affected by drowsiness and not impaired by the disease itself.
- Patients should only drive if they feel 100% safe to do so.
- The police use roadside tests to look for illicit use of strong opioids and other drugs which may impair driving performance. **Advise patients to carry evidence to confirm that the medicines have been prescribed for them e.g. a repeat prescription.** *(Ref: PCF8)*
- See **www.gov.uk/drug-driving-law** for further information.

Box 2 - Management of long-term pain for individuals with palliative care needs

1. Some patients with a palliative diagnosis have a long prognosis and may have pain for a number of years. For such individuals, consideration must be given to the potential long-term side effects of any treatments they may be given.

2. There is particular concern about the use of opioids for chronic pain. The clinical evidence shows limited effectiveness and patient safety concerns due to the risks associated with long-term use of opioids such as fractures and falls, endocrine abnormalities, immunomodulation, opioid induced hyperalgesia and dependence.

3. Based on the clinical evidence Public Health England and the Faculty of Pain Medicine have advised:
   - Opioids are very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain.
   - A small proportion of people may obtain good pain relief with opioids in the long term if the dose can be kept low and especially if use is intermittent (however it is difficult to identify these people at the point of initiation).
   - The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit.
   - If a patient is using opioids but is still in pain, the opioids are not effective and should be discontinued, even if no other treatment is available.
   - Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain is essential.

3. Drug treatments:
   - Should be reserved for when non-pharmacological therapies alone have failed.
   - Should be given on a trial basis initially.
   - Should only be continued with good objective evidence of improved function (not just pain perception).

4. The BNF advises that the prescriber has three main responsibilities:
   - To avoid creating dependence by introducing drugs to patients without sufficient reason.
   - To see that the patient does not gradually increase the dose of a drug, given for good medical reasons, to the point where dependence becomes more likely.
   - To avoid being used as an unwitting source of supply for addicts and being vigilant to methods for obtaining medicines.

For further guidance, refer to the GMMMG Opioid Prescribing for Chronic Pain Resource Pack **NHS Greater Manchester Integrated Care - Opioid Prescribing for Chronic Pain: Resource Pack (gmmmg.nhs.uk)** or seek specialist advice.

Commencing oral morphine *(Ref: PCF8)*

- Individuals can be started on either an immediate-release or a modified-release preparation.
- ALWAYS prescribe an immediate-release morphine preparation for breakthrough pain when prescribing MR morphine.
- The starting dose should usually be calculated to give a greater analgesic effect than the medication already in use, taking into account individual circumstances.
- The individual must be monitored closely, including for side effects. **See section on Management of opioid side effects**
- Always prescribe laxatives alongside strong opioids (usually a stimulant laxative unless contra-indicated).
- Depending on individual circumstances, an antiemetic should be prescribed for regular or p.r.n. use.

Table 4 - Morphine preparations and recommended frequency

Generic morphine	Dose intervals	Morphine brand names
Immediate-release oral morphine 10mg/5ml solution; Actimorph ™ 1mg, 2.5mg, 5mg oro dispersible tablets 10mg, 20mg, 50mg, 100mg tablets	4 hourly	Refer to BNF for brands currently available. **In Primary Care –** prescribe morphine preparations by brand name as modified-release preparations have different release characteristics and patient familiarity with one brand is important in ensuring safety. *(Ref: GMMMG Generic Prescribing Guidelines v.1)* **In hospitals and hospices –** generic prescribing may be required if the unit does not stock the brand which the patient usually takes.
Immediate-release morphine concentrated oral solution* 20mg/ml *(only on specialist advice)*	4 hourly	
Modified-release oral morphine (12 hourly preparations) 5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg tablets; 10mg, 30mg, 60mg, 100mg, 200mg capsules;	12 hourly	
Modified-release oral morphine (24 hourly preparation) 30mg, 60mg, 90mg, 120mg, 150mg, 200mg capsules	24 hourly	
Morphine injection 10mg/ml, 15mg/ml, 30mg/ml*	4 hourly as breakthrough dose or over 24 hrs SC via syringe pump	

***NB.** Concentrated preparations of morphine **must be used with caution,** as there are significant risks of overdose if a concentrate product is used in error for a normal strength product. Please note capsules that contain granules can be opened and sprinkled on cold, soft food or given via gastric/gastrostomy tubes ≥16French (Fr) with open distal end or lateral pores).

Suggested starting doses of oral morphine

- **Patient opioid-naïve (except in frail/elderly/ renal impairment) –** start oral morphine 5mg immediate-release 4 hourly or modified-release 10mg 12 hourly.
- **Patient opioid-naïve and frail/elderly –** start oral morphine 2-2.5mg immediate-release 4 hourly.
- **Patient previously receiving a regular weak opioid** (e.g. codeine 240mg/24h or equivalent – see Appendix 1 – Opioid Conversion charts) - start oral morphine 5mg immediate release 4 hourly or modified-release 10mg 12 hourly, but less if suspected to be a poor metaboliser of codeine. In frail/elderly - use a lower starting dose of 2.5mg immediate-release 4 hourly or modified-release 5mg 12 hourly.
- **Patient with severe renal impairment –** morphine should be avoided if possible and an alternative strong opioid used instead - see section on Symptom Management in Patients with Renal Impairment

Box 3 - Management of breakthrough pain

Breakthrough pain may occur either as a result of a predictable event (incident pain) e.g. on movement, or spontaneously without predictable precipitating factors. Some breakthrough pains are short-lived and resolve spontaneously, in which case the individual patient may not need to take breakthrough analgesia.

(i) Management of breakthrough pain other than incident pain

- An immediate-release strong opioid should be prescribed 2-4 hourly when required, up to a maximum of 6 doses in 24 hrs. Where possible, the regular and "when required" opioid should be the same drug, e.g. morphine modified-release and immediate-release.
- Doses are typically 1/10 to 1/6 of the total daily regular dose, **but as with the regular dose, there is need to consider individual variation.**

Example – calculation of p.r.n. dose based on 1/6 of regular 24 hr dose

- Patient is taking morphine modified-release 30mg twice a day – therefore the "when required" dose is calculated as follows: 30mg (12 hr) x 2 = 60mg divided by 6 = 10mg 4 hourly when required.

- The "when required" dose should usually be increased when the regular dose is increased. If 3 or more "when required" doses are needed per day, consider a review of pain management. **SEEK SPECIALIST ADVICE IF REQUIRED**.

(ii) Management of incident pain

- Where possible, a predictable painful activity should be timed to coincide with the peak plasma concentration after a regular or "when required" dose of morphine. For example, a dose of immediate-release strong opioid could be given at least 30 minutes before the precipitant of the pain. If this is not effective, consider seeking specialist advice regarding alternative methods for managing incident pain.

Titrating oral morphine dose

- When adjusting the dose of morphine, use of "when required" doses should be taken into account.
- Check with the patient that the morphine is effective before increasing the dose.
- IN GENERAL, increments should not exceed 33-50% of current regular dose every 24 hrs regardless of p.r.n. usage. This may be difficult to achieve with lower doses.

Examples of dose titration

  - Immediate-release oral morphine: 5→7.5→10→15mg 4 hourly.
  - Modified-release oral morphine: 10→15→20→30mg twice a day.
- Upward titration of the dose of morphine should stop when either the pain is relieved or unacceptable side effects occur. In the latter case, switching to an **alternative strong opioid should be considered** **(see page 19).**
- If the individual was commenced on regular immediate-release morphine, once pain control is achieved consider conversion to modified-release morphine at the same 24 hr total dose.
- Consider seeking specialist advice if:
  - The dose of morphine has been titrated three times without achieving pain control.
  - The patient requires three or more "when required" doses per day.
  - The total daily dose of oral morphine exceeds 120mg over 24 hrs.
  - The patient is experiencing unacceptable side effects.

When the oral route is not available (e.g. individual is vomiting or unable to swallow)

- **If analgesic requirements are stable -** consider initiating transdermal patches. See sections on **Buprenorphine** and **Fentanyl**.
- **If analgesic requirements are unstable -** consider initiating SC opioids **(see below)** *(Ref: NICE Guideline CG140 Palliative care for adults: strong opioids for pain relief accessed via https://www.nice.org.uk/guidance/cg140) or* **SEEK SPECIALIST ADVICE IF REQUIRED.**

Initiating SC opioids

- **Morphine is recommended as the first line strong opioid for SC use for individuals, except for individuals who have been taking oral oxycodone or those with severe renal impairment.**
- If individual has constant pain, prescribe morphine as regular 4 hourly SC injections or as a 24 hr continuous subcutaneous infusion via a syringe pump.

Conversion from oral to SC morphine:

- Oral morphine 5mg ≈ SC morphine 2.5mg.
- However, wide inter-individual variation exists and each individual should be assessed on an individual basis. **See Appendix 1 – Opioid Conversion Charts for further information about strong opioid conversions**
- Breakthrough doses of 1/10 to 1/6 of the regular 24 hr dose of opioid should be prescribed 2-4 hourly SC when required.

4. Alternative Strong Opioids

When morphine cannot be used, alternative strong opioids commonly used in palliative care include:

- Oxycodone (oral or SC).
- Buprenorphine (transdermal).
- Fentanyl (transdermal).

NB. The transdermal route is only suitable if analgesic requirements are stable.

Box 4 - Opioid switching

Explicit guidance on switching opioids is difficult because both the reasons for switching and the individuals circumstances differ.

Conversion ratios are an approximate guide only. Many variables will affect the conversion e.g. age, renal/hepatic function, concurrent medication, comorbidity, duration of opioid treatment, pharmacokinetics of drugs.

Consider a dose reduction of 50% when switching between opioids especially if

- Patient is on a high dose of opioid (e.g. morphine dose ≥1g/24h or equivalent).
- Opioid dose has been escalated rapidly.
- Patient is frail or elderly.
- Patient is experiencing side effects from the current opioid.

In such circumstances, "when required" doses can be used to make up any deficit while re-titrating to a satisfactory dose of the new opioid.

SEEK SPECIALIST ADVICE on the most appropriate alternative strong opioid and the appropriate conversion ratio.

See Appendix 1 – Opioid Conversion Charts for further information.

Oxycodone

- Oxycodone is a strong opioid and is more potent than morphine so care should be taken when prescribing.
- It is licensed for moderate to severe pain in individuals with cancer and post-operative pain and for the treatment of severe pain requiring the use of a strong opioid.

Place in therapy

- Moderate to severe pain with unacceptable level of side effects with morphine.
- Breakthrough medication for individuals using fentanyl or buprenorphine patches who have experienced an unacceptable level of side effects with morphine or have renal impairment.

Cautions

- Use first line in mild to moderate impairment, avoid in severe impairment.
- Use cautiously in mild hepatic impairment, avoid if possible in moderate to severe hepatic impairment.

Table 5 – Oxycodone preparations and recommended frequency

Generic oxycodone	Dose intervals	Oxycodone brands
Immediate-release oral oxycodone 5mg/5ml liquid 5mg, 10mg, 20mg capsules	2-4 hourly	Refer to BNF for brands currently available. **In Primary Care –** prescribe oxycodone preparations by brand name as modified-release preparations have different release characteristics and patient familiarity with one brand is important in ensuring safety. *(Ref: GMMMG Generic Prescribing Guidelines v.1)* **In hospitals and hospices –** generic prescribing may be required if the unit does not stock the brand which the patient usually takes.
Immediate-release oxycodone concentrated oral solution 10mg/ml* *(only on specialist advice)*	4 hourly	
Modified-release oral oxycodone preparations 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg tablets	12 hourly	
Oxycodone injection 10mg/1ml, 1ml & 2ml ampoules	4 hourly as breakthrough dose or over 24 hrs SC via syringe pump	
Concentrated oxycodone injection 50mg/ml, 1ml ampoules* ***(only on specialist advice)***	4 hourly as breakthrough dose or over 24 hrs SC via syringe pump	

***NB.** Concentrated preparations of oxycodone **must be used with caution,** as there are significant risks of overdose if a concentrate product is used in error for a normal strength product.

Dosing

- **If the individual is opioid naïve,** start either:
  - **Regular** immediate-release oxycodone liquid 1mg- 2.5mg 4 hourly.
  - **OR** modified-release oxycodone tablets 5mg twice a day.
- **If switching from an alternative strong opioid to oxycodone** – see Box 4 – Opioid switching and Appendix 1 – Opioid Conversion Charts. **SEEK SPECIALIST ADVICE IF REQUIRED.**
- **NOTE:** Oxycodone is approximately twice as potent as morphine when given orally (e.g. Oral oxycodone 10mg is approximately equivalent to oral morphine 20mg).
- Immediate-release oxycodone liquid should be prescribed for breakthrough pain at 1/10-1/6 of the total daily regular dose, 2-4 hourly when required. See Box 3 – Management of breakthrough pain for further guidance.

  Example – calculation of "when required" dose based on 1/6 of regular 24 hr dose:
  - Individual is taking oxycodone modified-release tablets 15mg twice a day - the "when required" dose is 30 divided by 6 = 5mg 4 hourly when required.

Titrating oral oxycodone dose

- When adjusting the dose of oxycodone, use of "when required" doses should be taken into account.
- Check with the individual that the oxycodone is effective before increasing the dose.
- IN GENERAL, increments should not exceed 33-50% of current regular dose every 24 hrs regardless of p.r.n. usage. This may be difficult to achieve with lower doses.
- **Examples of dose titration**
  - Immediate-release oral oxycodone: 5→7.5→10→15mg 4 hourly.
  - Modified-release oral oxycodone: 10→15→20→30mg twice a day.
- Upward titration of the dose of oxycodone should stop when either the pain is relieved or unacceptable side effects occur. In the latter case, switching to an alternative strong opioid should be considered.
- If the individual was commenced on regular immediate-release oxycodone, once pain control is achieved consider conversion to modified-release oxycodone at the same 24 hr total dose.
- **Consider seeking specialist advice if:**
  - The dose of oxycodone has been titrated three times without achieving pain control.
  - The individual requires three or more "when required" doses per day.
  - The total daily dose of oral oxycodone exceeds 60mg over 24 hrs.
  - The individual is experiencing unacceptable side effects.

Buprenorphine

- Although buprenorphine has both opioid agonist and antagonist properties, analgesic effects are generally similar to morphine.
- Constipation may be less severe.
- Only transdermal preparations of buprenorphine are recommended for routine use in palliative care.

Place in therapy

- Unacceptable level of side effects with morphine.
- Severe renal impairment (no centrally active metabolites).
- Tablet phobia or poor compliance with oral medication.
- Oral route is inappropriate.
- Individuals who have chronic cancer pain and low strength 7 day patches may be an option for opioid naïve patients.
- Frail/elderly.

Cautions

- Patches not suitable for acute pain or rapidly changing pain because of the time it takes to reach therapeutic levels. Only use for chronic stable pain.

Dosing

- There are multiple preparations of transdermal buprenorphine available varying in strength and length of action.
- 5micrograms of buprenorphine is equivalent to 12mg of oral morphine.

Table 6 – Buprenorphine preparations and recommended frequency of patch change

Frequency of patch change	Strengths available
7-day patch	5, 10, 15, 20micrograms/hr
4-day patch	35, 52.5, 70micrograms/hr
3-day patch	35, 52.5, 70micrograms/hr

- **If the patient is opioid-naïve -** commence a low patch strength i.e. buprenorphine 5-10micrograms/hr (equivalent to oral morphine 12-24mg/24hrs).
- **For individuals who are switching from an alternative opioid -** refer to Box 4 – Opioid Switching and Appendix 1 – Opioid Conversion Charts
- **Breakthrough analgesia -** For Individuals using transdermal buprenorphine, either immediate-release morphine or immediate-release oxycodone may be used for the management of breakthrough pain. The preferred choice will depend on a number of factors - see Box 3 – Management of breakthrough pain and Appendix 1 – Opioid Conversion Charts **CONSIDER SEEKING SPECIALIST ADVICE.**

Titrating buprenorphine patch dose

- Wait at least 72 hrs after starting a buprenorphine patch or increasing the patch strength before adjusting the dose. If after this time the individual needs 2 or more "when required" doses of analgesia for breakthrough pain the dose can be increased to the next strength patch.
- **Consider seeking specialist advice if:**
  - The dose of buprenorphine has been titrated three times without achieving pain control.
  - The Individual requires three or more "when required" doses per day.
  - The individual is on a buprenorphine patch above 52.5micrograms/hr.
  - The individual is experiencing unacceptable side effects.

If switching from a buprenorphine patch to an alternative strong opioid

- Note that on removal of the patch significant blood concentrations of buprenorphine persist for at least 24 hrs, therefore do not commence an alternative long acting opioid medication for at least 12 hrs. **SEEK SPECIALIST ADVICE IF REQUIRED.**

Management of patients with a buprenorphine patch in the last days and hours of life

- It is usual practice to leave the buprenorphine patch in place in the management of individuals in the last days and hours of life – see Pain Algorithm 4: Patient using fentanyl or buprenorphine patches becomes unable to swallow and **SEEK SPECIALIST ADVICE.**

Fentanyl

- Fentanyl is a strong opioid analgesic that is approximately 100 to 150 times more potent than oral morphine.
- Constipation is less severe than with other strong opioids.
- Better tolerated in renal impairment.
- Available as transdermal patches.
- Other formulations are also available e.g. transmucosal and parenteral preparations, but these are **ONLY TO BE PRESCRIBED ON SPECIALIST ADVICE.**

Place in therapy

- Unacceptable level of side effects with morphine.
- Severe renal impairment (no centrally active metabolites).
- Tablet phobia or poor compliance with oral medication.
- Oral route is inappropriate.

Cautions

- Patches not suitable for acute pain or rapidly changing pain because of the time it takes to reach therapeutic levels (12 – 24 hrs). Only use for chronic stable pain.
- Not suitable for opioid naïve individuals. Consider buprenorphine patches as alternative.
- Be aware of the potency of fentanyl in comparison with other opioids – a 25micrograms/hr fentanyl patch is equivalent to about 60mg of oral morphine per 24 hrs. **Check the dose carefully.**

Dosing

There are multiple brands of transdermal fentanyl available – refer to BNF for details.

Table 7 – Transdermal fentanyl preparations and recommended frequency of patch change

Frequency of patch change	Strengths available
Usually every 72 hrs, though on specialist advice some individuals may require patch changes every 48 hrs *(Ref: Scottish Palliative Care Guidelines)*	12, 25, 37.5, 50, 75, 100 micrograms/hr

- **If the individual is opioid-naïve –** fentanyl patches are not generally recommended as a first-line strong opioid. Consider buprenorphine patches for opioid naïve patients requiring transdermal strong opioid.
- **For individuals who are switching from an alternative opioid –** refer to Box 4 – Opioid Switching and Appendix 1 – Opioid Conversion Charts
- Approximately 10% of individuals previously taking regular morphine may experience withdrawal symptoms after changing to fentanyl giving symptoms of shivering, restlessness and bowel cramps. Pain control is not affected and the symptoms can be managed initially with breakthrough doses of immediate release strong opioid. **SEEK SPECIALIST ADVICE IF SYMPTOMS PERSIST.**
- As fentanyl causes less constipation than morphine or oxycodone, if a switch to fentanyl is made consider halving the dose of laxatives and then adjust further according to need.
- **Breakthrough pain –** For individuals using transdermal fentanyl, either immediate- release morphine or immediate-release oxycodone may be used for the management of breakthrough pain. The preferred choice will depend on a number of factors - see Box 3 – Management of breakthrough pain and Appendix 1 – Opioid Conversion Charts. **CONSIDER SEEKING SPECIALIST ADVICE.**

Box 5 – Fentanyl/Buprenorphine Safety Concerns

There have been several safety alerts highlighting the risk of unintentional opioid toxicity and overdose of fentanyl/buprenorphine, due to inappropriate dosing or accidental exposure.

Overdose Risk

- Inappropriate strength of fentanyl patches prescribed in opioid naïve patients.
- Failure to remove an old fentanyl patch before applying a new one.
- Exposure of the patch application site to a heat source (e.g. hot bath, hot water bottle, electric blanket, heating pad etc) or increased body temperature (e.g. fever).
- Concommitant use of fluconazole/miconazole (both can increase fentanyl efficacy).

Accidental exposure

- Poorly affixed fentanyl patches transferring to another person.
- Children applying improperly disposed patches to their body, believing the patches to be stickers or plasters.

Advice for healthcare professionals:

- Always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
  - Not exceeding the prescribed dose.
  - Following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application.
  - Not cutting patches.
  - Avoiding exposure of patches to heat including via hot water (bath, shower).
  - Ensuring that old patches are removed before applying a new one.
  - Storing patches (including used ones) safely, out of the sight and reach of children.
  - Disposing of them in a way which minimises accidental exposure to the drug, by folding the patch so the adhesive side adheres to itself and then placing it back in the original sachet. It can then be placed in household waste.
- Ensure that patients and caregivers are aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately (by dialling 999 and requesting an ambulance) if overdose is suspected.
- In patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hrs after patch removal.

Ref: MHRA (Oct 2018). Transdermal fentanyl patches: life-threatening and fatal opioid toxicity from accidental exposure, particularly in children **https://www.gov.uk/drug-safety-update/transdermal-fentanyl-patches-life-threatening-and-fatal-opioid-toxicity-from-accidental-exposure-particularly-in-children**

Titrating fentanyl patch dose

- Wait at least 48 hrs after starting a fentanyl patch or increasing the patch strength before adjusting the dose. If after this time the individual needs 2 or more "when required" doses of analgesia for breakthrough pain the dose can be increased by 12 to 25micrograms/hr.
- **Consider seeking specialist advice if:**
  - The dose of fentanyl patch has been titrated three times without achieving pain control.
  - The individual requires three or more "when required" doses per day.
  - The individual is on a fentanyl patch above 50micrograms/hr.
  - The individual is experiencing unacceptable side effects.

If switching from a fentanyl patch to an alternative strong opioid

- Note that on removal of the patch significant blood concentrations of fentanyl persist for at least 24 hrs, therefore do not commence an alternative long acting opioid medication for at least 12 hrs. **SEEK SPECIALIST ADVICE IF REQUIRED.**

Management of individuals with a fentanyl patch in the last days and hours of life

- It is usual practice to leave the fentanyl patch in place in the management of individuals inthe last days and hours of life – **see Pain Algorithm 4: Patient using fentanyl or buprenorphine patches becomes unable to swallow** and **SEEK SPECIALIST ADVICE.**

5. Management of Opioid Side Effects

- If side effects are intractable and reducing the individual's quality of life or limiting analgesic titration, consider changing to an alternative opioid. **SEEK SPECIALIST ADVICE.**
- If toxicity develops on a previously tolerated opioid dose, consider precipitating factors e.g. renal impairment, other biochemical abnormalities, sepsis or drug interactions.
  - Ensure the patient is well-hydrated.
  - Investigate for possible causes and treat as appropriate.
  - If pain is controlled, reduce the opioid dose by a third.
  - If pain is not controlled, **SEEK SPECIALIST ADVICE.**

Table 8 – Management of opioid side effects

Side effect	Management
Constipation (very common)	Prevent by prescribing concurrent laxative (give a stimulant laxative first line unless contra-indicated, add a softener if necessary **(see Constipation section of guidance)**.
Nausea and vomiting	Prescribe either haloperidol 500micrograms (use liquid rather than tablet due to expense) to 1.5mg at night OR metoclopramide 10mg three times a day. Prescribe for 5 days then stop if asymptomatic. Symptoms often improve after 5-7 days. If symptoms persist despite an antiemetic, consider other possible causes before switching to another opioid.
Drowsiness	Warn individual that drowsiness and poor concentration may occur at start of therapy, and when dose is increased, but usually reduces after a few days.
Delirium	Decrease dose if possible; consider adjuvant analgesic or alternative opioid. If symptoms persist, start haloperidol 500micrograms at night PO/SC *(use liquid rather than tablet due to expense)*, if necessary increase in increments of 500micrograms – 1mg – maximum 15mg/24 hrs dependent on renal and hepatic function **(see Delirium section of guidance)**. Higher doses can be used under specialist advice.
Myoclonus	Decrease dose if possible; if this dose of opioid is essential consider a benzodiazepine e.g. diazepam 2-5mg oral three times a day when required/ midazolam 2.5mg SC 4 hourly when required (dependent on renal and hepatic function). Seek specialist advice if not resolved in three doses.
Hallucinations	Decrease dose if possible; consider adjuvant analgesic or alternative opioid.
Dry mouth (very common)	Inform individual and advise good oral hygiene **(see Oral Care section of guidance)**
Respiratory depression	Unlikely to occur if opioids used and monitored correctly. Naloxone may be required **only if severe respiratory depression with reduced conscious level &/or hypoxia. (See section on management of respiratory depression)**.

6. Use of naloxone for the management of respiratory depression caused by prescribed therapeutic use of opioids

Ref: PCF8 Quick Clinical Guide: Reversal of opioid induced respiratory depression, Scottish Palliative Care Guidelines (last updated April 2020)

- Respiratory depression is uncommon if opioid doses are titrated carefully.
- If a patient on strong opioids becomes drowsy, consider whether this may be due to a cause other than the opioid e.g. deterioration of their illness/dying, or metabolic changes such as hypercalcaemia or uraemia.
- In patients receiving opioids for pain relief, traditional IV doses of naloxone (e.g. 400micrograms stat) should only be used in immediately life-threatening situations (i.e. unresponsive patient with/near respiratory arrest).
- In other circumstances, careful titration using lower doses of naloxone (e.g. 20-100micrograms IV) should be used to avoid a severe acute withdrawal syndrome and, in those receiving opioids for analgesia and hyperalgesia.
- Due to higher affinity and prolonged receptor binding of buprenorphine, higher doses of naloxone must be used - consider seeking specialist toxicology advice.

See Table 9 – Management of respiratory depression caused by strong opioids

Administering naloxone in care settings where there is no immediate access to the IV route.

- Naloxone may be administered intramuscularly (IM) when IV access is not immediately available.
- Onset of naloxone IM is 2-5 minutes (onset of naloxone IV is 1-2 minutes).
- 100micrograms naloxone IM should be given and repeated after five minutes if there is no improvement with the first dose.
- An IV line should be sited as soon as possible.

Ongoing treatment for patients who have required naloxone

- After the last dose of naloxone, monitor level of consciousness and respiratory rate every 15 minutes for 2h, then hourly for 6h after immediate-release opioid or hourly for 12h after modified-release opioid or opioid with a long half-life.
- Further boluses of naloxone may be required because naloxone is shorter-acting than morphine and other opioids – **SEEK SPECIALIST ADVICE.**
- **Review opioid regimen**
  - Consider possible causes for the opioid toxicity e.g. excessive dosing, drug interactions, reduced elimination due to renal impairment.
  - Wait until there is a **sustained improvement in consciousness and respiratory rate** before restarting a lower dose of opioid.

Seeking further advice

24 hr advice can be obtained from the National Poisons Information Service, 0344 892 0111

Table 9 – Management of respiratory depression caused by strong opioids

Situation	Respiratory rate (RR) (breaths/min), conscious level & oxygen saturation (SaO_2)	Recommended action(s)	Points to consider
Mild respiratory depression	RR ≥ 8 AND easily rousable, SaO_2 at baseline level	Monitor respiratory rate and SaO_2 Watch and wait Assess Airway/Breathing/Circulation	For patients in the community, consider admission to hospital if they cannot be monitored closely in their current setting. Consider omitting or reducing the next regular dose of opioid. This includes a patch or CSCI.
Severe but not immediately life-threatening respiratory depression	RR < 8 AND/OR difficult to rouse, AND/OR SaO_2 below baseline level	Assess Airway/Breathing/Circulation Administer oxygen if necessary to maintain SaO_2 >95% or normal target saturation levels. **Give naloxone** 100micrograms IV every 2 mins until RR ≥ 8. Lower doses of naloxone e.g. 20 micrograms IV are sometimes used. Titrate dose against level of respiratory function, (i.e. to achieve a respiratory rate ≥8 breaths/min and no cyanosis) **and** level of consciousness (i.e. patient easily rousable; they do not have to be fully alert).	For patients in the community, **URGENT** admission to hospital is required. Omit the next regular dose of opioid. This includes a patch or CSCI. Following review of opioid regimen, restart lower dose once conscious level has maintained improvement and respiratory rate is satisfactory. **SEEK SPECIALIST ADVICE IF REQUIRED.**
Immediately life-threatening respiratory depression	Minimal respiratory effort and patient unconscious	Assess Airway/Breathing/Circulation Administer oxygen if necessary to maintain SaO_2 >95% or normal target saturation levels. Give naloxone, administering each dose over 30 seconds. Assess after 1 minute and, if no response, move to next dose: Start with 400micrograms IV →800micrograms →800micrograms →2-4mg. If no response to 2-4mg, consider alternative diagnosis.	For patients in the community, **URGENT** admission to hospital is required. Omit the next regular dose of opioid. This includes a patch or CSCI. Following review of opioid regimen, restart lower dose once conscious level has maintained improvement and respiratory rate is satisfactory. **SEEK SPECIALIST ADVICE IF REQUIRED.**

If the combination of parameters of respiratory rate, conscious level or SaO_2 are not covered by advice above, then use clinical judgement – **SEEK SPECIALIST ADVICE**

7. Adjuvant Analgesics

Table 10 – Adjuvant analgesics

(Ref: PCF8, GMMMG Neuropathic Pain Guideline) https://gmmmg.nhs.uk/wp-content/uploads/2022/05/GMMMG-Neuropathic-Pain-Guidance-final-version-8.2-for-GMMMG-website.pdf

Also see Table 36 – Adjuvant analgesics in renal impairment.

Drug	Use	Comments
1st line		
▪ Amitriptyline 10-75mg at night. Start at 10mg; increase to 25mg after 3-7 days, and then by 25mg increments every 1-2 weeks, as tolerated and required.	Neuropathic pain May be combined with antiepileptic if either alone is only partially effective.	Onset of action may be less than a week in neuropathic pain. Helps sleep. Contraindicated in patients with history of arrhythmias; use with caution in other cardiovascular diseases. Monitor for side effects (See BNF). If helpful but poorly tolerated, consider duloxetine (see below).
▪ Gabapentin 300mg daily titrated to 300mg three times a day initially. ▪ Then by 300mg steps every 3-7 days up to 1200mg three times a day maximum.	Neuropathic pain May be combined with tricyclic antidepressant if either alone is only partially effective.	Dose increases may be limited by side effects (e.g. sedation, dizziness). **In renal impairment and frailer patients -** use lower starting dose (e.g. 100mg) and slower titration by 100mg steps rather than 300mg; **CONSIDER SEEKING SPECIALIST ADVICE.** N.B. Risk of abuse, now a Schedule 3 controlled drug.
▪ Pregabalin 75mg twice daily. If necessary increase by 75mg twice a day at intervals of 3 to 7 days, up to a maximum of 300mg twice a day.	**Use pregabalin if gabapentin effective but not tolerated due to side effects or if tablet burden is an issue.**	Titration may be limited by side effects (e.g. sedation, dizziness) Consider commencing lower doses e.g. 25mg twice daily in patients with renal impairment, concurrent opioids and frailer patients. Increase in 25mg twice daily increments every 3-7 days. N.B. Risk of abuse, now a Schedule 3 controlled drug.
▪ Duloxetine 30mg daily - increase in 30mg steps every 1 - 2 weeks, max 120mg daily.	Neuropathic pain and/or anxiety disorder	May be considered when other treatments have failed or not been tolerated, or as an alternative to gabapentin/pregabalin in patients with a history of substance misuse, particularly in a prison setting.
2nd line: If partial response to either tricyclic or antiepileptic, then consider **combination** of tricyclic and antiepileptic *(Ref: PCF8).*		

Other options for specific causes of neuropathic pain

Drug	Use	Comments
Corticosteroids		
■ Dexamethasone 8-16mg a day oral in 1-2 doses. ■ **Give in the morning to avoid sleep disturbance.** ■ Dexamethasone is 7 times more potent than prednisolone.	To decrease peri-tumour oedema e.g. ■ Nerve compression. ■ ↑ intracranial pressure. ■ Spinal cord compression. ■ Organ infiltration.	Dose will depend on specific cause – **see Table 33 – Corticosteroid use for the management of specific symptoms**. May also increase appetite, affect mood. Prescribe gastroprotection (e.g. a PPI) unless contra-indicated. ■ Stop if no response after 7 days. ■ Review and reduce dose every 3-7 days to avoid side effects. ■ Check blood glucose for 3 days initially then weekly. *(Ref: PCF8; End of Life Diabetes Clinical Care Recommendations 3rd edition, November 2021 accessed online:* **https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/public/2021-11/EoL_TREND_FINAL2_0.pdf** *)*

NSAIDs		
■ Ibuprofen 200-400mg three times a day (weak anti-inflammatory but lowest side effect risks). ■ Naproxen 250-500mg twice a day (low side effect risks but good anti-inflammatory).		■ Consider risks/Contra-Indications before using. ■ GI side effects and risk of thrombotic events (MI/Strokes) are reduced if lower doses are used for the shortest duration possible. ■ Prescribe gastroprotection (e.g. a PPI) unless contra-indicated. ■ If no improvement after 1 week, stop. ■ Monitor regularly for side effects, will need regular u&e checks if not in the dying phase. ■ If the patient is on chemotherapy consult the oncology team before commencing.
■ Cox-2 inhibitors e.g. Celecoxib 100mg twice daily, increased if necessary to 200mg twice daily (PCF8 NSAID drug of choice).	Bone pain/ soft tissue infiltration	■ Consider risks/Contra-Indications before using. ■ For high GI risk patients, prescribe gastroprotection (e.g a PPI) unless contra-indicated. ■ If no improvement after 1 week, stop. ■ Monitor regularly for side effects, will need regular u&e checks if not in the dying phase. ■ If the patient is on chemotherapy consult the oncology team before commencing.

NB the use of steroids and NSAIDS together should be avoided re increased risk of GI bleeding.

See Appendix 3 for analgesics to be initiated by Specialist Palliative Care only.

Other approaches to pain management (consider seeking specialist advice)

- Radiotherapy/chemotherapy/hormone therapy.
- Transcutaneous electrical nerve stimulation (TENS).
- Massage.
- Relaxation.
- Psychological support.
- Neural blockade/epidural/intrathecal analgesia. Neuro-destructive blocks e.g. intrathecal alcohol/ phenol, cordotomy.

Nausea and Vomiting

Approximately 70% of individuals with advanced cancer and up to 50% of individuals with non-malignant chronic disease have nausea and/or vomiting.

Assessment

- Review history, recent investigations and medication.
- Examination - look for underlying causes and likely physiological mechanisms.
- Investigations - only if outcome will affect management.

Table 11 - Management of reversible/treatable causes of nausea and vomiting

Cause	Specific management
Drugs – e.g. opioids, PPIs, NSAIDs, SSRIs, antibiotics, iron, digoxin	Stop unless the drug is essential, when an antiemetic can be added
Uncontrolled pain	Analgesia - non-oral route until vomiting settles
Anxiety	Determine fears; explain; anxiolytic – e.g. lorazepam
Cough	Cough suppressant
Urinary retention	Catheterise
Constipation	Laxatives
Liver metastases	Corticosteroids; anticancer treatment
Raised intracranial pressure	Corticosteroids (e.g. dexamethasone)
Electrolyte disturbances	Correct if possible and appropriate
Hypercalcaemia	Rehydration and intravenous bisphosphonate
Hydronephrosis	Urinary diversion or stent
Oral/oesophageal candidosis	Antifungal (fluconazole, nystatin, miconazole)
Infection (respiratory, UTI)	Antibiotic
Gastritis	Stop irritant drug if possible; add PPI
Bowel obstruction	See separate section below

Management

- Assess most likely cause(s) of symptom; may be more than one.
- Underlying cause may be apparent in 20-30% of cases.
- Remove or treat reversible cause(s) if identified.
- If vomiting or severe nausea, use a non-oral route for symptom control until nausea & vomiting is controlled. Consider changing to oral route after 3 days of good control.
- Avoid triggers (e.g. food smells); aim for small frequent meals.

Antiemetic Therapy

- Decide most likely **cause,** and prescribe appropriate antiemetic regularly and p.r.n. **(See below Table 12 – Management of specific causes of nausea and vomiting** and Table 13 - Antiemetics)
- Reassess, regularly (initially daily).
- Titrate dose as needed.
- If no response, reassess cause
  - **If likely cause is unchanged -** consider alternative route of administration, alternative antiemetic or broad-spectrum antiemetic.
  - **If likely cause has changed -** try appropriate antiemetic for that cause.
  - May need combinations of antiemetic therapy.
- If symptoms still not improving **SEEK SPECIALIST ADVICE.**
- For patients with renal impairment, see Table 37 – Antiemetics in renal impairment

Table 12 – Management of specific causes of nausea and vomiting

Cause	Type of antiemetic	Drug (see Table 13 for dosing & further guidance)
Gastritis, gastric stasis or functional bowel obstruction (peristaltic failure)	Prokinetic	Metoclopramide
Chemical cause e.g. opioids, hypercalcaemia, renal impairment	Antiemetic acting principally in chemoreceptor trigger zone	Haloperidol
Vestibular symptoms	Antiemetic acting principally in vestibular centre and vomiting centre	Cyclizine
Raised intracranial pressure	Antiemetic acting principally in vestibular centre and vomiting centre	Cyclizine in conjunction with dexamethasone
Multifactorial/unknown/ refractory	Broad spectrum	Levomepromazine

Ref: PCF8 Quick Clinical Guide: Nausea and Vomiting, Scottish Palliative Care Guidelines

Table 13 – Antiemetics (Based on info from PCF8 drug monographs and BNF)

Drug	Main action of drug	Suggested dose & route	Recommended use/comments
FIRST LINE			
Cyclizine † ‡	Antihistamine Antimuscarinic Action at vestibular system and vomiting centre	Oral – 50mg twice a day to three times a day & 50mg when required (max dose 150mg/24h) SC – 75-150mg/24h by CSCI & 25-50mg 4-6 hourly when required (max dose 150mg/24h)	Cerebral irritation; vertigo; visceral distortion/obstruction; oropharyngeal irritation PO bioavailability is 50%, so PO:SC conversion ratio is 2:1 May be **added to** haloperidol Constipating; delays gastric emptying
Haloperidol * ◊	Dopamine antagonist acts at chemoreceptor trigger zone	Oral – 500micrograms - 1.5mg at night & 500micrograms 2 hourly when required, maximum dose 10mg/24h (higher doses may be used - seek specialist advice) SC – 500micrograms - 1.5mg at night or CSCI & 500micrograms 2 hourly when required, maximum dose 10mg/24h (higher doses may be used – seek specialist advice)	Biochemical disturbance (drug, metabolic, toxic) May be **added to** cyclizine Use liquid rather than 500micrograms tablet due to expense
Metoclopramide * † ◊	Dopamine antagonist & prokinetic Acts at chemoreceptor trigger zone & GI tract	Oral – 10mg three times a day (higher doses may be used under specialist advice) SC – 30mg/24h by CSCI (higher doses may be used – seek specialist advice) p.r.n. doses usually 6hourly (can be given more frequently under specialist advice)	Gastric stasis, reflux, delayed gastric emptying NB. MHRA alert (2013) limiting dose and duration of use does not apply to palliative care **https://bnf.nice.org.uk/drug/metoclopramide-hydrochloride.html#importantSafetyInformations** Risk of acute dystonic reaction, especially in young women. Avoid in mechanical bowel obstruction, colic

Drug	Main action of drug	Suggested dose & route	Recommended use/comments
SECOND LINE			
Levomepromazine * ◊	Broad spectrum anti-emetic Dopamine, histamine, muscarinic antagonist (not prokinetic)	Oral – 6.25mg-25mg at night & 6.25mg 2 hourly when required (max 25mg/24 hrs) Can be given in divided doses Note can be sedative in higher doses; seek specialist advice SC – 5mg-25mg at night or by CSCI	**Replaces** previous antiemetic Usually second-line - may be used earlier if sedation is not a problem or is desirable (**more likely** in doses ≥ 25mg/24h) *Caution – epilepsy (lowered seizure threshold)*
Ondansetron (or other 5HT3 antagonist, doses differ)	$5HT_3$ antagonists	Oral – 4-8mg twice daily (higher doses may be used – seek specialist advice) SC – 16mg/24h by CSCI (higher doses may be used – seek specialist advice)	Mainly in chemotherapy, post-operatively Adjuvant in renal failure, gastric irritation or biochemical stimulus **Add to** previous antiemetic Note – profoundly constipating
Dexamethasone	Reduces inflammatory response, ? central effect	Oral – 8-16mg each morning or 2 divided doses, morning and lunchtime SC – 6.6mg-13.2mg each morning or 2 divided doses **(use 3.3mg/ml strength) stop if no benefit after 1 week otherwise taper down to lowest effective dose.**	Adjuvant antiemetic; cerebral oedema; liver metastases **Add to** previous antiemetic **See Corticosteroid section**

* - In Parkinson's syndromes, domperidone may be used in place of dopamine antagonists.
† Note - avoid adding cyclizine or other antimuscarinic drugs to metoclopramide, as they inhibit its prokinetic action.
‡ - Cyclizine, like other antimuscarinic drugs, may aggravate heart failure and should be avoided in those at risk.
◊ - Haloperidol, Metoclopramide and Levomepromazine can lower seizure threshold - consider using cyclizine as first line if patient has a history of seizures

Gastro-Intestinal Obstruction

Occurs in approximately 15% of all individuals with cancer; more frequent complication if advanced intra-abdominal cancer (e.g. colon up to 31%; ovary -50%).

Site of obstruction is small bowel in 50%; large bowel in 30%; both in 20%.

Table 14 - Common causes of intestinal obstruction

Mechanical	Functional
Cancer	Autonomic nerve damage
Constipation	Drugs – opioids, anticholinergics
Bowel wall infiltration	Postoperative
Stricture formation	Metabolic - hypokalaemia; hypercalcaemia
Extrinsic compression	Radiation fibrosis

Intestinal obstruction has mechanical or functional cause(s) – often more than one.

- Degree of obstruction may be partial or complete.
- Onset may be over hours or days; initial intermittent symptoms may worsen and become continuous, or may resolve spontaneously (usually temporarily).

Assessment/Signs and symptoms of bowel obstruction

- Nausea and vomiting (earlier and more profuse in higher obstruction).
- Pain due to abdominal colic or tumour itself.
- Abdominal distension (especially distal obstruction).
- Altered bowel habit (from constipation to diarrhoea due to overflow).
- Bowel sounds (from absent to hyperactive and audible).
- Digital rectal examination to assess faecal impaction.
- Radiology - if needed to distinguish faecal impaction, constipation and ascites.
- Rarely an emergency - take time to discuss situation with patient and family to allow them to make an informed choice about management.

Management

- Bowel obstruction may be reversible in some patients.
- For all patients - consider whether surgery may be appropriate, see Table 15 – Assessing whether surgery may be appropriate
- If surgery is not appropriate, see Table 16 - Medical management of gastro-intestinal obstruction symptoms

Table 15 – Assessing whether surgery may be appropriate

Consider if:	Poor surgical outcome likely if:	Surgery is likely contra-indicated if:
■ Individual willing. ■ Discrete and easily reversible mechanical cause of obstruction. ■ Prognosis >12 weeks if treated.	■ Previous abdominal radiotherapy. ■ Small intestinal obstruction. ■ Multiple sites. ■ Extensive disease. ■ Poor condition. ■ Cachexia. ■ Poor mobility.	■ Carcinomatosis peritonei. ■ Findings suggest intervention is futile. ■ Poor physical condition. ■ Short prognosis <12 weeks.

Table 16 - Medical management of gastro-intestinal obstruction symptoms

SEEK SPECIALIST ADVICE if individual is not responding or the situation is complex.

Treatment to try and resolve the obstruction	
Corticosteroids	■ Consider dexamethasone 8-16mg oral or 6.6-13.2mg SC daily (using 3.3mg/ml injection) if no contra-indications. ■ If no improvement after 5-7 days, or adverse side effects present, then stop steroids. ■ If improvement shown, reduce steroid dose gradually as symptoms allow.
Management of nausea +/- vomiting	
Functional or partial obstruction	■ Metoclopramide: 30mg/24h by CSCI (higher doses may be used on specialist advice). ■ Contraindicated in complete bowel obstruction. ■ Stop if precipitates colic; use antiemetics below.
Complete obstruction	**Use either:** ■ Cyclizine 75-150mg/24h by CSCI & 25-50mg SC 4-6 hourly when required, maximum dose 200mg/24h). ■ Haloperidol 500micrograms-1.5mg SC at night or by CSCI & 500micrograms SC 2 hourly when required, maximum dose 5mg/24h (higher doses may be used with specialist advice). **Or** use cyclizine & haloperidol in combination. **Or** substitute both with SC levomepromazine 5mg-25mg at night & 5mg SC 2 hourly when required, maximum dose 25mg/24 hrs.
Persistent/high volume vomiting	**SEEK SPECIALIST ADVICE**

Management of other symptoms	
Heartburn/acid reflux	Consider SC H2 blocker or PPI if available (specialist prescribing).
Constipation precipitating obstruction	■ Docusate sodium – maximum licensed dose is 500mg/day, but up to 200mg three times a day orally may be used (Ref PCF8). ■ Consider macrogols if impaction (can give up to 8 sachets dissolved in 1 litre of water taken over less than 6 hrs. Repeat for up to 3 days). ■ Laxatives risk inducing colic – ensure hyoscine butylbromide injection is available if needed. ■ Avoid stimulant, bulk or fermenting laxatives e.g. lactulose.
Abdominal pain	■ Follow pain control guidelines, using non-oral route.
Abdominal colic	■ Hyoscine butylbromide 60-120mg/24h by CSCI then **SEEK SPECIALIST ADVICE.** ■ Stop prokinetic drugs; bulk-forming, osmotic or stimulant laxatives.
Hydration	■ Assess need for IV or SC fluids on an individual patient basis. ■ Many are not dehydrated. ■ May still absorb oral fluid above level of obstruction. ■ SC fluid can be given up to 1-2L/24h.
Dietary intake	■ Allow low residue food and drink. ■ Parenteral nutrition generally has no role in patients with limited options for anti-cancer treatment or poor performance status (Ref: PCF8). However, it may be appropriate in selected cases with longer prognosis - multidisciplinary team decision.

Note – Higher doses of some drugs above may be used **– SEEK SPECIALIST ADVICE.**

Nasogastric intubation

- Do not use nasogastric (NG) tube for obstruction in patients with advanced illness **routinely.**
- May be considered for decompression of upper gastrointestinal (GI) tract if surgery is being considered, or faeculent vomiting which is responding poorly to drug treatment.
- Prolonged NG aspiration with IV fluids is not recommended as it rarely gives sustained relief. Use medical measures described above.

Venting percutaneous gastrostomy

- May be considered for symptom relief in individuals whose vomiting is not relieved by pharmacological means, though risk of blockage.

Ongoing Management

- Review treatment at least daily.
- If the obstruction does not resolve, the aim should be to:
  - Control pain and nausea.
  - Minimize vomiting as far as possible.
  - Permit sufficient oral fluids to maintain hydration.
- Discharge home, or management at home, requires careful planning.

Constipation

Constipation is usually caused by more than one factor. The more risk factors, the more likely constipation will occur.

Causes to consider

- Drug induced – review medication.
- Dehydration - review diuretics and fluid intake.
- Reduced mobility – e.g. patient may not be able to get to the toilet; lack of privacy.
- Altered dietary intake - review.
- Hypercalcaemia – **See Palliative Care Emergencies section of guidance page 70**
- Neurological **e.g. metastatic spinal cord compression, see page 73**; autonomic neuropathy).
- Gastro-intestinal obstruction – **See section on gastrointestinal obstruction**

Assessment

- History – past and present bowel habit, including use of laxatives and date of last bowel action; current medication; other causative factors.
- Abdominal palpation and auscultation, digital rectal examination.
- Investigations - if needed for treatment, e.g. abdominal x-ray; check calcium levels.
- **For intractable constipation, SEEK SPECIALIST ADVICE.**

Management

- Prevention is the best management of constipation.
- Generally, all patients prescribed an opioid should also be prescribed a stimulant laxative, with the aim of achieving a regular bowel movement without straining every 1–3 days.
- Encourage a good oral fluid & dietary intake, including fruit and fruit juice. The NHS.UK website provides guidance on increasing fibre intake **https://www.nhs.uk/live-well/eat-well/how-to-get-more-fibre-into-your-diet/**
- Use oral laxatives first line.
- About one third of individuals with palliative care needs, need rectal measures, either because of failed oral treatment or electively (e.g. frail bedbound patients, patients with paralysis) *(Ref: PCF8)*.
- Rectal measures should be avoided, where possible, in individuals who are neutropenic or thrombocytopenic, because of the risk, respectively, of infection or bleeding *(Ref: PCF8)*.

Table 17 – Pharmacological Management of Constipation

Clinical Situation	Agent type and examples	Comments
Soft bulky stools - low colonic activity	**Oral stimulant laxatives:** Bisacodyl 5mg at night increasing to 20mg at night. Senna 15mg at night increasing to 30mg twice a day. Sodium picosulfate liquid 5-10mg at night increasing to 30mg daily.	Start with low dose and titrate. May cause abdominal cramp. Suppositories also available.
Colon full, no colic	**Stimulant ± softening agent –** e.g. senna + docusate sodium.	Docusate sodium oral solution may cause a bitter aftertaste or burning sensation, minimised by drinking plenty of water after taking.
Colon full and colic present	**Macrogols e.g Movicol®, Laxido®** 1 sachet in 125ml water once daily, increase to 2-3 sachets per day.	Require adequate oral fluids to be effective.
Hard dry faeces	**Softening agents –** docusate sodium up to 500mg/day available as capsules or oral solution. Arachis oil enema (avoid if known nut allergy).	Useful in sub-acute obstruction. Higher doses may stimulate peristalsis.
Hard faeces - full rectum, colon	**Stimulant plus softener,** e.g. bisacodyl tablets or senna tablets/liquid plus docusate sodium. 2nd line – Macrogols (e.g. Movicol®, Laxido®) 2-3 sachets/day. 3rd line - Glycerol 4g suppository and Bisacodyl 10mg suppository If ineffective - Sodium Citrate enema	Require adequate oral fluids to be effective.
Faecal impaction	Arachis oil retention enema **(avoid if known nut allergy)** ± phosphate enema 2nd line – Macrogols (e.g. Movicol®, Laxido®) 8 sachets dissolved in 1 litre of water taken over less than 6 hrs Repeat for up to 3 days.	Warm before use. Give arachis oil at night, followed by phosphate enema in the morning. Keep dissolved solution in a refrigerator for maximum of 6 hrs. Limit to 2 sachets/h in heart failure.

For opioid-induced constipation resistant to the above methods – SEEK SPECIALIST ADVICE.

N.B. In paraplegic patients - Need to avoid either faecal incontinence or impaction. It can be preferable to provide a twice/thrice weekly rectal regime with the use of suppositories/enemas rather than oral laxatives. Follow specialist guidance depending on location of spinal injury.

Diarrhoea

Increase in the frequency of defecation and/or fluidity of the faeces.

Prevalence: 4% of individuals with advanced cancer (up to 50% of individuals on or after chemotherapy).

Assessment and management

- Establish cause - usually evident from history.
- Review diet (note some gastrostomy feeds can cause diarrhoea). Seek dietitian advice if required.
- Review medication.
- Clinical assessment includes a rectal examination and inspection of the stool.
- Exclude:
  - Infective cause.
  - Constipation/faecal impaction with overflow - a plain abdominal x-ray if overflow may help if suspected. Treat as for constipation **(see page 40).**
- Other investigations may be appropriate if the results will significantly affect management.
- If the individual is in the last days of life, treat symptomatically but do not investigate.

Table 18 – Management of diarrhoea according to cause

Cause	Management
Drugs - e.g. laxatives, magnesium antacids, PPI, NSAID	Review medication and stop if possible
Antibiotics - altered bowel flora	Stop antibiotic if possible Stool sample to exclude Clostridium difficile
Infection	Fluid and electrolyte support Stool sample for culture - treat with appropriate drug for identified bacteria
Overflow (constipation, partial obstruction)	Identify. Treat underlying constipation. Soften stool if partial obstruction. Avoid **specifically** constipating treatments
Acute radiation enteritis	Seek oncology advice
Chemotherapy	Seek oncology advice
Immunotherapy induced colitis	Seek oncology advice urgently
Secretory diarrhoea (e.g. tumour, fistula)	Seek oncology advice. May need surgical advice for fistula
Surgical resection (stomach, ileal, colon), bile salt diarrhoea	Colestyramine (on specialist advice)
Steatorrhoea	Pancreatic enzyme +/- PPI (reduces gastric acid destruction of enzymes)

Use of loperamide and codeine for diarrhoea

- Give loperamide 2mg after each loose stool. Maximum dose is 16mg a day.
- If not controlling diarrhoea, rapidly change to 2mg four times a day.
- This can be increased to 4mg four times a day if required.
- Substitute codeine 30mg four times a day orally if ineffective.
- Thereafter consider a combination of loperamide + codeine and seek specialist advice.

Ref: Scottish Palliative Care Guidelines

Fatigue

Fatigue could be a consequence of underlying disease process (e.g. cancer) or as a consequence of treatment (e.g. chemotherapy, radiotherapy).

Other causes of fatigue include:

- Anaemia: consider blood transfusion if appropriate.
- Dehydration: consider IV/SC hydration.
- Pain: optimise pain control.
- Iatrogenic: opioids, benzodiazepines, post chemotherapy.
- Poor nutrition: consider dietician referral, nutritional supplement drinks. Consider checking B12 and folate levels.
- Depression: consider antidepressants.
- Endocrine abnormalities: Addison's disease (consider steroid replacement) and hypogonadism (consider testosterone replacement where appropriate. Consult with an endocrinologist).

- Fatigue is often a combination of reversible and irreversible causes.

Management

- Initial management of fatigue should be to consider reversible causes.

Non-pharmacological management

- Paced exercise: individual programme of moderate aerobic exercise –fast walking, swimming, cycling.
- Cognitive behavioural therapy.
- Mindfulness programme.
- Acupuncture.

Pharmacological management

- Corticosteroids reduce the effect of pro-inflammatory cytokines, may stimulate appetite and improve a general feeling of wellbeing. Use should be considered on carefeul consideration of risks vs benefits.
- Consider need for gastric protection.
- Dexamethasone - 2-6mg orally once daily in the morning; assess after one week.
  - if beneficial, continue - reduce weekly to lowest effective dose.
  - if no benefit after 1 week, then stop.
  - side effects: fluid retention, candidosis, myopathy, insomnia, gastritis and steroid-induced diabetes. **See Corticosteroids section for more details**.

Anorexia

Anorexia - a reduced desire to eat/loss or absence of appetite.

Causes

- Paraneoplastic effect of cancer.
- Cachexia of chronic disease.
- Impaired gastric emptying.
- Medication - e.g. opioids, SNRIs.
- Poor oral hygiene, candidosis.
- Altered taste or smell.
- Anxiety, depression, delirium.
- Any of the causes of nausea.

Management of cancer-related anorexia

- Treat reversible causes.
- Explain that anorexia is common in cancer and is often difficult to manage.
- Listen to fears and anxieties of individual and family/carers - failure to eat can cause fear and conflict.
- Dietary advice.
  - Eat energy rich foods such as full fat milk, yoghurt and spreads.
  - Food fortification e.g. add cream to soups, butter to vegetables etc.
  - Encourage snacking and more frequent small portions rather than large meals.
  - Advise carers to avoid offering excessive amounts of food.
- Consider asking for dietician advice unless prognosis is short.

Pharmacological management

Corticosteroid may be considered on a risk/benefit balance for short-term improvement of appetite; effects are rapid but tend to decrease after 3-4 weeks. They may also help to reduce nausea, improve energy and a feeling of general wellbeing.

- Consider need for gastric protection.
- Dexamethasone - 2-6mg orally once daily in the morning; assess after one week.
  - if beneficial, continue - reduce weekly to lowest effective dose.
  - if no benefit after 1 week, then stop.
  - side effects: fluid retention, candidosis, myopathy, insomnia, gastritis and steroid-induced diabetes. **See Corticosteroids section for more details.**

Prokinetic

- If impaired gastric emptying is suspected, consider a trial of metoclopramide 10mg three times daily.

SEEK SPECIALIST ADVICE IF NO RESPONSE TO ABOVE MEASURES.

Breathlessness

Breathlessness (dysnoea) is common in patients with advanced disease, and tends to become more common and severe in the last few weeks of life.

Note: The guidance in this section does **NOT** apply if breathlessness is caused by respiratory depression. **Refer to section on Use of naloxone for the management of respiratory depression caused by prescribed therapeutic use of opioids**

Breathlessness/Dyspnoea - Definition and Causes

- An unpleasant subjective sensation that does not always correlate with known clinical pathology.
- The patient's distress indicates the severity.
- The causes of breathlessness are usually multi-factorial: physical, psychological, social and spiritual factors all contribute to this subjective sensation.
- It is important to recognise and treat potentially reversible causes of breathlessness.

Assessment

- History and clinical examination.
- Investigations if appropriate to the patient's condition, wishes and prognosis - these may include oxygen saturation, chest x-ray and further imaging.
- More invasive investigations such as blood gases may be relevant in specific patient groups or seek specialist advice.

Management

- Treat reversible causes.
- Non-pharmacological measures (see below).
- Drug treatments.
- Management will be dependent on clinical diagnosis.

Table 19 – Management of potentially treatable causes of breathlessness

Cause	Consider
Cardiac failure / pulmonary oedema	Diuretics/ACE inhibitors/nitrates/opioids. Liaise with heart failure team. May benefit from IV diuretics in the community setting, if available, if not, can consider SC diuretics
Pneumonia	Antibiotics where appropriate
Bronchospasm	Bronchodilators ± steroids
Anaemia	Iron supplementation (treat with oral iron first line, IV if no oral route or GI malignancy) May need to consider transfusion in line with palliative guidelines
Pulmonary embolism	Anticoagulation
Anxiety	Psychological support, anxiolytics
Superior vena cava obstruction	Consider high dose steroid - **see Palliative Care Emergencies section** Consider referral to oncologist for radiotherapy/chemotherapy stent
Tracheal/bronchial obstruction from malignancy	Consider referral to oncolgist for radiotherapy/stenting. Consider ENT advice
Lung metastases	Consider referral to oncologist for radiotherapy/chemotherapy
Pleural effusion **Pericardial effusion** **Ascites**	Consider drain/diuretics if appropriate

Non-pharmacological management of breathlessness

- Reassurance and explanation.
- Distraction and relaxation techniques.
- Positioning of patient to aid breathing.
- Increase air movement – fan/open window.
- Physiotherapy – decrease respiratory secretions and breathing exercises.
- Occupational therapy – modify activities of daily living to help with symptoms.
- Establish the meaning of breathlessness for the patient and explore fears.
- Psychological support – to reduce distress of anxiety and depression.

Pharmacological management of breathlessness

(i) Opioids

Decrease perception of breathlessness, decrease anxiety and decrease pain.

Opioid naïve patient

- Non-pharmacological interventions to be optimised ahead of use of opioids.
- Recent evidence suggests low dose modified release morphine gives better management of breathlessness compared to immediate release morphine.
- For example, suggested starting dose Morphine MR 5mg twice a day.

Individual already taking regular strong opioid for pain

- For breathlessness use an additional "when required" dose of strong opioid which is in the range of 25-100% of the 4 hourly strong opioid dose, depending on severity of breathlessness.
- For example, if individual is on oral morphine modified release 30mg twice a day for pain – the dose range for oral morphine immediate release dose for breathlessness is 2.5-10mg when required.
- Titrate according to response.
- Consider increasing the regular dose by a maximum of 25-50% if "when required" doses are beneficial.

Notes:

- Use with caution in patients with type 2 respiratory failure.
- There is emerging evidence of a ceiling effect of opioids (Johnson MJ, Currow DC. BMJ Supportive & Palliative Care 2020;10:287–295).

(ii) Benzodiazepines

Benzodiazepines do not relieve breathlessness per se but do have a role when anxiety exacerbates breathlessness. For individuals with anxiety who have a prognosis of more than 4 weeks, an SSRI should be considered. A benzodiazepine may be used to alleviate symptoms whilst awaiting the effect of an SSRI, or if prognosis is less than 4 weeks.

Note: Unless the individual is imminently dying, benzodiazepines are contra-indicated in acute severe pulmonary insufficiency, untreated sleep apnoea syndrome, severe hepatic impairment and myasthenia gravis.

They should be used with caution in individuals with type 2 respiratory failure.

See Anxiety section for further guidance, including drug dosages.

(iii) Corticosteroids

May reduce inflammatory oedema.

Table 20 – Use of corticosteroids for management of specific causes of breathlessness

Indication	24-hr dexamethasone dose (oral)
Superior vena cava obstruction (see page 69)	16mg
Stridor	8-16mg
Lymphangitis carcinomatosis **Post-radiotherapy** **Bronchospasm**	8mg

Review treatment with corticosteroids after 5 days.

- If symptoms have improved, reduce dose gradually to the lowest effective dose.
- If no improvement in symptoms, stop or reduce corticosteroid to previous maintenance dose.
- If individual has taken corticosteroids for less than 3 weeks this can be done abruptly.
- If corticosteroids taken for more than 3 weeks reduce dose gradually and stop.

See section on Corticosteroids for further details.

(iv) Oxygen therapy

- The evidence for efficacy is limited. Oxygen therapy may help dyspnoeic patients who are hypoxic (SaO2 < 92%, normal may be lower in some COPD patients) at rest or who become so on exertion. It may help other dyspnoeic patients due to facial or nasal cooling effect, in which case a handheld fan will have the same effect.
- Consider a trial of oxygen for hypoxic patients (SaO2 < 92%, normal may be lower in some COPD patients) and those where saturation measurements are not available. Discontinue unless of clear benefit.

- For individuals with COPD who are chronically hypoxic – do not use more than 28% oxygen, without specialist advice.
- Oxygen therapy should be considered on a risk/ benefit balance taking into account potential negative effects such as limitation on mobility, barriers to communication, and inconvenience.
- Safety implications must also be considered e.g. fire risk from smoking (including e-cigarettes) or other heat sources such as radiators, matches or lit candles.
- Seek guidance from Community Oxygen Service and respiratory physicians, and follow local guidelines.

(v) Nebulised medications

Table 21 - Nebulised medications

Drug	Dose	Comments
Sodium chloride 0.9% nebuliser solution	2.5-5ml when required or 4 hourly	Hydrating agent for viscous secretions
Salbutamol nebules	2.5-5mg when required or 4 hourly	Bronchodilator
Ipratropium nebules	250-500micrograms when required. Max four times a day.	Bronchodilator

Monitor the first dose for adverse effects. Stop after 3 days if no response.

Cough

- Assessment as to the likely causes(s) and purpose of the cough is essential.
- May be cancer-related/treatment-related or due to other diseases.
- Cough may serve a physiological purpose and therefore where possible expectoration/physiotherapy should be encouraged.

Management

- Treat specific causes. **See Below Table 22 – Management of specific causes of cough.**
- Consider PPI if cough associated with other symptoms of acid reflux.
- Obstructive sleep apneoa management - referral for CPAP.
- Consider pharmacological management if cough is persistent and treatment of underlying cause is not possible. **See Table 23 – Pharmacological management of cough**

Table 22 – Management of specific causes of cough

Cause	Management
Malignancy related	Consider referral to oncologist for radiotherapy/ chemotherapy/laser therapy. Consider corticosteroids
Treatment related	Medication review e.g. ACE inhibitor induced cough
Cardiac failure and pulmonary oedema	Diuretics/ACE inhibitors
Pneumonia	Antibiotics if appropriate
Asthma	Bronchodilators +/- steroids
COPD	Bronchodilators/steroids. To reduce sputum viscosity: Carbocisteine - see below
Infection	Physiotherapy/nebulised sodium chloride 0.9%/antibiotics. Maintain hydration
Recurrent laryngeal nerve palsy	Consider referral to an Ear, Nose and Throat (ENT) specialist
Pleural effusion	drainage +/- pleurodesis
Post-nasal drip	Trial of nasal steriods
Gastro-oesophageal reflux disease (GORD)	Over the counter preparations

Table 23 - Pharmacological management of cough

Cause	Dose	Comments
Simple linctus (NB. Not in GM formulary)	5ml 3-4 times a day	Locally soothing demulcent action Some antitussive effect
Immediate release morphine	2.5-5mg 4 hourly	Use if opioid naive
Carbocisteine	750mg three times a day, reducing to twice a day	Reduces sputum viscosity
Sodium chloride 0.9%	2.5ml nebulised 4 hourly when required	Helps expectoration of sticky mucinous secretions

In the event of acute infection it may not be advisable to use cough suppressants.

Respiratory Secretions

Excess respiratory secretions are common in individuals near the end of life. They are caused by fluid pooling in the upper airways, arising from one or more sources:

- Saliva (most common).
- Bronchial mucosa (e.g. inflammation/infection).
- Pulmonary oedema.
- Gastric reflux.

Management

- Whilst noisy or 'rattling' breathing may be distressing to family members, if a patient is semiconscious or unconscious they are not usually troubled by respiratory secretions. Explanation and reassurance should be offered.
- Position the individual semi-prone, to encourage postural drainage, unless the secretions are caused by pulmonary oedema or gastric reflux, when the individual should be more upright.
- Hypersalivation/drooling prior to end of life can be managed with atropine 1% eye drops (4 drops on the tongue or sublingually) 4 hourly p.r.n. /hyoscine hydrobromide 1mg patches every 3 days/amitriptyline 10-25mg at night. Mouth dryness or difficulty expectorating secretions can be a reason why patients stop these medications.
- Gentle suction of the upper airway is usually reserved for unconscious patients, as it can otherwise be distressing. Should be considered under specialist advice only.

See Algorithm 6: Are troublesome respiratory tract secretions present and **Table 40 – Antisecretory drugs in renal impairment** for further guidance.

Management of hypersalivation and sialorrhoea in Adult Patients **https://gmmmg.nhs.uk/wp-content/uploads/2023/01/MFT-Hypersalivation-pathway-update_FINAL-for-web.pdf**

(Ref: PCF8)

Oral Problems

Oral problems are common in individuals with palliative care needs. Careful assessment and early intervention are vital in order to optimise the individuals comfort and prevent more serious problems and complications.

Assessment

The mouth should be assessed carefully on a daily basis. Features of a healthy mouth include:

- The mouth is clean and moist with saliva.
- The gums, tongue and cheeks are healthy and pink.
- No holes in the teeth or broken fillings
- Dentures are clean and fit well.
- No mouth ulcers or undiagnosed red or white patches.
- Consider medications which may cause issues.

Preventative management

- Teeth and tongue should be cleaned at least twice daily for about 2 minutes with a small/medium head toothbrush and fluoride toothpaste. Any excess toothpaste should be spat out, but the mouth **should not** be rinsed with water immediately after brushing as this washes away the remaining toothpaste and reduces its protective effects.
- Dentures should be removed twice daily, cleaned with a brush and rinsed with water. They should be soaked overnight in water, or using the individuals usual solution (check product instructions as some solutions should be used for 15 minutes only). After soaking, the dentures should be cleaned with a brush again.
- Adequate oral fluid intake should be encouraged.
- Lips should be moisturised sparingly with lip balm. (If oxygen therapy in place, then a water soluble lubricant should be used).
- Diagnose and manage secondary oral infection.
- Opioids, diuretics, anticholinergics, oxygen (consider giving humidified oxygen and reviewing non-essential medications).
- Anti-coagulants may cause gums to bleed.
- Steroids and antibiotics – can cause candida infection (thrush) which can alter taste or cause pain.
- Oral miconazole gel or fluconazole capsules given with hepatorenal impairment or warfarin may be harmful.
- Avoid using foam sponges as they can cause choking (MHRA alert 2012).
- Avoid using lemon and glycerine swabs

Management of oral problems

Management will depend on the nature and cause of the problem. **See Table 24 – Management of oral problems**

References and further guidance:

Mouth Care Matters **http://mouthcarematters.hee.nhs.uk/wp-content/uploads/sites/6/2020/01/MCM-GUIDE-2019-Final.pdf**

NHS.UK How to keep your teeth clean **https://www.nhs.uk/live-well/healthy-teeth-and-gums/how-to-keep-your-teeth-clean/**

Mouth care guidance and support in cancer and palliative care 3rd edition (2019) **http://www.ukomic.com/documents/UKOMiC-Guidance-3rd-Edition.pdf**

Ref: What should be considered when choosing or prescribing saliva substitutes? UKMI (May 2019) **https://www.sps.nhs.uk/wp-content/uploads/2020/02/UKMI_QA_Saliva-Subsitutes_update_June-2019-1.pdf**

Table 24 – Management of oral problems

Problem	Management
Aphthous ulcers	■ Hydrocortisone oromucosal tablet 2.5mg four times a day for up to 5 days. Allow tablet to dissolve at site of ulcer. ■ Topical analgesic gels – choline salicylate 8.7% oral gel e.g. Bonjela® or local anaesthetic (e.g. lidocaine ointment 5%). ■ Antiseptic mouthwash, e.g. chlorhexidine gluconate 0.2%, may help prevent or treat secondary infection.
Viral ulcers	■ Aciclovir 200mg 5 times a day for 5 days. ■ Topical gels (see above).
Malignant ulcers	■ Consider antibiotic.
Radiation stomatitis	■ Benzydamine 0.15% mouthwash or spray. ■ Consider applying a mucosal protectant gel e.g. Episil®, Gelclair®, Oralife®, MuGard®. ■ Paracetamol 1g up to 4 times a day **(see page 13 regarding when dose reduction may be required)** ■ Opioid analgesics if above inadequate. ■ Seek advice from Oncology team if necessary.
Acute ulcerative gingivitis	■ Metronidazole 400mg three times a day orally for 3 days. ■ Antiseptic mouthwash – e.g. chlorhexidine gluconate 0.2% mouthwash **(NB. See notes below).**
Dry mouth	■ Review medications (opioids, antimuscarinics). ■ Increase oral fluid intake. ■ Saliva substitutes/moisturising agents – refer to BNF and GMMMG Formulary for full range of products available. • Avoid acidic saliva products in patients with their own teeth. – AS Saliva Orthana® oral spray & lozenges & Biotene Oralbalance® gel are neutral pH. – Glandosane® spray and Salivix® pastilles are acidic.* • Be aware that some saliva substitutes are porcine in origin. – Biotene Oralbalance® gel and Glandosane® spray **do not** contain animal-derived ingredients. – AS Saliva Orthana® & Salivix® **do** contain animal-derived ingredients.* • These products can only be prescribed on the NHS in line with ACBS criteria (i.e or patients suffering from dry mouth as a result of having (or having undergone) radiotherapy, or sicca syndrome). For other patients these preparations can be purchased over-the-counter. ■ Boiled sweets, ice cubes, sugar free chewing gum. ■ Consider sodium chloride 0.9% mouthwashes/sprays/nebulisers. ■ Pilocarpine - seek specialist advice. • Avoid in those with a lack of salivary function.
Coated tongue	■ Chewing pineapple chunks. ■ Brushing tongue with soft toothbrush.

Fungal infection	■ Nystatin oral suspension 100,000 units/ml 1 ml – 5 ml four times a day for 7 days. Hold in mouth for 1 min and then swallowed. Use after meals and at bedtime. Note, nystatin has a topical effect. The higher doses are unlicensed and will require enough quantity to be issued to cover at least a 7-day supply e.g. approx. 150ml. ■ Fluconazole 50mg daily for 7 days (14 days if dentures worn). Fluconazole 150mg as a single dose can be used if prognosis is short. (note reduce dose by 50% if eGFR < 50 ml/min). Fluconazole suspension is significantly more expensive than capsules. ■ Miconazole 20mg/1g oral gel - see BNF. ■ NB. Fluconazole and miconazole are enzyme inhibitors. There is a risk of interactions with many drugs e.g. fentanyl, buprenorphine. Seek specialist advice. ■ Review and reassess treatment after 5-7 days. If recurrent please seek specialist microbiological advice. ■ Dentures should be soaked overnight in a weak chlorine solution (e.g. Milton Sterilising Fluid ®).
Bacterial infection	■ Consider the use of antibiotics.
Dry Lips	■ Yellow/white soft paraffin or normal lip salve. • Contraindicated if patient having radiotherapy to head and neck. ■ If Oxygen therapy in place, then water soluble lubricant should be used.

Guidance regarding use of Chlorhexidine *(Ref: PCF8)*

- There is a risk of an anaphylactic reaction in individuals with a history of chlorhexidine allergy. Check the labels and instructions for use to establish if products contain chlorhexidine prior to use on individuals with a known allergy. See **https://assets.publishing.service.gov.uk/media/5485abd7e5274a4290000281/con197920.pdf**
- Chlorhexidine is inactivated by some toothpastes. Wait 30 minutes after using toothpaste before using chlorhexidine.
- Chlorhexidine inactivates nystatin. If using both, leave at least 30 minutes after chlorhexidine before using nystatin.
- Chlorhexidine mouthwash may contain alcohol. This may cause discomfort. Try diluting with water or use alcohol free product. *(Ref: PCF8)*

Hiccups

Hiccups lasting more than 48 hours are not uncommon in individuals with advanced disease and can be very distressing and exhausting. They can affect an individual's daily living and social functioning.

Assessment

- Careful assessment is required to identify the cause.
- Consider severity, duration and impact on a patient's quality of life.
- Causes include:
  - Gastric stasis and distension (the most common cause).
  - Gastro-oesophageal reflux.
  - Metabolic disturbances (for example uraemia, hypercalcaemia, magnesium deficiency).
  - Infection.
  - Irritation of diaphragm or phrenic nerve.
  - Hepatic disease/hepatomegaly.
  - Cerebral causes (for example tumour, metastases) .
  - Damage to phrenic nerve over its course from skull to diaphragm, for example shingles, pressure from mediastinal tumour.

Management of Hiccups

- Hiccups often stop spontaneously. Treatment is only required if hiccups are persistent and causing the individual discomfort and distress.
- Try simple physical manoeuvres initially and those that have worked previously.

Non-pharmacological management

- Simple measures or 'home remedies' can be effective. These include:
  - Sipping iced water or swallowing crushed ice.
  - Breathing into a paper bag, particularly if the patient is hyperventilating.
  - Interrupting normal breathing, for example holding breath.
  - Drinking from the wrong/opposite side of a cup.
  - Rubbing the soft palate with a swab to stimulate the nasopharynx.
- Acupuncture may be effective.

Pharmacological management

- Most studies of treatments for hiccups are small and of low quality and suggestions for drug treatment options are made cautiously.

See Table 25 – Pharmacological management of hiccups.

Table 25 – Pharmacological management of hiccups

Cause	Specific management
Gastric distension +/- gastro-oesophageal reflux	■ Peppermint water 10ml when required. ■ Metoclopramide 10mg three times a day (do not use metoclopramide concurrently with peppermint water as opposing action). ■ Antiflatulent e.g. Simeticone. ■ PPI.
Diaphragmatic or phrenic nerve irritation	■ Baclofen – seek specialist advice. ■ Antiepileptic – e.g. gabapentin – **SEEK SPECIALIST ADVICE.** ■ Nifedipine – **SEEK SPECIALIST ADVICE.** ■ Midazolam – **SEEK SPECIALIST ADVICE.**
Systemic causes e.g. biochemical, infection	■ Treat underlying cause. ■ Haloperidol 500micrograms (use liquid rather than tablet due to expense) to 1mg three times a day orally. ■ Midazolam – **SEEK SPECIALIST ADVICE.**
CNS tumour Meningeal: infiltration by cancer	■ Antiepileptic – e.g. gabapentin – **SEEK SPECIALIST ADVICE.** ■ Baclofen – **SEEK SPECIALIST ADVICE.**
Hepatic, mediastinal or cerebral compression/irritation by disease/tumour	■ Dexamethasone oral 4-8mg in the morning may reduce compression/ irritation. **Follow steroid advice, page 78** ■ Stop if no benefit after a week. ■ If beneficial gradually reduce dose.

Ref: PCF8, Scottish Palliative Care Guidelines

Pruritus (Itch)

Pruritus is an unpleasant sensation that provokes the urge to scratch. It is a common symptom and can be severe and distressing, causing discomfort, frustration, poor sleep, anxiety and depression. It may be localised or generalised if related to systemic disease and is often worse at night. Persistent scratching, and the 'itch-scratch-itch' cycle leads to skin damage excoriation and thickening.

Although pruritus is experienced in the skin, conjunctiva and mucous membranes the cause is often not peripheral in palliative patients and therefore not responsive to antihistamines.

Patients with itch usually have dry skin which can compound the problem.

Common causes

- Dermatological conditions- dry skin, eczema, scabies.
- Peripheral neuropathic causes- shingles.
- Drug allergies.
- Central neuropathic causes- brain tumours, multiple sclerosis.
- Central neurogenic causes- opioids, cholestasis, paraneoplastic.
- Mixed peripheral and central causes- uraemia.

Management of pruritus

- Correct the correctable.
- Manage dry skin with emollients.
- Review medication-if there is an obvious cause stop and prescribe an alternative.
- Manage dermatitis with emollients and topical steroids if needed.
- Always consider scabies with a chronic rash-manage with permethrin or malathion.
- Cholestasis related to common bile duct obstruction-consider stenting.
- Hodgkin's lymphoma-itch can resolve with oncological treatment of the condition.

Non-pharmacological management

- If skin becomes wet, dry the skin by patting gently.
- Avoid soap, use soap substitutes.
- Keep fingernails cut short.
- Keep skin cool and hydrated with emollients 2-3 times a day-keep creams and lotions in fridge.
- Avoid prolonged hot baths.
- Avoid overheating and sweating especially at night.
- Increase air humidity in the bedroom to avoid skin drying.
- Distraction techniques.
- Avoid rough clothing if possible.

Pharmacological management

- Are generally determined by the cause of the itch.

See Table 25a – Suggested management of pruritus.

Table 25a – Suggested management of pruritus

Cause	Specific management
Dry Skin	▪ Emollients 2-3 x a day long-term.
Primary Skin Diseases **e.g. Scabies** **Dermatitis** **Psoriasis**	▪ Appropriate treatment of underlying condition.
Marked inflammation of the skin	▪ Consider 1-week course of oral steroids (oral dexamethasone 2-4mg or prednisolone 10-20mg once a day in the morning).
Opioid Induced Itch	▪ Stat dose of Antihistamine followed by regular dose if stat dose beneficial e.g. chlorphenamine 4mg three times a day or non-sedating antihistamine (see BNF). ▪ Switch opioid (morphine more likely to cause itch). ▪ Ondansetron 8mg orally twice a day.
Cholestasis	▪ Sertraline 25mg-100mg once a day. **SEEK SPECIALIST PALLIATIVE CARE ADVICE IF NOT EFFECTIVE.**
Uraemia	Options: ▪ If localized, capsaicin cream 0.025% once daily- 4x a day depending on need. ▪ Gabapentin 100mg–400mg or pregabalin 25mg-75mg after haemodialysis. ▪ Sertraline 50mg once a day. **SEEK RENAL SPECIALIST ADVICE IF NOT EFFECTIVE.**
Paraneoplastic Itch	▪ Sertraline 50mg–100mg or paroxetine 5mg-20mg once daily. ▪ Mirtazapine 15mg–30mg nocte. **SEEK SPECIALIST PALLIATIVE CARE ADVICE IF NOT EFFECTIVE.**
Unknown Cause	▪ Trial of antihistamines e.g. chlorphenamine 4mg three times a day. ▪ Consider sedative antihistamine or phenothiazine at night. ▪ Sertraline 50mg-100mg or paroxetine once daily.
Hodgkin's lymphoma	▪ Prednisolone 30mg-60mg once daily. ▪ Cimetidine 400mg twice a day. **SEEK SPECIALIST HAEMATOLOGICAL ADVICE RE DURATION OF HIGH DOSE STEROIDS OR IF NOT EFFECTIVE.**

Ref: PCF8, Scottish Palliative Care Guidelines

Delirium and Confusion

Delirium is characterised by 4 core features:

- Disturbance of consciousness and attention.
- Change in cognition, perception and psychomotor behaviour.
- Develops over a short period of time and fluctuates during the day.
- Is the direct consequence of a general medical condition, drug withdrawal or intoxication.

- Delirium can have an acute or sub-acute onset (sub-acute seen commonly in the elderly) and should be distinguished from dementia.
- Validated tools to detect delirium include the 4AT and the Confusion Assessment Method (CAM).

Types of delirium

- **Hyperactive delirium –** predominantly restless and agitated.
- **Hypoactive delirium –** predominantly drowsy and inactive. Delirium is often overlooked and the symptoms may be mistaken for depression or dementia.
- **Mixed motor type –** with evidence of both hyperactive and hypoactive symptoms in the past 24 hrs.
- Delirium can be a great source of distress to individuals and carers and is associated with higher mortality.
- Identification and treatment of the underlying cause is vital.
- Causes of delirium can be multi-factorial so assessment is essential.
- Use of the mnemonic PINCHME is helpful in remembering the possible reversible causes of delirium (Pain/Infection/Nutrition/Constipation/Hydration & hypoxia/Medication & Metabolic/Environment).

Non-Pharmacological management

- Provide environmental and personal orientation. This may be helped by the presence of a family member or trusted friend.
- Manage individual in a quiet well-lit room.
- Support and correct any sensory deprivation (use of glasses/hearing aids etc).
- Ensure continuity of care by avoiding any potential disruptive interventions – e.g. moving individual to different bed or ward.
- Maintain hydration.
- Hallucinations, vivid dreams and misperceptions may reflect unresolved fears and anxieties: facilitated discussion may be necessary.
- Reassure relatives and carers that the individual's confusion is secondary to a physical condition and provide information about how they can best help the person – e.g. see information at **https://www.rcpsych.ac.uk/mental-health/problems-disorders/delirium**

Table 26 – Pharmacological management of underlying causes of delirium

Cause	Treatment
Drug related: ■ Opioids ■ Corticosteroids ■ Sedatives ■ Antimuscarinics that cross the blood/brain barrier	Reduce or stop suspected medication as appropriate or switch to suitable alternative.
Withdrawal: e.g. alcohol, nicotine, benzodiazepines, opioids	May be appropriate to allow the patient to continue to use responsible agent. Nicotine patches may be useful.
Metabolic: ■ Respiratory failure ■ Liver failure ■ Renal failure ■ Hypoglycaemia/hyperglycaemia ■ Hypercalcaemia ■ Adrenal, thyroid or pituitary dysfunction ■ Infection ■ Nutrition	Treat any reversible causes if possible. Consider oxygen see Respiratory Symptoms section of guidance. **See Palliative Care Emergencies section of guidance**
Raised Intracranial Pressure:	Dexamethasone in daily doses of up to 8mg oral twice a day or 6.6mg SC twice a day can be given for 1 week dependent on severity of symptoms. Then reduce over 2-4 weeks to lowest dose which maintains benefit. (If treated with radiotherapy, steroids should be continued until one-week post treatment, and then reduced as above). Consider trial of dose increase if symptoms recur.
Other: ■ Circulatory (dehydration, shock, anaemia) ■ Pain ■ Constipation ■ Urinary retention ■ Sleep ■ Environment	Treat reversible causes if possible and appropriate (e.g. IV fluids, transfusion) ■ **See Pain section of guidance** ■ **See Constipation section of guidance** Catheterise if patient able to comply

Pharmacological management of symptoms

- The evidence for the role of antipsychotics in managing delirium symptoms is variable.
- SIGN guidelines 157 conclude that whilst the evidence to support the use of pharmacological treatment is insufficient, expert opinion supports a role for medications in specific situations such as those with intractable distress or where safety of the patient or others is compromised.
- Regular review is imperative as sedative drugs may exacerbate symptoms.
- Use a step-wise approach to drug dosages.

Table 27 – Pharmacological management of delirium symptoms

Situation	Management
Delirium where sedation undesirable	Start with haloperidol 500micrograms oral/SC at night and 500 micrograms 2 hourly pm (use liquid rather than tablet due to expense). Increase regular dose in 0.5-1mg increments as needed. Median effective dose 2.5mg/24hr, maximum dose 10mg/24h. *(Ref: PCF8)*. If needing doses above 5mg, **SEEK SPECIALIST ADVICE.**
Agitated delirium where sedation would be beneficial	Olanzapine 2.5mg oral at bedtime. Titrate as necessary. Mean effective dose 5mg/24hr *(Ref PCF8)*. Levomepromazine dose 6.25mg-12.5mg-25mg (6.25mg in the elderly/frail) for agitation in the imminently dying (PCF8). If two or more doses given in 24 hrs, please **SEEK SPECIALIST ADVICE.** If patient has seizures or hepatorenal fallure, **SEEK SPECIALIST ADVICE BEFORE USAGE.**
Acutely disturbed, violent or aggressive; at risk to themselves or others	Haloperidol 1.5-3mg Oral/SC or IM repeat as needed after 20-30 min - **SEEK ADVICE FROM MENTAL HEALTH CRISIS TEAM.**

- Avoid antipsychotic drugs for people with conditions such as Parkinson's disease or dementia with Lewy bodies. The elderly are at an increased risk of adverse neurological and cardiac effects when treated with haloperidol for delirium.
- There is a risk of arrhythmias (QT prolongation) with antipsychotic medication therefore use for shortest duration possible at lowest dose possible.

References:

- NICE Clinical Guideline CG103 (2010) Delirium: prevention, diagnosis and management (Last updated 2023) https://www.nice.org.uk/guidance/cg103
- SIGN guidelines 157 - Risk reduction and management of delirium PCF8 https://www.sign.ac.uk/media/1423/sign157.pdf
- Dementia United (2019) A Greater Manchester Approach to Delirium - Dementia United dementia-united.org.uk

Anxiety in Advanced Illness

People with life-limiting illnesses may suffer general anxiety or panic for a number of reasons including uncertainty about the future, separation from loved ones, financial, work and social worries as well as unrelieved pain or other symptoms and screening tools may be useful.

Anxiety may be new to the individual but is more common in individuals with pre-existing anxiety disorders, such as generalised anxiety disorder or panic disorder.

Symptoms and signs of anxiety may be due to or exaggerated by organic problems such as:

- Hypoxia.
- Sepsis.
- Medications (e.g. antipsychotics; SSRIs; steroids).
- Drug or substance withdrawal (e.g. benzodiazepines/opioids/nicotine/alcohol).
- Metabolic causes (e.g. hypoglycaemia/ thyrotoxicosis/hypercalcaemia).
- Poorly controlled pain/other symptoms and screening tools may be useful.
- Dementia.

Management

- The severity of the underlying disease and the overall prognosis guides management decisions.
- Treat contributing factors such as pain and other symptoms, hypoxia, sepsis etc.
- If prognosis >4 weeks, use non-pharmacological measures and follow NICE guideline CG113 for management of generalised anxiety disorder and panic disorder https://www.nice.org.uk/guidance/cg113
- If prognosis <4 weeks, some non-pharmacological measures can still be helpful, but use of benzodiazepines may also be considered particularly if anxiety is severe.

Non-pharmacological measures

- Acknowledge and discuss anxiety and specific fears as well as patient's own views and understanding - important first step.
- Distraction.
- Relaxation Techniques.
- Counselling.
- Cognitive behavioural therapy (CBT).
- Consider involvement of local psychological or psychiatric services.
- Self-help (e.g. "bibliotherapy" - use of written material).
- Support groups.
- Community palliative care support, Day Hospice support or equivalent, if appropriate, befriending.
- Assess how family is coping and if any communication problems are amplifying the anxiety or provoking feelings of isolation.

Pharmacological Management

- See Table 28 – Pharmacological management of anxiety – prognosis less than 4 weeks

Table 29 – Pharmacological management of anxiety – prognosis more than 4 weeks

Table 39 – Benzodiazepines in renal impairment

Table 28 – Pharmacological management of anxiety – prognosis less than 4 weeks

Drug	Dose	Comments	Pharmacokinetics
Lorazepam*	500micrograms – 1mg orally or sublingually twice daily and p.r.n. Maximum dose 2mg in 24 hrs. **In elderly/debilitated** – maximum dose 2mg.	• 1mg tablets are scored. • Sublingual route is unlicensed – one study suggested more rapid absorption sublingual than oral but others have found no difference. Thus, it is likely that the amount of lorazepam absorbed sublingually is variable and formulation-dependent. The patient must have a sufficiently moist mouth for sublingual absorption to occur. • Note only some brands of lorazepam tablet will dissolve easily when placed under the tongue, so need to specify manufacturer on the prescription e.g. Genus, PVL or TEVA brands.	Tmax 2.5h (PO or sublingual) Half-life = 10-20h
Diazepam*	2mg three times a day, increased if necessary to 15mg in divided doses. Higher doses may be appropriate, **SEEK SPECIALIST ADVICE** **In elderly/debilitated** – 1mg three times a day, increased if necessary to 7.5mg daily in divided doses. Higher doses may be appropriate, **SEEK SPECIALIST ADVICE**	• Long acting.	Tmax 0.5-1.5h (PO) Half-life = 25-50h; active metabolite up to 200h
Midazolam*	2.5-5mg SC 1 hourly p.r.n. If symptoms persist, seek specialist advice.	• If oral route not available. • Rapid onset, short acting. • If multiple doses are required then consider administration via 24 hr CSCI at a starting dose of 5-10mg.	Tmax 0.5h (SC) Half-life = 1-4 h

***Note:** Older patients are more sensitive to the effects of benzodiazepines. Benzodiazepines can cause physical and psychological dependence, and can cause paradoxical agitation on occasions. Short term use only for 2-4 weeks. Benzodiazepines with long half-lives accumulate when given repeatedly and undesirable effects may manifest only after several days or weeks. *Ref: BNF, PCF8*

Table 29 – Pharmacological management of anxiety – prognosis more than 4 weeks

Medication	Comment
SSRI e.g. Sertraline 25mg once daily (see BNF for titration) If sertraline is ineffective switch to alternative SSRI or SNRI If SSRI or SNRI not tolerated, consider pregabalin – BNF advises starting dose of 150mg daily in 2-3 divided doses. May need to start at lower dose in elderly/debilitated e.g. 25mg twice daily.	Ref: NICE guideline CG113 for management of generalised anxiety disorder and panic disorder **https://www.nice.org.uk/guidance/cg113**

Depression

Depression is common in a palliative care setting and is under-recognised. Estimates of the prevalence of depression vary, but it is probable that at least 25% of individuals with advanced illness will develop a significant mood disorder.

It is important to note that:

- Untreated depression may increase the impact of existing symptoms and reduce the effectiveness of usual interventions.
- Physical consequences of life-limiting illnesses can mimic symptoms of depression.

Screening for depression

Screening for depression should be undertaken in all settings using screening tools or questions such as:

- "During the last month, have you often been bothered by feeling down, depressed or hopeless?"
- "During the last month, have you often been bothered by having little interest or pleasure in doing things?"
- Sensitively ask about the risk of suicide or self-harm.

Management

- Explore the individuals understanding of his/her illness.
- Address and treat current causes of physical and psychological distress.
- **If prognosis less than 4 weeks - SEEK SPECIALIST ADVICE.**
- **If prognosis more than 4 weeks -** see Box 6 (opposite) – Non-pharmacological management of depression and **Table 30 – Pharmacological management of depression – prognosis more than 4 weeks for summaries of management options**. See NICE guideline CG90 Depression in adults: recognition and management **https://www.nice.org.uk/guidance/ng222** for more details.
- Refer to a mental health specialist if treatment-resistant, recurrent symptoms, atypical or psychotic depression and/or significant risk of suicide.

Box 6 - Non-pharmacological management of depression

- Distraction.
- Relaxation.
- Sleep and anxiety management advice.
- Complementary therapies.
- Day Hospice support or equivalent if appropriate.
- Guided self-help.
- Specific psychological treatments including cognitive behavioural therapy (CBT).
- Exercise.

Table 30 – Pharmacological management of depression - prognosis more than 4 weeks

Drug	Comments
Selective serotonin reuptake inhibitors (SSRIs) e.g. Sertraline 50-200mg once daily Citalopram 10-40mg once daily (20mg maximum in patients over 65 years)	• Recommended by NICE in routine care. • Useful for mixed anxiety and depressive disorders. • May provoke anxiety "flare" (manage with benzodiazepines as needed). • May be fewer interactions with citalopram and sertraline than other SSRIs. • Incidence of sexual dysfunction <10%.
Mirtazapine 15-45 mg at night	• Response rate equivalent to other antidepressants (70%). • Rapid onset of action (one to two weeks). • May increase appetite. • Does not cause nausea and vomiting. • Causes sedation at low dose so given at night. • Not associated with cardiac toxicity or sexual dysfunction.
Duloxetine 60mg once daily. (Higher doses may be used on specialist advice)	• May be beneficial if also has neuropathic pain. • Incidence of sexual dysfunction (30%).
Venlafaxine 75mg daily, increased if necessary up to 300mg daily. (Higher doses may be used on specialist advice)	• **Note venlafaxine has several cautions and contra-indications -** see BNF and NICE guideline CG90: Depression in adults: recognition and management.

For patients with renal impairment see Table 38 – Antidepressants in renal impairment

If no response after 2-4 weeks or only partial response after 6-8 weeks:

Increase dose – if no tolerability issues.

Consider combining with a second antidepressant if a previous switch was unhelpful. **NICE suggests primary care prescribers due to the possibility of serotonin syndrome SEEK SPECIALIST ADVICE before adding a second drug.**

Switching antidepressants *(Ref PCF8)*

Switch from	Switch to mirtazapine, duloxetine or venlafaxine
Citalopram 20mg once daily **Sertraline 50mg once daily** **Paroxetine 20mg once daily**	• Stop the SSRI and start the alternative antidepressant the following day.
Fluoxetine 20mg once daily	• Stop fluoxetine, wait at least 4 days before starting the alternative antidepressant.
Amitriptyline 25mg once daily (taken for <6 weeks)	• Stop amitriptylline and start the alternative antidepressant the following day.

For doses above those in the table a cross taper is needed. Reduce dose weekly in steps to dose listed above then switch.

Seizures

Seizures occurring in individuals with palliative care needs are commonly associated with cerebral tumours (70% of individuals have seizures), cerebrovascular disease, epilepsy or biochemical abnormalities (e.g. hyponatraemia, hypercalcaemia, hypoglycaemia, uraemia). [2]

Assessment

Consider other causes e.g. vasovagal episode, postural hypotension, arrhythmia, hypoglycaemia, extrapyramidal side effects from dopamine antagonists.

Is there a history of seizures? If already prescribed antiepileptics, check if patient has been taking them. Check for drug interactions. Have any drugs lowered seizure threshold? [2]

See specialist advice where diagnosis of seizures is in doubt.

Pharmacological management

If no focal lesion identified, seek specialist advice. Antiepileptics are not usually started until a second seizure occurs. [1]

If an irreversible focal lesion is identified, e.g. a cerebral tumour, then further seizures are likely. Anti-epileptics are generally recommended after a first seizure. [1]

Anti-epileptics should **not** be used *prophylactically* in the absence of a history of seizures. [1]

For choice of antiepileptic in palliative care consider factors such as; drug interactions, co-morbidities, route, time to effect. [1]

Consider prescribing Midazolam in anticpation of need in all patients at risk of seizures with brain metastases.

Drug	Comments
Levetiracetam	Is generally a first-line choice for focal seizures in palliative care, there are no clinically significant drug interactions and it can be administered oral/IV/SC/ continuous SC infusion (CSCI). (The dose is the same oral/IV/SC). [1] • Start with Levetiracetam 250–500mg oral twice a day. • If starting with 250mg twice a day, increase automatically after 2 weeks to 500mg twice a day (the minimum effective dose in most people). • If necessary, increase by 250–500mg twice a day every 2 weeks. • A response, if it occurs, is generally seen with relatively low doses, e.g. levetiracetam 1g – 1.5g/24h. • The dose should be reduced in patients with renal impairment. • Normal dose can be used in patients with hepatic impairment. • Consider anticipatory supply of injectable levetiracetam for use in CSCI if patient is likely to lose their swallow soon/ deteriote quickly (can be difficult to opbtain the community). **IF SEIZURES PERSIST SEEK SPECIALIST ADVICE.**

Convulsive status epilepticus [1]

General measures – protect airway, oxygen, IV access, protect from injury, check blood glucose

Drug	Comments
Midazolam	• 10mg buccal/SC/IM stat or IV over 2min; repeat once after 10min if needed. The **midazolam** injection formulation can be given buccally in status epilepticus. **Midazolam** oromucosal solutions for buccal administration, authorized for children and adolescents, are available.

Managing seizure in the last days of life [1] (see flowchart)

Seizures are frightening for individuals and those closest to them. Explain the management plan, educate and address any concerns such as desired management of further seizures, management of risk of seizure recurrence if stopping anti-epileptic drugs, for example due to swallowing difficulties.

- Midazolam is generally used first-line because of familiarity, availability, benefit in concurrent symptoms and compatibility with other drugs CSCI.
- manage acute seizures with midazolam 10mg buccal/SC/IM stat or IV over 2min; repeat once after 10min if needed.
- Oral antiepileptics have a long half-life. However, If the individual is in last days of life and unable to take oral antiepileptics ongoing management should be considered. E.g. **midazolam** 10-30mg/24h CSCI (seek specialist advice).
- If it is desirable to avoid sedation, consider alternative e.g levetiracetam CSCI. Conversion of oral to CSCI of levetiracetam is 1:1.
- If seizures persist, seek specialist advice.

References

1. Palliative Care Formulary 8th edition.
2. Scottish Palliative Care Guidelines: Scottish Palliative Care Guidelines - Seizures

Insomnia

Assess the person's beliefs about what they regard as normal sleep and the impact of insomnia on their activities and quality of life. Ask about duration of insomnia and any possible contributing factors.

Management

- **Correct contributory factors where possible** e.g. pain, delirium, depression, anxiety, obstructive sleep apnoea, drugs e.g. alcohol, corticosteroids *(Ref PCF8)*.

Non-pharmacological measures

- Establish fixed times for going to bed and waking up.
- Try to relax before going to bed.
- Maintain a comfortable sleeping environment – not too hot, cold, noisy or bright.
- Avoid napping during the day.
- Avoid caffeine, nicotine and alcohol within 6 hrs of going to bed.
- Consider complete elimination of caffeine from the diet.
- Avoid exercise within 4 hrs of bedtime (although exercise earlier in the day is beneficial).
- Avoid eating a heavy meal late at night.
- Avoid 'blue light' displays on electronic devices witihn 2 hrs of bedtime.
- Avoid watching or checking the clock throughout the night.
- If unable to sleep, don't lie there worrying about it. Get up (if possible), do something relaxing until feeling sleepy again, then go back to bed.

Pharmacological management

- If symptoms are severe, medication may be considered.
- A hypnotic drug that may help with the underlying cause may be useful, e.g. for delirium consider quetiapine, for depression consider mirtazapine.
- Low doses of short acting Z-drugs (Zolpidem and zopiclone) and benzodiazepines increase the risk of falls.
- If a Z-drug or benzodiazepine is required, choose one with a short half-life if possible **See Table 31 below – Pharmacological management of insomnia.**
- Consider alternative management if using for more than 4 weeks as dependence may occur. *(Ref PCF8)*

Table 31 – Pharmacological management of insomnia

Drug	Standard dose	Dose – elderly/frail	Half-life	Comments
Zolpidem	10mg at bedtime (oral)	5mg at bedtime (oral)	2 hrs	Cost effective options
Zopiclone	7.5mg at bedtime (oral)	3.75mg at bedtime (oral)	3.5 hrs	Cost effective options
Temazepam	10-20mg at night	10mg at night	8-15 hrs	Controlled drug prescription requirements apply (liquid available but high cost)
Lorazepam	Not recommended due to length of half-life		10-20 hrs	
Midazolam	2.5mg SC at bedtime		1-4 hrs	Consider if oral route unavailable. Controlled drug prescription requirements apply

Ref: PCF8; NICE Clinical Knowledge Summary Insomnia – **https://cks.nice.org.uk/insomnia**

The place of melatonin for insomnia in palliative care is uncertain. It may be considered as an alternative if Z-drugs / benzodiazepines are not tolerated.

Melatonin is indicated for persistent insomnia in people over 55years of age (evidence for efficacy is less with younger adults).

Recommended dose is melatonin MR 2mg once daily after food. Take 1-2 hrs before bedtime. Review for effect after 3 weeks. *(Ref PCF8)*

Palliative Care Emergencies

Neutropenic sepsis

This is a medical emergency which requires immediate hospital investigation and treatment.

Presentation

- Consider in any individual who has had recent anticancer therapy (including chemotherapy, immunotherapy, trial therapy or radiotherapy) and/or allograft <2 years or autologous <6 months who is deteriorating, especially if it is unexpected.
- Occurrence most likely 7-14 days after anticancer therapy but can be up to 6 weeks post treatment.
- Early signs – flu-like symptoms, temperature of <36°C and greater than or equal to 37.5°C.
- Late signs – anxiety, confusion, cold and clammy, hypotension, tachycardia, diarrhoea.
- Remember – pyrexia may be absent in some infected patients who are dehydrated, severely 'shocked' or taking paracetamol, NSAIDs or steroids.

Management

- If condition suspected, **DO NOT DELAY.** Individual should be managed as per the sepsis 6 pathway (IV antibiotics IV Fluids, oxygen, blood cultures, lactate and hourly urine output).
- Antibiotics (please see local antimicrobial policy) should be administered within one hour of clinical suspicion of neutropenic sepsis; do NOT delay the administration of antibiotics whilst awaiting FBC/Neutrophil count results.
- The Christie Hotline is available for 24 hr advice at 0161 446 3658.

Hypercalcaemia

Definition

- Corrected serum calcium >2.7mmol/L (some variation between laboratories).

Presentation

- Common in cancer of breast, myeloma, lung, head and neck, kidney, thyroid and cervix.
- May develop insidiously.
- Severity of symptoms are related to speed of rise of calcium.

Symptoms

- Common symptoms include malaise, weakness, anorexia, thirst, nausea, constipation and polyuria. **There should be a low threshold for checking calcium levels in individuals with these symptoms.**
- Symptoms in more severe hypercalcaemia include vomiting, ileus, delirium, seizures, drowsiness and coma.
- Pain can be precipitated or exacerbated by hypercalcaemia.

Investigations

- Onset of symptoms raising clinical suspicion should be investigated.
- Blood should be checked for urea and electrolytes (U&Es), estimated glomerular filtration rate (eGFR), liver function tests (LFTs) and corrected calcium.
- Other bloods to consider parathyroid hormone, magnesium, phosphate and vitamin D.

Management/Treatment

In Primary Care - SEEK SPECIALIST ADVICE

Points to consider prior to treatment

- First episode or long interval since previous episode.
- Individual reports good quality of life prior to episode.
- Treatment can take time to work (around a week) and may not be approriate if prognosis is very poor – **SEEK SPECIALIST ADVICE.**
- Individual is willing and able to have intravenous treatment and blood tests.

If adjusted calcium < 3mmol/L and patient asymptomatic:

- Check urea, electrolytes, creatinine, eGFR.
- Review medications e.g. those that impact on renal function especially diuretics/vitamins/ supplements containing calcium/ACE inhibitors.
- Correct dehydration - IV fluids 0.9% sodium chloride, 2-3 Litres/24h or ensure equivalent adequate oral fluid intake.
- Recheck in 2 to 3 days and treat if calcium is rising.

If patient symptomatic & adjusted calcium <3mmol/L, or adjusted calcium >3mmol/L (can be potentially life threatening)

- Review medications e.g. those that impact on renal function especially diuretics/vitamins/ supplements containing calcium/ACE inhibitors.
- Treat with IV fluids 0.9% sodium chloride 2-4 L/24h. The amount and rate of hydration depends on renal function, calcium level and cardiovascular status.
- Administer IV bisphosphonate: EITHER zoledronic acid OR pamidronate disodium (according to local guidelines/BNF/SPC) – **do not give both.**
- If eGFR <30 ml/min do not give bisphosphonate **SEEK SPECIALIST ADVICE.**
- Hypercalcaemia carries a poor prognosis, consider commencing Advance Care Planning.

Table 32 – Onset and duration of effect of bisphosphonates

	Pamidronate disodium	Zoledronic acid
Onset of effect	< 3 days	< 4 days
Maximum effect	5-7 days	4-7 days
Duration of effect	2.5 weeks	4 weeks

Monitor for Recurrence:

- If symptoms persist repeat calcium levels and renal function after 7 days. Re-treat with bisphosphonate if clinically indicated.
- If serum calcium refractory to treatment seek specialist advice.
- Repeat bisphosphonate infusion every 3-4 weeks if symptoms recur.
- Check plasma calcium concentration and renal function before each dose.
- Consider dental hygiene measures to prevent osteonecrosis.

Superior Vena Cava Obstruction (SVCO)

- Compression/invasion or thrombosis of superior vena cava due to tumour or nodal mass within mediastinum.
- Commonest causes (95%) – lung cancer, non-Hodgkin lymphoma.

Symptoms and signs of SVCO

- Swelling of face, neck, arms.
- Headache.
- Dizziness.
- CNS depression.
- Seizures.
- Dyspnoea.
- Dilated veins – neck, trunk, arms.
- Hoarse voice.
- Stridor.

Management

Admit the individual to hospital if they are in the community, unless they are in the last days of life, in which case **SEEK SPECIALIST ADVICE.**

(i) Immediate management

- Sit individual up.
- Administer oxygen if hypoxic.
- Dexamethasone 16mg oral/13.2mg SC followed by 8mg twice a day oral/6.6mg SC twice a day (morning and lunch) on subsequent days.
- Consider Furosemide 40mg IV or oral.
- Co-prescribe a Proton Pump Inhibitor (PPI) alongside high dose steriod treatment and monitor blood glucose levels.

(ii) Seek specialist oncological advice re ongoing management

- Endovenous stent.
- Thrombolysis if stent blocked by thrombus.
- Radiotherapy and/or chemotherapy may be offered depending on primary tumour site/ histology.
- Advance Care Planning should be considered.

Outcome

Placement of an endovenous stent offers the most rapid and effective initial symptomatic relief. Overall prognosis in patients with SVCO is poor. Without treatment, SVCO may cause death within a few days. Even with treatment, one year survival is only 17%. *(Ref: Palliative Adult Network Guidelines, 2016).*

Metastatic Spinal Cord Compression (MSCC)

The Greater Manchester Cancer Services MSCC pathway and Network Guidance on the assessment and management of MSCC is available at: https://www.christie.nhs.uk/patients-and-visitors/services/metastatic-spinal-cord-compression-mscc/information-about-mscc-for-healthcare-professionals

- Affects 5-10% of patients with cancer.
- Spinal metastases: most common in prostate, lung, and breast cancer and myeloma.
- Catastrophic event – aim is to prevent establishment of paresis.
- Symptoms may be vague, there should be a high index of suspicion. A normal neurological examination does not exclude spinal cord compression, so investigate if a patient has concerning symptoms.
- Patients with cancer and neurological signs or symptoms of spinal cord compression should be treated as an oncological emergency.

Symptoms

- Back/Spinal Pain:
  - May radiate in a radicular 'band-like' pattern.
  - Severe progressive or unremitting.
  - May be exacerbated by straining (for example, coughing, sneezing or bowel movements) or by standing, sitting or moving.
  - May be nocturnal pain preventing sleep.
  - May not be present.
- Nerve root pain in limbs.
- Claudication (muscle pain or cramping in the legs when walking or exercising).
- Weakness of limbs (out of proportion to general condition of patient).
- Difficulty walking.
- Sensory changes – tingling, numbness, "my legs don't belong to me".
- Difficulty passing urine – usually a late presentation.
- Constipation or faecal incontinence.

Signs

- Localised spinal tenderness.
- Weakness of limbs.
- Reflexes - absent/increased.
  - Extensor plantars.
  - Clonus may be present.
- Altered sensation – look for a sensory level.
- Distended bladder.

Management/Treatment

- **Immobilise without delay (including for transfer to hospital) for individuals with:**
  - Suspected MSCC AND neurological symptoms or signs suggesting spinal instability.
- **Consider immobilisation for individuals with:**
  - Suspected spinal metastases OR MSCC AND moderate to severe pain associated with movement.

- **Commence high dose steroids immediately if there is clinical suspicion of MSCC,** even if diagnosis not confirmed.
  - Dexamethasone 16mg oral/13.2mg SC followed by 8mg twice a day oral/6.6mg SC twice a day (morning and lunch) on subsequent days.
  - Then continue dexamethasone 8mg twice a day or 16mg once daily orally until either MSCC has been excluded, surgery has been completed or radiotherapy has been started.
  - For patients undergoing radiotherapy, maintain on 8mg oral each morning until completion of treatment.
- Co-prescribe a Proton Pump Inhibitor (PPI) alongside high dose steroid treatment and monitor blood glucose levels.
- Assess if it is appropriate to commence thromboprophylaxis.
- Urgent MRI of the whole spine must be done within 24 hrs of clinical suspicion (if MRI is contraindicated a CT of the whole spine with thin slices and saggital reconstruction should be done).
- Urgent same day referral to the Network MSCC coordinator or out of hours contact the Christie Hotline (Christie Hospital, 0161 446 3658, **https://www.christie.nhs.uk/patients-and-visitors/services/metastatic-spinal-cord-compression-mscc/contact-the-mscc-service** for advice re. radiotherapy and/or chemotherapy.
- The Network MSCC coordinator (or oncology team out of hours) may advise referral for specialist spinal opinion for possible surgical decompression if:
  - No underlying diagnosis has been made.
  - There are limited levels of spinal cord. compression on imaging
  - Minor neurological impairment is present.
  - There is progressive weakness despite previous radiotherapy at this level.
  - Evidence of spinal instability and estimated life expectancy of at least six months with general condition suitable for general anaesthesia and surgery.
  - Taper dexamethasone (and discontinue) over 1-2 weeks after completion of radiotherapy or surgery. If there is neurological deterioration during the dose reduction, the dose should be increased again to the previous satisfactory dose, and maintained at that level for a further 2 weeks before attempting to taper the dose again. *(Ref: PCF8)*

    For more information on immobilisation and/or spinal instability see NICE Guidance: Spinal Metastases and Metastatic Spinal Cord Compression (September 2023): https://www.nice.org.uk/guidance/ng234/resources/spinal-metastases-and-metastatic-spinal-cord-compression-pdf-66143896133317

Aims of Treatment

- The earlier treatment is commenced the greater chance of preventing permanent paralysis, loss of bowel and bladder control, devastating loss of independence and quality of life and markedly reduced survival.
- Maximisation of recovery of neurological function.
- Local tumour control.
- Pain control.
- Improve spinal stability.
- Good communication with individual and those identified as important to them.
- Good nursing care, pressure area care, psychological support and rehabilitation.

Cauda Equina Compression – Lumbar Spine Below L1

Presentation

- Lumbar pain with loss of power in lower limbs and loss of sphincter control.

Symptoms/Signs

- Weakness of legs, loss of lower limb tendon reflexes, sciatic pain, urinary hesitancy and peri-anal numbness.

Cause

Spinal metastases, breast, prostate, lung cancer and myeloma most common.

Treatment

As for spinal cord compression - give high dose dexamethasone 16mg stat dose orally or 13.2mg IV or SC (using 3.3mg/ml strength), followed by radiotherapy.

Recurrence

Consider steroids as above.

Catastrophic Haemorrhage

- Catastrophic haemorrhage can be a frightening experience for both patients and carers, though this can be minimised by good anticipatory planning.
- Bleeding may be frank or occult.
- It may be a terminal event in both advanced cancer and non-malignant disease. Commence Advance Care Planning if not already in place.

Types of haemorrhage

- Haemoptysis.
- Haematemesis.
- Rectal/vaginal haemorrhage.
- Melaena.
- Haematuria.
- Surface bleeding.
- Nose bleed.
- Oesophageal varices.

Signs and symptoms

- Visible bleeding.
- Hypotension.
- Cool extremities.
- Anxiety.

Anticipatory management for patients at high risk of catastrophic haemorrhage

- Plan ahead where possible.
- Consider stopping any anticoagulation medication. Consider whether commencing tranexamic acid is clinically indicated?
- Consider whether admission for urgent blood transfusion, IV fluids etc. would be appropriate if a bleed was to occur.
- Develop a proposed management plan, ideally discussed with the individual and those closest to them and staff.
- Record management plan in case notes and communicate this to all team members.
- Provide dark coloured towels to disguise blood loss.

Pharmacological management

- Anticipatory prescribing of an anxiolytic (midazolam 5-10mg IV, IM, buccal or sublingual *(Ref: PCF8)*.
- **The SC route should not be used in catastrophic bleeds due to peripheral shut down and therefore unpredictable absorption of the medication.**
- For individuals in the community, consider training a family member in the use of buccal or sublingual midazolam (Note: buccal or sublingual route is not appropriate if a large amount of blood is likely to come out of the mouth).
- **Note: If the individual has a massive haemorrhage and is clearly dying, support and non pharmacological interventions are more important until help arrives than trying to give medication; the individual will usually lose consciousness rapidly and may be frightened especially if left alone.**

Catastrophic bleed

- Manage as per anticipatory plan.
- Keep patient warm and **ensure they are not left alone.**
- Use anxiolytic as needed if the individual is distressed.
- Support the individual and family.

Further care

- **If bleeding stops -** consider whether there is a risk of further haemorrhage. Further management will depend on overall clinical status and discussion with individual and those closest to them in relation to whether acute interventions are appropriate.
- **If bleeding continues at a slower rate –** consider whether any interventions to try and stop the bleeding are appropriate. It may be necessary to commence and continue an infusion of anxiolytic (midazolam) if the individual is in the last hours of life.
- **Following a catastrophic haemorrhage**
  - Offer support and debriefing to family and team members – may need to be ongoing for a period of time after the event.
  - Dispose of clinical waste appropriately.

Ref: PCF8, Scottish Palliative Care Guidelines

Corticosteroids

Corticosteroids are used extensively in palliative care. **Dexamethasone** is the preferred choice due to its relatively high anti-inflammatory potency and lower incidence of fluid retention and biochemical disturbance.

- Whilst highly effective they should be used with caution and be constantly monitored to prevent avoidable complications.
- Standard starting doses for the different indications are not well established and doses given below are for guidance only and need to be tailored according to the individual patient's overall condition.
- Give corticosteroids as a single dose in the morning, or as a divided dose in the morning and at lunchtime, to minimise risk of insomnia.
- Clinical response must be reviewed within 7 days.
- Titrate down to minimum effective dose as soon as is possible.

Table 33 – Corticosteroid use for the management of specific symptoms

Indication	Suggested starting dose/usage
Anorexia	Dexamethasone - 2-4mg orally once daily in the morning; assess after one week ■ If beneficial, continue - reduce weekly to lowest effective dose. ■ If no benefit after 1 week, then stop. Although enhanced effect can still be present at 4 weeks, short courses are recommended to reduce risk of side effects.
Adjuvant analgesic	For cancer-related pain (e.g. liver capsule pain, nerve compression): ■ Dexamethasone 8-16mg a day orally in 1-2 doses.
Antiemetic	For chemotherapy-induced nausea and vomiting: follow Oncology guidelines. Refractory nausea and vomiting: ■ Dexamethasone 8-16mg orally OR 6.6mg-13.2mg IV or SC each morning or 2 divided doses (use 3.3.mg/ml strength).
Obstructive syndromes	E.g. bowel obstruction, upper airways compression, SVCO, lymphangitis carcinomatosis: ■ Dexamethasone 8 - 16mg orally or 6.6mg-13.2mg IV or SC each morning or 2 divided doses (use 3.3.mg/ml strength)

Spinal cord compression	■ Dexamethasone 16mg stat dose oral or 13.2mg IV or SC (using 3.3mg/ml strength). ■ Then continue dexamethasone 8mg twice a day (morning and lunchtime) or 16mg once daily orally until either metastatic spinal cord compression has been excluded, surgery has been completed or radiotherapy has been started. ■ For patients undergoing radiotherapy, maintain on 8mg oral each morning until completion of treatment. ■ Taper (and discontinue) over 1-2 weeks after completion of radiotherapy or surgery. If there is neurological deterioration during the dose reduction, the dose should be increased again to the previous satisfactory dose, and maintained at that level for a further 2 weeks before attempting to taper the dose again. *(Ref: PCF8)*
Raised intracranial pressure	Dexamethasone 8 - 16mg daily or 6.6-13.2mg SC (using 3.3mg/ml strength) for one week dependent on severity of symptoms, and then reduce over 2-4 weeks to lowest dose which maintains benefit. (If treated with radiotherapy, steroids should be continued until one-week post treatment, and then reduced as above). Consider trial of dose increase if symptoms recur.

Box 7 – Equivalent doses of corticosteroids

Conversion between dexamethasone and prednisolone:
Dexamethasone 1mg is approximately equivalent to Prednisolone 7.5mg.

Conversion between oral and SC dexamethasone:
Traditionally conversion from oral to SC dexamethasone was made on a 1:1 basis.
The injectable formulations now contain either dexamethasone 3.3mg/ml or 3.8mg/ml. Using a 1:1 conversion results in complex dose calculations and unnecessary waste. Therefore, as the dose of dexamethasone is titrated to effect it can be considered that 4mg orally is equivalent to 3.3mg/ml or 3.8mg/ml injection.

Table 34 - Adverse effects of corticosteroids

Adverse effect	Comments
Glucose metabolism	Steroids can increase blood glucose levels. All patients on steroids should have regular blood glucose checks – follow local guidance **https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/public/2021-11/EoL_TREND_FINAL2_0.pdf**
Insomnia	Give corticosteroids as a single dose in the morning, or as a divided dose in the morning and at lunchtime, to minimise risk of insomnia.
Dyspepsia	Give after food. Co-prescribe PPI if history of peptic ulcer disease or patient also taking aspirin, NSAIDs, SSRIs or is anticoagulated.
Psychiatric disturbance	e.g. depression, mania, psychosis, delirium.
Change in appearance	"Moon face", truncal obesity, effect on body image.
Musculoskeletal problems	Proximal myopathy, osteoporosis, avascular bone necrosis.
Increased susceptibility to infection	Especially oral/pharyngeal candidosis - examine mouth regularly.
Skin changes	Thinning, bruising, acne, impaired wound healing.
Other	Hypertension, oedema, pancreatitis.

Monitoring and stopping treatment

- Use the lowest effective dose for the shortest period of time.
- Close careful monitoring is essential.
- Rapid withdrawal of a corticosteroid may result in a corticosteroid withdrawal syndrome. This may cause an array of symptoms and signs similar to pseudorheumatism (myalgia, arthralgia, malaise, rhinitis, conjunctivitis, painful itchy skin nodules, weight loss and pyrexia) and/or a hypo-adrenal crisis (malaise, profound weakness, hypotension).
- Corticosteroids may be stopped without tapering the dose if total treatment duration of less than 3 weeks AND daily dexamethasone dose of 4mg or less AND symptoms unlikely to relapse.
- Some patients may need a maintenance dose of low dose dexamethasone.
- **Gradual dose reduction is advisable if any of the following:**
  - Risk of recurrent severe symptoms.
  - 3 or more weeks treatment.
  - Daily dose of more than 4mg dexamethasone for more than one week.
  - Had a second dose in the evening.
  - Repeated courses of steroids.
  - Taking a short course of steroids within a year of stopping long-term treatment.
  - Other possible causes of adrenal suppression.

- Reduce daily dose gradually to dexamethasone 4mg/day according to symptoms, then more slowly by 1-2mg weekly. The individual must be reviewed regularly and the dose increased if symptoms worsen.
- If physiological stress, e.g. from infection, trauma, surgery, occurs within 1 week of stopping the corticosteroid, additional corticosteroid cover should be prescribed to compensate for adrenal suppression.

Steroid treatment card: Patients on systemic steroids for more than 3 weeks must be given a steroid card.

Steroids in last days of life

- For ongoing symptom control, continue at the most convenient SC dose.
- If recent and/or low oral dose prescription for appetite stimulation, discontinue.

Ref: PCF8; North West Coast Clinical Network (November 2021) Palliative Care Consensus Guidance for Cheshire & Merseyside and Lancashire & Cumbria , Lancashire and South Cumbria Consensus Guidance.

Section 2

Specific Situations

Symptom Management in Patients with Renal Impairment

(Reference PCF8 & www.renaldrugdatabase.com)

This section gives general guidance about prescribing in individuals with renal impairment. Caution is required and a low threshold for seeking specialist advice is advised if the estimated glomerular filtration rate (eGFR) <30ml/min.

Be aware that the eGFR does not take into account body weight. In individuals of low body weight the eGFR may overestimate renal function which can potentially lead to drug overdosing.

Individuals with renal impairment may have increased central nervous system (CNS) sensitivity therefore use low starting doses and titrate all medicines cautiously.

For individuals on haemodialysis or peritoneal – **SEEK SPECIALIST ADVICE.** The renal handbook (5th edition) can be a useful resource https://www.medicinainterna.net.pe/sites/default/files/The_Renal_Drug_Handbook_The_Ultimate.pdf

Analgesics

1. **Paracetamol** at standard doses is safe in mild-moderate renal impairment, but dose should be reduced in severe renal impairment (Max 3g/24hrs if eGFR<10ml/min).

2. **Non-steroidal anti-inflammatory drugs (NSAIDs)** should be avoided if possible, unless an individual is already on dialysis. If an NSAID is prescribed, the lowest effective dose should be used and renal function should be re-checked within 5-7 days of starting the drug. If the renal function deteriorates, consider risk versus benefit ratio.

3. **Opioids** should be used cautiously if eGFR<30ml/min, **seek specialist advice.** Monitor for signs of opioid toxicity which may include reduced respiratory rate, hallucinations, myoclonic jerks, drowsiness and confusion.

Use of an unfamiliar opioid may present risks. Therefore, it may be safer to use a familiar opioid cautiously rather than switching to a renally safer alternative that the prescriber and those administering it are unfamiliar with.

Consider

- Will there be any issues with obtaining a supply? (e.g. will it be in stock at a community pharmacy?).
- How easy will it be to administer? (e.g. will the individual be able to self-administer or will health care professionals need to be involved?).
- How familiar is the prescriber with management of dose, titration and adverse effects?

Table 35 – Strong opioids in renal impairment

Drug	Accumulation risk	Dose
Morphine	Active metabolites may accumulate	Avoid if possible, but if have to use then adjust starting dose according to eGFR: eGFR 20-50mL/min: 75% of normal dose. eGFR 10-20mL/min: Use small doses (50% of dose), eg. 2.5-5mg and extended dosing intervals. Titrate according to response. eGFR <10mL/min: Use small doses. Eg.1.25-2.5mg and extended dosing intervals. Titrate according to the response. Avoid slow release oral preparations as any side effects may be prolonged.
Oxycodone	Active metabolites may accumulate	eGFR 20-50mL/min: Start with 75% of dose. Titrate dose as in normal renal function. eGFR 10-20mL/min: Start with 75% of dose. Titrate dose as in normal renal function. eGFR <10mL/min: Start with small doses e.g. 50% of dose. Has been used in CKD 5 patients; start with lowest dose and gradually increase dose according to response.
Buprenorphine patch	No active metabolites Possible accumulation of parent drug	Use normal dose.
Fentanyl patch	No active metabolites Possible accumulation of parent drug	eGFR 10-50ml/min – start at 75% of normal dose, titrate according to response. eGFR <10ml/min – start at 50% of normal dose, titrate according to response.

Ref: https://ukkidney.org/sites/renal.org/files/RAsec/Final%20OPIATE~4.pdf

Table 36 – Adjuvant analgesics in renal impairment

Drug	Accumulation risk	Dose
Amitriptyline	Possible accumulation	Use with caution
Gabapentin	Parent drug may accumulate	See latest version of BNF for dose guidance
Pregabalin	Parent drug may accumulate	See latest version of BNF for dose guidance
Duloxetine	Accumulation of parent drug	Avoid if possible. Contraindicated if eGFR<30ml/min.

Antiemetics

- For all antiemetics use low starting doses and titrate cautiously. Individuals are likely to have increased cerebral sensitivity.
- In general, all antiemetics commonly used in palliative care can be used cautiously at low doses in severe renal impairment. Therefore, choose the most appropriate antiemetic according to cause of nausea/vomiting and effectiveness.

Table 37 – Antiemetics in renal impairment

Drug	Accumulation risk	Dose
Cyclizine	No active metabolite	Start low dose, titrate cautiously
Haloperidol	Possible accumulation of parent drug or active metabolite in severe renal impairment	Start low dose, titrate cautiously
Levomepromazine	Possible accumulation of active metabolite	Start low dose, titrate cautiously
Metoclopramide	Possible accumulation in severe renal impairment	Start low dose, titrate cautiously
Ondansetron	No active metabolite	Use at normal dose

Antidepressants

- For all antidepressants start at low dose and titrate cautiously.
- In renal impairment there may be increased sensitivity to drugs acting on central nervous system (CNS).

Table 38 – Antidepressants in renal impairment

Drug	Accumulation risk	Dose
Sertraline	No active metabolite	Start with 25mg daily, titrate cautiously
Citalopram	Active metabolites	Use with caution in severe renal impairment, increased risk of QT prolongation, titrate cautiously
Mirtazapine	Active metabolites and parent drug may accumulate	Avoid if possible

Benzodiazepines

- Uraemia may cause or contribute to agitation in the dying phase.
- Consider use of haloperidol if patient suffering from delirium rather than agitation/anxiety

Table 39 – Benzodiazepines in renal impairment

Drug	Accumulation risk	Dose
Lorazepam	No active metabolite Does not accumulate	Use low starting dose and titrate cautiously
Clonazepam	Possible accumulation	Use low starting dose and titrate cautiously
Midazolam	Possible accumulation	Use low starting dose and titrate cautiously

Antisecretory drugs

Table 40 – Antisecretory drugs in renal impairment

Drug	Accumulation risk	Dose
Hyoscine butylbromide	No active metabolite Does not accumulate	Use normal dose
Glycopyrronium	Active metabolite may accumulate	Reduce dose by 50%

Management of Diabetes at the End of Life

Management will vary depending on whether the patient is in the last months, weeks or days of life.

Managing diabetes in the last months of life

Refer to the detailed guidance in the End of Life Guidance for diabetes Care (November 2021)

www.diabetes.org.uk/professionals/position-statements-reports/diagnosis-ongoing-management-monitoring/end-of-life-care

Managing diabetes in the last weeks of life

Explore with the individual and those identified as important to them about changing the approach to diabetes management, including:

- The aim of management – avoiding hypoglycaemia rather than avoiding longer term complications due to hyperglycaemia.
- The value or otherwise of continuing to monitor blood glucose readings.
- The method and frequency of checking blood glucose levels.
- The type of management – oral hypoglycaemics and/or insulin.

Devise a management plan with the individual and those identified as important to them. Ensure the local diabetes specialist team are involved if the individual remains on insulin. Aim to:

- Keep invasive tests to a minimum.
- Be alert to symptoms that may be due to hypo or hyperglycaemia and have appropriate medication/interventions available to address these if they develop.

Aim for a target blood glucose reading of 6-15mmol/L.

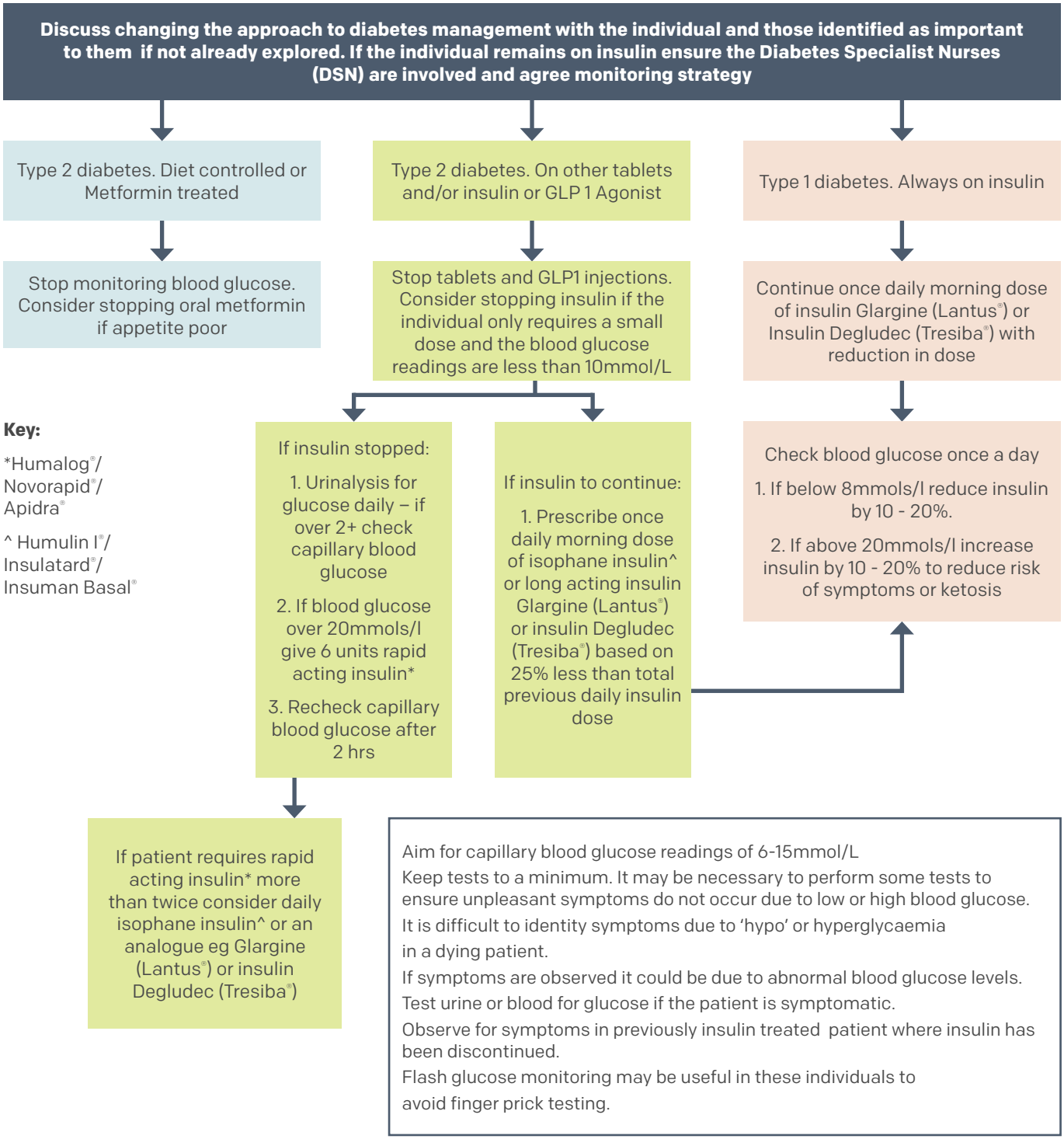
Managing diabetes in the last days of life

Follow Figure 2 – Management of Diabetes algorithm for the last days of life

Seek advice from the local diabetes specialist team if required.

Figure 2 – Management of Diabetes

Algorithm for the last days of life



Extracted from End of Life Guidance for Diabetes Care (November 2021) Diabetes

NOTE: Although this algorithm taken from the End of Life Guidance for Diabetes Care Clinical Care Recommendations includes Insulin Degludec as an alternative to insulin Glargine, the former is only recommended for restricted use across GM, so **Insulin Glargine should be used.**

Management of Implantable Cardioverter Defibrillators (ICDS) in the last weeks and days of life

An implantable cardioverter defibrillator (ICD) is a small device that is placed in the chest or abdomen and links to the heart. It uses electrical pulses or shocks to help control life-threatening arrhythmias. Individuals with an ICD in situ sometimes develop end-stage heart failure or another life limiting condition, in which case a stage may be reached when it is no longer medically appropriate for the device to be used.

It is important, wherever possible, to plan ahead and discuss with the individual , and those important to them, whether to deactivate the ICD.

- In general, maintaining an ICD in active defibrillation mode is inappropriate if the individual has an active DNACPR order.
- However, it is possible that a competent individual may decline a full resuscitation attempt because of the loss of dignity this could involve, but they may decide to keep their ICD active.
- **If the ICD is to be kept active, consider obtaining a ring magnet from the local Cardiology department** so the ICD can be deactivated when the individual is dying. See section **What to do if a patient is dying and their implantable defibrillator is still switched on for further guidance**

Triggers for conversations around switching off an ICD

- Refractory symptoms despite optimal therapy.
- At least three hospital admissions with decompensation in less than six months.
- Deteriorating physical function.
- Cardiac cachexia.
- Resistant hyponatraemia.
- Serum albumin of less than 25g/L.
- Have been experiencing multiple shocks.
- Comorbidity with a poor prognosis, such as terminal cancer.
- Continuation is inconsistent with the individual's goals of care.

There is information for individuals and carers regarding deactivating the shock function of an ICD towards the end of life at **https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/icds-and-end-of-life/icd-deactivation-faqs**

Decisions regarding switching off an ICD

When an individual is heading towards the end of their life, if time allows, it can be arranged with the Cardiology department at the local acute hospital for the defibrillator to be switched off in anticipation of the last hours of life. This generally needs to be done in normal working hours.

Turning off the defibrillator means that the individual will not be shocked should they have a ventricular tachyarrhythmia. If it is a combined defibrillator and pacemaker device, the pacemaker will continue to function, as it is only the defibrillator component that is turned off.

What to do if a patient is dying and their implantable defibrillator is still switched on

If an individual dies with their defibrillator functioning, it will repeatedly shock during the periods of ventricular tachyarrhythmia (VT or VF) that may precede asystole in a dying heart. This can be distressing to the individual, family and staff. There is also a risk of shock to anyone touching the individual.

If urgent deactivation by a cardiac physiologist using a programmer cannot be arranged immediately, the ICD can be deactivated (after discussion and careful consideration of its consequences) by taping a **ring magnet** securely on the skin overlying the device. **Suitable magnets are available from local Cardiology Departments.**

With the magnet in situ, there is no risk of shock to anyone touching the individual e.g. family or those identified as important to the individual, or during normal nursing cares. Do not attempt to remove the defibrillator.

What to do after a patient has died

The magnet should be left in place until the ICD is switched off and the magnet can then be removed without risk of shock to the individual or staff.

If an individual dies with a functioning defibrillator in situ, it needs to be turned off before it is removed. The local cardiology centre will need to be contacted to do this.

It is necessary for the device to be removed after death regardless of what happens to the body after death. It is essential that the undertakers are informed that a device is still in situ when the body is moved. It is essential that the device is removed if the body is cremated.

Ref: https://www.bhf.org.uk/informationsupport/publications/healthcare-and-innovations/deactivation-of-implantable-cardioverter-defibrillators-towards-the-end-of-the-life

Symptom Management in individuals with Advanced Dementia

A prognostic indicator tool may be helpful to assess whether an individual is in the end of life stage e.g. Gold Standards Framework Proactive Identification Guidance https://goldstandardsframework.org.uk/cd-content/uploads/files/PIG/Proactive%20Identification%20Guidance%20v7%20(2022).pdf

General Assessment

- A comprehensive, holistic assessment is an essential cornerstone in meeting an individual's needs and managing their symptoms effectively. The following considerations are particularly important when assessing a person with dementia:
- Is the individual able to self-report symptoms including pain?
- Involve other people who know the individual. This may include family members, professional carers and other clinicians. This is vital for understanding the person's 'normal state' so that changes in behaviour can be identified & understood in context to help identify underlying cause (e.g. breakthrough pain) in apparently distressed individuals.
- Consider using "This Is Me" www.alzheimers.org.uk/get-support/publications-factsheets/this-is-me or similar to ensure individual's history and preferences are recorded and shared with staff.
- Use supportive communication strategies: ask short questions and allow additional response time; use gestures; minimise distractions and external noise; address any sensory impairments; seek confirmation of any assumptions made; consider use of first language.
- Is the person compliant with medication?
- Consider sub-type of dementia (where known) as this may affect presentation of symptoms and management.
- Consider the carer's needs including their support needs and coping strategies.

Assessment of Mental Capacity

- Does the individual have capacity to consent (with support) to examination/investigation/taking medications?
- Undertake formal assessment of mental capacity according to the MCA and hold best interests meeting if necessary.

Assessment of Distress and Pain

- People with dementia may not report their pain so it is always important to ask them.
- They may not associate their experience with the word pain, so use alternative words such as aching, hurting, sore, and uncomfortable.
- Focus on current pain and ensure assessment is made during both periods of activity and of rest.

- Visual tools in the form of rating scales (numerical rating scale, verbal rating scale, pain thermometer), body diagram, descriptive words and pictures may support people with communication difficulties to self-report their pain.
- When a person is not able to accurately report how they feel, observing their behaviour and facial gestures can indicate when they are distressed.
- The following behaviours are likely to be a sign of distress which may be an indication of pain, discomfort or an emotional need: Agitation, walking around more than usual, withdrawal, night-time waking, not eating/ drinking or any behaviour that signals a change from the person's normal behaviour.
- Knowing about a person, their routines, habits and life story and the context in which the distressed behaviour occurs, can help to distinguish pain and other causes of distress such as hunger, anxiety, boredom.
- If a person is unable to say whether they have pain it is important to look to rule out other potential causes of distress before assuming it is pain.

There are several tools available to support pain assessment in people with dementia, including **PAIN-AD** https://geriatrictoolkit.missouri.edu/cog/painad.pdf and **Abbey Pain Scale** https://www.apsoc.org.au/PDF/Publications/APS_Pain-in-RACF-2_Abbey_Pain_Scale.pdf

- When using these tools, watch for over-identification of pain. Is distress due to another cause?
- **Disability Distress Assessment Tool** helps healthcare professionals and carers record a person's behaviour and recognise signs they are distressed. It also has a clinical decision check list to help determine the possible cause of their distress http://www.wamhinpc.org.uk/sites/default/files/Dis%20DAT_Tool.pdf

Medication use – general considerations

- Consider non-drug management options first.
- Optimise current medications: consider concordance, individuals specific factors, consider use of compliance aid e.g. Dosette box.
- People with dementia are particularly vulnerable to the side effects of drugs that exacerbate confusion e.g. anticholinergics, amitriptyline. The Anticholinergic Burden Calculator http://www.acbcalc.com/ can be used to assess the anticholinergic burden of existing medications and to aid decision making about alternatives with a lower anticholinergic burden.
- In Parkinson's Dementia and Lewy Body Dementia, be aware of side effects of dopamine agonists (confusion, hallucinations and delusions).
- Use oral medication as first line wherever possible.
- If the person is unhappy taking oral medications, consider:
  - Switching from tablets to syrup/liquids.
  - Giving tablets with jam/yoghurt.
  - Oro-dispersible preparations.
  - Change to a once daily/slow release preparation if available.

  Liaise with pharmacist. NB. Administration of covert medication for individuals who lack capacity may occasionally be needed. This will require a best interest decision.
- Prioritise essential medications (in dying phase, symptom management is the priority).
- If necessary, SC injections can be given regularly or when required.
- Consider a syringe pump if the person needs regular SC medication, but if they are likely to move about and forget to carry/take the syringe pump or to pull at the infusion line, continuing with regular injections may be more appropriate.

Pain Management

- Identify and, where possible, treat any contributing causes e.g. constipation, pressure sores.
- If unclear if individual has pain, consider a trial of regular analgesia.
- Start with regular paracetamol, consider stronger analgesia if necessary.
- Consider topical preparations such as non-steroidal anti-inflammatory gels and non-pharmacological measures such as heat pads and warm baths for mild-moderate localised pain in acute and chronic musculoskeletal conditions such as arthritis.
- If unable to swallow oral medications and the individual is thought to be in the last months of life but not obviously in last days of life, the transdermal route may be considered **Pain Management section re transdermal preparations**

Eating and Swallowing Problems

- Nutritional problems, loss of appetite, swallowing problems and weight loss are common issues in dementia, especially as the severity of illness increases.
- Overall there is no conclusive evidence that Clinical Assisted Nutrition provides benefit for people with advanced dementia, either in terms of prolonging life or improving quality of life for people with dementia. **https://www.ncbi.nlm.nih.gov/pubmed/19370678**
- NICE recommends that tube feeding should not normally be used for people living with severe dementia, unless the reasons for the person's problems with eating, drinking or swallowing are treatable and it's expected that they will be able to start eating and drinking normally afterwards.

  Ref: NICE Decision Aid Enteral (tube) feeding for people living with severe dementia (2018) **https://www.nice.org.uk/guidance/ng97/resources/enteral-tube-feeding-for-people-living-with-severe-dementia-patient-decision-aid-pdf-4852697007**
- Exclude reversible causes for not eating e.g. thrush.
- Ensure good mouth care.
- Consider if appropriate to refer to Speech and Language Therapist for assessment.
- Consider mental capacity with all feeding decisions and if the patient lacks capacity a best interest decision would need to be made.
- For those with swallowing difficulties comfort feeding small amounts of appropriately thickened fluids/soft food may provide enjoyment of eating and result in perceived alleviation of hunger or thirst (risk feeding).

Nausea and Vomiting/Constipation

- Follow the general guidance for managing these symptoms – **see Nausea and Vomiting** and **Constipation sections**

Agitation, aggression, distress and psychosis

- Neuropsychiatric symptoms are nearly universal in dementia and agitation is among the most distressing for individuals, those identified as important to them and carers.
- Consider specific causes e.g. pain, side effect of medication, emotional, activity (e.g. dressing) or environment (e.g. lighting, unfamiliar surroundings).
- Address where possible by person-centred non-drug approaches.

Antipsychotics

- Low-strength antipsychotics have historically been prescribed to treat behavioural and psychological symptoms associated with dementia (BPSD) but produce only limited benefits and are associated with an increased risk of stroke and mortality, as well as other serious adverse events such as sedation, extrapyramidal side effects, dehydration, falls, chest infections and accelerated cognitive decline.
- NICE Guideline 97 "Dementia: assessment, management and support for people living with dementia and their carers" (June 2018) **https://www.nice.org.uk/guidance/ng97/**

chapter/Recommendations#managing-non-cognitive-symptoms recommends that antipsychotics should only be used for people who are living with dementia who are either at risk of harming themselves or others, or experiencing agitation, hallucinations or delusions which are causing them severe distress.

- Before starting antipsychotics, discuss the benefits and harms with the person, those identified as important to them and carers (as appropriate). Consider using a decision aid to support this discussion e.g. NICE patient decision aid on **antipsychotic medicines for treating agitation, aggression and distress in people living with dementia.** The antipsychotic should be used at the lowest dose that helps the person, and for the shortest possible time. Stop if there is no clear ongoing benefit after discussion with the patient and their family members or carers (as appropriate).
- **Dopamine receptor antagonists should be avoided if possible in Lewy Body dementia** as these individuals are more prone to severe side effects.

Delirium

- Delirium is extremely common in patients with advanced dementia. See Delirium section
- Non-pharmacological management is the mainstay of treatment.
- **Avoid dopamine receptor antagonists in Lewy Body Dementia if at all possible –** they can have marked adverse effects which may not recover with cessation of the drug.

References

- NICE Guideline 97 "Dementia: assessment, management and support for people living with dementia and their carers" (June 2018) https://www.nice.org.uk/guidance/ng97/chapter/Recommendations
- GMMMG Low Strength Antipsychotic Prescribing in Dementia: A GP Resource Pack (2021) https://gmmmg.nhs.uk/wp-content/uploads/2021/08/GMMMG-Antipsychotics-in-dementia-GP-resource-pack-FINAL.pdf
- NHS Yorkshire and Humber Clinical Networks Guidelines for Healthcare Professionals: Symptom Management in End of Life Care for People with Dementia.
- North West Coast Strategic Clinical Network Palliative Care Guidelines in Dementia 2nd edition, Version 3.9 – March 2018.

Section 3

Care of the dying

Priorities of care for the dying person

- Recognition that the person may be dying and entering the last days and hours of life.
- Sensitive communication between staff and the dying person and those identified as important to them.
- Involve the dying person and those identified as important to them in decisions about treatment and care to the extent that the dying person wants.
- Support the needs of families and others identified as important to the dying person including any questions or concerns they may have.
- Individualised care should be used to support a person at the end of life. The Strategic Clinical Networks (SCN) Individual Plan of Care and Support for the Dying Person in the Last Days and Hours of Life is available to support this care.
- Senior responsible clinician to agree an holistic individual plan of care including symptom control to be delivered.

References:

The above is based on the Five Priorities for Care of the Dying Person. The Priorities for Care are that, when it is thought that a person may die within the next few days or hours https://assets.publishing.service.gov.uk/media/5a7e301ced915d74e33f09ee/One_chance_to_get_it_right.pdf

National Palliative and End of Life Care Partnership; Ambitions for Palliative and End of Life Care - A National Framework for Local Action 2021-2026 ambitions-for-palliative-and-end-of-life-care-2nd-edition.pdf (england.nhs.uk)

Symptom Management

Symptoms which may occur in the last days and hours of life include:

- Pain.
- Nausea and vomiting.
- Respiratory – secretions, dyspnoea, stridor.
- Psycho-neurological – anxiety, panic, convulsions, delirium and agitation in last days.
- Urinary incontinence/retention.

General principles of symptom management at the end of life

- Identification and regular review of symptoms is essential.
- Symptom control must be tailored for the individual. Reversible causes for any symptom must be assessed and managed effectively when considering prescribing or administering symptom-specific medications.
- Consider the use of non pharmacological measures.
- All medications, including the prescribing of anticipatory medications must:
  - Be targeted at specific symptoms.
  - Be prescribed with a clinical rationale for the starting dose.
  - Have their purpose, use and side effects explained to the dying person and (with the consent of the individual) those close to them if possible.
  - Symptom control using prescribed medications should be reviewed regularly and adjusted as needed for the individual.

Anticipatory prescribing

- Anticipatory prescribing is designed to enable prompt symptom relief at whatever time the individual develops distressing symptoms.
- It is based on the premise that although each dying person is an individual, many symptoms which may develop during the last days of life can be predicted and measures put in place so these can be addressed quickly and effectively if they do occur.

NICE Guideline Care of Dying Adults in the Last Days of Life **https://www.nice.org.uk/guidance/ng31** gives the following recommendations about anticipatory prescribing:

- Use an individualised approach to prescribing anticipatory medicines for people who are likely to need symptom control in the last days of life.
- Specify the indications for use and the dosage of any medicines prescribed.
- Assess what medicines the person might need to manage symptoms likely to occur during their last days of life, such as:
  - Agitation.
  - Anxiety.
  - Breathlessness.
  - Nausea and vomiting.
  - Troublesome respiratory secretions.
  - Pain.

- Discuss any prescribing needs with the dying person, those important to them and the multi-professional team.
- Ensure that suitable anticipatory medicines and routes are prescribed as early as possible. Review these medicines as the dying person's needs change.
- When deciding which anticipatory medicines to offer take into account:
  - The likelihood of specific symptoms occurring.
  - The benefits and harms of prescribing or administering medicines.
  - The benefits and harms of not prescribing or administering medicines.
  - The possible risk of the person suddenly deteriorating (for example, catastrophic haemorrhage or seizures) for which urgent symptom control may be needed.
  - The place of care and the time it would take to obtain medicines.
- Before anticipatory medicines are administered, review the dying person's individual symptoms and adjust the individualised care plan and prescriptions as necessary.
- If anticipatory medicines are administered:
  - Monitor for benefits and any side effects at least daily, and give feedback to the lead healthcare professional.
  - Adjust the individualised care plan and prescription as necessary.
- The BMA has also produced guidance designed to help GPs with their prescribing in this important field **https://www.bma.org.uk/advice-and-support/gp-practices/prescribing/anticipatory-prescribing-for-end-of-life-care**

Maintaining Hydration

Nutrition and hydration are often emotive topics for the individual and those identified as important to them when approaching the end of life. There is need for ongoing sensitive discussions about goals of care and realistic expectations of treatment.

NICE Guideline Care of Dying Adults in the Last Days of Life gives the following recommendations about maintaining hydration: **https://www.nice.org.uk/guidance/ng31**

1. Support the dying person to drink if they wish to and are able to. Check for any difficulties, such as swallowing problems or risk of aspiration. Discuss the risks and benefits of continuing to drink, with the dying person, and those involved in the dying person's care.

2. Offer frequent care of the mouth and lips to the dying person, and include the management of dry mouth in their care plan, if needed. Offer the person the following, as needed:
   - Help with cleaning their teeth or dentures, if they would like .
   - Frequent sips of fluid.

3. Encourage people important to the dying person to help with mouth and lip care or giving drinks, if they wish to. Provide any necessary aids and give them advice on giving drinks safely.

4. Assess, preferably daily, the dying person's hydration status, and review the possible need for starting clinically assisted hydration, respecting the person's wishes and preferences.

5. Discuss the risks and benefits of clinically assisted hydration with the dying person and those important to them. Advise them that, for someone who is in the last days of life:
   - Clinically assisted hydration may relieve distressing symptoms or signs related to dehydration, but may cause other problems. **See recommendation 9**
   - It is uncertain if giving clinically assisted hydration will prolong life or extend the dying process.
   - It is uncertain if not giving clinically assisted hydration will hasten death.

6. Ensure that any concerns raised by the dying person or those important to them are addressed before starting clinically assisted hydration.

7. When considering clinically assisted hydration for a dying person, use an individualised approach and take into account:
   - Whether they have expressed a preference for or against clinically assisted hydration, or have any cultural, spiritual or religious beliefs that might affect this documented in an advance statement or advance decision to refuse treatment.
   - Their level of consciousness.
   - Any swallowing difficulties.
   - Their level of thirst.
   - The risk of pulmonary oedema.
   - Whether even temporary recovery is possible.
8. Consider a therapeutic trial of clinically assisted hydration if the person has distressing symptoms or signs that could be associated with dehydration, such as thirst or delirium, and oral hydration is inadequate.
9. For people being started on clinically assisted hydration:
   - Monitor at least every 12 hrs for changes in the symptoms or signs of dehydration, and for any evidence of benefit or harm.
   - Continue with clinically assisted hydration if there are signs of clinical benefit.
   - Reduce or stop clinically assisted hydration if there are signs of possible harm to the dying person, such as fluid overload, or if they no longer want it.
10. For people already dependent on clinically assisted hydration (enteral or parenteral) before the last days of life:
    - Review the risks and benefits of continuing clinically assisted hydration with the person and those important to them.
    - Consider whether to continue, reduce or stop clinically assisted hydration as the person nears death.

Table 41 - Potential indications and complications of clinically assisted hydration at the end of life

Potential indications	Potential complications
Symptomatic dehydration Thirst (may be unrelated to fluid status) Reversible renal impairment Opioid toxicity Excess sedation Distress of the individual/those identified as important to them	Line discomfort/ infection Fluid overload Worsening secretions Increased symptom burden as a result of the above Distress of the individual/those identified as important to them

- Clinically assisted hydration may be given either SC or IV. SC fluids usually involve less discomfort and have fewer potential adverse effects than the IV route.
- SC fluids should not be used for severe dehydration and may be difficult to administer in people with widespread oedema.
- Isotonic or hypotonic solutions only should be used (e.g. 0.9% sodium chloride).
- Rate of infusion will vary by individual, but is usually around 1 litre of fluid per 24 hrs.
- There may be practical difficulties when considering clinically assisted hydration in the community setting. Equipment and training may be required. Refer to local guidelines and policies.

Syringe Pumps

The syringe pump is a portable battery-operated device used to give medication continuously via the SC route, usually over a 24 hr period. A number of pumps are available, although the most commonly used pumps across Greater Manchester and Eastern Cheshire is the BD Body GuardTM and T34 ambulatory syringe pump (please check your locality guidelines).

In palliative care, the delivery of medication via the continuous SC route is useful when the oral route is inappropriate such as;

- Dysphagia.
- Intractable nausea +/or vomiting.
- Malabsorption.
- Inability to administer medication via oral route i.e. head/neck cancers.
- Intestinal obstruction.
- Profound weakness/cachexia.
- Unconsciousness.
- Patient choice e.g. aversion to oral medication; dislike of alternative routes (e.g. rectal).
- Care in the last days and hours of life.
- Only prescribe an anticipatory syringe driver in the last days of life if the individual is already established on oral medication and is likely to lose this route.

For most drugs, this method of administration is unlicensed.

However, other routes of administration may be useful and limit the need for a syringe pump e.g. rectal, transdermal and sublingual. Furthermore, **pain control is no better via the SC route than the oral route if the patient is able to swallow and absorb the drug(s).**

It is important to consider the following:

- If the SC route in not available, can the drug(s) be given by another route.
  - Rectal (e.g. NSAID).
  - Sublingual (e.g. lorazepam).
  - Transdermal (e.g. fentanyl).
- Whether the drug can be given as a once daily injection (e.g. dexamethasone, haloperidol, levomepromazine).
- It is best to avoid giving several ‘once’ daily injections SC. However, consider this as an alternative or if this is the individuals choice.
- Drugs are generally more bioavailable by injection than orally. This means that the dose of drug given via the syringe pump is likely to be lower than the dose previously given orally.
- Syringe pumps can take a variety of syringe sizes. The minimum recommended size is 20ml. Dilute the mixture to the maximum volume the syringe pump will take to minimise problems with site irritation. See local policies for recommendations relating to the volumes that can be accommodated in different size syringes.
- It takes a few hours before the drugs are sufficiently absorbed for an effect to be seen. If symptoms are controlled start the syringe pump 1-2 hrs before the effect of medications are due to wear off. If symptoms are uncontrolled, set up the syringe pump immediately. It may be necessary to cover the ‘lag time’ with a stat SC dose of the relevant drug if a delay would be unacceptable for symptom control.

- Protect the contents of the syringe from light with a holster.
- Good communication is vital to expel myths around the use of syringe pump.

Care in the last days or hours of life

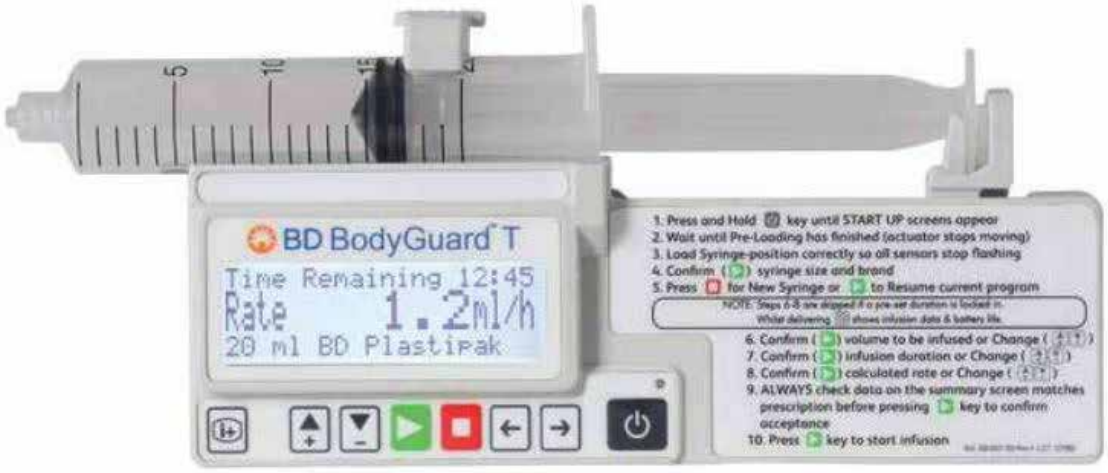
- If an individual is well symptom controlled using other routes of administration these can be maintained in the dying phase, a syringe pump does not have to be set up as a matter of routine.
- In the last days of life, it is recommended to leave transdermal fentanyl or buprenorphine patches in situ (continuing to change as prescribed) with additional analgesia administered SC.
- Avoid inserting the cannula in:
  - Oedematous SC tissue.
  - Very restless/confused patients.
  - Excessive bleeding and a lack of clotting (bleeding diathesis). However, if an individual's platelet count is low, SC injections are less likely to cause bleeding than intramuscular injections. Please check with the medical team.

Advantages of using a syringe pump

- Continuous infusion avoids peaks and troughs in plasma drug level.
- Avoids repeated injections.
- The syringe is generally replenished daily.
- Independence and mobility maintained as the pump is light weight and can be worn in a holster.
- Control of multiple symptoms with a combination of drugs.

Disadvantages

- Irritation or erythema and swelling at the cannula site which may interfere with the rate and absorption.
- May be seen as a 'terminal' event by the individual and those identified as important to them.
- Lack of reliable compatibility data for some mixtures.
- Possible infection.



Drug compatibility

- It is common practice to administer 2 or 3 drugs in the same syringe. Drug compatibility should be checked for all combinations of drugs mixed in one syringe including the diluent.
- A predictor of drug compatibility is pH. The majority of drugs given by syringe pump are acidic. Alkaline drugs include dexamethasone, diclofenac, furosemide, ketorolac and phenobarbital. Consequently, combinations involving these drugs tend to be incompatible and separate infusions are usually recommended. For most drug combinations, water for injection is the suggested diluent, as there is less chance of precipitation.
- Generally, incompatible drugs cause precipitation and thus cloudiness in the syringe. Do not use if this happens. Change both the syringe and the giving set.
- Some drugs are not suitable for SC injection as they are irritant to the skin; e.g. diazepam, prochlorperazine, chlorpromazine.

For more information on compatibility of drugs via CSCI:

http://book.pallcare.info/index.php?op=plugin&src=sdrivers

Good practice regarding syringe pumps:

- Before setting up the syringe pump explain to the individual and those identified as important to them:
  - The reason for using this route and method.
  - How the device works.
  - Advantages and possible disadvantages.
- All staff should receive training and be familiar with their local syringe pump before using.
- Follow local protocol for use.
- All syringe pumps in use should be serviced regularly; see local guidelines.
- After use all syringe pumps should be cleaned and decontaminated as per local guidelines.
- Label the syringe with the list of drugs, date and time the syringe pump is commenced.
- Use of a designated syringe pump chart which includes a monitoring section can prompt checks that the syringe pump is functioning properly (Note: Some areas have a combined prescription and monitoring chart for syringe pumps).
- Checks should include the remaining volume, site condition, rate setting and appearance of the contents of the syringe.
- If the site becomes inflamed or painful, review contents of syringe and re-site using a fresh cannula.
- Site irritation may be reduced by diluting the drugs in a greater volume of diluent or using sodium chloride 0.9% as the diluent or substituting a plastic cannula.
- When prescribing the drugs to be placed in the syringe pump, ensure that the correct SC breakthrough doses are prescribed (i.e. for analgesia 1/6 of the total 24 hr dose of opioid).
- Assess symptom control and adjust the prescription at appropriate intervals.
- Some individuals are able to revert from a syringe pump to oral/transdermal medication. When this seems possible, convert the drugs sequentially rather than all at once.

Always follow your local policies and guidelines for managing the syringe pump

Algorithms for Symptom Management in the Last Days of Life

- The following algorithms give a general guide to managing symptoms in the last days of life.
- It is recognised that many organisations and localities across the region have developed their own local guidelines, tailored specifically for their needs. **Local guidelines should be followed where available and management must be individualised according to the needs of the specific individual receiving care.**

- Please note that there are **four separate algorithms** for managing pain in different circumstances:
  - Algorithm 1 – Individual not already on strong opioids who becomes unable to swallow.
  - Algorithm 2 – Individual taking regular oral morphine who becomes unable to swallow.
  - Algorithm 3 – Individual taking regular oral oxycodone who becomes unable to swallow.
  - Algorithm 4 - Individual using fentanyl or buprenorphine patches who becomes unable to swallow.
- Algorithms 5 to 8 give guidance for managing symptoms other than pain:
  - Algorithm 5 - Restlessness and/or agitation in the last days to hours of life.
  - Algorithm 6 - Respiratory tract secretions.
  - Algorithm 7 - Breathlessness.
  - Algorithm 8 - Nausea and/or vomiting.
- Algorithm 9 gives guidance on managing an individual who is taking anti-epileptics for seizures (including prophylaxis) who becomes unable to swallow.

Pain Algorithm 1

INDIVIDUAL NOT ALREADY ON REGULAR STRONG OPIOIDS BECOMES UNABLE TO SWALLOW (e.g. no regular morphine, oxycodone or fentanyl)

If the patient is known to be intolerant to morphine or morphine not effective, SEEK SPECIALIST ADVICE

Is the patient in pain?

Yes

p.r.n. SC Morphine

- Give morphine 2.5-5mg SC 2-4 hourly p.r.n.
- If 2 or more p.r.n. doses are required in 24 hrs **and** morphine is effective review and consider starting morphine via CSCI.

No

Pre-emptive Prescribing

Prescribe morphine.

2.5-5mg SC 2-4 hourly p.r.n. in case pain occurs.

Continuous SC Morphine

Start a CSCI via a syringe pump over 24 hrs

- Calculate starting dose based on p.r.n. doses required - a cautious starting dose is advised to minimise risk of opioid toxicity.
- Usual starting dose 5-10mg over 24 hrs – **seek specialist advice if you think higher doses may be needed.**
- Calculate p.r.n. 'breakthrough' dose as 1/6 to 1/10 of the total 24 hr dose of SC morphine and prescribe this dose 2-4 hourly SC p.r.n.

Review Pain at Each Visit

- Is morphine effective?
- If the patient needed more than 2 p.r.n. doses in 24 hrs consider if the 24 hr CSCI dose needs increasing.
- Recalculate CSCI dose by adding p.r.n. doses to amount in CSCI **(Do not increase CSCI dose by more than 50%).**
- If patient needs more than 3 p.r.n. doses in 24 hrs or morphine is not effective **seek specialist advice.**

KEY MESSAGES – PAIN

- Consider and eliminate reversible causes for pain (constipation, urinary retention, spiritual and psychological causes).
- Would a pain chart be of benefit?
- Refer to the opioid conversion charts **Appendix 1** for information.
- When calculating CSCI increase based on p.r.n. use, exclude doses used for incident pain.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Pain Algorithm 2

INDIVIDUAL TAKING REGULAR ORAL MORPHINE BECOMES UNABLE TO SWALLOW

If the patient is taking ORAL OXYCODONE follow algorithm 3 when commencing a continuous SC infusion

Is pain controlled on current dose?

Yes

Commence CSCI via a Syringe Pump

- Convert the dose of oral morphine to the SC equivalent (see key messages below).
- Calculate breakthrough dose in case required (see key messages below).

No

Commence CSCI via a Syringe Pump

- Convert the dose of oral morphine to the SC equivalent (see key messages below).
- Consider increasing total 24 hr dose of SC morphine by 33-50%.
- Give the increased total 24 hr dose of SC morphine via syringe pump over 24 hrs.
- Calculate new breakthrough dose (see key messages below).

Review Pain at Each Visit

- Is morphine effective?
- If the patient needed more than 2 p.r.n. doses in 24 hrs consider if the 24 hr CSCI dose needs increasing.
- Recalculate CSCI dose by adding p.r.n. doses to amount in CSCI **(Do not increase by more than 50%).**
- If patient needs 3 or more p.r.n. doses in 24 hrs or morphine is not effective **seek specialist advice.**

KEY MESSAGES - PRESCRIBING SC MORPHINE

- To calculate the dose of SC morphine, divide total dose of oral morphine by 2.
- Calculate the breakthrough dose of morphine as 1/6 to 1/10 of the total 24 hr dose of SC morphine and prescribe this dose 2-4 hourly SC p.r.n.
- If symptoms are controlled start CSCI 2-4 hrs before the next dose of regular oral opioid is due; if symptoms are not controlled, start CSCI immediately.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Pain Algorithm 3

INDIVIDUAL TAKING REGULAR ORAL OXYCODONE BECOMES UNABLE TO SWALLOW

If the patient is taking ORAL MORPHINE follow algorithm 2 when commencing a continuous SC infusion

Is pain controlled on current dose?

Yes

Commence CSCI via a Syringe Pump

- Convert the dose of oral oxycodone to the SC equivalent (see key messages below).
- Calculate breakthrough dose in case required (see key messages below).

No

Commence CSCI via a Syringe Pump

- Convert the dose of oral oxycodone to the SC equivalent (see key messages below).
- Consider increasing total 24 hr dose of SC oxycodone by 33-50%.
- Give the increased total 24 hr dose of SC oxycodone via syringe pump over 24 hrs.
- Calculate new breakthrough dose (see key messages below).

Review Pain at Each Visit

- Is oxycodone effective?
- If the patient needed more than 2 p.r.n. doses in 24 hrs consider if the 24 hr CSCI dose needs increasing.
- Recalculate CSCI dose by adding p.r.n. doses to amount in CSCI **(Do not increase by more than 50%).**
- If patient needs 3 or more p.r.n. doses in 24 hrs or oxycodone is not effective **seek specialist advice.**

KEY MESSAGES - PRESCRIBING SC OXYCODONE

- To calculate the dose of SC oxycodone, divide total dose of oral oxycodone by 2.
- Calculate the breakthrough dose of oxycodone as 1/6 to 1/10 of the total 24 hr dose of SC oxycodone and prescribe this dose 2-4 hourly SC p.r.n.
- If symptoms are controlled start CSCI 2-4 hrs before the next dose of regular oral opioid is due; if symptoms are not controlled , start CSCI immediately.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Pain Algorithm 4

INDIVIDUAL USING FENTANYL OR BUPRENORPHINE PATCHES BECOMES UNABLE TO SWALLOW

IMPORTANT

CONTINUE CURRENT FENTANYL OR BUPRENORPHINE PATCH PRESCRIPTION, CHANGING PATCHES AS PRESCRIBED

Pre-Emptive Prescribing

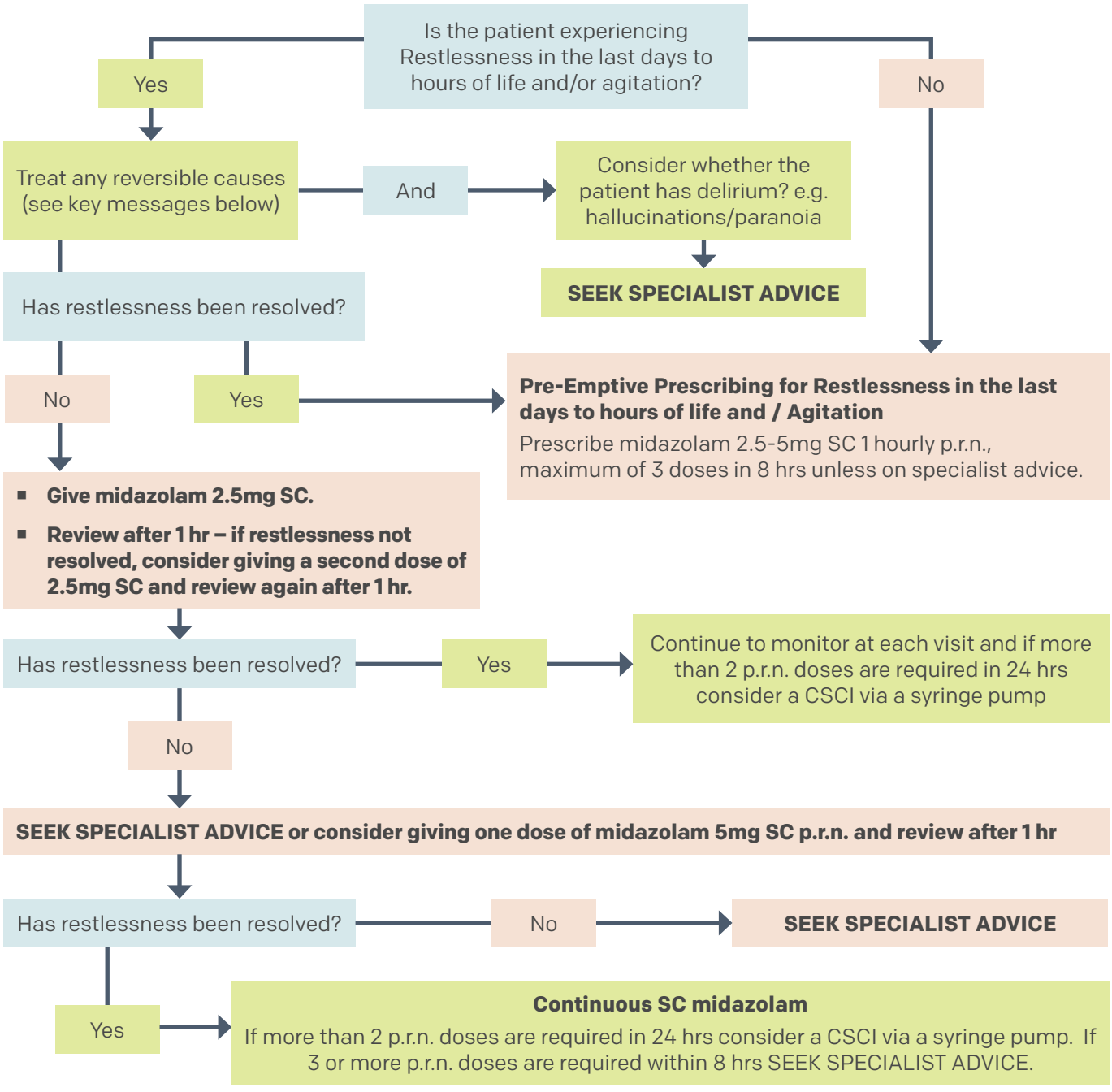
- Prescribe SC opioid for breakthrough pain 2-4 hourly p.r.n in case pain occurs.
- If patient has been taking an oral opioid for breakthrough pain, the same drug should usually be prescribed SC.
- Calculate dose or consult conversion chart **(Appendix 1)** as a guide for the p.r.n. dose of SC opioid that is relevant for the strength of patch.

If pain not controlled or if needing more than 2 p.r.n doses over 24 hrs, consider a CSCI in addition to the patch - seek Specialist Palliative Care advice.

If eGFR<30ml/min, SEEK SPECIALIST PALLIATIVE CARE ADVICE.

Algorithm 5

IS THE INDIVIDUAL EXPERIENCING **RESTLESSNESS IN THE LAST DAYS TO HOURS OF LIFE** AND/OR AGITATION?

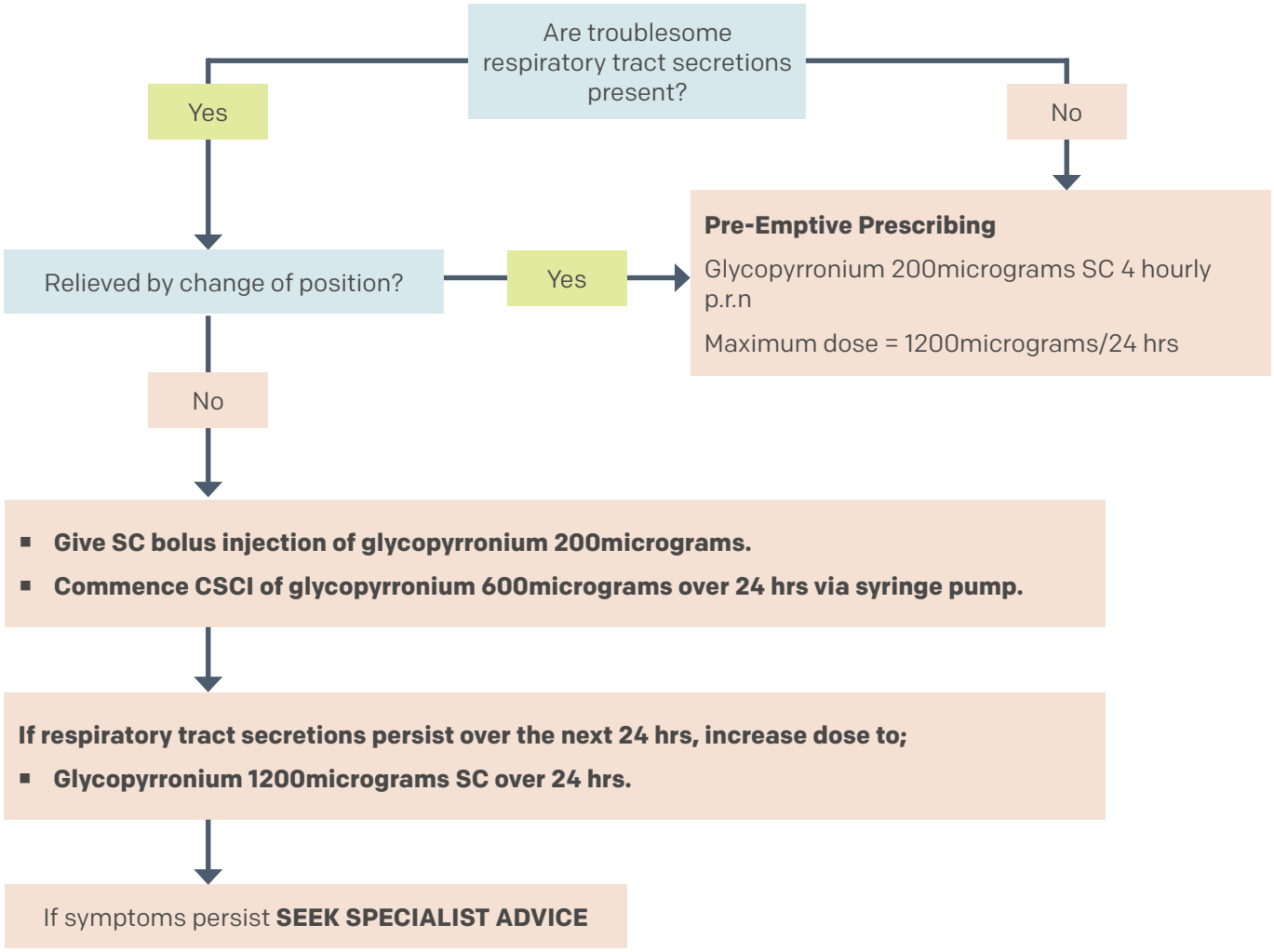


KEY MESSAGES –RESTLESSNESS IN THE LAST HOURS TO DAYS OF LIFE AND AGITATION

- Document that reversible causes of agitation have been considered (pain, constipation, urinary retention, overheating, infection, nicotine withdrawal, high calcium levels).
- If requiring 3 or more p.r.n doses within 8 hrs seek urgent specialist advice.
- Consider adding any p.r.n doses given in previous 24 hrs to syringe pump dose.
- The p.r.n dose of midazolam should be the amount in the syringe pump divided by 6.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Algorithm 6

ARE TROUBLESOME **RESPIRATORY TRACT SECRETIONS** PRESENT?

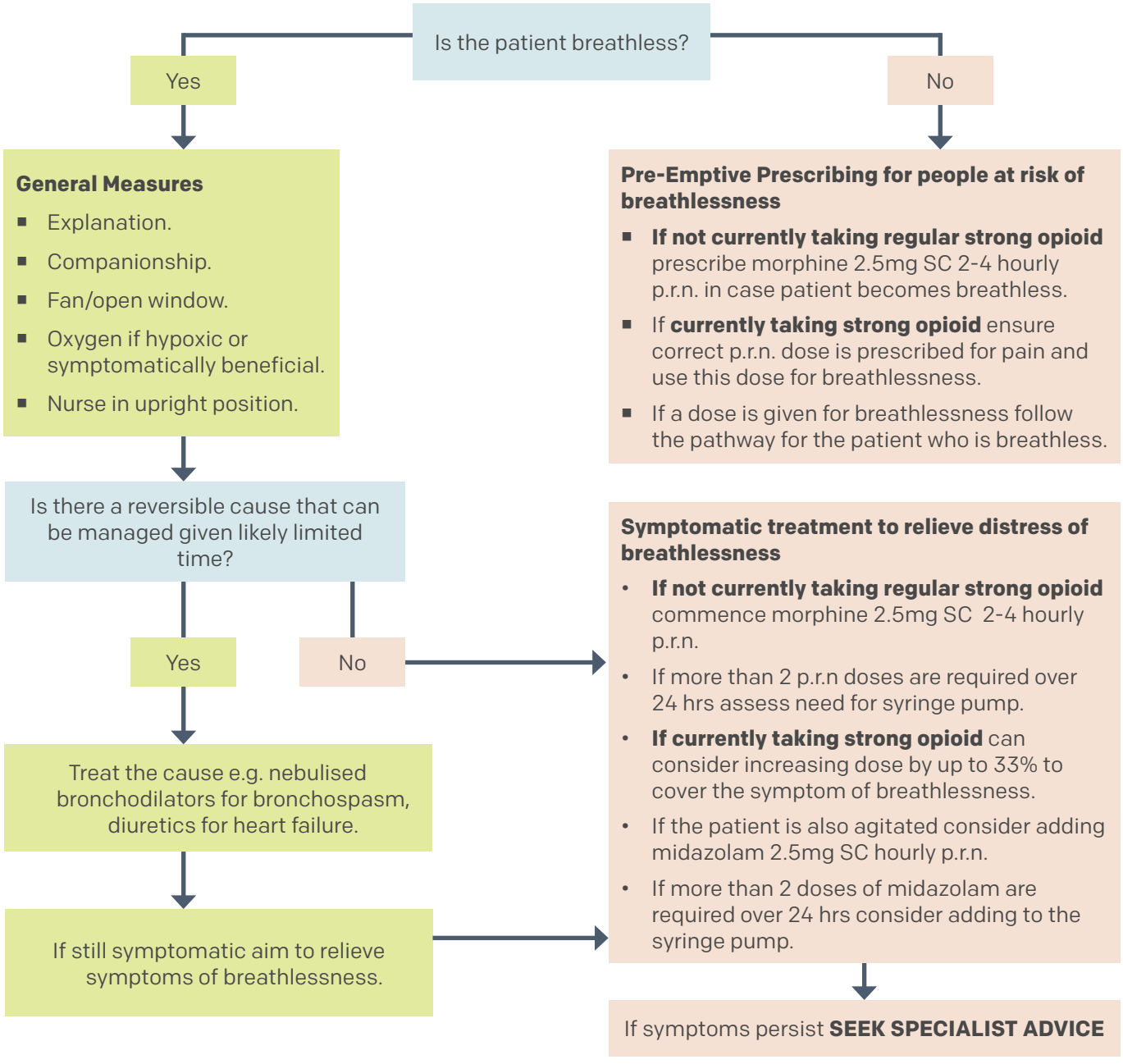


KEY MESSAGES – TROUBLESOME RESPIRATORY SECRETIONS

- Treatment must be commenced at **onset** of secretions. Medication may prevent new secretions being produced but will not remove secretions already present.
- If there is a delay in commencing a syringe pump when appropriate, administer regular glycopyrronium 200micrograms 6 hourly until syringe pump available.
- Alternative antimuscarinic drugs can be used according to local guidelines, e.g. hyoscine butylbromide (Buscopan®) 20mg SC 4 hourly p.r.n., 60-120mg CSCI or hyoscine hydrobromide 400micrograms SC 4 hourly p.r.n, 1.2mg – 2.4mg CSCI over 24 hrs.
- Troublesome respiratory secretions may be most upsetting for family and those close to the patient. Discussion of these symptoms with them is important.
- Palliative treatment with antibiotics may be appropriate if they are likely to help reduce purulent secretions and increase the comfort of the patient.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Algorithm 7

IS THE INDIVIDUAL **BREATHLESS?**

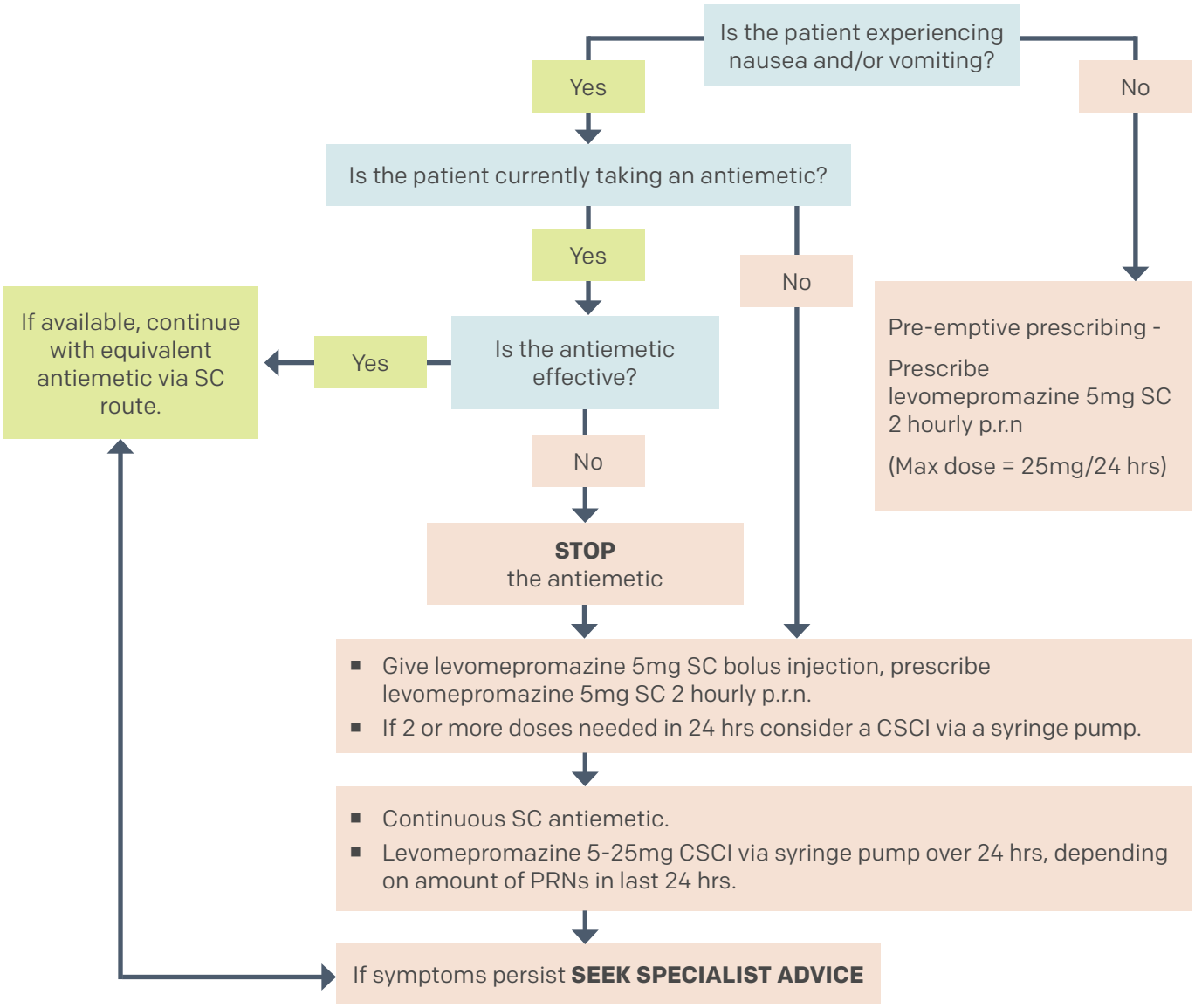


KEY MESSAGES – BREATHLESSNESS

- Treatment for reversible causes of breathlessness include; bronchodilators, diuretics and antibiotics.
- Simple measures such as a calm environment, a fan or open window can be just as effective as medication.
- If 3 or more p.r.n doses are required within 8 hrs seek specialist advice.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Algorithm 8

IS THE INDIVIDUAL EXPERIENCING **NAUSEA AND/OR VOMITING?**

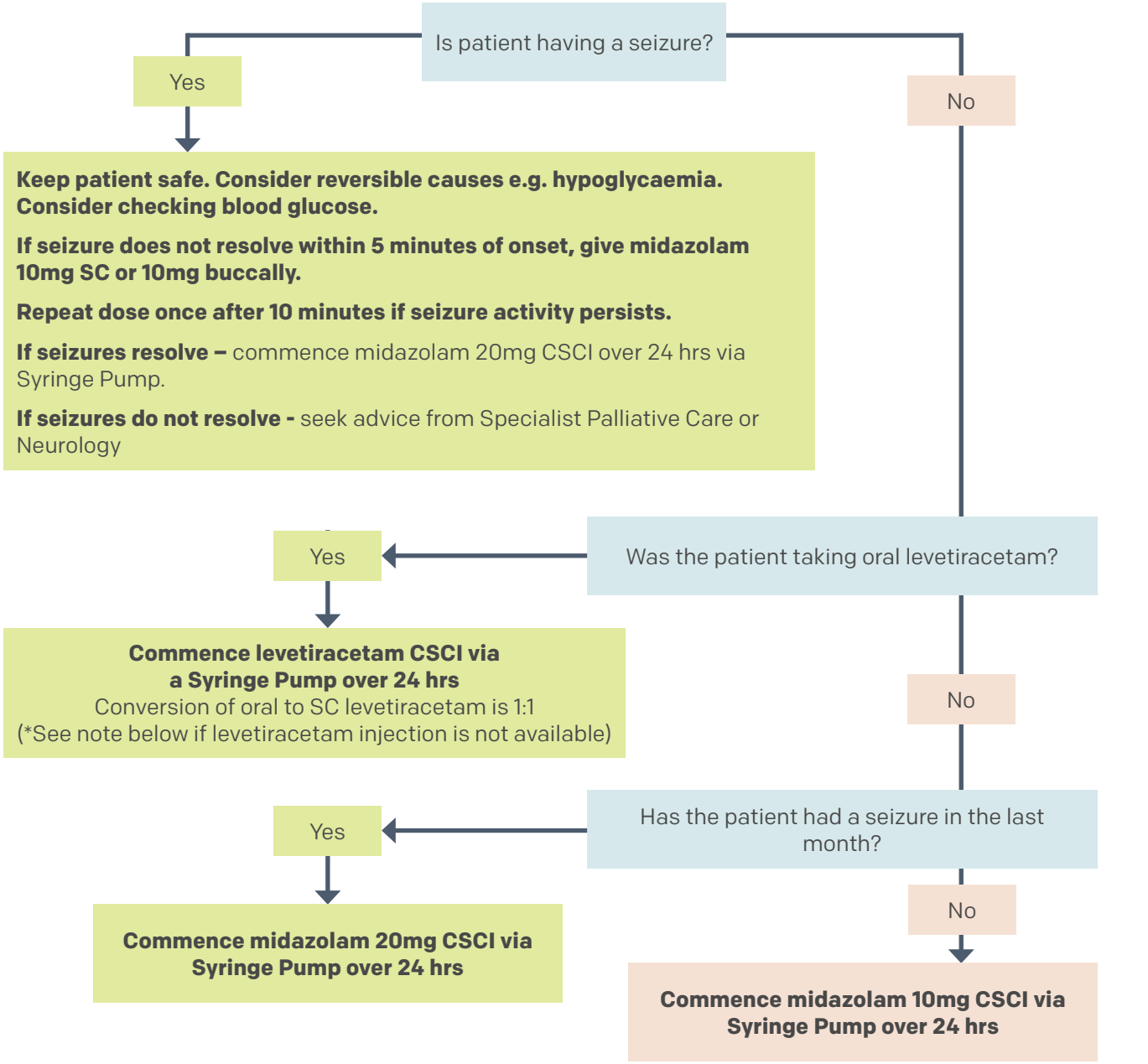


KEY MESSAGES – NAUSEA AND VOMITING

- Patients with complete bowel obstruction and nausea or vomiting should not receive metoclopramide.
- Alternative antiemetics may be prescribed according to local guidelines, e.g. cyclizine 25-50mg SC 4-6 hourly p.r.n. OR 75-150mg by CSCI over 24 hrs (not recommended in heart failure, use water for injection if diluent needed); or haloperidol 500micrograms – 1.5mg stat, 1.5 – 5mg CSCI.
- Metoclopramide and cyclizine should not be prescribed simultaneously.
- For patients with Parkinsonism or Parkinson's Disease seek specialist advice.
- Simple measures such as treating constipation and keeping the patient away from strong food smells may also help.
- If eGFR<30ml/min, **SEEK SPECIALIST PALLIATIVE CARE ADVICE.**

Algorithm 9

INDIVIDUAL TAKING ORAL ANTI-EPILEPTICS FOR SEIZURES OR SEIZURE PROPHYLAXIS BECOMES UNABLE TO SWALLOW



SEEK SPECIALIST ADVICE regarding titration of medication in CSCI if seizures are not controlled on the initial dose.

***If levetiracetam injection is not available, midazolam may be used as an alternative if the patient is thought to be imminently dying or whilst awaiting supplies.**

Note: Some anti-epileptics have a long half-life and may continue to be effective for 2-3 days after the last oral dose. SEEK SPECIALIST ADVICE if the patient is likely to die within the next 24 hrs, as it may not be necessary to commence a CSCI, unless they have a history of recent seizures.

PCF8 Scottish Palliative Care Guidance

Section 4

Appendices

Appendix 1 - Opioid Conversion Charts

Ref: PCF8, BNF

- The conversion tables below act as a guide but **consideration must be given to the wide inter-individual variation that exists.**
- Each patient should be assessed on an individual basis.
- Be cautious when converting between different opioids.
- Consider a dose reduction when switching opioids, particularly if the switch is being made because of opioid toxicity.
- Breakthrough p.r.n doses within these charts are based on 1/6 of the total regular daily dose of opioid, but the dose required by an individual may vary between 1/6 and 1/10.

Table 42 - Dose conversions of weak opioids to oral morphine

Drug	Conversion	Maximum dose in 24 hrs (mg)	Approximate oral morphine equivalent in 24 hrs (mg)
Codeine	To obtain equivalent oral morphine dose divide by 10	240	24
Dihydrocodeine		240	24
Tramadol		400	40

Table 43 - Recommended strong opioid dose conversion ratios

Convert from	Convert to	Calculation
Oral morphine	SC morphine	Divide by 2
	Oral oxycodone	Divide by 2
	SC oxycodone	Divide by 3
Oral oxycodone	SC oxycodone	Divide by 2*
	SC morphine	Equivalent
SC morphine	SC oxycodone	Divide by 1.5

***Note:** The UK manufacturer recommends a conversion ratio for oral: SC oxycodone of 2:1. However, PCF8 advises that this may be too conservative for some patients as mean oral bioavailability is 75%. A conversion ratio of 1.5:1 has therefore been recommended in the GMEC SCN Palliative Care Pain and Symptom Management Guidelines since 2015, but it is acknowledged that some centres prefer to use 2:1 and some conversion charts use this conversion also.

Table 44 - Opioid Conversion Chart – Morphine and Oxycodone

The following chart provides guidance for the following circumstances:

- Calculating 4 hourly breakthrough doses for oral or SC morphine and oral or SC oxycodone, according to total 24 hr dose.
- Converting between oral morphine and SC morphine.
- Converting between oral morphine and oral oxycodone.
- Converting between SC morphine and SC oxycodone.
- Converting between oral oxycodone and SC oxycodone.

Route	Morphine (mg)				Oxycodone (mg)			
	Oral		SC		Oral		SC	
Frequency	24h total MR	4 hourly p.r.n	CSCI 24h	4 hourly p.r.n	24h total MR	4 hourly p.r.n	CSCI 24h	4 hourly p.r.n
Dose	20	2.5	10	1.25	10	1.25	5	0.5
	30	5	15	2.5	15*	2.5	10	1.25
	60	10	30	5	30	5	20	2.5
	90	15	45	7.5	45*	7.5	30	5
	120	20	60	10	60	10	40	5
	150	25	75	12.5	75*	12.5	50	7.5
	180	30	90	15	90	15	60	10
	240	40	120	20	120	20	80	15

**See paragraph 3 below*

Notes:

1. Doses are based on the conversion ratios given in Table 43 - Recommended strong opioid dose conversion ratios, but these are only a guide and **individual assessment, monitoring and titration is essential.**
2. Where feasible, suggested doses have been rounded to provide a dose which can be administered easily. However, when converting from oral MR morphine to oral MR oxycodone, please note that some of the doses for MR oxycodone based on the recommended conversion ratio do not correspond to available formulations. These doses are marked * and will need to be rounded either up or down, according to the individual circumstances.

   Prescribers should seek specialist advice if unsure about the appropriate dose to use.
3. The table does not indicate incremental steps – **dose increases are normally 33-50% steps.**
4. SC injection volumes more than 2ml are uncomfortable; note: oxycodone injection is available as 10mg/ml or 50mg/ml; morphine is 30mg/ml; consider using alternative opioid or 2 injection sites per p.r.n. dose if injection volume is more than 2ml.

Table 45 - Converting from oral codeine or oral morphine to transdermal buprenorphine

Oral codeine dose (mg/24 hrs)	Oral morphine dose (mg/ 24 hrs)	Buprenorphine patch strength (micrograms/hr)	Suggested 4 hourly p.r.n dose of oral morphine (mg)	Suggested 4 hourly p.r.n dose of oral oxycodone (mg)
		7-day patch		
120	12	5*	2	1
240	24	10	5	2.5
	48	20	7.5 - 10	3.75 - 5
		3- or 4- day patch		
	84	35	15	7.5
	126	52.5	20	10
	168	70	30	15

*For patients on 7-day buprenorphine patch 5micrograms/h, p.r.n. codeine may be adequate

Table 46 - Converting from strong opioid regimes to buprenorphine patches

Strong opioid	When to apply first patch	Comments
Immediate-release strong opioid	Apply patch Continue regular 4 hourly immediate release strong opioid for 12 hrs	Prescribe immediate release strong opioid for 'breakthrough' pain 2-4 hourly when required. **Table 45** Converting from oral codeine or oral morphine to transdermal buprenorphine.
Modified-release strong opioid (12 hourly)	Apply patch at same time as last dose of modified release strong opioid	
Modified-release strong opioid (24 hourly)	Apply patch 12 hrs after last dose of modified release strong opioid	
Continuous SC infusion over 24 hrs (CSCI)	Apply patch – discontinue CSCI 12 hrs after application of patch	

Commencing fentanyl patches and conversion charts

- Fentanyl patches are not recommended for patients who are opioid naïve or those who need rapid tritration of dose.
- Consider buprenorphine patches for opioid naïve patients requiring transdermal strong opioid.

Table 47 – Conversion from oral morphine or oral oxycodone to transdermal fentanyl

Oral morphine dose over 24 hrs (mg)	Oral morphine breakthrough dose 4 hourly when required (mg)	Transdermal fentanyl dose (micrograms/hr)	Oral oxycodone dose over 24 hrs (mg)	Oral oxycodone breakthrough dose 4 hourly when required (mg)
30	5	**12**	15*	2.5
60	10	**25**	30	5
90	15	**37**	45*	7.5
120	20	**50**	60	10
150	25	**62**	75*	12.5
180	30	**75**	90	15
240	40	**100**	120	20

* See notes on Table 44 - Opioid Conversion Chart – Morphine and Oxycodone These doses for MR oxycodone do not correspond to available formulations and will need to be rounded either up or down, according to the individual circumstances. This conversion table assumes morphine to fentanyl potency is 1:100. For some brands of patches converting at a potency of 1:150 is required.

Table 48 - Converting from strong opioid regimes to fentanyl patches

Strong opioid	When to apply first patch	Comments
Immediate-release strong opioid	Apply patch, continue regular 4 hourly immediate release strong opioid for 12 hrs	Prescribe immediate-release strong opioid for breakthrough pain 2-4 hourly when required Table 47 Conversion from oral morphine or oral oxycodone to transdermal fentanyl
Modified-release strong opioid (12 hourly)	Apply patch at same time as last dose of modified release strong opioid	
Modified-release strong opioid (24 hourly)	Apply patch 12 hrs after last dose of modified release strong opioid	
Continuous SC infusion over 24 hrs (CSCI)	Apply patch, discontinue CScE 8-12 hrs after application of patch	

Appendix 2 - General Principles and Responsibilities when Asking for Advice About Palliative Care Patients

Asking for advice from a Specialist Palliative Care telephone helpline

Being prepared with as much information as possible will help both you and the person giving you advice to get the best out of the process. Before you pick up the phone think about the information you have, what additional information may be needed and where that might be found.

Remember that the person giving advice is unlikely to know the individual and will be relying heavily on your clinical assessment. It is important that, whenever possible, you see the individual and take a history from them in person before seeking advice. Ideally, seek advice whilst with the individual as this means that questions can be clarified with them immediately. Where this is not possible, ensure that you have up to date contact information on the individual and those identified as important to them so issues can be clarified quickly, if needed.

The person giving advice will only be able to offer a limited number of options, which will be aimed at holding a situation until the individual can be reviewed by their own caring team or a member of the specialist palliative care team.

Framework to help you ask for advice effectively

Setting	
Hello, I am	State name and role and where you work clearly.
I am calling about	State name of individual and their location.
I am seeing this individual because	State in what capacity you are seeing the individual e.g. on call doctor asked to see the individiual by family.
I would like	State clearly what you want – advice, discussion, clarification, admission, urgent review etc.
Background/Objective Assessment	
Individual has	State diagnosis.
Individual's condition	State what has changed – condition, new symptom and the time frame for this change.

They have the following	State the key issue(s) you need help with – e.g. they are in severe pain despite having three doses of breakthrough pain medication. State a summary of your clinical assessment – I am worried that they may have bone metastases. State what their observations are (if relevant).
Relevant Factors	
I am concerned because	State what the individuals previous condition was reported to be, e.g. pain free and alert. List the reasons why you need help, such as pain relief is not working, pain has suddenly got worse, those identified as important to the individual are really distressed and panicking etc.
I have already done	State what measures you have already started, e.g. I have given an antiemetic. Any other factors that you feel may play a part in any management plan e.g. the elderly wife feels exhausted.
If you are not clear what is going on, and/or uncertain about potential causes, say so clearly	I am not sure what the problem is. I am not sure why this is happening now. I am not sure what would be the appropriate thing to do.
Also give a clear indication of how worried you are by using phrases such as:	I am very worried. I am concerned. I just want to check that
Recommendations	
I wondered if	State clearly if you want confirmation of your proposed management plan or if you want more detailed advice.
I was planning to	Check if a plan is appropriate; "Would be OK to give a fourth breakthrough – the last one was two hours ago?" "I do not think this family will cope – would it be appropriate to admit?"
Follow Up	
What if advice does not work	As the caller, state clearly your follow up plans; "I will ring the patient back in an hour to see if things have improved." If you are going off duty, ensure there is a plan as to how the outcome of the advice will be followed up.
What will happen next day?	As the caller clearly state what you will do to follow up on the management plan and what, if anything, you expect from the specialist palliative care team.

Summary

Summarise what has been discussed and the plan highlighting what you are going to do and what you expect the person giving advice to do (e.g. hand over the issue to the relevant person the next working day).

Double check drug names and doses if specific advice has been given around these. If you do not understand or lack confidence to follow advice say so.

Either the person giving the advice or the person receiving advice should ensure that a summary of the advice is read back as a double check that what has been proposed is understood by both parties.

Even at this stage do not be frightened to say if you are unclear about something or you are concerned about the effect of the advice. If

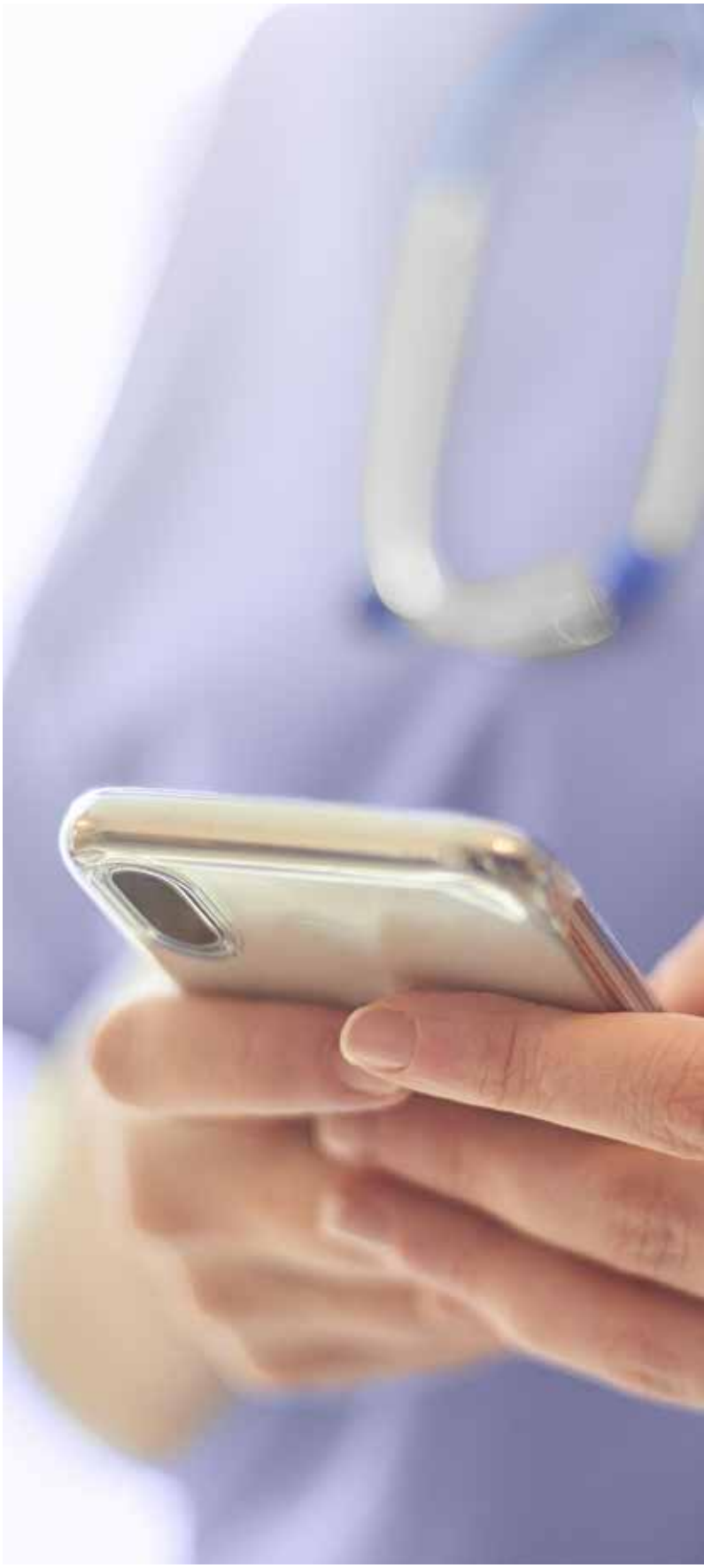
needed, suggest that you phone back once you have checked out your concerns with a colleague etc.

If you remain unsure, say so and suggest what you would feel able to do.

Write clearly in the individuals notes the outcome of the phone call and what should be done if the plan does not hold the situation. Sign, time and date the entry.

ALWAYS ENSURE THAT THE PATIENT IS REVIEWED TO CHECK THE IMPACT OF THE ADVICE GIVEN. IF THE PATIENT IS NOT SETTLED, ASK FOR MORE ADVICE.

Ref: North West Coast Strategic Clinical Networks Palliative and End of Life Care Guidance: Seeking Palliative Care Advice and Key Features of Common End of Life Diseases, September 2017



Appendix 3: Specialist Medication Prescribing in Palliative and Supportive Care

Individuals with specialist palliative and supportive care needs may be prescribed drugs that are unfamiliar to non-specialist prescribers. The Greater Manchester and Eastern Cheshire Strategic Clinical Networks document https://www.england.nhs.uk/north-west/wp-content/uploads/sites/48/2019/03/Specialist-Medication-Proforma.pdf provides a framework for good practice, and guidance on clinical responsibility for secondary and tertiary care when planning discharge or prescribing for outpatients.

'When clinical and/or prescribing responsibility for an individual is transferred from secondary to primary care, the primary care prescriber should have the appropriate competence to prescribe the necessary medicines. Therefore, it is essential that the transfer of care involving medicines that a primary care prescriber would not normally be familiar with, should not take place without the sharing of information with the primary care prescriber and their mutual agreement to the transfer of care'.

EL (91)127 ''Responsibility for prescribing between Hospitals and GPs'', DH

Prescribers should follow their local formulary guidance when deciding which medication, it is appropriate to prescribe in Primary Care and local Specialist Palliative Care. Specialist Palliative Care and Tertiary Care should familiarise themselves with individual locality formularies when deciding which medications are appropriate to prescribe or recommend in outpatients or those individuals who will be discharged into the community.

It is recommended that the list of medications below should only be initiated by specialist supportive and palliative care teams/hospices when prescribed for individuals with supportive and palliative care needs.

Specialist Medication List

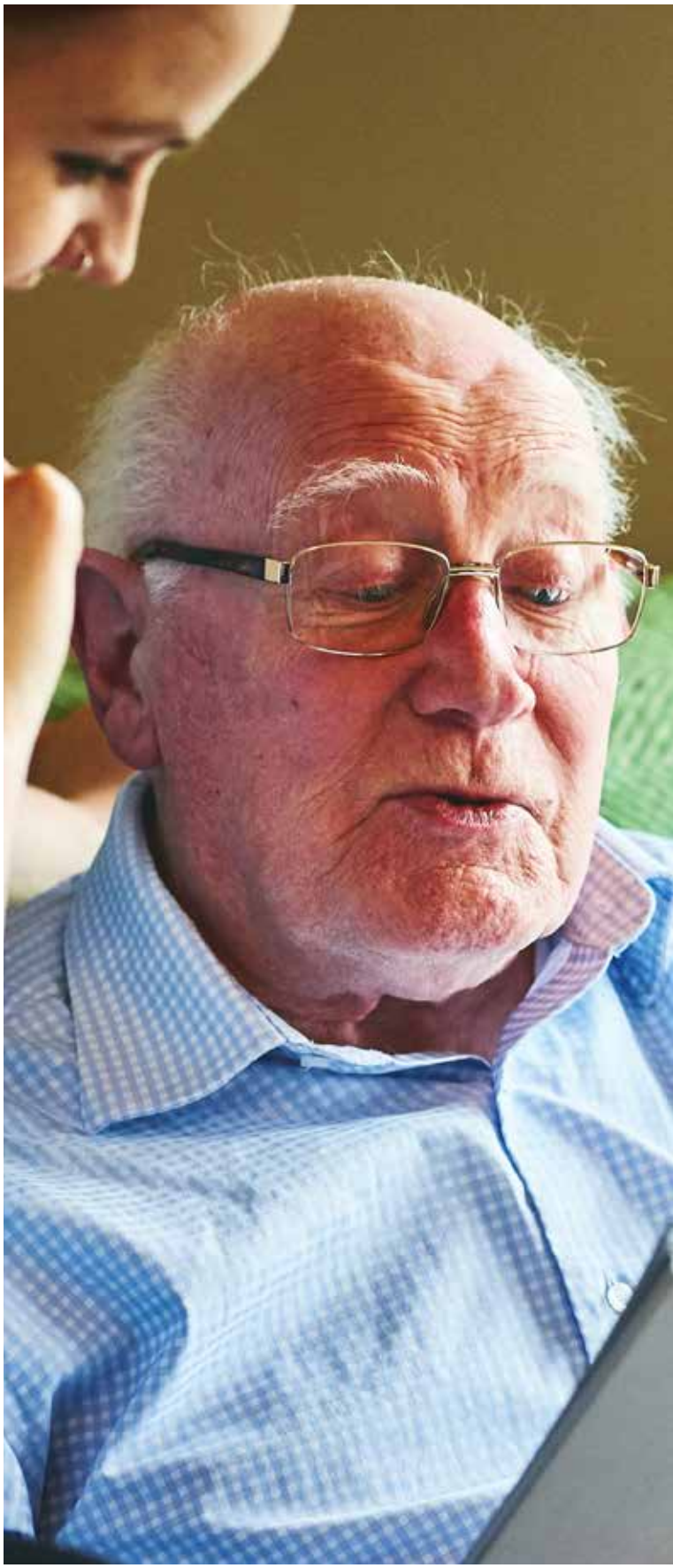
- Ketamine.
- Methadone.
- Alfentanil.
- Octreotide (Greater Manchester Medicines Management Group RED status – only specialist clinician prescribed).
- Methylnaltrexone.
- Naloxegol.
- Tapentadol.
- Ketorolac.
- Clonazepam (SCly).
- Transmucosal release Fentanyl preparations.
- Lidocaine plasters.
- Oxycodone and naloxone combination products.
- Melatonin.

NB. For further advice on which medicines should be initiated by specialists, please consult the **GM RAG list.**

Prescribing Specialist Medication – Responsibilities of Specialist Palliative Care

- To provide information, discuss and agree treatment with the individual.
- To provide a specific patient information leaflet, when available.
- To initiate treatment and titrate specialist medication.
- In circumstances of prescribing specialist medication, a direct conversation should take place between the specialist and the individuals GP.
- Agreement should be reached before the prescription issued or individual discharged into the community.
- To clarify where the individual can obtain an ongoing supply of medication and liaise with the community pharmacist.
- To communicate in writing with the individuals GP and local Specialist Palliative Care Team so that both are aware of the individual in advance of the discharge or outpatient medication being initiated in the community.

Ref: Greater Manchester and Eastern Cheshire Strategic Clinical Networks Specialist Medication Proforma Final: June 2018



Section 5

References and Abbreviations

Key References

BNF Online https://bnf.nice.org.uk/

Diabetes UK. End of Life Diabetes Clinical Care Recommendations 3rd edition (Nov 2021) https://www.diabetes.org.uk/for-professionals/improving-care/clinical-recommendations-for-professionals/diagnosis-ongoing-management-monitoring/end-of-life-care

Greater Manchester Medicines Management Group. Neuropathic Pain Guidelines (May 2022) https://gmmmg.nhs.uk/?s=neuropathic+pain

National Institute for Health and Clinical Excellence (NICE) Guidelines:

Palliative Care guidelines:

- Palliative Care for Adults: strong opioids for pain relief (2016). Clinical Guideline CG140 https://www.nice.org.uk/guidance/cg140
- Care of dying adults in the last days of life (December 2015). NICE Guideline NG31 https://www.nice.org.uk/guidance/ng31

Other relevant NICE guidelines:

- Metastatic spinal cord compression: Diagnosis and management of patients at risk of or with metastatic spinal cord compression. Clinical Guideline CG75 (November 2008). http://www.nice.org.uk/guidance/cg75
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- Parker SM et al (2023) British Thoracic Society Clinical Statement on Chronic Cough in Adults; Thorax 78 (supplement 6) pages 3-19

All weblinks correct as of July 2024

Abbreviations

ACBS	Advisory Committee on Borderline Substances
BNF	British National Formulary
caps	Capsules
CD	controlled drug - preparation subject to prescription requirements of the Misuse of Drugs Act (UK). (See BNF)
CKD	Chronic Kidney Disease
CNS	Clinical Nurse Specialist
COPD	Chronic obstructive pulmonary disease
COX, COX2I	cyclo-oxygenase, cyclo-oxygenase type 2 inhibitor
CPAP	Continuous Positive Airway Pressure
CSCI	Continuous Subcutaneous Infusion
CT	Computed Tomography
DNACPR	Do Not Attempt Cardiopulmonary Resuscitation
EAPC	European Association for Palliative Care
eGFR	Estimated Glomerular Filtration Rate
ENT	Ear, Nose and Throat
g	gram(s)
GI	Gastrointestinal
GMMMG	Greater Manchester Medicines Management Group
hr	hour(s)
IM	Intramuscular
IV	Intravenous
L	Litre(s)
MHRA	Medicines and Healthcare products Regulatory Agency

micrograms	not abbreviated
mg	milligram
ml	millilitre
min	minute(s)
mmol	millimoles
MR	Modified Release
MRI	Magnetic Resonance Imaging
nocte	at night
LTOT	Long Term Oxygen Therapy
NSAID	Non-steroidal anti-inflammatory drug
PCF8	Palliative Care Formulary 8th edition
p.o	By mouth
PPI	Proton pump inhibitor
p.r	By rectum
p.r.n.	When required
®	Trade mark
Ref	Reference
RR	Respiratory Rate
SaO2	Oxygen Saturation
SC	Subcutaneous
SIGN	Scottish Intercolegiate Guideline Network
SNRI	Serotonin-noradrenaline reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
SPC	Summary of Product Characteristics
stat	Immediately
TD	transdermal

TENS	Transcutaneous electrical nerve stimulation
Tmax	Time to peak concentration
PENS	Percutaneous electrical nerve stimulation
UK	United Kingdom
URTI	Upper respiratory tract infection
UTI	Urinary tract infection
u&e	Urea and Electrolytes
WFI	Water for injection
WHO	World Health Organization
≈	Is approximately equivalent to

Get in Touch

Specific Palliative and end of life care enquiries:

england.gmec-scn@nhs.net

www.peolc.net

https://www.england.nhs.uk/north-west/gmec-clinical-networks/

GENERAL ENQUIRIES

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Twitter: @GMEC_SCN

Twitter: @NHS_GM