NHS
North East and North Cumbria
Clinical Networks

Palliative and End of Life Care Symptom Control Guidelines

for cancer and non-cancer patients

Sixth edition: 2025
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INTERACTIVE INDEX

To return to this Interactive Index **Click** on the folio number at the bottom of the page being viewed 

Click on the folio number to take you to that page/ start of the titled section 

OPIOID DOSE CONVERSION CHART

ESSENTIAL NOTES ON USING THIS CHART - The dose conversions give guidance but **YOU MUST EXERCISE CLINICAL JUDGMENT** as well as looking up the dose.

When changing to a new opioid because of toxicity or unacceptable side-effects, always start with a dose that is approximately 2/3rd of the calculated equivalent and titrate. This will reduce risk of toxicity and increase likelihood of a successful switch.

If you have any doubt, you must seek specialist advice. Always document your reasons for switching and your calculations in the patient's clinical record.

	ORAL opioid. Dose in ***mg*** per 24 hours (**morphine** is ***first line*** oral opioid of choice)		Opioid by ***SUBCUTANEOUS INFUSION*** Doses are for medication in syringe driver in ***mg*** / ***24hrs*** (**morphine** is ***first line*** injectable opioid of choice)			Opioid by ***TRANSDERMAL PATCH*** (Dose in ***micrograms*** / ***hour***)	
Opioid	**Morphine**	**Oxycodone**	**Morphine injection**	**Oxycodone injection**	**Alfentanil injection**	**Fentanyl patch (72 hourly)**	**Buprenorphine patch (7 day & 3-4 day)**
Conversion calculation rule		Divide oral **morphine** dose by 1.5 **(Note a)**	Divide oral **morphine** dose by 2	Divide oral **oxycodone** dose by 2 **(Note b)**	Divide oral **morphine** dose by 30	**(Note c)**	**(Note d)**
	20	~15	10	7.5	~0.5	N/A	10 (7 day)
	30	20	15	10	1	12	15 (7 day)
	60	40	30	20	2	25	25 (7 day)
	120	80	60	40	4	50	52.5 (3-4 day)
	180	120	90	60	6	75	70 (3-4 day)
	240	160	120	80	8	100	105 (3-4 day)
PRN dose	**IR oral opioid - 1/10 -1/6 of 24hr oral dose up to 1-hrly**		**SC bolus inj - 1/10-1/6 of 24hr CSCI dose up to 1-hrly**		SC bolus injection: - Starting dose should be **250micrograms up to 1-hrly** - If CSCI dose **> 2mg, PRN dose 1/10 to 1/6 of 24hr CSCI dose up to 1-hrly** **(Note e)**	N/A	N/A
Further information	**See pages 6-9**		**See pages 8-9 and 28-29**		**See pages 8-9 and 29**		**See pages 6-9 and 28**

Note (a): PCF9 advises morphine: oxycodone = 1.5:1. In practice, halve the morphine dose to derive oxycodone dose and then re-titrate.

Note (b): When changing oxycodone from oral to subcutaneous, PCF9 advises oral: SC = 1.5:1. In practice, especially if the switch is needed for poor oral absorption, halving the dose offers a more cautious conversion from which re-titration may follow.

Note (c): We follow the dose ratio in PCF9 which is morphine: fentanyl = 100:1.

Note (d): Data sourced by PCF9 suggests that TD buprenorphine is between 70 and 115 times more potent than oral morphine. PCF9 advocates a ratio of 100:1 as a compromise. Therefore, as a guide, a buprenorphine 5microgram/hr patch would be equivalent to 12mg oral morphine per day. Based upon this potency ratio, buprenorphine and fentanyl patches may be considered of similar potency (this does not translate conveniently into examples on the chart above).

Note (e): Alfentanil when given as a PRN has a short duration of action (approx. 1hr); consequently, in patients with renal impairment, low dose IR oxycodone (oral/injection) given PRN with an increased dose interval may offer a more practical solution and provide better symptom control.

INDEX

Key resources

- Palliative Care Formulary (PCF) 9 & online; Wilcock A, Howard P, Toller CS, Droney J, Charlesworth S, Royal Pharmaceutical Society of Great Britain [accessed May 2025]
- British National Formulary (BNF) online; BMJ Publishing Group Ltd and Royal Pharmaceutical Society of Great Britain [accessed May 2025]

Frequently used abbreviations

AKI	acute kidney injury
BD	twice daily
CSCI	continuous subcutaneous infusion
eGFR	estimated glomerular filtration rate
GI	gastrointestinal
hr(s)	hour(s)
hrly	hourly
IR	immediate release
IV	Intravenous
mg	milligrams
min(s)	minute(s)
mL	millilitres
mmol/L	millimoles per litre
MR	modified release
NSAID	non-steroidal anti-inflammatory drug

OD	once daily
OM	in the morning
ON	at night
PO	by mouth
PPI	proton pump inhibitor
PR	rectal
PRN	as required
PTH	parathyroid hormone
QDS	four times daily
SC	subcutaneous
SU	sulfonylurea
TD	transdermal
TDS	three times daily
UTI	urinary tract infection

INTRODUCTION

Welcome to the Sixth Edition of the North East and North Cumbria (NENC) Clinical Networks Palliative and End of Life Care Symptom Control Guidelines. These guidelines have been written by a group of medical, pharmacy and nursing specialists working in palliative care in hospitals, hospices and the community across our region.

Palliative care is an approach that aims to improve the quality of life of patients and their families/carers facing problems associated with life-threatening illness, regardless of diagnosis. It prevents and relieves suffering through identification, assessment and treatment of symptoms and other problems, whether physical, psychosocial or spiritual.

It is also important to consider future health problems, and to plan treatment and care to support a patient's wishes. An excellent resource for supporting and documenting discussions about Advance Care Planning is ***Deciding right***, a regional initiative recognised by all organisations across NENC. More information can be found on **http://northerncanceralliance.nhs.uk/deciding-right/**

Much of the support provided to patients is from healthcare professionals who are not specialists in palliative care and who aim to meet the needs of the patients and their families within the limits of their knowledge and competence.

These symptom control guidelines have been written to help these clinicians in the management and treatment of adult patients with palliative and end of life care needs.

These guidelines are a place to begin. If symptoms fail to respond to treatment or if you are concerned that this guidance may not be appropriate to the clinical situation, please seek specialist advice from your local palliative care service.

This guidelines booklet is small, simple and accessible, and presents a consensus view on symptom management based on available evidence, expert opinion and regional practice. The guidelines are not intended to replace established textbooks and formularies that already exist. They have been updated to reflect recent changes in practice, and in response to feedback and requests for additional information from users of the fifth edition.

Please note that drug dose guidance – and especially the stated relative potencies of different opioid drugs – is drawn from the Palliative Care Formulary online and 9th Edition (PCF9). Where the recommendations differ from the BNF, we have tried to highlight this in the text.

The use of drugs beyond licence ("off-label") in palliative care and pain management practice is currently both necessary and common and should be seen as a legitimate aspect of clinical practice. (See PCF9, pages xxi-xxvi).

The group takes no responsibility for any consequences of any actions taken because of using these guidelines. Readers are strongly advised to ensure that they are acting in line with current accepted practice and legislation, as these may change. No legal liability is accepted for any errors in these guidelines, or for the misuse or misapplication of the advice presented here.

We are immensely grateful for the hard work and commitment by all the contributors to this sixth edition:
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For further information and/or an electronic version of these guidelines, please visit https://northerncanceralliance.nhs.uk/

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PAIN Unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is a highly subjective phenomenon. *"Pain is what the patient says hurts"*

PAIN ASSESSMENT– it is essential to try to determine the CAUSE of the pain to guide management

Essential elements:

- Careful initial assessment and documentation - **identifying the probable cause(s) of the pain(s) leads to more appropriate treatment.**
- Regular review – progress of symptoms, effects of interventions, identify changing / new pains.
- Multiple sites and types of pain are common – assess and plan management for each pain.

Each pain should be assessed for:

- Site, severity, radiation and characteristics of its timing / frequency / variation.
- Quality - use patient's descriptions (e.g. burning, shooting, throbbing, 'toothache').
- Exacerbating and relieving factors include effects of drug and non-drug interventions.
- Associated symptoms and features and impact on daily activities / sleep.
- Consider additional factors that may contribute to 'total pain' below.

Completing the picture:

- Clinical examination - to determine the likely type and cause of pain.
- Relevant investigation, if appropriate, should be considered:
  - Renal and hepatic function (which may influence drug choice).
  - X-rays / scans (MRI scan of spine if nerve root compression / metastatic spinal cord compression suspected).

Pain scores or scales
Subjective, self-rated severity scales (e.g. 1-10) help review effectiveness of interventions.

Non-verbal cues / scale can also be used

Assessing impact of pain and interventions useful e.g. on sleep / Activities of Daily Living / mobility

"Review, review, review": success in pain management depends upon regular review of pain and its causes, as well as the effectiveness and acceptability of treatment for the patient, and impact of interventions on daily functioning and sleep.

Concept of TOTAL PAIN

Where significant changes in the patient's pain experience occurs in response to complex psychosocial factors.

Explore:

- Patient's understanding, fears and concerns.
- Previous experience of pain and expectations of treatment.

PRESCRIBING FOR PAIN IN PALLIATIVE CARE

Principles for managing chronic non-cancer pain vary depending on the cause and is beyond the scope of these guidelines.

When prescribing for pain in palliative patients, a step-wise approach provides a framework for pain management based on pain severity, character and cause. Opioids are central to this and are valuable drugs for the safe and effective relief of moderate to severe pain in patients with advanced cancer. As strong opioids are readily available in the UK, weak opioids are no longer indicated for pain in palliative patients as low dose morphine has greater and more rapid analgesic effect with comparable safety profile.

Morphine is the first line opioid of choice unless the patient is intolerant of morphine and/or eGFR <30 ml/min/1.73 m²

ANALGESIC LADDER

STEP 1
Non-opioid (Paracetamol and/or NSAID) +/- adjuvant

STEP 2
Strong opioid* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant
(*e.g. morphine, oxycodone – see pages 6-8; for adjuvants – see pages 10-11)

PAIN DEFINITIONS

Background pain – predictable regular / continuous level of pain managed by regular analgesia. Use lowest dose of drug possible to avoid toxicity – supplement with PRN doses.

Breakthrough pain – a transient exacerbation of pain which occurs either spontaneously (e.g. colic, stabbing in nerve injury) or in relation to a specific trigger (e.g. weight bearing, swallowing, coughing) despite relatively stable background pain. The latter is also known as **incident pain**. Typically, breakthrough pain is managed with PRN opioids prescribed at 1/10th to 1/6th of background opioid dose (ie regular 24hr dose) up to 1-hrly. Set maximum (e.g. 6 doses/24hrs) – ensure patient review if exceeds this.

An increase in breakthrough requirements may not necessarily require an increase in background opioids, particularly if background pain is well controlled.

SAFE OPIOID PRESCRIPTION AND TITRATION

- **Start and titrate cautiously –** reduce doses (+/- extend **PRN** intervals) if frail / elderly / renal/hepatic impairment. Modified release preparations may accumulate in end stage organ failure; seek specialist advice.
- Understand the **differing properties, adverse effects** and **potencies of different opioids** (pages 2 & 8).
- **Route** – use oral route if possible; use non-oral route if dysphagia, vomiting, bowel obstruction, terminal phase.
- **Breakthrough IR opioid dose is calculated as 1/10th to 1/6th of total background** opioid dose **max. 1- 2hrly.**
- **Review effectiveness** of any previous increases in the regular dose and/or if PRNs relieved pain.
- **Increase background** opioid dose **by 33-50% (max. 50%), not more often than every 48 hrs** (7 days for patches). At end of life, increases of CSCI doses may be more frequent.
- Sudden escalation in pain or **PRN** usage, outside of patient's usual, requires re-evaluation.
- **Incident pain:** where a high number of PRN breakthrough doses relate to incident pain and the patient's background pain remains well controlled, there is no need to increase background doses.
- **Monitor for efficacy, side effects and signs of opioid toxicity / sedation.**
- Some types of pain do not respond well to opioids and require **adjuvant analgesics** (pages 10-11) / interventions.
- Make patients aware of **driving regulations** when on opioids (https://www.gov.uk/drug-driving-law).

COMMON CONCERNS over the use of opioids

Addiction – Psychological dependence is rare when opioids are carefully titrated in a patient with severe pain. In patients with a history of substance misuse, liaise with specialist team but do not withhold pain relief. Addiction must be differentiated from pseudo-addiction, whereby patients may seek analgesia for genuine, unmet pain requirements.

Tolerance - Increasing doses without benefit may indicate tolerance or a pain that is poorly responsive to opioids.

Respiratory depression – Opioids may cause respiratory depression, but it is usually counteracted by pain. Careful dose titration, clinical judgement and regular review allow safe use in most patients.

OPIOID TOXICITY – for Emergency Treatment, see page 26

Features: sedation, myoclonic jerks, hallucinations, confusion, reduced respiratory rate. **Severe cases may be life threatening.** Can occur due to fever / heat in those with transdermal patches.

Pin-point pupils may indicate that a patient is receiving opioids but may not be indicative of toxicity.

Actions: **refer to page 26** for emergency treatment. Consider checking renal and hepatic function. Seek specialist advice on opioid dose reduction, opioid switch and/or alternative analgesics.

COMMON SIDE EFFECTS of opioids

Constipation – common, persists, worse with dose increase. Prescribe stimulant laxative, adding a softener if needed (see section on constipation page 15).

Nausea/vomiting – common when commencing opioids, usually settles within days. Prescribe PRN anti-emetic in anticipation of need (e.g. haloperidol 0.5 -1.5mg PRN OD or metoclopramide 10mg PRN TDS) for the first week, titrating to response. If nausea and vomiting persist, assess and refer to pages 12-13.

Drowsiness – common during early days of treatment, then often settles. Reassure patient, unless severe or cognitive impairment. Consider dose reduction, alternative analgesic or seek advice on opioid switch.

Dry mouth – common and persistent. Ensure good oral hygiene. Consider artificial saliva products or saliva stimulants. Refer to page 14.

FLOWCHART FOR OPIOID INITIATION / TITRATION USING MORPHINE

Morphine is the first line opioid of choice **unless** patient is intolerant of morphine or **eGFR** <30 ml/min/1.73 m² (see pages 8 & 18 for opioids in renal failure, or seek specialist advice)

Using Immediate Release morphine (IR)

Using Modified Release morphine (MR)

- Use lower starting doses than in these examples if elderly and/or frail.
- In hepatic impairment, start with IR doses and titrate slowly; increase interval between doses (page 18)
- If taking codeine or tramadol, stop these drugs and use conversion table (page 8), or seek specialist advice to calculate appropriate starting dose of strong opioid.

Start IR morphine

5mg regularly QDS e.g. Oramorph (2.5ml of 10mg/5ml solution) OR Actimorph

Prescribe same dose PRN 1-hrly for breakthrough pain.

Start MR morphine

10mg regularly 12-hrly (e.g. Zomorph)

Prescribe IR morphine
5mg PRN 1-hrly for breakthrough pain
e.g. Oramorph (2.5ml of 10mg/5ml solution) OR Actimorph.

If patient appears **sedated / signs of toxicity** at any time, reduce **morphine** dose and/or frequency of PRN doses. Consider stopping **morphine** +/-switching to alternative. Seek advice if needed.

Review every 24-48 hours.

If pain uncontrolled, increase regular dose by 33-50%. Prescribe the nearest practical dose.

Prescribe the same dose 1-hrly as required for breakthrough pain.

When pain is controlled, convert to 12-hrly MR **morphine** – by adding up the **regular** doses of **morphine** in last 24hrs, divide by two and prescribe nearest practical dose 12-hrly.

Recalculate breakthrough PRN dose, which should be 1/10th to 1/6th of new total daily MR dose. Prescribe 1-hrly as required.

Review after 48 hours.

If pain is uncontrolled, increase regular dose by 33-50%. Prescribe the nearest practical dose.

Recalculate breakthrough PRN dose, which should be 1/10th to 1/6th of new total daily MR dose. Prescribe 1-hrly as required.

If pain controlled, continue same dose. Encourage patient to use breakthrough medication as needed. Review regularly.

ONGOING TITRATION

If dose escalations have been ineffective and/or the dose is greater than MR **morphine 60mg BD**, consider adjuvant analgesic (see pages 10-11) and/or referral to specialist palliative care.

DIFFERENT OPIOIDS

	Opioid	Preparations	Conversion ratio Opioid: oral morphine	Notes
WEAK OPIOIDS	**Codeine**	**IR:** oral (lasts 4-6 hrs)	10:1	Weak opioid. Metabolised to morphine with significant inter-patient variation. **Caution needed** with conversions to other opioids – consider initial switch to IR oral morphine 2.5-5mg PRN for 48 hours to assess needs.
	Tramadol	**IR:** oral **MR:** oral (12 hourly)	10:1	Weak opioid. Neuropathic effect and serotonin syndrome risk (inhibits 5HT3 and NA reuptake). If withdrawing, should be gradual.
STRONG OPIOIDS	**Morphine**	**IR:** oral / injectable **MR:** oral (12 hourly)	N/A	**First line opioid of choice if no significant renal impairment.**
	Oxycodone	**IR:** oral / injectable **MR:** oral (12 hourly)	See Opioid Conversion Chart*	Alternative to morphine if adverse effects / signs of toxicity / moderate renal impairment. Avoid in severe hepatic impairment.
	Alfentanil	**IR:** injectable	See Opioid Conversion Chart*	Often used in renal failure. PRN - short acting so often impractical (see below).
	Buprenorphine	Transdermal patch**	See Opioid Conversion Chart*	Can be used in renal impairment/failure. 7-day patch (doses 5microg/hr - 20microg/hr) OR 3-4 day patches (doses >35microg/hr).
	Fentanyl	Transdermal patch**	See Opioid Conversion Chart*	IR preps are also available but prescribe under specialist guidance only.

*For further information/calculations, see Opioid Dose Conversion Chart page 2.

**Risk of toxicity with patches if fever/heat. Less constipating than oral opioid preparations.

OPIOIDS AND RENAL IMPAIRMENT (for more information, refer to page 18)

- Caution needed – limited excretion of active metabolites can lead to accumulation and toxicity
- Opioids with non-active metabolites are safer in severe renal impairment (alfentanil, fentanyl, buprenorphine)
- Some opioids are cleared by dialysis which may result in pain flare afterwards

Mild-moderate renal impairment (eGFR 30-60 ml/min/1.73 m²):

- Reduce dose, lengthen time / interval between PRN doses, titrate PRN and MR opioids more cautiously, and review regularly.
- Morphine can be used with caution; oxycodone may be preferred.

Severe renal impairment (eGFR < 30 ml/min/1.73 m²):

- **For stable pain:** buprenorphine patch for mild pain / opioid naïve patient; fentanyl patch if higher opioid requirements in an already opioid tolerant patient
- **For severe / unstable pain or at end of life:** use alfentanil injection via CSCI. Seek specialist advice if unfamiliar with alfentanil or considering using other opioids.

Due to short duration of action of alfentanil (approx. 1hr), low dose ***IR*** oxycodone (oral/injection) given PRN with increased (longer) dose intervals may offer a more practical option and provide better symptom control. Monitor closely for signs of toxicity.

- **Avoid** REGULAR codeine, morphine and oxycodone.

OPIOIDS AND HEPATIC IMPAIRMENT (for more information, refer to page 18)

- **If co-existing renal impairment, seek specialist advice.**
- Start at low IR doses and titrate slowly; increase interval between doses; avoid MR opioids where possible. Ensure patient does not become constipated.
- **Use cautiously:** morphine, or alfentanil (with specialist support)

  If regular use of IR morphine is effective and tolerated, MR morphine can be used cautiously.

  If unavoidable: oxycodone - use low dose and reduced frequency.
- **DO NOT use** weak opioids
- **Seek specialist advice if needed.**

SWITCHING BETWEEN DIFFERENT ROUTES OF ADMINISTRATION

- **Always use the opioid dose conversion chart guidance** (page 2) when changing route / drug / formulation.
- Don't forget to discontinue / cross off the previous opioid prescription.
- **Continuous subcutaneous infusion (CSCI)** - delivers opioid injection via a pump, usually over 24 hours. Takes 4 hours to reach effective serum levels. Prescribe PRN opioid in addition, usually via SC route.
- **Transdermal (TD) patches** – slow onset and offset over days dependent on type used. Patches cannot be used to manage acute exacerbations / escalation of pain; **use only for stable pain**. Patches should not generally be increased more frequently than once a week.
- If the opioid switch is because of **opioid toxicity**, check renal and hepatic functions, and seek specialist advice on opioid choice and dose.
- **Breakthrough doses** may be needed to cover transition periods created due to differing pharmacokinetics of individual drugs and routes of administration.
- Fentanyl and buprenorphine are less constipating than morphine or oxycodone. Therefore, when starting transdermal fentanyl or buprenorphine, pre-existing laxatives should be reduced in patients with opioid induced constipation.

FROM: \ TO:	IR oral opioid	MR oral opioid	Syringe driver (CSCI)	Transdermal opioid (patch)
IR oral opioid	Direct swap	See page 7	Start syringe driver, prescribe IR opioid PRN	Apply patch immediately and use IR opioid PRN
MR oral opioid 12hr dosing	Stop MR opioid and give first IR dose	Straight switch when next dose due	Start CSCI 2hrs before next oral MR dose would have been due. Use IR opioid PRN	Apply patch when take last MR dose. Use IR opioid PRN
Syringe driver (CSCI)	Stop CSCI and give first IR opioid dose	Stop CSCI and give first MR dose at same time. Use IR opioid PRN.	Can switch medication immediately (if switching due to renal or hepatic impairment, seek specialist advice).	Stop CSCI 8-12 hrs after patch applied. Use IR opioid PRN to bridge gap till stable dose
Transdermal opioid (patch)	Remove patch and continue PRN	*See information below*	*See information below*	*Seek specialist advice (eg buprenorphine to fentanyl patch)*

Switching between strong opioids e.g. from morphine to fentanyl

Reduce calculated dose by 25-50% as patient may not be as tolerant to the new opioid and thus at risk of opioid toxicity with an equipotent switch.

Risk of opioid toxicity increases in patient with any of the following: frailty, acute illness, recent large increases in opioid dose, hepatic or renal impairment; thus a larger dose reduction may be needed – seek specialist advice if uncertain.

Transdermal opioid patch to MR oral opioid

Remove FENTANYL patch 6 hours before giving first dose of oral MR opioid. For first 24 hours (i.e. first 2 doses), give HALF the calculated equivalent dose since the transdermal opioid will take time to be cleared from plasma and subcutaneous reservoir. After 24 hours, increase to the calculated equivalent dose if clinically indicated by pain.

(If switching high doses or if switching from BUPRENORPHINE patch, seek specialist advice).

Transdermal opioid patch to continuous subcutaneous opioid infusion

If the patient is in the last hours to days of life, leave the opioid patch in place and continue to change it at the correct time interval; add a syringe driver (CSCI) with injectable medication alongside to make up the additional opioid treatment needed. Consider opioid equivalence of patch when deciding CSCI dose (see Conversion chart on page 2, and information on page 28) or seek specialist advice.

In other situations where a change from a patch is required, remove FENTANYL patch and start syringe driver 6 hours later using HALF the calculated opioid equivalent dose for the first 24 hours, then adjust according to symptom control and need for breakthrough analgesia.

For BUPRENORPHINE patch, seek specialist advice.

ADJUVANT ANALGESIA

An adjuvant analgesic is a drug whose primary indication is for something other than pain, but which can have additional analgesic benefits as well as opioid sparing action. Understanding the cause of the pain will allow for the best choice of adjuvant to be used in pain management alongside ongoing analgesia.

Consider seeking specialist input where disease modifying treatment may have analgesic properties (e.g. radiotherapy for bony tumours).

For management of neuropathic pain, see page 11.

Type of pain	Adjuvant	Medication
Neuropathic *(central or peripheral nervous system pain)*	Anti-convulsants	**Pregabalin, Gabapentin** (see page 11)
	Anti-depressants	**Duloxetine, Amitriptyline** (see page 11)
	Other (under specialist palliative care support)	**Clonazepam, Clonidine, Ketamine, Methadone, Oxcarbazepine**
Inflammatory *(trauma or inflammatory response)*	Anti-inflammatory	**Paracetamol** **NSAID** (see below for further information*)
	Corticosteroids	**Dexamethasone** (see page 16)
Somatic *(pain of the musculoskeletal system)*	Anti-inflammatory	**Paracetamol** **NSAID** (see below for further information*)
	Skeletal Muscle relaxants	**Baclofen** (with specialist support) **Benzodiazepines** (with specialist support)
Visceral *(injury or stretching or spasm of internal organs eg bowel colic, bladder spasm)*	Anti-inflammatory	**Paracetamol** **NSAID** (see below for further information*)
	Corticosteroids	**Dexamethasone** (liver capsule pain – see page 16)
	Smooth muscle relaxants	**Urinary antispasmodics (e.g. oxybutynin)** **Hyoscine butylbromide or glycopyrronium injection**
Pressure effect *(infiltration and compression from tumour or oedema)*	Anti-inflammatory	**Paracetamol** **NSAID** (see below for further information*) **Dexamethasone** (see page 16)
	Corticosteroids	

***Choice of NSAIDs in palliative care**

Palliative Care Formulary suggests **celecoxib** as the choice of oral NSAID over non-selective NSAIDs (ibuprofen, naproxen) due to a lower GI bleeding risk, nil effect on increasing bleeding time, and a lower colitis risk.

Despite having a lower GI injury risk, gastroprotection is still usually advised when prescribing celecoxib in palliative care. Celecoxib and non-selective NSAIDs have a similar risk profile in cardiovascular and renal side effects.

Dose: 100mg PO BD; if necessary, increase up to 200mg PO BD.

NEUROPATHIC PAIN

'Pain caused by a lesion or disease of the somatosensory system'

Specific pain type caused by 'malfunction' in the processing of somatosensory signals leading to a change in pain intensity and character, often with a reduced responsiveness to opioids.

Causes include direct nerve damage to peripheral or central nerves (including in the brain and spinal cord), or 'invisible' processing malfunctions and electrical changes in the nerves that can be induced by chemical / physiological changes including nociceptive pain signal present for >3 months (e.g. chronic pain, cancer-related chronic pain).

Features of nerve compression: pain in a dermatomal pattern or with radicular radiation (e.g. nerve root pattern).

Patient descriptors: may include burning, stabbing, shooting, 'toothache'-like pain.

Associated features: include numbness (may be painful), tingling or weakness. Pain may be worse on movement.

Patient may have **allodynia** (pain to light touch) or **hyperalgesia** (excessive pain to mild pain stimuli).

Step 1 Pregabalin or Duloxetine → **Step 2** Pregabalin and Duloxetine → **Step 3** Seek specialist advice

First line drugs for neuropathic pain include anti-depressants (e.g. duloxetine, amitriptyline) and anti-epileptics (e.g. pregabalin, gabapentin). Choice may be influenced by individual patient, drug characteristics and/or availability. Pregabalin is usually preferred over gabapentin due to patient compliance with twice daily dosing regimen.

Low dose combined treatment may be effective if a higher dose of a single drug does not control the pain.

If direct cancer-related nerve compression is a cause, dexamethasone can help to reduce pressure on a nerve and any associated pain

Drug	Additional indications	Cautions	Common side effects	Typical dosing schedule
Duloxetine *OD: capsule / suspension.* *Can open capsules and sprinkle into apple juice/sauce.* *DO NOT add contents to water.*	Depression Anxiety Hot flushes Stress incontinence Chemo-induced peripheral neuropathy	Avoid in renal impairment (eGFR<30 ml/min/1.73 m²) and in hepatic impairment Epilepsy (lowers seizure threshold) Avoid stopping abruptly.	**Drowsiness, headache, dry mouth,** dizziness, tremor, hypertension	**Starting dose: 30mg OD** **Increase to: 60mg OD after 1-2 weeks** **Maximum: 60mg BD** (Consider **amitriptyline** if **duloxetine** not tolerated; no benefit if it is ineffective. Starting dose: **10mg ON** and titrated cautiously every 3-7days)
Pregabalin *BD: capsule / solution.* *Can open capsule & mix in water / teaspoon of soft cold food.*	Seizures, spasticity, anxiety	Absence seizures, psychotic illness. Renal impairment: reduce dose and speed of titration. Do not stop suddenly (lowers seizure threshold). Increased risk of respiratory depression if prescribed in combination with opioid; unlikely to occur when drugs titrated carefully. Avoid in patients with severe heart failure (gabapentin is preferred to pregabalin if unavoidable).	**Sedation,** dizziness, ataxia, constipation *Slowing titration can reduce side effects.*	**Starting dose: 75mg BD** **Increase by: 75mg BD** every 3-7 days **Maximum dose: 300mg BD** **Elderly/frail:** start **25-50mg BD; increase by 25-50mg BD every 3-7 days** **eGFR 31-60:** start **25mg TDS.; max dose 150mg BD** **eGFR 15-30:** start **25-50mg OD; max dose 150mg OD** **eGFR <15 and dialysis patients:** seek specialist advice
Gabapentin *TDS: tablet / capsule / solution* *Can open capsule & mix in water / teasp of soft cold food.*	Seizures, spasticity,			**Starting dose: 300mg ON** **Increase by: 300mg every 2-3 days** **Usual effective dose: 600mg TDS** **Elderly/frail:** start **100mg OD; increase by 100mg every 2-3 days** **eGFR 31-50:** start **300mg ON; max dose 300mg TDS** **eGFR 15-30:** start **100mg ON; max dose 300mg BD** **eGFR <15:** seek specialist advice

NAUSEA AND VOMITING

1. Attempt to determine cause by careful evaluation and relevant investigation. Treat reversible causes where appropriate and possible.

Prompts to consider underlying cause – suggestions and not a complete list		
Infection:	UTI, pneumonia, gastro-enteritis, oropharyngeal candidiasis, meningitis.	See A
Metabolic:	renal impairment, hypercalcaemia, tumour toxins.	See A
Drug-related:	opioids, diuretics, NSAIDs, antibiotics, chemotherapy.	See A
Gastric stasis:	pyloric tumour / nodes, ascites, hepatomegaly, opioids, anticholinergic drugs, autonomic neuropathy.	See B
GI disturbance:	constipation, gastritis, ulceration, obstruction, hepatomegaly, ascites.	See B & E
Organ damage:	distension, distortion, obstruction, radiotherapy.	See C & D
Neurological:	raised intracranial pressure, vestibular disease, motion sickness.	See F
Psychological:	anxiety, associations of sights/smells.	See G

2. Choose anti-emetic according to cause of nausea/vomiting (see page 13 for drug details)

Causes	Information and possible features	Suggested treatment hierachy
A Chemical cause	Renal impairment, hypercalcaemia, other metabolic upset, drugs, infection. Persistent, often severe, nausea unrelieved by vomiting.	First: **haloperidol** Then: **levomepromazine**
B Gastric stasis	Fullness/regurgitation, early satiety, belching, reduced appetite, nausea relieved by vomiting (often large volume and undigested). Functional obstruction (failure of GI motility). Partial bowel obstruction (flatus PR, no colic).	**Metoclopramide** or **domperidone** (avoid if complete obstruction – see **row E)** Also consider trial of **steroids (see page 16)**
C Chemotherapy or radiotherapy	Useful to distinguish between 'acute' and 'delayed' phase. If anticipatory, see row G.	Acute: follow oncology guidelines for **ondansetron** and/or **corticosteroids**, **aprepitant** Delayed: Follow oncology guidelines
D Organ damage	Harm to thoracic, abdominal or pelvic viscera caused by malignancy or treatment.	**Cyclizine** Also consider trial of **steroids (see page 16)**
E Bowel obstruction	May be high, low or multi-level. High causes regurgitation, forceful vomiting of undigested food. Low causes colicky pain, large volume (possibly faeculent) vomits.	For detailed management of bowel obstruction, see the guideline on **page 20**
F Raised intracranial pressure/ intracerebral causes	Headache, visual disturbance, other neurological signs.	**Cyclizine** Also consider **steroids (see page 16)**
G Psychological factors	e.g. anxiety, fear, anticipation.	Consider non-drug treatment options first, then **benzodiazepine**, then **levomepromazine**
H Cause unknown	Terminal phase or patient too ill for investigation.	Consider **cyclizine,** or **haloperidol** if chemical cause most likely, or **levomepromazine**
I Post-operative	Consider site of surgery, risk factors, anaesthetic used.	Dependant on likely cause – to be discussed with surgical/anaesthetic team

3. Route and regime

- Patients with nausea/vomiting generally absorb drugs poorly by the oral route.
- ***Prescribe SC for at least 24 hours*** if there is vomiting, obstruction and/or poor symptom control.
- Start at low dose and titrate according to symptoms/as tolerated. Use with caution in organ failure.
- Prescribe chosen anti-emetic regularly – see next page for frequency.
- Levomepromazine can be considered *in addition* to existing antiemetic agent as required for refractory symptoms. Avoid use with haloperidol.

4. Review – reassess symptom control within 24 hours

- Review drug choice if symptoms persist or worsen.
- Review route: consider switch to SC if poor control of symptoms, or from SC to oral once nausea/vomiting effectively controlled.
- If cause/symptom resolves, consider whether anti-emetic can be discontinued.

COMMONLY USED ANTI-EMETIC DRUGS
(see PCF9 for more detail; cautions/contraindications from BNF)

CYCLIZINE – antihistaminic, anticholinergic anti-emetic. Antimuscarinic effect may reduce efficacy of prokinetics. Caution in advanced heart failure. May cause cognitive impairment/drowsiness.

DOSE: **PO: 50mg TDS. SC: 25-50mg TDS. CSCI: 75-150mg/24hrs**. Consider lower dose in frail patients and in those with Parkinson's disease. In CSCI, dilute to maximum possible volume with water for injection to reduce risk of skin irritation and seek specialist advice if problem persists.

HALOPERIDOL – centrally acting anti-emetic. Most potent D2 antagonist. Long acting so can be given as once daily dose, usually at night. Illogical to combine with metoclopramide because both act by central dopamine antagonism. Contra-indicated in Parkinson's disease. May prolong QT interval with risk of cardiac dysrhythmia.

DOSE: **starting dose 0.5-1.5mg PO/SC OD or over 24hours via CSCI**; **Maximum PO/SC/CSCI 3mg/24hrs**. Higher doses under specialist advice.

METOCLOPRAMIDE - prokinetic and centrally acting anti-emetic. Antimuscarinics may reduce efficacy of prokinetics. Contra-indicated in Parkinson's disease, complete obstruction and recent GI surgery. May prolong QT interval with risk of cardiac dysrhythmia. May precipitate/worsen colic. Note regulatory advice (MHRA/EMA) on dose and duration related to neurological side effects, although longer treatment durations are frequently used in palliative care.

DOSE: **PO/SC: 10mg TDS to 20mg QDS**. **CSCI: 30-60mg/24hrs**. Higher doses and long-term use under specialist advice.

Second line antiemetic:

LEVOMEPROMAZINE - broad spectrum anti-emetic. Consider for refractory/persistent symptoms. Long acting so can be given as once daily dose, usually at night. Risk of sedation and hypotension (even at low dose). Avoid in Parkinson's disease. May prolong QT interval with risk of cardiac dysrhythmia. Some specialists recommend low doses for **SC PRN use (2.5 - 5mg)** to reduce the risk of sedation.

DOSE: **PO/SC: starting dose 6.25mg OD or 6.25mg via CSCI over 24hrs**; if required, dose can be progressively increased up to a **maximum of 25 mg/24hrs**. If unfamiliar with levomepromazine or considering higher doses, **please seek specialist advice.**

More specific and targeted anti-emetics include:

DEXAMETHASONE – corticosteroid. Adjuvant anti-emetic. Stop if no obvious effect within 3-7 days. If continued, seek specialist advice due to long term side effects. For injectable dose guidance, see page 16.

DOSE: **PO/SC: 4-8mg per day** (given before noon). **16mg initially in raised intracranial pressure**.

DOMPERIDONE - prokinetic anti-emetic. Antimuscarinics may reduce efficacy of prokinetics. Domperidone does not cross blood/brain barrier so avoids extrapyramidal effects of metoclopramide, and therefore may be used more safely in patients with Parkinson's Disease. May prolong QT interval with risk of cardiac dysrhythmia. Note regulatory advice (MHRA/EMA) on dose and duration related to cardiac side effects.

DOSE: **PO: 10mg TDS**. Higher doses and long-term use under specialist advice.

HYOSCINE BUTYLBROMIDE – antimuscarinic. Reduces GI motility and secretions. Antimuscarinic effect may reduce efficacy of prokinetics. Limited efficacy by mouth, therefore avoid by oral route.

DOSE: **SC: 20mg PRN 1-hrly up to six doses/24hrs**. **CSCI: 60mg-120mg/24hrs**.

OCTREOTIDE – somatostatin analogue. Reduces GI secretions, beneficial in inoperable bowel obstruction to reduce large volume vomits. Only under specialist supervision.

DOSE: prescribe under specialist guidance.

OLANZAPINE – centrally active broad-spectrum antiemetic. May be useful in patients intolerant to haloperidol and/or levomepromazine and has an emerging role in chemotherapy-induced nausea and vomiting.

DOSE: prescribe under specialist guidance

ONDANSETRON – 5HT3 receptor antagonists. Only recommended post-op and in the acute phase of chemotherapy/radiotherapy treatment. Can cause significant constipation.
For other indications only use under specialist guidance. First line use is rarely appropriate in palliative care. Be aware may prolong QT interval with risk of cardiac dysrhythmia.

DOSE: follow oncology guidelines: **PO/SC: 4mg BD**. **CSCI: 8mg/24hrs**. For higher doses, seek specialist advice.

MOUTH CARE

Mouth assessment and mouth care should be part of routine care for every palliative patient.
Ensure regular mouth care is carried out with regular brushing of teeth or cleaning with a 360^{o} toothbrush.

Common Oral Symptoms	Treatment / care
Dry mouth Appears dry, reduced saliva – can lead to cracking and bleeding	Regular mouth care and prompts of fluid. Consider using sugar-free chewing gum to help prompt saliva stimulation. Review and stop contributory medications, if appropriate. Artificial saliva products (for example **Oralieve® oral balance gel**) are available. Ensure that mouth is rinsed/cleansed before re-application.
Oral Thrush (oral candidiasis) Patchy white coating (can turn brown with severe cases) on tongue- can feel 'fuzzy, furry' and cause altered taste. May also present with red, raw-looking lesions in the mouth, particularly in patients with dentures. Altered swallow and retrosternal discomfort may indicate oesophageal candidiasis – in this case start treatment for moderate to severe infections	**Mild symptoms:** 1st line treatment: **Nystatin 4-6 ml QDS for 7-14 days**. (NICE recommends miconazole oral gel as 1st line treatment, if available; however, many potential drug interactions). 2nd line treatment: **Fluconazole 100 or 200mg OD for 7-14 days**. (Fluconazole interacts with multiple drugs and can increase serum levels. Please check interactions before prescribing). **Moderate to severe infections, oesophageal candidiasis and immunosuppression:** 1st line treatment: **Fluconazole 200 or 400mg OD for 14-21 days**. (Fluconazole interacts with multiple drugs and can increase serum levels. Please check interactions before prescribing). If symptoms persist despite treatment, consider mouth swab. **Dentures** - ensure dentures are thoroughly cleaned and soaked for several minutes in chlorhexidine every day, and rinsed before re-insertion; failure to do so will increase risk of recontamination and reduce effectiveness of anti-fungal treatment.
Painful mouth Ulceration, inflammation, mucositis (can occur after treatment radiotherapy/ chemotherapy)	Can try coating agent e.g. **Gelclair® QDS**. Check for ill-fitting dentures. Seek specialist advice from oncology or palliative care

If mouthcare becomes a significant burden (impacting on oral intake, nausea etc), please seek specialist palliative care advice.

For further information: https://cks.nice.org.uk/topics/palliative-care-oral/

CONSTIPATION

If you are concerned your patient may have a bowel obstruction, please refer to the section on 'Emergencies - bowel obstruction' on page 20.

Assessment: A comprehensive assessment of the patient and their symptoms should be carried out including their normal and current bowel function.

Causes: Consider possible causes of constipation including medications, hypercalcaemia, hypokalaemia, dehydration, poor oral intake, immobility, tumour burden and concurrent disease (diabetes, hypothyroidism, Parkinson's disease).

Management: Consider non-pharmacological approaches including increased fluid intake, patient privacy, review of constipating medications and accessible toilet facilities.

Hard - Consider a softener laxative ← Is stool **hard** or **soft**? → **Soft -** Consider a stimulant laxative

Option A (osmotic laxative)	Option B (stimulant ± softener)
Macrogol 3350 sachet (e.g. Laxido® / Movicol) **1 to 3 sachets daily**, each made up with 125ml of water per sachet. If faecal impaction, consider a higher **dose (max 8 sachets/24 hrs)** for 3 days.	Stimulant (**e.g. Senna** tablets/solution) **15mg ON** and titrate to **30mg ON** if needed or **bisacodyl tablets 5mg - 10mg ON**. If stools become hard, add in softening agent such as **docusate sodium capsule 100 - 200mg BD or TDS** (limited evidence of efficacy). If significant colic occurs, the stimulant laxative should be discontinued and consider softener alone or switch to option A.

Review – if still constipated

If either A or B unsuccessful, consider A+B

Consider performing a rectal (PR) examination.

PR: soft impacted stool

Consider **bisacodyl** suppositories +/- enema to stimulate bowel.

PR: hard impacted stool

Consider **glycerin** suppositories +/- **arachis oil** enema (except in peanut allergy) to soften stool.

Titrate laxatives to achieve regular stool frequency and optimal consistency – regular oral laxatives may be required, particularly in opioid induced constipation.

NEUROGENIC CONSTIPATION:

For patients with known spinal cord compression or sacral nerve damage who have lost sensation and/or control of bowels, seek advice from palliative care team to help establish a bowel management regime.

OPIOID-INDUCED CONSTIPATION:

Peripherally acting μ opioid receptor antagonists (PAMORAs) e.g. **naloxegol** or **naldemedine** may be considered in opioid induced constipation where other measures have failed to achieve adequate bowel motions. They should only be used under specialist guidance. PAMORAs are contra-indicated in gastrointestinal (GI) obstruction and patients at risk of GI perforation.

CORTICOSTEROIDS IN PALLIATIVE CARE

DRUG CHOICE, FORMULATION AND INDICATIONS

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. (Dexamethasone 750micrograms ~ Prednisolone 5mg ~ Hydrocortisone 20mg).

If patient is awaiting biopsy or on / due to commence immunotherapy, consider discussing with oncologist prior to commencing steroids.

Route and formulations: tablets (including soluble), oral solution, injection.

Dexamethasone should be prescribed in terms of the 'base' *(dexamethasone)* rather than the 'salt' (dexamethasone *phosphate* or dexamethasone *sodium phosphate*). Tablets are formulated as the base.

Conversion between oral and subcutaneous doses of dexamethasone		
Oral dose of **dexamethasone**	Equivalent subcutaneous dose	Volume of injection (3.3mg/ml)
8mg	6.6mg	2ml
6mg	4.95mg	1.5ml
4mg	3.3mg	1ml
2mg	1.65mg	0.5ml

Indications, doses and recommendations for titration

Standard starting doses for different indications are not well established and must take account of patient factors. High dose dexamethasone injection (>6.6 mg) is large volume (>2 ml) and so should be split between separate sites when given SC. Ensure the daily dose(s) is administered before noon to minimise insomnia. Clinical response must be reviewed within 7 days. Titrate down to minimum effective dose, if discontinuation not possible (usually every 5-7 days to ascertain effect). Consider temporary increase in steroid dose when significant intercurrent illness, trauma or surgery occurs to compensate for reduced adrenocortical response (and conversion to SC if unable to take oral).

Anorexia: 2 - 4mg OD. Review the response. Short courses (1-2 weeks) are recommended to reduce risk of side effects.

Adjuvant analgesic: 8 -16mg OD for cancer-related pain (e.g. liver capsular pain, nerve compression).

Anti-emetic: for chemotherapy, follow oncology guidelines. Refractory nausea and vomiting: **8mg OD or BD**.

Obstructive syndromes e.g. bowel obstruction, upper airways compression, superior vena cava obstruction, lymphangitis carcinomatosis: **8 - 16mg daily**.

Metastatic spinal cord compression: 16mg OD until surgery or radiotherapy if appropriate. Maintain on **8mg OD** during radiotherapy. After surgery or completion of radiotherapy, reduce dose gradually over 1-2 weeks and stop. If do not proceed to surgery or radiotherapy, reduce gradually. If neurological function deteriorates at any time, consider increasing to previous effective dose for a further 2 weeks before reducing again.

Raised intracranial pressure: 8-16mg OD for one week, and then reduce over 2-4 weeks, maintaining each dose increment for at least 5 days to assess response, aiming for 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. If symptoms due to brain tumour, liaise with neuro-oncology team for management plan.

ADVERSE EFFECTS

Glucose metabolism: Steroids can increase blood sugar levels. **See detailed guidance on page 17.**

Insomnia: Give OD or BD dose, ensuring last dose is before noon to prevent insomnia.

Dyspepsia: Give after food. Co-prescribe PPI if at risk of peptic ulcer disease or patient also taking antiplatelets, NSAIDs, SSRIs or is anti-coagulated.

Increased susceptibility to infection: especially oral/pharyngeal candidiasis – treat with anti-fungal **(see page 14)**

Other: Psychiatric disturbance (depression, mania, psychosis, delirium); **change in appearance** (moon face, truncal obesity, negative body image); **musculoskeletal problems** (proximal myopathy, osteoporosis, avascular bone necrosis); **skin changes** (thinning, bruising, acne, impaired wound healing); other: hypertension, oedema, pancreatitis.

SAFE USE: MONITORING AND STOPPING TREATMENT

Use the lowest effective dose for the shortest period. Close careful monitoring is essential. Stop after 7-10 days if the desired effect is not achieved. **The prescriber must take responsibility for steroid monitoring.** The patient and other involved professionals must be informed of the indication for steroid use and the plan for dose reduction and monitoring.

Steroid withdrawal: stop without tapering dose if total treatment duration of less than 3 weeks AND daily dexamethasone dose of 6mg or less AND symptoms unlikely to relapse.

Gradual dose reduction: necessary if any of the following: 3 or more weeks treatment, daily dose of more than 6mg dexamethasone for more than 1 week, risk of recurrent severe symptoms, repeated courses of steroids, other possible causes of adrenal suppression. Daily dose can be reduced rapidly (e.g. halving dose) to 4mg/day, then more slowly by 1-2mg weekly in order to prevent a hypo-adrenal crisis (malaise, profound weakness, hypotension).

Steroids at end of life: for ongoing symptom control, continue and switch to the most convenient SC dose. If recent or low dose prescription for appetite stimulation, discontinue. If long-term, consider low maintenance dose to prevent adrenal crisis.

Steroid Treatment Card (blue): should be issued by pharmacy to patients on systemic steroids for > 3 weeks.

Steroid Emergency Card (red): should be issued to patients at risk of adrenal crisis if steroids are stopped abruptly.
(www.england.nhs.uk/2020/08/steroid-emergency-card-to-support-early-recognition-and-treatment-of-adrenal-crisis-in-adults)

CONTROL OF GLUCOSE IN PATIENTS ON CORTICOSTEROIDS

Patients NOT known to have Diabetes

Check capillary or venous glucose on all patients before starting on steroids, to determine individual risk. Random blood glucose over 7.8mmol/L means individual is "At Risk" of developing diabetes with steroids. Random venous glucose over 11mmol/L needs second check to confirm pre-existing unknown diabetes.

Type 2 Diabetes

No hypo symptoms and NOT on a **SU** or **Insulin**.

Test before evening mealtime.

Commence:

Gliclazide 40mg OM and increase in **40mg increments** every morning if needed, **up to 240mg max dose** in morning dose.

If failing to achieve target, consider starting **insulin**.

Assuming no hypoglycaemic symptoms:

If on maximum dose of **gliclazide**, will need to switch to **insulin** and switch to blood glucose testing

- Start morning **Isophane insulin (e.g. Humulin I) 10 units** on first day of steroids
- Seek advice from local diabetes team if required
- Aim blood glucose 6-15mmol/L before tea

Increase morning **insulin** if glucose before evening meal is above target

- **Increase morning insulin dose by 4 units**
- Review daily until stable, increasing dose as needed.

Diabetes – Insulin treated

Reassess glucose control and usual testing regime

Once a day basal insulin regimen:

- Transfer **basal insulin** to morning.
- Titrate up **insulin** dose by 10 – 20% daily according to pre-evening meal capillary blood glucose levels.
- Consider twice daily **basal insulin** or
- Commence **gliclazide** to achieve glucose targets.

Twice daily pre-mixed insulin regimen:

This will need an increase in morning **insulin** dose according to teatime glucose reading.

Basal bolus insulin regimen:

- Increase in both breakfast and lunchtime mealtime **insulin** doses **and**
- Transfer **basal insulin** to morning with possible increase in this dose to prevent high teatime readings.

Assuming no hypoglycaemic symptoms:

Increase **insulin** doses if serum glucose before lunch or evening meal is above 15 mmol/L

- Increase morning and/or lunchtime dose by:
  4 units if daily dose below 20 units
  8 units if daily dose 20-50 units
  12 units if daily dose above 50 units.
- Review daily until stable.

Target Glucose: Aim for between 6 – 15mmol/l.

Remember: Never stop **insulin** in people with known type 1 diabetes.

NOTE: if **steroids** are reduced or discontinued, your patient could be at risk of significant hypoglycaemia especially if on **SU** or **insulin**. **PLEASE** reduce the dose of these agents in tandem with steroid dose reduction.

If unsure at any stage about next steps or need specific advice on how to meet your patient's diabetes needs, please **contact your local Diabetes Specialist Team**.

For further information see links below:

- End of Life Guidance for Diabetes Care
  https://trenddiabetes.online/portfolio/end-of-life-guidance-for-diabetes-care/
- Joint British Diabetes Societies 08 Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy
  https://abcd.care/resource/current/jbds-08-management-hyperglycaemia-and-steroid-glucocorticoid-therapy

HEPATIC IMPAIRMENT

- Indicators of severe hepatic impairment include Child-Pugh C, bilirubin >50, significant ascites, hepatic encephalopathy, raised INR/prolonged prothrombin time, known cirrhosis or significant metastatic disease in liver.
- Constipation can increase hepatic encephalopathy; laxatives should be prescribed with opioids and anticholinergic medicines.
- **Seek specialist advice if the patient has hepatorenal syndrome.**

Analgesia – non-opioids	Analgesia – opioids	Agitation	Antisecretory	Antiemetics
Paracetamol PO/IV: reduce dose, **max 2g/24hours.** **AVOID** NSAIDs: increased risk of renal dysfunction and haemorrhage. **Pregabalin & Gabapentin PO:** dose as per frail / elderly population **(see page 11)**. **Duloxetine PO:** seek specialist advice. **Amitriptyline PO:** caution, start with low dose of **5mg-10mg ON.**	**AVOID** tramadol and codeine **Morphine PO/SC:** reduce dose and increase dosing interval. **AVOID** if concurrent renal failure. **AVOID** oxycodone **Fentanyl patches:** can be considered for stable pain. **Alfentanil SC:** reduce dose and increase dosing interval.	**Lorazepam PO/SL:** use cautiously, give smaller doses with an increased dosing interval. **Midazolam SC:** use cautiously, give smaller doses with an increased dosing interval **AVOID** diazepam and temazepam: risk of sedation and masking encephalopathy. Consider shorter acting benzodiazepine such as midazolam. **Haloperidol PO/SC**: can be used for delirium, start at low dose **0.5mg PRN 1-hrly**. **Levomepromazine:** seek specialist advice.	**Hyoscine butylbromide PO/SC:** can be used at usual doses. **Glycopyrronium PO/SC**: can be used at usual doses.	Try to establish the cause of nausea and vomiting **(see page 12).** **Metoclopramide PO/SC**: use low dose (starting at **5mg TDS or 15mg / 24hr via CSCI**), titrating up to **30mg/24hrs** if needed. **Haloperidol PO/SC:** can be used for chemical causes, start at low dose **0.5mg PRN 1-hrly.** **AVOID** cyclizine

RENAL IMPAIRMENT

- The following guidance is for patients with severe renal impairment (eGFR < 30 ml/min/1.73 m²). In all cases, low starting doses with cautious titration is indicated.
- For patients undergoing renal replacement therapy, specialist advice should be sought as dialysis can remove and therefore reduce the efficacy of many drugs

Analgesia – non-opioids	Analgesia – opioids	Agitation	Antisecretory	Antiemetics
Paracetamol PO/IV: dosing unchanged. **AVOID** NSAIDs, as further deterioration in renal function may be precipitated. **Pregabalin & Gabapentin PO:** significant accumulation may occur (**see page 11** and seek specialist advice). **Duloxetine PO: AVOID if** eGFR < 30 ml/min/1.73m2. **Amitriptyline PO:** Caution; start at **10 mg ON**; adverse effects may be more prevalent.	**AVOID** morphine, codeine, and tramadol in severe impairment. **Oxycodone PO/SC:** use cautiously at reduced doses with an increase in dosing interval **(see page 8)**. **Alfentanil SC:** dosing unchanged. **Fentanyl, and buprenorphine TD:** dosing unchanged.	**Midazolam SC:** can generally be given at usual doses, although increased CNS sensitivity can occur, and lower cumulative doses may be sufficient. **Haloperidol PO/SC:** start with smaller doses, **0.5 mg PRN 1-hrly**. **Levomepromazine PO/SC:** start with smaller doses, **6.25 – 12.5 mg PRN BD.**	**Hyoscine butylbromide SC/PO:** can be used at usual doses. **Glycopyrronium PO/SC:** can be used with a 50% reduction in dose	Establish cause of nausea and vomiting **(see page 12)**. **Haloperidol PO/SC:** smaller starting doses may be sufficient, i.e. **0.5 mg PRN 1-hrly.** **Cyclizine PO/SC**: patients may be more prone to sedative and antimuscarinic effects; as a result, lower doses (i.e. **25 mg PRN 8-hrly)** may be sufficient. **Metoclopramide PO/SC:** can accumulate; start with **5 mg TDS or 15mg/24hr via CSCI.** **Levomepromazine PO/SC:** initiate at smaller doses (≤ **6.25 mg PRN 8-hrly)** and titrate cautiously.

PARKINSON'S DISEASE (PD)

- Centrally acting D2 receptor antagonists must be avoided as they can exacerbate PD and precipitate potentially fatal Parkinsonism-Hyperpyrexia Syndrome (i.e. **metoclopramide, haloperidol, prochlorperazine, levomepromazine** and **olanzapine**).
- Patients with PD often lose their swallow. Usual oral medication regimens can be given via NG or enteral feeding tubes if appropriate, following PDMedCalc guidance (www.pdmedcalc.co.uk). Alternatively, transdermal **rotigotine** can be used to replace oral antiparkinsonian medication, using the conversion available at www.pdmedcalc.co.uk. In many cases transdermal **rotigotine 2 – 4 mg/24 hr** may be sufficient replacement at the end of life to minimise the risk of neuropsychiatric reactions.

Analgesia – non-opioids	Analgesia – opioids	Agitation	Antisecretory	Antiemetics
Paracetamol PO/IV: dosing unchanged; reduce dose if body weight < 50 kg. **NSAIDs PO/SC:** caution in frail populations due to increased risk of renal dysfunction and GI bleeding. **Pregabalin & Gabapentin PO:** dose as per frail elderly population **(see page 11)**. **Duloxetine PO:** seek specialist advice. **Amitriptyline PO:** seek specialist advice.	**AVOID** tramadol and codeine **Morphine & Oxycodone PO/SC**: dosing unchanged; selection largely determined by renal and hepatic function. **Alfentanil SC:** dosing unchanged; selection largely determined by renal and hepatic function. **Fentanyl TD:** can be considered for stable pain.	**Midazolam SC:** can be given at usual doses. **AVOID** haloperidol, olanzapine and levomepromazine, as they can exacerbate PD.	**Hyoscine butylbromide PO/SC:** can be used at usual doses. **Glycopyrronium PO/SC:** can be used at usual doses.	**Cyclizine PO/SC:** use smaller doses (SC **max 75mg/24hrs**). **Domperidone PO:** dosing unchanged; only available as oral formulations. **Ondansetron PO/SC:** dosing unchanged; contraindicated if patient receiving apomorphine. **AVOID** metoclopramide, haloperidol, prochlorperazine, levomepromazine, and olanzapine, as they can exacerbate PD

MYASTHENIA GRAVIS (MG)

- If the oral route is no longer viable, please consult a specialist regarding the potential for converting the patient's usual oral acetylcholinesterase inhibitor to an alternative route of administration.
- Please be aware drugs with anticholinergic properties can worsen MG and/or precipitate a potentially fatal myasthenic crisis.
- MG is not a terminal condition; patients typically die ***with*** not ***from*** MG.

Analgesia – non-opioids	Analgesia – opioids	Agitation	Antisecretory	Antiemetics
Paracetamol PO/IV: dosing unchanged. **NSAIDS PO/SC:** dosing unchanged. **Pregabalin & Gabapentin PO:** seek specialist advice. **Duloxetine PO:** dosing unchanged. **AVOID** amitriptyline, as anticholinergic action may worsen MG.	Generally, **opioids** do not worsen MG but can exacerbate pre-existing neuromuscular respiratory depression	**Benzodiazepines PO/SC:** contraindicated in unstable MG or in those with respiratory insufficiency unless imminently dying. Can be used cautiously in patients with stable MG. **Antipsychotics PO/SC:** can worsen MG but may be used cautiously, with preference towards those with little antimuscarinic activity, e.g. haloperidol.	**Hyoscine butylbromide and glycopyrronium PO/SC:** for respiratory secretions, prioritise non-pharmacological options (reassurance, patient positioning and suction). **The use of SC antimuscarinics requires specialist input.**	Prioritise drugs which do not have antimuscarinic effects - **metoclopramide, ondansetron, granisetron and domperidone**

EMERGENCIES – BOWEL OBSTRUCTION

1. RECOGNITION

Risk factors/possible causes:
Malignant - progression or recurrence of intra-abdominal cancer (especially bowel, ovary, pancreas).
Non-Malignant – surgical adhesions, incarceration of hernia, ileus, faecal impaction.
Medication - including opioids, anticholinergics, 5HT3 antagonists (e.g. ondansetron)

Clinical presentation:
Symptoms - depend on level(s) of obstruction, and if partial or complete obstruction.
Abdominal pain, colic, nausea, vomiting, bloating.
Vomiting may be large volume in high obstruction; nausea may be relieved by vomiting.
Diarrhoea can occur in partial obstruction. In complete obstruction no faeces or flatus will be passed.
On examination - abdominal distension, tender abdomen, tinkling/reduced bowel sounds, dehydration.

2. IMMEDIATE ACTION - IS ADMISSION APPROPRIATE?

Consider patient's wishes, Emergency Health Care Plans, clinical records and guidance from family/others.
If YES - admit as an emergency. Give **medication for symptom relief** immediately e.g. SC dose of opioid analgesic (appropriate to analgesic history – see page 28-29) and anti-emetic (either metoclopramide 10mg SC if no colic or cyclizine 25 - 50mg SC if colic present)
On admission: perform clinical examination, take baseline bloods (electrolyte disturbance can contribute to peristaltic dysfunction), commence IV fluid resuscitation, consider CT scan and **seek urgent surgical opinion**. If large volume vomiting, consider NG tube for decompression.
If NO – or if admitted and surgical decision is for supportive care only - see section 3 below. In addition, for patients with intra-abdominal cancer, consider a trial of dexamethasone 6.6mg OD SC (or IV). Review effect after 5 days: discontinue if no effect or reduce gradually if benefit.

3. ONGOING MANAGEMENT

Treat any background constant pain with opioid/24hr via CSCI - see pain section on **page 28-29**.

All symptom control medications to be given SC to ensure systemic delivery.
Other critical medications may not be absorbed e.g. anti-seizure drugs, long-acting opioids, Parkinson's medication, and should be given by a non-oral route where possible. Caution: Parkinson's Disease - seek specialist advice for management plan due to risks of adverse reactions to antiemetics.

Is colic present and/or bowel obstruction clinically complete?

NO

Prescribe **metoclopramide 30mg/24hr CSCI and 10mg PRN SC 6-hrly**. If it is unclear whether partial or complete obstruction, avoid **metoclopramide**

Review after 24 hours

If still vomiting but **NO COLIC**, increase **metoclopramide to 60mg/24hr CSCI**.	If **COLIC PRESENT**, discontinue all **metoclopramide** prescriptions.

Review after 24 hours

If vomiting continues and **NO COLIC**, contact palliative care team for specialist advice.	If **COLIC** present, discontinue all **metoclopramide** prescriptions.

YES

For vomiting/nausea: start **cyclizine 75mg or 150mg/24hrs CSCI**
Prescribe **cyclizine 25mg SC PRN TDS (max 150mg/24hr** including PRN and CSCI**), or haloperidol 0.5-1.5mg SC PRN 1hrly (max 3mg/24hr).**

For colic: start **hyoscine butylbromide 60mg/24hrs CSCI.**
Also prescribe **hyoscine butylbromide 20mg PRN SC 1-hrly (max 180mg/24hrs** including CSCI**).**
NB: cyclizine and hyoscine butylbromide should run in separate CSCIs.

Review after 24 hours
If vomiting/nausea persist, combine c**yclizine AND haloperidol 1.5mg/24hrs CSCI**. Alternatively switch to levomepromazine **12.5mg SC OD** (or over 24hrs CSCI) **AND** prescribe **6.25mg SC PRN 1-hrly up to 25mg/24hrs** (including regular and PRN doses).
If colic persists, increase **hyoscine butylbromide to 120mg/24hr CSCI.**

Review within 24 hours
If symptoms persist, seek specialist advice.

EMERGENCIES – SEIZURES

1. RECOGNITION

- Seizures (generalised or partial) occur in 10-15% of palliative care patients. They can increase in severity and frequency towards the end of life.
- Causes include pre-existing epilepsy, primary and secondary brain tumours, raised intracranial pressure, metabolic disturbances (hypoglycaemia, electrolyte abnormalities, hepatic encephalopathy, renal impairment), infections, drug side effects/interactions (including alcohol withdrawal) and treatment complications (after neurosurgery and/or radiotherapy).
- Exclude other causes of loss of consciousness or abnormal limb/facial movement e.g. vasovagal episode, postural hypotension, arrhythmia, hypoglycaemia (check blood glucose level), extrapyramidal side effects from dopamine antagonists, alcohol.
- Identify if a patient is prescribed anti-epileptic drug therapy, if they can take oral medication, whether they have missed any doses or had exposure to seizure threshold lowering risk factors.

2. ACUTE MANAGEMENT

The flowchart below is intended for use where standard medical protocols are unavailable or not assessed to be in the patient's best interest.

Acute management

Step 1: General measures
- ABCDE approach
- Protect airway
- Protect patient from injury (lie on their side and remove hazardous obstacles)
- Note time of seizure onset
- Call for help
- Check blood sugar
- Consider reversible causes and treat if appropriate

Seizure not self-limiting (> 5 mins in duration)

Step 2: Initial management

Midazolam 10 mg, can be given SC, IV, IM or buccally

If onging seizure activity repeat doze after 10 mins. Seek specialist advice if seizures do not terminate with midazolam.

Ongoing seizure activity

Step 3: Further measures

Levetiracetam 1 - 2 g IV or via a short subcut infusion over 15 - 30 minutes, **if unavailable seek specialst advice.**

If already on levetiracetam or seizures ongoing, seek specialist advice for consideration of additional anti-epileptic options.

3. ONGOING MANAGEMENT

- For those with intracranial tumours, anti-epileptic drugs are normally commenced following a single unprovoked seizure.
- Choice of anti-epileptic drug should be guided by seizure type, potential for drug interactions and patient co-morbidities. Consider discussion with epilepsy specialist to individualise patient treatment plan.
- Be aware patients immediately post-ictal may have prolonged drowsiness.

Ongoing management

After seizure has been terminated, initiate or optimise maintenance anti-epileptic therapy if acutely reversible cause cannot be addressed:

- If patient has oral access, initiate new or titrate pre-existing antiepileptic therapy (NB: levetiracetam is typically first line in patients with seizures secondary to central malignancy – **seek specialist advice.**
- If patient unable to take oral medication, consider subcutaneous infusion (CSCI) of one of the following:
  - Midazolam starting at 20 or 30 mg over 24 hrs
  - Levetiracetam starting at 1000 mg over 24 hrs OR convert from oral therapy to CSCI on a 1:1 bais.
  - **NB:** *For patients previously established on complex antiepileptic regimens, 2 or more antiepileptics via CSCI may be required,* ***seek specialist advice***
- Consider optimisation of corticosteroids if seizure secondary to brain tumour or metastases

- Levetiracetam can be helpful if wishing to avoid sedation. At high doses, 2 syringe drivers may be needed due to the large volume. It is usually diluted with WFI but can cause site irritation. If mixed with other drugs, sodium chloride 0.9% should be used as the diluent instead (refer to syringe driver and drug compatibilities page 35). Dose reduction may be required in renal impairment. Side effects include mood changes, headache and nasopharyngitis.
- For any palliative patient with an ongoing risk of seizures, it is helpful to have an **Emergency Health Care Plan** in place (see ***Deciding right***). Include and educate families on future seizure management.
- Where appropriate, advise patients not to drive following a seizure and to review **DVLA driving guidance**.
- Be aware of future use of drugs which may reduce seizure threshold e.g. haloperidol, levomepromazine.

EMERGENCIES – METASTATIC SPINAL CORD COMPRESSION (MSCC)

This guidance applies only to patients with a known cancer diagnosis

Patients with suspected Metastatic Spinal Cord Compression must be assessed *as a priority* and treated as an *emergency*.

Discuss with MSCC co-ordinator at nearest Cancer Centre or Acute Oncology Out of Hours.

Management should depend on the patient's wishes and whether the MSCC may be amenable to surgical or oncological intervention. A personalised care plan will help to support the patient's wishes and holistic needs in the community setting if MSCC is unable to be treated.

1. RECOGNITION

Consider spinal metastases (requires MRI scan within 1 week) in a cancer patient with back pain with any of the following features:

- Progressive, severe or unremitting pain. Pain may be aggravated by moving or straining (for example, coughing, sneezing or bowel movements).
- Pain may be worse at night.
- Localised tenderness.
- Claudication (muscle pain or cramping in the legs when walking or exercising).

Consider MSCC (requires MRI scan within 24 hours) in patients with the following features:

- Limb weakness, altered gait, unsteadiness or falls.
- Pain in a nerve root distribution, often bilateral (radicular pain) down arms or legs.
- Urinary retention, dribbling or incontinence; faecal incontinence or constipation.
- Altered or reduced sensation.

Cauda equina syndrome (requires MRI scan within 24 hours) may present with:

- Sciatic pain, often bilateral.
- Weakness/wasting of gluteal muscles.
- Bladder or bowel problems, including retention and incontinence.
- Sacral (saddle) anaesthesia and/or loss of anal sphincter tone.

Do not be reassured by X-rays as these are normal in 10-20% cases.

2. IMMEDIATE ACTION

- **Offer dexamethasone as soon as possible to any patients with features of MSCC or cauda equina. Also consider dexamethasone in patients with features of spinal metastases with severe pain or haematological malignancy (See NICE NG234 for further information):**
  - Outpatients: **16mg BY MOUTH or 13.2mg SC** (if given SC, volume needs to be divided into two sites, 2mls each). Continue daily in the morning whilst awaiting treatment.
  - Inpatients: **13.2mg IV or SC**. Continue daily in the morning whilst awaiting treatment.
- **Prescribe PPI for gastric protection.**
- **Assess pain and give adequate analgesia** (including an opioid if necessary)
- **Immobilisation (nurse the patient flat):**
  - **Immediately** if pain or symptoms/signs suggest spinal instability
  - **Consider** if moderate or severe pain with movement
- Assess and address holistic care needs from diagnosis, including providing information and decision-making support appropriate to each individual.

3. REFERRAL FOR INVESTIGATION

Community Patient:

If appropriate, depending on the patient's wishes and stage of illness, admit to your local hospital as an emergency for full neurological assessment. The acute receiving team will make arrangements for urgent whole spine MRI scan (or CT scan if MRI scan contraindicated).

Hospital/Hospice Inpatient:

Contact MSCC co-ordinator (or Acute Oncology out of hours) immediately for any patients with features of MSCC or cauda equina, **or within 24 hours** for patients presenting with symptoms of spinal metastases but no features of MSCC. These discussions will facilitate urgent whole spine MRI scan (or CT scan if MRI scan contraindicated), emergency virtual MDT discussion between radiologist, oncologist and spinal surgeon, and appropriate decision making.

See NICE NG234: Spinal metastases and metastatic spinal cord compression: www.nice.org.uk

EMERGENCIES – MALIGNANT HYPERCALCAEMIA

1. BACKGROUND

Malignant hypercalcaemia affects up to 30% of patients with advanced malignancy. It is strongly associated with breast, lung, haematological and genito-urinary tract malignancies. Most cases (80%) occur due to tumour secreted parathyroid hormone-related protein but may also occur because of bone metastases. The diagnosis is a poor prognostic sign (median survival 3-4 months), although prognosis may be longer in those with haematological malignancies.

2. RECOGNITION

Measure serum corrected calcium in **any** patient with **suspected/confirmed** cancer whose **condition deteriorates rapidly**. Normal range 2.20 - 2.60 mmol/L.

Consider if:

- previous hypercalcaemia
- contributory medications (calcium supplements, thiazide diuretics, lithium, other nephrotoxics)

Investigate:

- Assess symptoms and duration
- Determine fluid balance status
- Bloods – corrected calcium, U+Es, PTH, phosphate, magnesium, Vitamin D i**n al**l.

Excluding U+Es, do not delay bisphosphonate in *symptomatic* hypercalcaemia awaiting results above.

Signs / symptoms

Note: Symptom severity is related to the **rate of increase** in serum calcium, rather than the absolute level

Anorexia	Polyuria & thirst	Nausea & vomiting
Constipation	Abdominal pain	Drowsiness
Confusion	Cognitive dysfunction	Fatigue
Seizures	Dysrhythmias	Coma

STOP & THINK **Hypercalcaemia can occur as a terminal event in a patient expected to die soon from progressive cancer. Consider if appropriate to attempt to correct this potentially fatal event. If not, manage symptomatically.**

Corrected Ca^{2+} >2.60 mmol/L

- PTH low (or low-normal) indicitive of malignant cause. PTH high (or high-normal) consider hyperparathyroidism.
- **Calcium serum levels > 3.4 mmol/L** require **urgent correction** due to risk of **cardiac dysrhythmia and coma**.

Review medications

Stop calcium supplements and thiazide diuretics and **consider stopping** nephrotoxics if acute kidney injury present e.g. **diuretics, ACE inhibitors and nonsteroidal anti-inflammatory drugs**.

***Note:** Replace vitamin D if deficient / insufficient (to minimise risk of bisphosphonate induced hypocalcaemia)*

Rehydration and Bisphosphonate administration:

- **Rehydrate** with sodium chloride 0.9% IV, volume according to individual patient need. **Caution** if risk of fluid overload.
- **If Corrected Ca^{2+} < 3.0 mmol/L AND *symptomatic,* OR ≥ 3.0 mmol/L: <u>treat</u>** with **bisphosphate** after rehydration.
- **If Corrected Ca^{2+} < 3.0 mmol/L AND *asymptomatic,* consider** treatment with **bisphosphate** after rehydration – balance risk of hypercalcaemia recurrence vs. bisphosphonate side-effects (NB: hypercalcaemia likely to reoccur without **bisphosphonate treatment**.

Bisphosphonate treatment:

- Give **zoledronic acid 4mg in 100mL sodium chloride 0.9% via intravenous infusion over 15 min.** (***Note*** - some centres dose reduce zoledronic acid if CrCl 30 – 60 ml/min, check local guidance)

If creatinine clearance < 30 ml/min, <u>DO NOT</u> give bisphosphate and SEEK SPECIALIST ADVICE.

- **Notable adverse effects:** 'Flu-like syndrome/pyrexia is common – treat with paracetamol. Osteonecrosis of jaw is rare but significant side-effect – consider dental option if symptoms. Rebound ***hypocalcaemia*** may occur – maximal within the first 10 days.

4. FOLLOW UP

- Expect **clinical** improvement 24-72 hours, and biochemical improvement 4-7 days after bisphosphonate.
- **After 7 days**, if no clinical/biochemical response consider giving additional **4mg of IV zoledronic acid**.
- If still no response, seek specialist advice on 2nd line management.
- Malignant hypercalcaemia often indicates worsening disease; **consider** oncology input
- **Malignant hypercalcaemia can reoccur** - discuss symptoms with patient and family/carers and consider checking serum calcium and renal function if clinically appropriate.
- **Consider** advance care planning / completion of an **Emergency Health Care Plan**.

EMERGENCIES – HAEMORRHAGE

1. RECOGNITION

- Bleeding is common in advanced disease, and death from major haemorrhage can occur.
- Catastrophic internal bleeding is more common than external bleeding.
- Catastrophic bleeding is often preceded by smaller herald bleeds.

Clinical presentation of a major haemorrhage may include:

- Cardiovascular compromise – hypotension, tachycardia (>100 beats/min = significant recent bleed).
- Identifiable bleeding source, e.g. haematemesis, melaena, haemoptysis, vaginal or PR bleeding, haematuria, superficial/fungating tumours (particularly head and neck cancers).
- Swelling, bruising, petechiae, discolouration, pain to potential internal bleed site.

2. ANTICIPATORY MANAGEMENT

- Review ongoing risk/benefit of prescribed anticoagulants, antiplatelets, steroids and NSAIDs.
- Consider bleeding risk in those with clotting disruption and consider correction of any coagulation disorder.
- Review cardiopulmonary resuscitation status and treatment options with the patient and family. Consider if investigation/intervention is indicated and document an **Emergency Health Care Plan (EHCP)**. Provide an emergency contact number for family/carer.
- Dark towels should be available nearby to reduce the visual impact of blood if haemorrhage occurs.
- Prescribe **crisis dose midazolam for catastrophic bleed** i.e. **10mg IV/IM/SC/buccal** as a one-off dose for distress associated with a major haemorrhage. Repeated doses may be required under specialist guidance in the event of ongoing bleeding and distress. Explain to families/carers the aim is for sedation to minimise distress for the patient. The prescription should **highlight that this indication is separate to routine anticipatory prescribing of midazolam** (i.e. **2.5mg or 5mg IV/IM/SC/buccal**).
- Note: buccal administration is inappropriate in haematemesis and large oral bleeds.

3. IMMEDIATE ACTION

If a patient is close to death from underlying cancer, it is usually appropriate to consider major haemorrhage as a terminal event and not to intervene with resuscitation measures.

If resuscitation is appropriate

- Apply local pressure to any obvious bleeding.
- Admit as emergency. Secure IV access.
- Start rapid infusion of sodium chloride 0.9%.
- Cross match and follow local haemorrhage protocols.
- Seek specialist help on further management.

If resuscitation is inappropriate

- Remain calm; this will help a dying patient to achieve a peaceful death.
- Call for help and stay with the patient whilst providing reassurance/explanation to the patient and family.
- Use dark towels to absorb blood.
- Consider the use of crisis dose midazolam (for catastrophic bleed) to relieve distress in a patient that may be imminently dying. This should be readily available; someone staying with the patient takes priority.
- Administer medications for symptom relief as needed.

4. ONGOING MEASURES

- Consider referral for radiotherapy or embolisation if the patient has an erosive tumour.
- ORAL: tranexamic acid 1g 8-hourly (avoid in haematuria)
- TOPICAL: tranexamic acid (500mg/5ml injectable formulation) soaked on gauze (access in community may be difficult, plan in advance); adrenaline 1 in 1000 (1mg/ml) soak on gauze (short term only due to the risk of ischaemic necrosis and rebound vasodilation); silver nitrate sticks for visible (smaller) bleeding points.
- Contact specialist palliative care for potential alternative options.
- Consider electrical/chemical cauterisation, radiotherapy or embolisation, CT angiogram if source unclear, surgical/non-surgical management as appropriate.
- Treat any superimposed infection.

5. FOLLOW UP

- If the patient survives a significant bleed, consider blood transfusion. Manage pain. Consider further advance care planning discussion.
- Support family, carers and staff following experience of haemorrhage.

EMERGENCIES – MALIGNANT SUPERIOR VENA CAVA OBSTRUCTION

This guidance applies only to patients with a known cancer diagnosis

1. RECOGNITION

- 95% of cases of superior vena cava obstruction (SVCO) are caused by malignant tumour in the mediastinum preventing venous drainage from the head, arms and upper trunk.
- Commonest in lung cancer. Can also occur in lymphoma and some other cancers.
- Onset usually over weeks or months but occasionally occurs rapidly over days.
- Patient may deteriorate rapidly.

Clinical Presentation:

- Breathlessness, cough, chest pain, stridor and cyanosis are common.
- Facial swelling and feeling of fullness, redness / plethora, headache, periorbital oedema, engorged conjunctivae, visual disturbances.
- Swelling of the arms, prominent distended veins on neck and chest wall, non-pulsatile raised jugular venous pulse.

2. IMMEDIATE ACTION

- Sit upright, chair may be preferable. Consider loosening or removing restrictive clothing and supporting arms with pillows.
- High dose steroids may be helpful prior to definitive treatment. Give **dexamethasone 16mg stat** (oral or equivalent dose IV or SC – **see page 16**) **and continue 16mg daily as morning dose**; also prescribe PPI for gastric protection.
- Give oxygen if available and manage other symptoms (see guidelines on breathlessness **page 33** and agitation **page 31**).
- Discuss URGENTLY with the local Acute Oncology Team and arrange appropriate imaging.
- Anticoagulation may need to be considered if evidence of thrombus.

3. FOLLOW UP

- If the obstruction is resolved by stent insertion or other intervention, the dexamethasone should be reduced gradually and possibly stopped. Consider ongoing prophylactic anticoagulation.
- If the obstruction cannot be resolved with intervention, the dexamethasone should be gradually reduced to the lowest effective dose.

If SVCO suspected in a patient at the end of life or an individual who is too unwell or unwilling to have investigations, prognosis may be days:

- manage symptoms in patient's preferred care setting. Agree an **Emergency Health Care Plan**.
- consider symptomatic measures, including steroids (as above), and nursing at 45 degrees for comfort.

In the event of acute severe breathlessness, see guidelines on treatment of severe frightening breathlessness (page 33)

RECOGNITION:

- Respiratory rate (RR) < 8/min AND difficult to rouse, OR
- RR < 12/min, difficult to rouse AND cyanosed / oxygen saturation < 90% on pulse oximeter.
- Other signs may include myoclonic jerks, altered mental status (progressing to coma), delirium with hallucinations, ↓BP, ↓tidal volume and ↓chest wall expansion.
- Pupil size is an unreliable indicator of opioid toxicity in patients taking regular opioids.

ACTION:

- **Naloxone should not typically be administered to patients receiving opioids when death is imminent, as a slow respiratory rate is a normal occurrence. Seek specialist advice.**
- **Follow local guidance where this exists.**
- Stop offending opioid (including CSCI and remove TD patches).
- Secure IV access (if possible and clinically appropriate).
- If required, administer oxygen to maintain SpO2 >95 % (88-92 % if risk of C02 retention).
- **If toxicity is mild (i.e. patient alert or rouses easily)** consider close monitoring and omitting opioids until there is a sustained improvement in respiratory rate, naloxone may not be required in this circumstance.
- **Naloxone administration (administer according to severity, see graphic below):**
  - IV administration is preferred due to rapid onset of action. If this is not possible naloxone can be given IM or SC, alternatively a nasal spray product is available for use in immediately life-threatening respiratory depression.
  - **For buprenorphine induced respiratory depression,** standard doses of naloxone are ineffective. Administer 2mg IV naloxone over 90 seconds, then start a continuous IV infusion of naloxone at 4mg/hr until respiratory rate is satisfactory. **Seek specialist advice.**
  - Once acute toxicity has resolved, seek specialist advice regarding ongoing analgesic management. Ongoing management will be influenced by likely cause of toxicity, i.e. recent dose titration, drug-drug interaction, change in clinical pharmacokinetics or overdose (intentional and unintentional).

Severe, but not imminently life-threatening Partial reversal	Life-threatening *A slow respiratory rate is a normal part of dying and should not be mistaken for opioid toxicity.* Full reversal
RR < 8/min, with respiratory drive and effort	**Unresponsive with/near resiratory arrest (i.e. no or minimal respiratory effort)**
STEP 1: Administer **20 – 100 micrograms of naloxone IV***	**STEP 1:** Administer **naloxone 400 micrograms IV**
STEP 2: Repeat previous step every 2 minutes until respiratory rate satisfactory	**STEP 2:** If no response, administer **naloxone 800 micrograms IV,** wait 1 min then repeat this step
STEP 3: Aim is to reverse respiratory depression, NOT analgesia	**STEP 3:** If no response, administer naloxone 2 – 4 mg IV; if no response, consider alternative diagnosis

STEP 4:

Consider an intravenous infusion of **naloxone** if respiratory depression recurs despite three repeated bolus doses of **naloxone**, particularly if the patient has received long-acting opioid preparations (e.g. MR products, methadone, or transdermal fentanyl) or drug elimination likely to be prolonged due to physiological change (e.g. AKI). **Please seek specialist advice.**

* ***20 microgram doses:*** *dilute 400 micrograms of naloxone to 10 ml with sodium chloride 0.9% and administer 0.5 ml doses.*
* ***100 microgram doses:*** *dilute 400 microgram of naloxone to 4 ml with sodium chloride 0.9% and administer 1 ml doses.*

DIABETES MANAGEMENT IN THE LAST DAYS OF LIFE

Discuss changing the approach to diabetes management (i.e. the value of and potential method for glucose testing including the type of glucose lowering treatments – tablets or **insulin**) with your patient and/or their family if not already explored. If your patient remains on **insulin**, ensure your local diabetes specialist team are involved and agree a monitoring and management strategy.

Type 2 diabetes
Diet controlled or **Metformin**

→ Stop monitoring blood glucose

Type 2 diabetes on tablets
and / or **insulin** or **GLP1 agonist**

→ Stop **oral hypoglycaemics** and **GLP1 agonist**. Consider stopping **insulin** depending on dose[2]

→ Either

If insulin stopped:

- If glucose over 20mmols/L, give **6 units of short-acting insulin.**
- Recheck capillary blood glucose after 2 hours.

→ If your patient requires **short-acting insulin** more than twice a day, consider a daily **long-acting insulin** e.g. **Glargine (Lantus)** or **Degludec (Tresiba)**

If insulin is to continue:

- Prescribe **once daily long-acting insulin analogue** giving a dose at midday based on an **overall 25% reduction in total daily insulin dose.**

→ Check blood glucose once a day at teatime:

- **If below 8 mmols/L, reduce insulin dose by 10-20%**
- **If above 20 mmols/L, increase insulin dose by 10-20%** to reduce risk of/or symptoms of ketosis.
- **Alter dose by 2 units if daily dose below 50 units**.
- **Alter dose by 4 units if daily dose 50 units or more.**

Type 1 diabetes
always on **insulin**[1]

→ Continue once daily long-acting **basal insulin** analogue at midday with reduction in dose[3]

Key to Insulins

Short-acting insulins (mealtime or corrective dose) e.g. **NovoRapid(ASPART)** ® /**Humalog (LISPRO®, Trurapi** ®)
Long-acting insulins (once daily basal/background) **insulin** e.g. **Glargine/LANTUS®, Degludec/TRESIBA®**

- Keep invasive glucose tests to a minimum. It is necessary to perform some tests to ensure unpleasant symptoms do not occur due to low or high blood glucose levels.
- Aim for capillary blood glucose between 6 – 15mmol/L
- It is very difficult to identify symptoms of very low or high glucose levels in a dying patient. If symptoms are observed, and if clinically appropriate to do so, check glucose levels (urine or capillary blood) if necessary.

1 Some patients with Type 1 diabetes may be using wearable technology e.g. **insulin pumps** or **Continuous Glucose Monitoring Systems (LIBRE or DEXCOM)**. Please contact local diabetes teams to discuss management.

2 **Patients on over 48 units of insulin daily are likely to develop symptoms without insulin.**

3 **Reduce long-acting insulin dose by 25% as well as discontinuing short-acting insulin.**

Prescribe insulin correctly by brand name; ensure correct dose units and strength.

For further information and/or advice, please contact your local specialist diabetes team
or refer to End of Life Guidance for Diabetes Care
https://trenddiabetes.online/portfolio.end-of-life-guidance-for-diabetes-care/

PAIN IN THE LAST DAYS OF LIFE

(For patients with rapidly deteriorating renal function and/or patients with eGFR<30 ml/min/1.73 m², consider advice on page 29)

- **Unless specifically indicated, morphine is the first line injectable opioid of choice.**
- **Other opioids are indicated if previous morphine intolerance and/or renal failure *(eGFR<30 ml/min/1.73 m²).***
- **Seek specialist advice if you consider that an alternative opioid may be indicated and/or patient is no longer able to take oral adjuvant analgesia.**

YES — **Is patient already on opioid drugs?** — **NO**

For patient on **morphine** or **oxycodone**, follow guidance below. For patients on other opioids, refer to grey box below or seek advice.

Patient on morphine or oxycodone:

- Divide 24-hour total dose of **REGULAR ORAL** opioid by 2 and prescribe this as **morphine** or **oxycodone CSCI over 24 hrs**.
- Start CSCI 2 hours before next oral opioid dose would have been due (or immediately if a dose has been missed).
- Discontinue oral opioid.
- Prescribe 1/10th to 1/6th opioid syringe driver dose as breakthrough medication to be given **SC PRN up to 1-hrly** (rounded to the nearest measurable dose).

Scenario 1: "planning ahead"

Patient not in pain:

- Prescribe **morphine 2.5mg SC PRN up to 1-hrly**.
- If patient later develops pain, proceed to next box.

Scenario 2: "act now"

Patient in pain:

- Give **morphine 2.5mg** SC stat.
- If effective, prescribe and start **morphine 10mg/24hr CSCI**.
- Prescribe **morphine 2.5mg SC** for breakthrough pain to be given PRN **up to 1-hrly**.

Review within 24hrs

If pain is controlled, make no changes.

If extra medication has been needed for pain, and is effective:

- increase syringe driver dose by 33-50% of regular dose.
- adjust breakthrough dose to 1/10th to 1/6th of syringe driver opioid dose to be given **SC PRN up to 1-hrly** (rounded to the nearest measurable dose).

Patient on regular weak opioid: e.g. **codeine, tramadol**

- Stop oral **weak opioid**.
- Start **morphine 10mg/24hrs** or **20mg/24hrs** CSCI soon after last oral dose *(use **20mg/24hrs** if previous weak opioid was at maximum daily dose)*.
- Prescribe **morphine 2.5-5mg SC PRN 1-hrly** for breakthrough pain.

Review regularly and adjust as above.

TRANSDERMAL PATCHES (e.g. fentanyl, buprenorphine) for a patient in the last days of life:

If pain controlled: continue transdermal patch(es). Remember to carry on changing the patch(es) regularly as previously (usually 72hourly, but may be less frequent with some strengths of buprenorphine)

Prescribe breakthrough doses of morphine (1/10th to 1/6th of the regular 24hr dose); if morphine is not appropriate (e.g. eGFR<30 ml/min/1.73 m²), seek specialist advice about an alternative injectable opioid.

Consult the chart on page 2 to calculate the correct breakthrough dose of opioid.

If pain not controlled:

If 2 or more breakthrough doses are needed in 24 hours, continue the patch(es) and start a CSCI with morphine (or other opioid).

The morphine (or other opioid) dose in the CSCI should represent a 33-50% increase of the regular 24hr dose.

Remember to combine the dose of the patch(es) and the dose in the CSCI to work out the new breakthrough dose (1/10th - 1/6th of the opioid **TOTAL** daily dose)

If further CSCI dose increases are needed, DO NOT increase the **TOTAL** regular 24hr opioid dose (patch and CSCI) by more than 50%

IF YOU ARE IN ANY DOUBT ABOUT THESE CALCULATIONS, SEEK SPECIALIST ADVICE.

PAIN IN THE LAST DAYS OF LIFE IN RENAL IMPAIRMENT

Key points

- This guidance applies to the patient with rapidly deteriorating renal function and/or eGFR<30 ml/min/1.73 m².
- * Whilst alfentanil is the preferred background opioid in renal failure, it has a short duration of action (<1hr) so oxycodone generally offers better symptom control and is a more practical option for PRN use; for this reason, common practice within palliative care is to prescribe an alfentanil CSCI alongside PRN oxycodone. This should be clarified and highlighted within special instructions on the prescription chart.
- If oxycodone is used as a PRN, it should be prescribed 2-hrly due to prolonged half-life in renal impairment
- **DO NOT prescribe oxycodone via CSCI in renal impairment without specialist support.**
- **Seek specialist advice and support if unfamiliar with prescribing alfentanil or other opioids in renal failure, and/or patient has hepatic and renal impairment and/or using transdermal opioids.**

YES — **Is patient already on opioid drugs?** — **NO**

Patient already on strong opioids

- See conversion chart **(page 2)** to calculate dose of CSCI **alfentanil**.
- Start CSCI 2 hrs before next oral opioid dose would have been due (or immediately if a dose has been missed).
- Discontinue oral opioid.
- **If unfamiliar with alfentanil use or patient has signs of opioid toxicity, seek specialist advice.**
- Prescribe **oxycodone 1-2mg SC PRN 2-hrly** OR ***250microg alfentanil SC PRN 1-hrly** for breakthrough pain.
- For patients on more than **alfentanil 2mg/24hrs CSCI**, seek specialist advice for PRN opioid dose

Review DAILY
If pain is controlled, make no changes

If extra medication has been needed for pain:

- Increase **alfentanil** syringe driver dose by 33-50%
- Continue previous PRN dose
- For patients on more than **alfentanil 2mg/24hrs CSCI,** seek specialist advice for further titration of PRN opioid dose

Continue to review regularly and **seek specialist advice if multiple dose increases/ pain persists.**

Patient on regular weak opioid
(e.g. **codeine, tramadol**)

- Stop oral weak opioid.
- Start **alfentanil 1mg/24hrs** by CSCI soon after last oral dose or seek advice about prescribing oxycodone.
- Prescribe **oxycodone 1mg SC 2-hrly as required** OR ***alfentanil 250microg SC 1-hrly as required** for breakthrough pain.
- Review and titrate further as needed.
- **Seek advice if uncertain.**

Scenario 1: "planning ahead"
Patient not in pain:

- Prescribe **oxycodone 1mg SC PRN 2-hrly** OR ***alfentanil 250 micrograms SC 1-hrly as required.**
- If patient needs pain relief, proceed to next box.

Scenario 2: "act now"
Patient in pain:

- Give **oxycodone 1mg SC** or ***alfentanil 250 micrograms** SC stat.
- If effective, prescribe and start **alfentanil 1mg/24hrs CSCI** or *seek advice about prescribing oxycodone.*
- Also prescribe **oxycodone 1mg SC PRN 2-hrly** OR ***alfentanil 250 micrograms SC PRN 1-hrly** for breakthrough pain.

Review within 24hours
If pain is controlled, make no changes

If extra medication has been needed for pain:

- Increase **alfentanil CSCI** to **1.5mg/24hrs**
- Continue current doses of **oxycodone** OR ***alfentanil** SC for breakthrough pain

Review DAILY
If pain is controlled, make no changes.

If extra medication required for pain:

- Increase alfentanil dose in syringe driver dose by 33-50%
- Adjust breakthrough dose to **oxycodone 2mg SC PRN 2-hrly** or continue ***alfentanil 250microg SC PRN 1-hrly.**

Continue to review regularly.

Seek specialist advice if multiple dose increases/pain persists.

For further information on alfentanil, refer to PAIN section page 8.
*See note in 'Key points' box at top of page

NAUSEA AND/OR VOMITING IN THE LAST DAYS OF LIFE

This guideline for the management of nausea/vomiting in the last days of life should be read in conjunction with the general guideline on nausea/vomiting on pages 12-13. Prescription should reflect the likely cause of the nausea and vomiting.

In **RENAL IMPAIRMENT** (eGFR<30 ml/min/1.73 m²): Use reduced dose HALOPERIDOL, or LEVOMEPROMAZINE second line.

In **HEART FAILURE:** caution with CYCLIZINE. METOCLOPRAMIDE or HALOPERIDOL may be preferred.

In **HEPATIC FAILURE:** use reduced dose of antiemetic – choice depends on cause - see pages 12 & 18

In **PARKINSON'S DISEASE:** avoid METOCLOPRAMIDE, HALOPERIDOL, LEVOMEPROMAZINE. Use reduced dose CYCLIZINE or seek specialist advice.

Planning ahead, in case nausea/vomiting develops:

Prescribe **cyclizine 25-50mg SC PRN 6-hrly** (max TDS),
or **haloperidol 0.5 – 1.5 mg SC PRN 1-hrly (max 3mg/24hr)**

OR

prescribe **levomepromazine* 6.25mg** (some areas prefer **2.5-5mg**) **SC PRN 1-hrly up to QDS**.

If patient develops nausea/vomiting, titrate levomepromazine as per "**UNCONTROLLED nausea/vomiting**" box below.

Nausea/vomiting already controlled:

Patients already taking an oral anti-emetic who reach the last days of life should have the anti-emetic continued to ensure on-going symptom control; however, **this current anti-emetic should be switched to the subcutaneous route via CSCI over 24hours.** This may require a change of drug if not available as SC preparation.

Also prescribe 'as required' dose of the same drug, or levomepromazine* **6.25mg** (some areas prefer **2.5-5mg**) **SC PRN 1-hrly up to 25mg/24hrs** (max including PRN and regular doses). Avoid using **levomepromazine*** with **haloperidol**.

NEW nausea/vomiting in a patient not currently treated with an anti-emetic

If a chemical cause is LIKELY:

- Prescribe **haloperidol 0.5-1.5mg SC OD** or via CSCI over 24hrs
- Also prescribe **haloperidol 0.5-1.5mg SC PRN 1-hrly**, up to **3mg/24hrs** (max including PRN and regular doses)

If a chemical cause is UNLIKELY:

- Prescribe **cyclizine 75 – 150 mg/24hrs CSCI**.
- Also prescribe **cyclizine 25mg SC PRN 6-hrly up to TDS** (max 150mg/24hr including regular and PRN doses) **OR levomepromazine* 6.25mg** (some areas prefer **2.5-5mg**) **SC PRN 1-hrly up to 4 doses/24hrs**

Some areas commence regular **levomepromazine* 6.25mg/24hrs SC OD** or via CSCI/24hrs, and **levomepromazine 6.25mg** (some areas prefer **2.5-5mg**) **SC PRN 1-hrly** up to 25mg/24hrs (max including regular and PRN doses).

REVIEW AFTER 24hours: If symptoms are controlled, continue as before.

If either nausea or vomiting persists, change anti-emetic to levomepromazine as below and/or seek specialist advice

UNCONTROLLED nausea/vomiting in a patient already on an anti-emetic

Review the possible causes, but do not delay changing the anti-emetic regime or arrange burdensome investigations in an end-of-life care situation.

If a first-line antiemetic fails to control nausea/vomiting, replace it with **levomepromazine* 12.5mg/24hrs SC** (either CSCI or SC bolus injection*). Also prescribe **levomepromazine* 6.25mg** (some areas prefer **2.5-5mg**) **SC PRN 1-hourly, up to 25mg/24hrs** (max including regular and PRN doses).

If refractory nausea and vomiting, seek specialist advice.

***Notes on levomepromazine**

Levomepromazine has a broad spectrum of action. Some areas use **levomepromazine** as first-line anti-emetic and prefer **2.5-5mg** as a **PRN QDS** dose.

The effects of this drug may last up to 24hrs; once daily SC dosing is an alternative to CSCI.

Any dose may have a sedative effect. The sedative effect may be clinically useful - this drug is also used in the management of terminal agitation and restlessness (see page 31). Where even mild sedation is an unacceptable side-effect, **start at a dose of 2.5mg SC**.

RESTLESSNESS / AGITATION / DELIRIUM IN THE LAST DAYS OF LIFE

NB: this guidance covers agitation in the last days of life. Agitation / delirium at an earlier stage may require different management - seek advice.

Agitation in the last days of life is common and is distressing for patients and families. It can be difficult to distinguish between restlessness, agitation and delirium. Possible sedating effects of medicines used to manage distress should be discussed and agreed with the patient and /or their caregiver.

Common presentation: restless; pulling at clothes/sheets; shouting, physical aggression, signs of fear.

Treat reversible causes: e.g. urinary retention; faecal impaction; pain or other symptoms. Opioid toxicity may present with similar symptoms, as may drug withdrawal (alcohol, nicotine, benzodiazepines, gabapentinoids, illicit drugs) – seek advice.

Support a calm environment: e.g. familiar voices and faces; gentle and usual routine; side / quiet room; calming music.

BENZODIAZEPINES: to prevent withdrawal or rebound agitation, regular / long-term benzodiazepines should be replaced by a continuous subcutaneous midazolam infusion

[Diazepam 5mg PO = Lorazepam 0.5mg PO = Temazepam 10mg PO = **Midazolam** 2.5mg SC].

Note: these are approximations. Appropriate caution and monitoring are required if switching between drugs. If switching from a long-acting drug (e.g. diazepam or clonazepam) a washout period may be required. If switching at a high dose, consider reducing by 30-40%. ***Seek specialist advice if needed***.

In **RENAL FAILURE:** MIDAZOLAM is a good first choice as toxin accumulation in renal failure increases seizure risk.
In **HEPATIC FAILURE:** use reduced dose MIDAZOLAM and/or HALOPERIDOL. For further information, see page 18

ANTICIPATORY *(Just in case)* **PRESCRIBING**

Prescribe *either:* **midazolam 2.5-5mg SC PRN 1-hrly** or **haloperidol 1.5mg SC (0.5-1mg in frail/elderly) PRN 1-hrly (max 5mg/24hr)**.

Some centres prescribe **levomepromazine** as an alternative/additional option **12.5-25mg SC PRN 1-hrly (12.5mg in frail/elderly), max 50mg/24hrs then seek specialist advice**.

IF SYMPTOMS DEVELOP, REVIEW AND COMMENCE REGULAR TREATMENT AS BELOW

RESTLESSNESS or AGITATION PRESENT (anxiety prominent)

Give Midazolam 2.5mg - 5mg SC stat

If stat dose effective, start syringe driver:
Midazolam 10mg/24hr CSCI.
and continue **midazolam 2.5-5mg SC PRN up to 1-hrly**
(use lower dose in the range if frail/elderly)

Review within 24 hrs

If breakthrough doses needed and effective, increase **midazolam** syringe driver dose by 50% or the equivalent of the extra doses given in the previous 24hrs.

Continue breakthrough doses of **midazolam 2.5-5mg SC PRN 1-hrly**.

Continue to review daily and titrate dose as clinically indicated. Common dose range **midazolam 10-60mg/24hrs CSCI**.

If **midazolam** CSCI dose >30mg/24hrs and agitation continues, consider adding **haloperidol or levomepromazine**.

DELIRIUM PRESENT

Give REGULARLY:
Haloperidol 1.5mg SC (0.5-1 mg in frail/elderly) OD or BD (and continue PRN as above)
or
Levomepromazine 12.5-25mg SC (12.5mg in frail/elderly) OD or via CSCI/24hr (and continue PRN as above). Note: may be more sedating

Review within 24 hrs

If symptoms are controlled, continue as above

(Both drugs are long acting so can be given as SC doses or CSCI).

If symptoms are not controlled, increase **haloperidol to 5mg/24hrs SC/CSCI**, or increase **levomepromazine** by equivalent of extra doses given to a **maximum of 50mg/24hrs**, then seek specialist advice.

Levomepromazine is an effective sedative.
It can be prescribed with **midazolam** (if **midazolam** partially effective) and/or used to replace **haloperidol**.
Use breakthrough dose **12.5-25mg SC** (12.5mg in frail/elderly) **PRN 1-hrly**.
Although 1-hourly doses can be given, seek specialist advice if more than 50mg/24 hours is needed.

Unresolved or severe symptoms
Some patients become extremely agitated when they are dying and may require very high doses of drugs to manage their symptoms. **Specialist advice should be sought**. It is vital that patients are not left in distress.

RESPIRATORY TRACT SECRETIONS IN THE LAST DAYS OF LIFE

Secretions which have already accumulated will not be removed by medication.
Early treatment improves the prospect of achieving symptom control. An unconscious patient may not be distressed; however explanation and reassurance to family/carers can help their distress.

Considerations when choosing an anti-secretory drug:

Hyoscine butylbromide and **glycopyrronium** are broadly similar in effectiveness, controlling secretions in up to 2/3rd of patients. Consider that secretions may continue to accumulate despite treatment.

In RENAL FAILURE: prescribe HYOSCINE BUTYLBROMIDE or half the stated GLYCOPYRRONIUM dose (see page 18)

If MYASTHENIA GRAVIS present: seek specialist advice (see page 19)

SECRETIONS PRESENT

General measures

- Assess if secretions causing distress to patient, and balance with potential side effects of drugs (eg dry mouth, urinary retention).
- Alter position to shift secretions.
- **Give explanation and reassurance to relatives/carers**
- Give regular mouth care.

Consider potentially reversible causes:

Pulmonary oedema – consider **furosemide** by SC infusion (seek specialist advice).

Chest infection – consider **antibiotics** for palliation of respiratory symptoms.

Gastric reflux – seek specialist advice.

Anti-secretory prescribing

Give stat dose of antisecretory agent:
Hyoscine butylbromide 20mg SC or
Glycopyrronium 200 micrograms SC

Commence CSCI if stat dose effective*:
Hyoscine butylbromide 60mg/24hrs CSCI or
Glycopyrronium 600micrograms/24hrs CSCI

Extra doses (use same PRN medication as CSCI):
Hyoscine butylbromide 20mg SC PRN 1hrly or
Glycopyrronium 200 micrograms SC PRN 1hrly
(maximum 6 doses in 24hrs in addition to CSCI dose).

SECRETIONS ABSENT

Pre-emptive discussion with relatives/carers that noisy secretions may occur but may not distress patient.

Medications to prescribe in anticipation:

Options:
Hyoscine butylbromide 20mg SC PRN 1-hrly
or
Glycopyrronium 200micrograms SC PRN 1-hrly

Specify maximum 6 PRN doses/24hrs

If doses required
Then manage as for 'secretions present' and consider starting syringe driver*

Review after 24hours, or sooner if indicated
If extra doses needed, increase CSCI dose to:
Hyoscine butylbromide 120mg/24hrs CSCI
OR **Glycopyrronium 1200micrograms/24hrs CSCI**

Use same PRN medication as CSCI:
Hyoscine butylbromide 20mg SC PRN 1hrly or
Glycopyrronium 200 micrograms SC PRN 1hrly
(maximum 3 doses in 24hrs in addition to CSCI dose)

If symptoms not controlled, seek specialist advice.

NB: For those who don't respond to antisecretory agents, non-pharmacological options are integral, such as patient repositioning, management of associated symptoms (e.g. breathlessness and agitation) and providing reassurance.

*Ideally CSCI should be commenced after initial PRN dose. However, in situations where this cannot be immediately facilitated (e.g. out of hours in community), ongoing PRN doses may be acceptable until prescribing review possible.

BREATHLESSNESS IN THE LAST DAYS OF LIFE

BREATHLESSNESS PRESENT

General measures:
- Calm environment
- Reassurance and support.
- Cool room.
- Gentle air flow with fan, directed at the nose/mouth
- Give hourly mouth care.
- Oxygen if helpful (but only if low saturations).

Patient not already on opioid for pain
(**for patients with renal impairment**, see advice to the right and on page 9)
- give **morphine 2.5mg SC** stat
- also prescribe **morphine 2.5mg SC PRN 1-hrly**
- commence **morphine 10mg/24hrs CSCI**

Patient already on opioid
- give **midazolam 2.5mg SC** stat
- also prescribe **midazolam 2.5mg SC PRN 1-hrly**
- commence **midazolam 10mg/24hrs CSCI**

(**Midazolam** is a useful option in patients with renal impairment if there is doubt about opioid choice).

RISK OF BREATHLESSNESS

Planning ahead

Patient **not on opioid**: prescribe **morphine 2.5mg SC PRN 1-hrly** (see below for advice if renal impairment present)

Patient on opioid analgesia: prescribe **midazolam 2.5mg SC PRN 1-hrly**.

Review within 24hours

If 2 or more doses needed, manage as for breathless patient and consider starting syringe driver

Specific situations

Heart failure: consider furosemide by continuous subcutaneous infusion. Seek specialist advice.

Severe renal impairment: consider replacing **morphine** with alternative opioid e.g. **oxycodone 1-2mg SC PRN 2-hrly**

or

alfentanil 250 micrograms SC PRN 1-hrly and/or 1mg/24hrs CSCI

Review within 24hours

If 2 or more breakthrough doses of morphine or midazolam needed in 24hrs, assess effectiveness and increase **CSCI** dose by 33-50%. Continue to allow breakthrough doses hourly as required. Consider increasing the breakthrough dose of **morphine** and **midazolam** to **5mg** if CSCI increased.

Usually for breathlessness management, the dose of morphine should not need to exceed 15mg/24hrs CSCI. If symptoms are not improving, seek specialist palliative care advice.

EMERGENCIES – SEVERE FRIGHTENING BREATHLESSNESS

Severe frightening breathlessness is an emergency and may be a terminal situation.
Therapeutic sedation is an appropriate treatment in this emergency situation - and only proportional sedation, sufficient to relieve the frightening sensation, should be given.

Review the patient. Consider treating possible reversible causes. Consider use of oxygen if hypoxic.
If no reversible cause and felt to be a terminal event
- administer **midazolam 5-10mg SC**.
- repeat up to twice at 30-minute intervals until the patient is calm (for some, this will mean being asleep).

When the patient is calm, set up a syringe driver with midazolam:
- **start at 20mg/24hrs CSCI** and prescribe **5mg SC PRN every 15-30 mins** for frightening symptoms.
- review every few hours and titrate further as necessary to maintain good symptom control.
- some patients may require higher doses of midazolam in CSCI; seek specialist advice as needed.

Treatment with an opioid may also be appropriate to reduce sensation of breathlessness. Consider using **morphine 2.5-5mg SC stat** and **morphine 2.5-5mg SC PRN 1-hrly**. If needed, consider starting **morphine 10mg or 15mg/24hr CSCI**.

WITHDRAWAL OF VENTILATION
Specialist support is advised. Midazolam and opioids can be used to alleviate anticipated and ongoing symptoms.

SYRINGE DRIVERS AND DRUG COMPATIBILITIES

Principles of medicines compatibility and syringe drivers

The law states that the instruction / direction to mix medicines must be in writing; therefore, the prescriber must indicate which medicines to mix in each syringe driver.

The compatibility information below only refers to mixing of 2 drugs in a syringe driver. If using 3 or more drugs in one syringe driver, ensure that the combination is compatible (including the diluent being used). If unsure, seek specialist advice.
After initial mixing, check for cloudiness or separation (precipitation); if present, wait.

- If fully resolves, continue and monitor closely.
- If doesn't resolve, discard solution and contact prescriber for alternative combination.
- Monitor all syringe drivers regularly for signs of incompatibility (crystallisation).
- Be aware that an "alarming" syringe driver could be due to incompatibility of the medicines.

The NENC PEoLC Network does not advocate anticipatory syringe driver prescribing or the prescribing of dose ranges in syringe drivers, although small dose ranges on PRN medications are acceptable (e.g. 2.5mg to 5mg). NICE (NG31 2015) states that prescribing should be individualised with regards to anticipatory medicines, and practitioners should monitor for benefits/side effects and adjust the individualised care plan/prescription as necessary. Best practice also considers learning from the Gosport War Memorial Hospital inquiry (2018) which highlighted unsafe practices around anticipatory prescribing.

Choosing a diluent

Water for injection is recommended as the diluent of choice as there is less likelihood of incompatibility.
The purpose of the diluent is to reduce the risk of site irritation. If there is inflammation at the injection site:

- Increase the diluent to the maximum volume (this should always be done in advance for drugs which are known to be irritant e.g. cyclizine, levetiracetam, levomepromazine).
- Consider switching to sodium chloride 0.9% and seek specialist advice regarding compatibilities
- If site irritation continues, seek specialist advice. Consider the addition of low dose dexamethasone to CSCI, if compatibility data permits.

To use this table

- Find the first medicine you want to mix in the left-hand column.
- Look along the row and search for the other medicine you want to mix.
- If the medicine is in the '☑YES compatible' box then go ahead and mix the two medicines with water as the diluent.
- If the medicine is in the '☒NOT COMPATIBLE' or '?CONCENTRATION SPECIFIC COMPATIBILITY' box, then follow the instructions in this box and check the strengths and concentrations to see if the two medicines can be mixed or not.

MEDICINE Indication ***Diluent: water for injection***	**DOSE (subcutaneous)**		**COMPATIBILITY- 2 MEDICINES**	
	Per 24hrs *If on regular opioids -use opioid conversion chart (page 2)	**PRN** (Doses normally ≥ 1 hour apart, seek specialist advice if symptoms not controlled)	☑ **YES COMPATIBLE** (assuming only 2 drugs mixed)	☒ **NOT COMPATIBLE or ? CONCENTRATION SPECIFIC COMPATIBILITY**
MORPHINE Pain / Dyspnoea *(10mg/mL, 30mg/mL)*	*10mg No upper limit for pain; if used for dyspnoea, see p28 (increase dose by 33-50% at a time)	2.5 - 5mg OR 1/10th-1/6th of total daily dose of morphine	☑ Cyclizine ☑ Hyoscine butylbromide ☑ Glycopyrronium ☑ Levomepromazine ☑ Metoclopramide ☑ Midazolam: generally regarded as *compatible* (although precipitation may occur, seek advice if injection site reactions occur)	? Haloperidol *incompatible* at high concentrations of haloperidol >1mg/mL or morphine>10mg/ml (e.g. this would be >170mg of morphine in 17ml, which is unlikely to be prescribed outside of specialist palliative care)
OXYCODONE Pain / Dyspnoea *(10mg/mL, 50mg/mL)* *If using oxycodone 50mg/ml, compatibilities may vary - seek specialist advice*	*5mg No upper limit (increase dose by 33-50% at a time)	2.5mg OR 1/10th–1/6th of total daily dose of oxycodone	☑ Haloperidol ☑ Hyoscine butylbromide ☑ Glycopyrronium ☑ Levomepromazine ☑ Metoclopramide ☑ Midazolam	? Cyclizine *incompatible* at high concentrations # If cyclizine is 150mg in **23mL or 24mL**, max oxycodone **≤70mg** -Oxycodone + cyclizine is a problematic combination, always dilute to maximum & monitor.
ALFENTANIL Pain / Dyspnoea (1mg/2mL) *Often not practical for PRN use due to short half-life, especially in community. Seek specialist advice for alternatives*	1mg No upper limit (increase dose by 33-50% at a time)	250 micrograms OR 1/10th–1/6th of total daily dose of alfentanil	☑ Haloperidol ☑ Hyoscine butylbromide ☑ Glycopyrronium ☑ Levomepromazine ☑ Metoclopramide ☑ Midazolam	? Cyclizine *incompatible* at high concentrations # If cyclizine is 150mg in **23mL or 24mL**, max alfentanil dose is **5.5mg**
# examples given of doses, assuming use of a syringe driver using either 17mL or 23mL/24mL as max total volume after dilution. Volume will depend on device being used and local policy/guidelines				

SYRINGE DRIVERS AND DRUG COMPATIBILITIES

MEDICINE Indication ***Diluent: water for injection***	DOSE (subcutaneous)		COMPATIBILITY- 2 MEDICINES	
	Per 24hrs *If on regular opioids -use opioid conversion chart (page 2)	**PRN** (Doses normally ≥ 1 hour apart, seek specialist advice if symptoms not controlled)	☑ **YES COMPATIBLE** (assuming only 2 drugs mixed)	☒ **NOT COMPATIBLE or ? CONCENTRATION SPECIFIC COMPATIBILITY**
MIDAZOLAM Agitation / Dyspnoea (10mg/2ml)	10mg No upper limit, but consider seeking specialist advice if not responding to 30mg (Increase by 33-50% at a time)	2.5 - 5mg	☑ Alfentanil ☑ Haloperidol ☑ Hyoscine butylbromide ☑ Glycopyrronium ☑ Levomepromazine ☑ Metoclopramide ☑ Oxycodone	? Cyclizine *incompatible* at some concentrations # If Cyclizine is 150mg in **23mL or 24mL**, max Midazolam **20mg** -Morphine (see MORPHINE section)
MIDAZOLAM Seizures (10mg/2ml)	30mg (Start at lower dose 20mg to avoid excessive sedation)	10mg		
CYCLIZINE Nausea and vomiting (50mg/ml)	75-150mg (Always dilute as much as possible with water e.g. up to 23mL)	25-50mg (max dose 150mg / 24hrs) ***NOTE: minimum dose interval 6 hours***	☑ Haloperidol ☑ Morphine	- Alfentanil (see ALFENTANIL section) ☒ Glycopyrronium *not known*, no data available ☒ Hyoscine butylbromide *incompatible* ☒ Levomepromazine *not recommended* ☒ Metoclopramide *not recommended* - Midazolam (see MIDAZOLAM section) - Oxycodone (see OXYCODONE section)
METOCLOPRAMIDE Nausea and vomiting (10mg/2ml)	30mg, increase gradually to 60mg if needed (higher doses under specialist guidance only)	10mg	☑ Alfentanil ☑ Glycopyrronium ☑ Haloperidol ☑ Midazolam ☑ Morphine ☑ Oxycodone	☒ Cyclizine *not recommended* ☒ Hyoscine butylbromide *not recommended* ☒ Levomepromazine *not recommended*
HALOPERIDOL Nausea and vomiting (5mg/mL)	0.5 - 3mg	0.5 - 1.5 mg	☑ Alfentanil ☑ Cyclizine ☑ Glycopyrronium ☑ Hyoscine butylbromide ☑ Metoclopramide ☑ Midazolam ☑ Oxycodone	☒ Levomepromazine *not recommended* -Morphine (see MORPHINE section) *Haloperidol is long acting so can be given as a bolus injection if compatibility is an issue*
HALOPERIDOL Agitation (5mg/mL)	0.5 - 5mg	0.5 – 1.5 mg		
LEVOMEPROMAZINE Nausea and vomiting (25mg/mL)	6.25 - 12.5mg	2.5 - 6.25mg	☑ Alfentanil ☑ Glycopyrronium ☑ Hyoscine butylbromide ☑ Midazolam ☑ Morphine ☑ Oxycodone	☒ Cyclizine *not recommended* ☒ Haloperidol *not recommended* ☒ Metoclopramide *not recommended* *Levomepromazine is long acting so can be given as a bolus injection if compatibility is an issue*
LEVOMEPROMAZINE Agitation (25mg/mL)	12.5 - 25mg; increase gradually if needed. Seek specialist advice for doses >50mg (Dilute high doses as much as possible)	12.5mg		
HYOSCINE BUTYLBROMIDE Chest secretions / Colic / spasm pain (20mg/mL)	60 - 120mg	20mg	☑ Alfentanil ☑ Haloperidol ☑ Levomepromazine ☑ Midazolam ☑ Morphine ☑ Oxycodone	☒ Cyclizine *incompatible* ☒ Glycopyrronium *not recommended* ☒ Metoclopramide *not recommended*
GLYCOPYRRONIUM Chest secretions (200microg/mL)	600microg – 1.2mg	200microg	☑ Alfentanil ☑ Haloperidol ☑ Levomepromazine ☑ Metoclopramide ☑ Midazolam ☑ Morphine ☑ Oxycodone	☒ Cyclizine *not known*, no data available ☒ Hyoscine butylbromide *not recommended*
LEVETIRACETAM Seizures (100mg/mL)	Oral **:** SC conversion 1:1	Use midazolam injection	Limited compatibility information suggests that it is compatible with haloperidol, hyoscine *butylbromide*, levomepromazine, metoclopramide, midazolam, morphine, oxycodone ***using sodium chloride 0.9% as diluent***	
# examples given of doses, assuming use of a syringe driver using either 17mL or 23mL/24mL as max total volume after dilution. Volume will depend on device being used and local policy/guidelines				

Evidence – The information in chart is from the Palliative Care Formulary 9th Edition and based on clinical observations in palliative care services.

Sixth edition: 2025
Next review date 2030