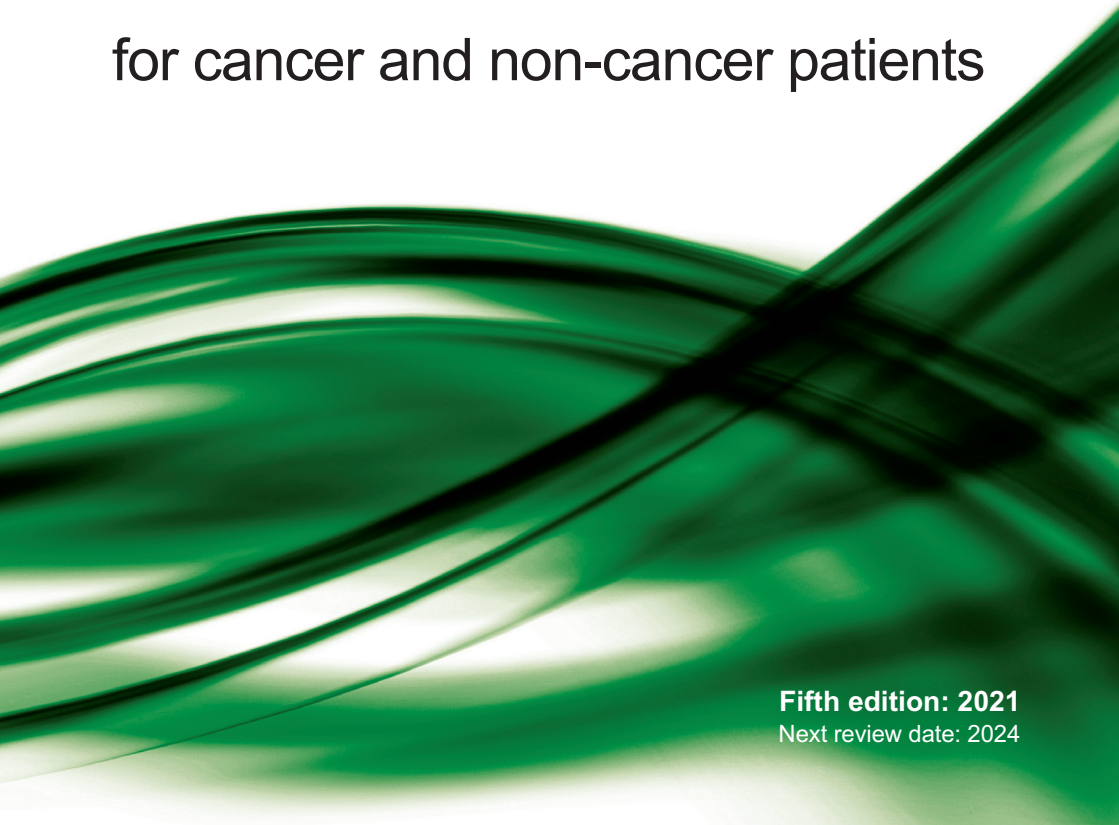
NHS
North East and North Cumbria
Clinical Networks

Palliative and End of Life Care Symptom Control Guidelines

for cancer and non-cancer patients



Fifth edition: 2021
Next review date: 2024

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)
	300	200	150	100	10	125	
	360	240	180	120	12	150	
	480	320	240	160	16	200	
	600	400	300	200	20	250	
	720	480	360	240	24	300	
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 inj -1/10 of 24hr CSCI dose up to 1-hrly**	N/A	N/A

Note (a): PCF7 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, PCF7 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 PCF7 which is morphine:fentanyl = 100:1 (BNF states 150:1). **Note (d):** Data sourced by PCF7 suggests that TD buprenorphine is between 70 and 115 times more potent than PO morphine. PCF7 advocates a ratio of 100:1 as a compromise. Therefore, as a guide, a buprenorphine 5 microgram/hr patch would be equivalent to 12mg PO 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).

INTRODUCTION

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

These guidelines have been written for any clinician responsible for the management and treatment of adult patients with palliative and end of life care needs, regardless of diagnosis.

They 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 and expert opinion. The guidelines are not intended to replace excellent textbooks and formularies that already exist. They have been updated to reflect any recent changes in practice, and in response to feedback and requests for additional information from users of the Fourth edition.

Please note that drug dose guidance – and especially the stated relative potencies of different opioid drugs – is drawn from the Palliative Care Formulary 7th Edition (PCF7). 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 PCF7, pages xix-xxiv).

The group takes no responsibility for any consequences of any actions taken as a result 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 to the effort and commitment made by all the contributors to this edition: Jane Bond, Jessica Briggs, Max Charles, Felicity Dewhurst, Hannah Edge, Jonathan Hindmarsh, Kate Howorth, Angela Laybourne, Francesca Mastaglio, Clare MacGregor, Emma McDougall, Rahul Nayar, Lauren Peters-Jones, Clare Raffel, Grace Rowley, Hassan Tahir, Pamela Saunders, Donna Wakefield, Jane Walker, Tom Ward and Lizzie Woods. With their hard work, the Fifth edition has now been successfully completed.

For further information, please visit https://northerncanceralliance.nhs.uk/

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For PAGE INDEX, KEY RESOURCES and FREQUENTLY USED ABBREVIATIONS
See inside back cover (Page 35)

PALLIATIVE AND END OF LIFE CARE

The National Institute for Health and Care Excellence (NICE 2020) defines palliative care as:

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

The principles of palliative care are relevant to patients with both malignant and non-malignant diagnoses. It may be delivered in conjunction with disease modifying treatment, and usually becomes a more important part of management as the disease progresses.

Much of the support given to people is from professionals who are not specialists in palliative care and should aim to meet the needs of the person and their family within the limits of their knowledge and competence. The aim of general palliative care is to provide:

- Information for the person and their carers with 'signposting' to relevant services.
- Accurate and holistic assessment of a person's needs.
- Co-ordination of care teams in and out of hours and across boundaries of care.
- Basic levels of symptom control.
- Psychological, social, spiritual, and practical support.
- Open and sensitive communication with the person, their carers and professional staff.

Specialist advice should be sought or the person referred to specialist services when necessary.

Key principles of symptom management

- Detailed assessment in partnership with patient and carers.
- Diagnose cause of symptom(s) using knowledge of pathophysiology and disease processes.
- Investigations and treatment should be appropriate to the stage of disease and prognosis, balancing benefit and harm (as defined by the patient).
- Choose the most appropriate treatment for the individual, balancing benefit against side effect, burden and considering factors such as route of administration.
- Avoid making too many changes at once or review will be complex.

Care planning and decision making

In palliative care it is hugely important to be open to, and to consider, future health problems and to plan care to support a patient's wishes and minimise distress. An excellent resource for supporting decision making is ***Deciding Right***, a North East initiative for making care decisions in advance.
See https://northerncanceralliance.nhs.uk/deciding-right/

Key aspects of ***Deciding right***, reproduced directly from the website, are that it:

- Applies to all ages, care situations and settings
- Emphasises the partnership between the individual, carer or parent and the clinician
- Places the Mental Capacity Act (MCA) at the centre of shared decision-making
- Enables professionals and organisations to comply with the MCA by filling the gap in practice, not just the knowledge gap
- Recognises the individual with capacity as key to making care decisions in advance.
- Empowers the individual who lacks capacity to have decisions made in their best interests.
- Enables information to be recognisable in all care settings.
- Introduces emergency health care plans as an important adjunct in all settings to tailor care to the individual with complex needs.
- Ensures that, wherever possible, documentation and information is suitable for all ages (children, young people and adults).

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 - **identify the probable cause of the pain(s).**
- 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 determining the likely type and cause of pain.
- Relevant investigation, if appropriate, should be considered:
- Renal function (which may influence drug choice).
- X-rays / scans (MRI spine if nerve root compression / MSCC 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 / ADLs / 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 & 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.

Considerations when prescribing analgesia:

Route	Use oral route if possible. Non-oral route if dysphagia, vomiting, bowel obstruction, terminal phase.
Background pain	Background pain is predictable regular / continuous level of pain managed by continuous opioid. Use lowest dose of drug possible to avoid toxicity – supplement with PRN doses.
Breakthrough pain	Pain occurring despite regular opioids - predictable (e.g. aggravated by movement) or spontaneous. Managed with PRN opioids prescribed at 1/10th to 1/6th of background dose; up to 1-**hourly**. Set maximum (e.g. 6 doses / 24hrs) – ensure patient review if exceeds this.
Incident pain	Pain occurring secondary to predictable inciting event (e.g. movement or receiving care / turning). Utilise PRN breakthrough medication given just before / at start of event, combined with low dose (or no) background opioids to limit side effects. An increase in breakthrough requirements for incident pain may not require an increase in background opioids if background pain is well controlled.
Transdermal patch (TD)	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.
Syringe driver (CSCI)	Continuous subcutaneous infusion (CSCI): deliver IR opioid injection usually over 24hrs via pump. Takes 4 hours to reach effective serum levels. Prescribe PRN opioid via subcutaneous route.
Adverse effects	Prescribers must know the adverse effects and contraindications of all medications. Consult BNF if unsure or discuss with local palliative care team.

PRESCRIBING FOR PAIN

A step-wise approach (e.g. **WHO analgesic ladder**) provides a framework for palliative pain management based on pain severity and character / 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 disease (malignant and non-malignant). As strong opioids are readily available in the UK, weak opioids are no longer indicated as low dose morphine has greater and more rapid analgesic effect. **Morphine is the first line opioid of choice in patients without significant impairment.**

Modified WHO analgesic ladder

STEP 1 **Non-opioid (Paracetamol and/or NSAID) +/- adjuvant**
STEP 2/3 **Opioid* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant** (* e.g. morphine, oxycodone – see page 7 & 8)

SAFE OPIOID TITRATION

- **Start and titrate cautiously** – reduce doses (+/- extend PRN intervals) if frail / elderly / renal/hepatic impairment.
- Understand the **differing properties** and **potencies of different opioids** (pages 2 & 8).
- **Breakthrough IR opioid of 1/10th to 1/6th of total background** dose max. 1- 2hrly.
- Increase in **background** doses **by 30-50% (max. 50%), not more often than every 48 hrs** (72hours for patches).
- **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** (p10) / 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 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.

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 21

Features: sedation, myoclonic jerks, hallucinations, confusion, reduced respiratory rate. Pin-point pupils may indicate that taking opioids. Can occur due to fever / heat in those with transdermal patches. **Reduce opioid dose by 30-50%.** Check renal and hepatic function. Seek specialist advice on alternative analgesics or opioid switch.

COMMON SIDE EFFECTS of opioids

Constipation – common, persists, worse with dose increase. Prescribe stimulant laxative, adding a softener if needed (see section on Constipation pages 14 and 15).

Nausea/vomiting – common when commencing opioids, usually settles within days. Prescribe anti-emetic 'as required' (e.g.haloperidol 0.5-1.5mg o.n. or metoclopramide 10mg t.d.s.) for the first week, titrating to response.

Drowsiness – fairly 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.

FLOWCHART FOR OPIOID TITRATION USING MORPHINE

Pain uncontrolled on paracetamol +/- adjuvant analgesic

Using Immediate Release Morphine (IR)

- Use lower starting doses than in these examples if elderly, frail or renal impairment.
- If taking codeine or tramadol, stop these drugs and use conversion table or seek specialist advice to calculate appropriate starting dose of strong opioid.

Start IR morphine
e.g. Oramorph (10mg/5ml)
5mg (2.5ml) regularly 4hrly.

Omit dose during night if sleeping.

Prescribe same dose 1-2hrly as required for breakthrough pain.

Review after 24 hours.

If sedated / signs of toxicity, reduce dose.

If pain controlled, continue same dose and review in 24hrs.

If pain uncontrolled, add up previous 24hr use (regular and as required doses) to recalculate new 4hrly dose. Prescribe nearest practical dose; **do not exceed a 50% increase.**

Review after further 24 hours.

If pain uncontrolled, follow as above.

When pain is better controlled, convert to 12hrly MR morphine. Add up total morphine use in 24hrs, divide by two and prescribe nearest practical dose.

Adjust breakthrough dose,

Using Modified Release Morphine (MR)

- Use lower starting doses than in these examples if elderly, frail or renal impairment.
- If taking codeine or tramadol, stop these drugs and use conversion table or seek specialist advice to calculate appropriate starting dose of strong opioid.

Start MR morphine
e.g. Zomorph, MST **10mg 12hrly.**

Prescribe IR morphine
e.g. Oramorph (10mg/5ml)
5mg (2.5ml) 1-2hrly as required for breakthrough pain.

Review after 24 hours.

If pain controlled, continue same dose and review in 24hrs.

If pain uncontrolled, encourage use of breakthrough medication and review in 24hrs.

Review after further 24 hours.

If pain is still uncontrolled, recalculate the MR morphine dose by adding the value of breakthrough given in the previous 24hrs but **do not exceed a 50% increase**. Prescribe the nearest practical dose.

Adjust breakthrough dose.

DIFFERENT OPIOIDS

Opioid	Preparations	Conversion ratio Opioid: oral morphine	Notes
Morphine	IR: oral / injectable MR: oral (12 hourly)	N/A	**First line opioid of choice if no significant renal impairment.**
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).
Oxycodone	**IR:** oral / injectable **MR:** oral (12 hourly)	See Opioid Conversion Chart*	Alternative to morphine if adverse effects / signs of toxicity / moderate renal impairment.
Alfentanil	**IR:** injectable	See Opioid Conversion Chart*	Often used in renal failure. Reduce dose in liver failure. PRN - short acting so often impractical (see below).
Hydromorphone	**IR:** oral / injectable	1 : 5 - 7.5	Older opioid; occasionally used in renal impairment.
Buprenorphine	**MR:** 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	**MR:** transdermal patch	See Opioid Conversion Chart*	Less constipating vs morphine. Risk of toxicity with patches if fever/heat. IR preps are also available; prescribe under specialist guidance only (see page 10).

***For further information and calculations, see Opioid Dose Conversion Chart on page 2**

OPIOIDS AND RENAL IMPAIRMENT - Acute kidney injury, chronic and end-stage renal failure

- 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 30-60ml/min):

- reduce dose, lengthen time / interval between PRN doses, titrate PRN and MR more cautiously, and review regularly.
- codeine, morphine, oxycodone, hydromorphone and tramadol can be used with caution.

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

- **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
- Avoid ***regular*** codeine, morphine and oxycodone. Low dose *immediate release* (IR) oxycodone (oral/injection) given PRN with increased dose intervals may be appropriate in an opioid tolerant patient without signs of toxicity.

Seek specialist advice if needed.

OPIOIDS AND HEPATIC IMPAIRMENT

General principles of prescribing in hepatic impairment: start at low dose and titrate slowly; lengthen time/interval between doses; avoid long acting drugs where possible. Ensure patient does not become constipated. **Seek specialist advice if needed.**

- **Generally safer**: fentanyl patch – low dose; only use if stable pain and already opioid tolerant
- **Use cautiously**: buprenorphine patch, morphine. (If co-existing renal impairment, follow guidance above or seek specialist advice)
- **Avoid if possible** (if unavoidable, use low dose and reduced frequency): oxycodone, hydromorphone
- **Under specialist guidance only**: codeine, methadone, tramadol; alfentanil (duration of action will become prolonged)

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.
- If the opioid switch is because of **opioid toxicity**, check eGFR 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.
- **Switching between medications** e.g. from morphine to fentanyl: **reduce calculated dose by 30%** (patient may not be as tolerant to the new opioid and thus at risk of opioid toxicity with an equipotent switch).

FROM: \ TO:	IR oral opioid	MR oral opioid	CSCI (syringe driver)	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
CSCI (syringe driver)	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 6hrs 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)*

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 does if clinically indicated by pain. (For BUPRENORPHINE patch, seek specialist advice on appropriate timings)

Transdermal opioid patch to continuous subcutaneous opioid infusion –

If the patient is considered to be in the last hours to days of life, leave the opioid patch in place and continue to change it at the right time intervals, and add a syringe driver with injectable medication alongside to make up the additional opioid treatment needed.

In other situations where a change in 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 on timing).

SPECIALIST ADVICE FOR PAIN MANAGEMENT

SEEK SPECIALIST ADVICE IF:	• Complex pain, pain refractory to usual measures, severe pain at end of life. • Adverse effects of medication limits use of analgesia. • Renal/hepatic dysfunction causing side effects. • Pain associated with more than usual distress, particularly where non-physical factors are involved. • Use of specialist drugs e.g. alfentanil. • Complex drug titrations / conversions.

ANALGESIC DRUGS PRESCRIBED UNDER SPECIALIST GUIDANCE ONLY

These drugs are initiated by specialists, usually in an inpatient setting, for management of complex pain. GPs may be requested to prescribe these drugs for their patients in the community (potentially under a shared care agreement) whilst the patient remains under the care of a palliative medicine specialist who will advise about dosing.

Drug	Preparation	Notes
Ketamine	Capsules /oral solution (both as special order); injection	Anaesthetic drug. Used for neuropathic, inflammatory, ischaemic limb and procedure related pain not responding to other treatments. Contra-indicated if high blood pressure. Side effects include symptoms due to upper gastrointestinal, hepatobiliary, urinary, and neuropsychiatric toxicity.
Methadone	Tablets / oral solution / injection	Strong opioid analgesic used as alternative for those who fail to respond or who are intolerant to other strong opioids. Has a very long and variable half-life and duration of action.
Fentanyl (fast acting)	**IR:** sublingual / nasal / buccal	Rapid onset 5-10mins; lasts 40-60mins. Used PRN for painful procedures / movement related pain.

ADJUVANT ANALGESIA

ADJUVANT DRUGS Specific indications for use of adjuvant analgesics	***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:*** **ANTIDEPRESSANTS (e.g. amitriptyline, duloxetine):** neuropathic pain, tenesmoid pain. Particularly useful when sleep is disturbed. **ANTICONVULSANTS (e.g. pregabalin, gabapentin):** neuropathic pain, tenesmoid pain. **CORTICOSTEROIDS:** raised intracranial pressure, liver capsule pain, soft tissue infiltration, compressive effects of cancer (e.g. nerves and viscous structures). **MUSCLE RELAXANTS (e.g. baclofen, benzodiazepines):** muscle cramp/spasm, myofascial pain. **ANTISPASMODICS (e.g. hyoscine butylbromide):** bowel colic, bladder spasm.

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).

First line drugs for neuropathic pain include **anti-depressants** (**e.g. amitriptyline**) and **anti-epileptics** (**gabapentin** and **pregabalin**). All have comparable efficacy and tolerability. Local prescribing variations may include duloxetine and nortriptyline. Choice may be influenced by individual patient characteristics, drug characteristics and cost. Consider a step-wise approach as below.

If direct nerve compression is a cause: Dexamethasone can help to reduce pressure on a nerve and any associated pain. Radiotherapy may also be useful if the nerve compression is due to a tumour mass. Gabapentin / pregabalin can help to reduce the associated neuropathic pain, as can amitriptyline / duloxetine (though to a lesser extent).

Step 1: Amitriptyline or Gabapentin / Pregabalin → **Step 2:** Amitriptyline and Gabapentin / Pregabalin → **Step 3:** SPCT advice

Drug	*Additional indications*	*Cautions*	*Common side effects*	*Typical dosing schedule*
Amitriptyline *Once daily*: *tablet / syrup*	Difficulty sleeping. Depression & anxiety (high dose >50mg usually required). Bladder spasm and urinary urgency.	**Avoid in cardiac disease** (all types) May reduce seizure threshold. Caution in glaucoma and hepatic impairment. **Use with caution with other anti-depressants**: risk serotonin syndrome.	**Dry mouth & sedation** Postural hypotension, reduced sodium, urinary hesitancy, delirium	**Starting dose:** 10mg o.n. **Increase to**: 25mg o.n. after 3-7days **Increase by**: 25mg every 7-14 days **Maximum:** 150mg o.n. if successive increases are beneficial and tolerated **Note:** sedating especially in combination with opioids / antiepileptics. Side effects often limit dose to 30-60mg daily (10-20mg in elderly / frail).
Gabapentin *TDS: tablet / capsule / solution* *Can open capsule & mix in water / teasp of soft cold food*	Seizures, spasticity.	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.	**Sedation**, dizziness, ataxia, constipation *Slowing titration can reduce side effects*	**Starting dose:** 300mg o.n. **Increase by:** 300mg every 2-3 days **Maximum dose:** 1200mg t.d.s. **Elderly/frail: start 100mg o.d; increase by 100mg every 2-3 days** **eGFR 15-30:** start 100mg o.d; max dose 300mg b.d. **eGFR <15:** seek SPCT advice
Pregabalin *BD: capsule / solution* *Can open capsule & mix in water / teasp of soft cold food*	Seizures, spasticity. Anxiety.			**Starting dose:** 75mg b.d. **Increase by:** 75mg b.d. every 3-7 days **Maximum dose:** 300mg b.d. **Elderly/frail: start 25-50mg b.d; increase by 25-50mg b.d. every 3-7 days** **eGFR 15-30:** start 25-50mg o.d; max dose 150mg o.d. **eGFR <15:** seek SPCT advice

See NICE CG173: Neuropathic pain in adults. www.nice.org.uk/guidance/cg173

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 hierarchy*
A Chemical causes	Renal impairment, hypercalcaemia, other metabolic upset, drugs, infection. Persistent, often severe, nausea unrelieved by vomiting.	First: haloperidol. Then: levomepromazine.
B Gastric stasis	Fullness/regurgitation, 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. Also consider trial of steroids.
C Chemotherapy or radiotherapy	Useful to distinguish between 'acute' and 'delayed' phase.	Acute: follow oncology guidelines for ondansetron and/or corticosteroids, aprepitant. Delayed: levomepromazine.
D Organ damage	Harm to thoracic, abdominal or pelvic viscera caused by malignancy or treatment.	Cyclizine.
E Bowel obstruction	May be high, low or multiple levels. High causes regurgitation, forceful vomiting of undigested food. Low causes colicky pain, large volume (possibly faeculent) vomits.	For detailed management of bowel obstruction please see the guideline on page 16.
F Raised intracranial pressure/intra-cerebral causes	Headache, visual disturbance, other neurological signs.	Cyclizine Also consider steroids – see page 22.
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		Ondansetron / granisetron.

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 accordingly to symptoms/as tolerated. Use with caution in organ failure.
- Prescribe chosen anti-emetic regularly – see below for frequency.
- Levomepromazine can be considered *in addition* as required for refractory symptoms. Caution if also on regular 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 PCF7 for more detail; cautions/contraindications from BNF)

CYCLIZINE – antihistaminic, anticholinergic anti-emetic. Some specialists believe that the anticholinergic effects of cyclizine block the action of metoclopramide and recommend that these two drugs are not combined. Caution in advanced heart failure and Parkinson's disease. May cause cognitive impairment/drowsiness.
DOSE: PO: 50mg t.d.s. SC: 25-50mg t.d.s. Syringe Driver: 75-150mg/24hrs. If SC use causes skin irritation, dilute to maximum possible volume with water for injection 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: PO/SC: 0.5-3mg o.n. Syringe Driver: 0.5-3mg/24hrs. (5mg max dose if necessary).

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). Caution in Parkinson's disease. May prolong QT interval with risk of cardiac dysrhythmia. Some specialists recommend very low doses for SC PRN use (2.5-5mg) to avoid any risk of sedation.
DOSE: PO/SC: 6.25-25mg o.n. Syringe Driver: 6.25-25mg/24 hrs.

METOCLOPRAMIDE - prokinetic and centrally acting anti-emetic. Some specialists believe the action of metoclopramide is blocked by cyclizine and recommend that these drugs are not combined. Contra indicated in Parkinson's disease, complete obstruction and recent GI surgery. May prolong QT interval with risk of cardiac dysrhythmia. Be aware of regulatory advice (MHRA/EMA) on dose and duration related to neurological side effects.
DOSE: PO/SC: 10mg t.d.s. to 20mg q.d.s. Syringe Driver: 30-60mg/24hrs. Higher doses and long-term use under specialist supervision.

More specific and targeted anti-emetics include:

APREPITANT – a neurokinin receptor antagonist. An adjunct in chemotherapy induced nausea/vomiting.
DOSE: follow oncology advice.

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 22.
DOSE: PO/SC: 4-8mg per day (given before noon). 16mg initially in raised intracranial pressure.

DOMPERIDONE - prokinetic anti-emetic. Action blocked by anticholinergic effect of cyclizine: do not combine. Domperidone does not cross blood/brain barrier so avoids extrapyramidal effects of metoclopramide. May prolong QT interval with risk of cardiac dysrhythmia. Be aware of regulatory advice (MHRA/EMA) on dose and duration related to cardiac side effects.
DOSE: PO: 10mg t.d.s. Higher doses and long-term use under specialist supervision

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 1-hrly as required up to six doses/24hrs. Syringe Driver: 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 those patients intolerant to haloperidol and/or levomepromazine.
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; some centres use first line in patients with Parkinson's disease. Be aware may prolong QT interval with risk of cardiac dysrhythmia.
DOSE: follow oncology guidelines: PO/SC: 4-8mg b.d.-t.d.s. Syringe Driver: 16mg SC/24hrs.

CONSTIPATION

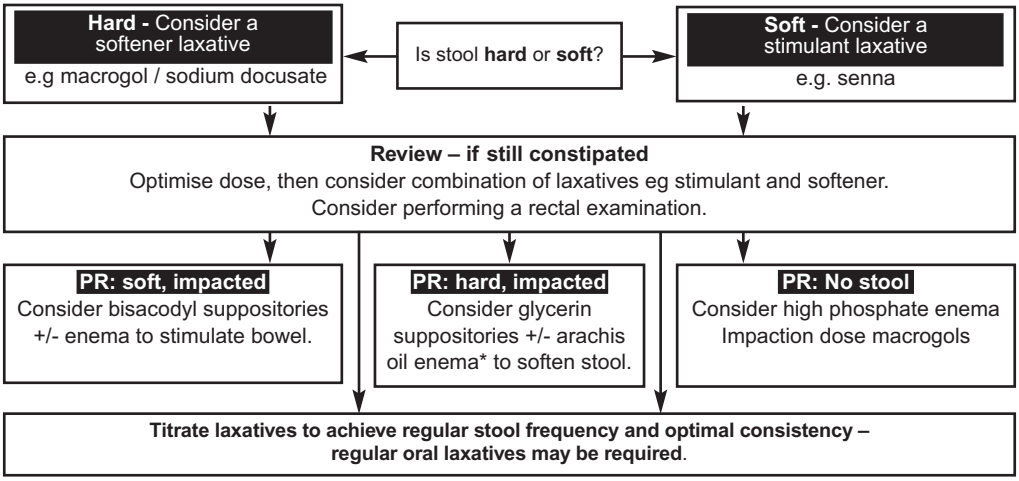
Common reversible causes to consider:

- Immobility / weakness
- Fluid depletion – poor fluid intake, increased losses e.g. vomiting, fistulae
- Intra-abdominal and pelvic disease
- Biochemical – hypercalcaemia, hypokalaemia
- Reduced food intake
- Medication – including opioids, diuretics, anti-cholinergics, ondansetron, chemotherapy
- Pain on defecation
- Environmental – lack of privacy, problems getting to a toilet

Management

Manage any reversible causes where possible, encourage fluids especially fruit juice.
Anticipatory prescribing – consider prescribing a laxative when starting medication that can cause constipation. If concerned there may be bowel obstruction, refer to the section on 'managing bowel obstruction'.

PCF7 suggests that 'compliance with laxatives may be limited by palatability, undesirable effects (e.g. colic, flatulence), volume needed and polypharmacy. Patient preference and tolerability should be considered. Concurrent prescriptions of several different laxatives should be avoided as laxative doses should be titrated every 1–2 days according to response, up to the maximum recommended or tolerable dose before changing to an alternative'.



Neurogenic constipation

In patients with spinal cord compression or sacral nerve damage who have lost sensation and/or control:

- Avoid oral stimulant laxatives which may cause uncontrolled bowel function
- Oral faecal softeners will prevent faeces becoming dry and hard
- Consider initiating a 3-day bowel regime (i.e. aim for a formed, not hard, stool and use stimulant suppositories to evacuate the bowel every 1-3 days)

Commonly used laxatives

	Examples	Information	Dose
Stimulant laxatives	*Senna* *Bisacodyl*	Reduces bowel transit time. Think carefully before using if possibility of bowel obstruction.	15-30mg at night orally 5-10mg at night orally
Osmotic laxatives	*Macrogols (e.g. Movicol, Laxido)*	Volumes may be difficult for some patients to manage. They retain water in the gut lumen which encourages peristalsis.	Start with 1-3 sachets daily orally (total volume 125mls per sachet)
	Lactulose	Lactulose can cause flatulence, bloating and abdominal cramps, not generally used first line. Used in hepatic encephalopathy.	15ml b.d. orally
Softeners	*Docusate*	Reduce surface tension and so improve water penetration of the stools.	100-200mg b.d / t.d.s orally
Combination stimulant/ softener laxatives	*Co-Danthramer* *Co-Danthrusate*	Dantron may cause red discolouration of urine and can cause painful skin damage. Avoid if patient is incontinent of urine or faeces. Only licensed for use in constipation in terminally ill patients as potential carcinogenic risk.	Seek specialist advice
Suppositories	*Bisacodyl* *Glycerin*	Stimulant (10mg per suppository) Softener (4g per suppository)	1-2 suppositories PR 1-2 suppositories PR
Enemas	*Arachis oil* *Microlax* *Phosphate*	Softener. *Contraindicated if nut allergy Osmotic / Softener Osmotic	1 PR 1 PR 1 PR
PAMORAs **Only to be used under specialist advice**	*Methylnaltrexone* *Naloxegol* *Naldemedine*	Peripherally acting μ-opioid receptor antagonists. Used in opioid induced constipation where other measures have failed to achieve adequate outcome.	Injection Oral Oral Seek specialist advice

EMERGENCIES – BOWEL OBSTRUCTION

1. RECOGNITION

Risk factors/possible causes:

- **Disease** - presentation, progression or recurrence of intra-abdominal malignancy (especially bowel, ovary, pancreas). Adhesions from previous surgery/radiotherapy. Acute ischaemia, incarceration of hernia, ileus, faecal impaction.
- **Medication** - opioids, anticholinergics (e.g. tricyclic antidepressants, hyoscine salts), diuretics, 5HT3 antagonists, phenothiazines, chemotherapy.

Clinical presentation:

- Pattern and severity of symptom(s) depends on level(s) of obstruction and if partial or complete obstruction.
- Vomiting may be large volume and faeculent; nausea may be relieved by vomiting.
- Constipation and/or overflow diarrhoea.
- Abdominal pain - constant or colicky; abdominal distension, palpable tumour mass, tympanic percussion, tinkling/abnormal bowel sounds.

2. IMMEDIATE ACTION - IS ADMISSION APPROPRIATE?

Consider patient's wishes, documented emergency health care plans or other records, and guidance from family/others.

If YES - admit as emergency. Give **medication for symptom relief** during transfer e.g. SC dose **opioid analgesic** (appropriate to analgesic history) and dose of **anti-emetic** (either metoclopramide 10mg SC if no colic or cyclizine 50mg SC if colic).

On admission check blood count and renal function; perform erect chest and supine abdominal X-ray; consider CT scan; start IV fluid resuscitation; consider decompression of distended gut with wide bore NG tube. **Consider constipation** and manage appropriately (see page 14). **Seek urgent surgical opinion.**

If NO – or if admitted but surgical decision is for supportive care only - see ONGOING MANAGEMENT below. In cases of advanced cancer, consider trial of corticosteroids with dexamethasone (e.g. 6.6mg injectable formulation SC or IV) alongside guidance below. Review effect after 5 days - discontinue if no effect; reduce gradually if benefit. Change to oral when possible.

3. ONGOING MANAGEMENT

Treat any background constant pain with opioid via 24hr subcutaneous infusion

Is colic present and/or bowel obstruction clinically complete?

NO

Prescribe metoclopramide 30mg/24hr SC via syringe driver and 10mg SC as required 6-hrly.

Review after 24 hours

If still vomiting but NO COLIC, increase metoclopramide to 60mg/24hr SC via syringe driver.	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

If colic continues: start hyoscine butylbromide 60mg/24hrs SC via CSCI. Also prescribe hyoscine butylbromide 20mg SC as required 8hrly.
For vomiting / nausea: start cyclizine 75-150mg/24hrs SC via CSCI ***OR*** haloperidol

Review within 24 hours
If colic persists, increase hyoscine butylbromide to 120mg/24hr via CSCI
If vomiting / nausea persist, stop cyclizine or haloperidol, and start levomepromazine 12.5mg SC o.d. (or via CSCI over 24hr) AND prescribe 6.25mg SC as required up to q.d.s.

Review within 24 hours
If symptoms persist, seek specialist advice from palliative care team about further dose increases and/or use of octreotide.

EMERGENCIES – SEIZURES

1. RECOGNITION

- Seizures can be frightening for the patient and their family.
- Seizures can become more severe or frequent at the end of life.
- Seizures (generalised or partial) occur in 10-15% of palliative care patients.
- Common causes include pre-existing epilepsy, brain tumours, raised intracranial pressure, metabolic disturbance (hypoglycaemia, electrolyte abnormalities, hepatic encephalopathy, renal impairment), infection.

For any palliative patient at risk of having a seizure, it is helpful to have an Emergency Health Care Plan in place (see ***Deciding right***).

2. IMMEDIATE ACTION for treatment of status epilepticus:

- 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.
- If appropriate, put the patient in the standard recovery position. Ensure patient safety and protect airway. Give oxygen if available and patient cyanosed.

Community/inpatient:

- Give buccal midazolam 10mg (using oromucosal solution or injectable formulation).
- Alternatively, give midazolam injection 10mg SC.
- Repeat after 10mins if seizure not resolved.

Inpatient with IV access present (or immediately possible):

- IV lorazepam 2mg/min up to 4mg.
- Repeat once after 10-20 mins if seizure not resolved.

If further treatment needed, seek specialist advice from neurologists or palliative care team.

3a. FOLLOW UP - SEIZURE MANAGEMENT IN THE NON-DYING PATIENT

- Consider investigation for reversible causes.
- If history of seizures, review and optimise patient's anti-epileptic medication. Exclude drug interactions reducing regular antiepileptic medication efficacy.
- After a first seizure, consider commencing regular anti-epileptic medication.
- If brain tumour or metastases, consider optimisation of corticosteroids.

Seek advice from local neurology team if needed

3b. FOLLOW UP - SEIZURE MANAGEMENT IN LAST DAYS OF LIFE

- If the patient is no longer able to take or absorb their oral anticonvulsants, **subcutaneous antiepileptic medication should be prescribed instead**.
- Midazolam 20-30mg SC/24hr via CSCI should be commenced, with midazolam 5-10mg buccal or 5-10mg SC 'as required' for further seizure control.
- Alternatively, if a patient is already taking levetiracetam orally and it is felt important to avoid sedation, this can be given via CSCI over 24 hours (note: accessing this in the community can sometimes be difficult).
  - The dose is calculated using a 1:1 ratio for oral to SC conversion.
  - 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, 0.9% sodium chloride should be used as diluent instead. Refer to syringe driver and drug compatibilities page 34.

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 Registrar out of hours.

Management of patients in the community should depend on the patient's wishes and whether the MSCC is amenable to surgical or oncological intervention.

1. RECOGNITION

Consider MSCC in any cancer patient with severe back pain in a nerve root distribution, particularly if pain is severe, recent onset or worsening, felt as a band around the body or radiating down arm(s) or leg(s), exacerbated by coughing or straining, not relieved by rest. Please note that pain often precedes neurological signs.

DO NOT WAIT FOR LATE SYMPTOMS/SIGNS TO APPEAR.
Do not be reassured by X-rays as these are normal in 10-20% cases.

Late symptoms/signs include:

- Limb weakness, altered gait, unsteadiness, falls. Consider MSCC in any cancer patient who goes 'off their legs'.
- Urinary retention, dribbling or incontinence; faecal incontinence or constipation.
- Altered or reduced sensation.

Cauda equina syndrome – tumour pressure below L1/L2 – may present with:

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

2. IMMEDIATE ACTION

- **Give dexamethasone:**
- Community/outpatients: 16mg BY MOUTH or 13.2mg SC (if given SC, volume needs to be divided into two sites, 2mls each).
- Inpatients: 13.2mg IV (or SC).
- **Prescribe PPI for gastric protection.**
- **Give adequate analgesia** (opioid if necessary) to enable comfortable transfer for admission/investigation.
- **Aim to nurse the patient flat** if pain or symptoms/signs suggest spinal instability.

3. REFERRAL FOR INVESTIGATION

Community Patient:

Admit to your local hospital as emergency for full neurological assessment and the acute receiving team will make arrangement for whole spine MRI.

Hospital/Hospice Inpatient:

Between 0900-1700, contact the MSCC co-ordinator as well as the Acute Oncology Registrar at the nearest Cancer Centre.
This discussion will guide appropriate decisions and facilitate emergency virtual MDT discussion between radiologist, oncologist and spinal surgeon.
Out of hours, contact the Acute Oncology Registrar on call for your region.

See NICE CG75: Metastatic Spinal Cord Compression: www.nice.org.uk

EMERGENCIES – MALIGNANT HYPERCALCAEMIA

This guidance applies only to patients with a known cancer diagnosis

1. RECOGNITION

Exclude in any patient with advanced cancer whose condition deteriorates rapidly.
Symptom severity is related more to the rate of rise in serum calcium, rather than the absolute level.
Onset may be insidious with symptoms not evident until corrected calcium is well above normal, or the patient may be symptomatic with modest elevation of calcium.
Most common paraneoplastic syndrome in patients with advanced cancer, most commonly due to tumour secretion of parathyroid hormone related protein. May occur in the absence of bone metastases. Strongly associated with breast, lung, haematological and genito-urinary tract malignancies.
Reflects poor prognosis. Median survival 3-4 months, worse if resistant to treatment.
Clinical Presentation:

- Confusion, drowsiness, and eventually coma.
- Thirst and polyuria. Dehydration may lead to pre-renal failure.
- Nausea and vomiting. Constipation.
- Worsening pain or pain responding poorly to treatment.

2. IMMEDIATE ACTION

Assessment

- Check 'Corrected/Adjusted Calcium' level in venous blood. Normal range 2.20 - 2.60 mmol/L
- Also check renal function (U&E) and vitamin D level (replace if deficient as per local guidelines; this does not need to delay treatment of hypercalcaemia).

Management:
Stop and think. Hypercalcaemia may indicate that the patient is approaching the end of life and treatment may not be appropriate. If so, manage patient symptomatically.

- **Admit** to hospital/hospice unless it is agreed that intervention is not appropriate.
- Review medications – consider stopping diuretics/ACE inhibitors; stop vitamins/supplements containing calcium.
- **Patient should be well hydrated with IV 0.9% sodium chloride**. Caution if risk of fluid overload.
- If calcium <3.0mmol/L and patient asymptomatic: recheck calcium level after 24 hours of rehydration and treat if calcium level rising.
- If patient symptomatic and calcium >3mmol/L; administer IV bisphosphonate (either pamidronate or zoledronic acid according to local guidelines).

Zoledronic acid*: give 4mg in 100mL sodium chloride 0.9% intravenous infusion over 15 min.

Disodium pamidronate*: stated dose in 500mL sodium chloride 0.9% IV infusion over 2hrs.

Corrected calcium (mmol/L)	<3.0	3.0 – 3.5	3.6 – 4.0	> 4.0
Pamidronate dose	15 - 30mg	30 - 60mg	60 - 90mg	90mg

*No dose adjustment is needed in mild-moderate renal impairment for patients being treated with Zoledronic acid or Pamidronate for **tumour induced hypercalcaemia**. If possible, avoid use in severe renal impairment (eGFR<30) and seek specialist advice.

Adverse effects: 'Flu-like syndrome/pyrexia is common – treat with paracetamol. Osteonecrosis of jaw is a rare but significant side effect – consider dental opinion if symptoms. Rebound ***hypocalcaemia*** may occur.
Denosumab can be used for treatment of refractory hypercalcaemia of malignancy (currently unauthorised indication). It can be prescribed for patients with renal impairment. Seek specialist advice from palliative care team and/or oncology.

3. FOLLOW UP

Expect clinical improvement in 24-72 hours. Check for **biochemical** improvement in 4-7 days.
If effective, treatment may be repeated for subsequent episodes.
After 7 days, if no clinical/biochemical response consider giving additional 4mg Zoledronic acid.
If no response, seek specialist advice on use of denosumab, calcitonin and need for further investigation e.g. PTH. Consider prophylaxis with oral bisphosphonate.

On discharge, ask primary care / community team to monitor symptoms and check calcium and renal function if there is clinical suspicion of recurrent hypercalcaemia.

EMERGENCIES – MAJOR HAEMORRHAGE

1. RECOGNITION

- Bleeding of all types occurs in **14%** of patients with advanced disease.
- Haemorrhage causes death in approximately **6%** patients.
- Catastrophic external haemorrhage is less common than internal unseen bleeding.

Clinical Presentation

- Cardiovascular compromise – hypotension, tachycardia (>100 beats/min = significant recent bleed).
- Identifiable bleeding source e.g. haematemesis, melaena, haemoptysis, PV or PR bleeding, haematuria.
- Erosion of an artery by a malignant ulcer or superficial/fungating tumour – especially in those with head and neck tumours.

2. ANTICIPATORY MANAGEMENT

- Massive haemorrhage is often preceded by smaller bleeds. Oral/topical treatment may help (see below). When planning ahead, agree and document an **Emergency Health Care Plan**.
- Review risk : benefit balance of anticoagulants.
- Consider risk of bleed in those with advanced haematological malignancy causing clotting disruption. Correct any coagulation disorder if possible.
- Consider referral for radiotherapy or embolisation if patient has an erosive tumour.
- Review cardiopulmonary resuscitation status and treatment options with patient and family. Document carefully.
- Dark towels should be available nearby to reduce the visual impact of blood if haemorrhage occurs.
- Prescribe anticipatory midazolam (10mg IV/IM/SC/buccal/sublingual) as a crisis one-off dose for major haemorrhage. Explain to families/carers that aim is for sedation and to relieve distress.

3. IMMEDIATE ACTION

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

An Emergency Health Care Plan, if present, should guide management.

If resuscitation is inappropriate

Try to remain calm; this will help a dying patient to achieve a peaceful death.

- The priority is to stay with the patient, giving as much reassurance/explanation as possible to patient and family.
- Use dark towels to absorb blood loss.
- Consider the use of crisis midazolam (10mg by appropriate route) to relieve distress in a patient that may be imminently dying. This should be readily available; someone staying with the patient takes priority.

If resuscitation is appropriate

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

3. FOLLOW UP

- Ensure support available for family and staff following experience of haemorrhage.
- If the patient survives the haemorrhage, consider blood transfusion.

To prevent rebleeding:

- **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); Sucralfate paste (2g/5mL aqueous gel) applied directly to ulcer under non-adherent dressing; Adrenaline 1 in 1000 (1mg/ml) soak on gauze (short term only due to the risk of ischaemic necrosis and rebound vasodilation).
- Consider diathermy, radiotherapy or embolisation.

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 is the most common symptom.
- Facial swelling and feeling of fullness, redness, headache, periorbital oedema, engorged conjunctivae.
- Swelling of the arms, prominent distended veins on neck and chest wall, non-pulsatile raised jugular venous pulse.
- Cough, chest pain, stridor, cyanosis.
- Visual disturbance.

2. IMMEDIATE ACTION

- Sit upright, chair may be preferable. Limited use of steroids may be helpful prior to definitive treatment. Give dexamethasone 16mg stat (oral or equivalent dose IV or SC) 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 32 and agitation page 30).
- 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 dose that manages symptoms.

If SVCO suspected in patient at end of life / too unwell for / unwilling to have investigations, prognosis likely to be days:

- manage symptoms in patient's preferred care setting. Agree an **Emergency Health Care Plan**.
- consider steroids (as above), anticoagulation with treatment dose low molecular weight heparin, symptomatic measures, and nursing at 45 degrees for comfort.

EMERGENCIES – OPIOID TOXICITY

RECOGNITION - Emergency management of opioid toxicity is indicated if:

- respiratory rate (RR) < 8/min **AND** difficult to rouse, **OR**
- RR < 12/min **AND** difficult to rouse **AND** cyanosed / oxygen saturation < 90% on pulse oximeter.

ACTION (please follow local guidance where this exists)
Aim is to reverse respiratory compromise whilst maintaining adequate analgesia; full reversal of analgesia may cause acute withdrawal syndrome and abrupt return to pain that is difficult to control.

- Stop opioid. Remove any transdermal opioid patches.
- Secure IV access.
- Dilute 400 micrograms naloxone in 10mls 0.9% sodium chloride.
- Give 0.5ml (i.e. 20 micrograms naloxone) every 2mins IV until respiratory recovery.
- Review renal function, pain and analgesic requirements.
- Administer oxygen to maintain SaO2>95% (88-92% if pre-existing respiratory disease)

N.B. Modified release opioids may require reversal by naloxone ***infusion***. This is especially true of transdermal formulations with a subcutaneous reservoir (fentanyl, buprenorphine) or methadone which is highly protein bound. Seek specialist advice if needed.

The National Poisons Information Service (0344 892 0111) will provide specialist advice on management of opioid toxicity 24 hours a day.

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. (Potency: dexamethasone 1mg ~ prednisolone 7.5mg).

If patient is on immunotherapy, consider discussing with oncologist prior to commencing steroids.

Route and formulations: tablets (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.

Prescribing injections can appear confusing. (Dexamethasone base 3.3mg/mL = dexamethasone sodium phosphate 4.3mg/mL = dexamethasone phosphate 4.0mg/mL). For clarity, prescribe as base and therefore in multiples of the commonly available 3.3mg/ml form.

For practical purposes: 3.3mg/ml injection may be considered equal to 4mg in tablet form
(see www.ukmi.nhs.uk/filestore/ukmiaps?ProductsafetyassessmentforDexamethasone_Sept_2014.pdf)

Standard starting doses for the different indications are not well established and must take account of patient factors. High dose dexamethasone (>6.6mg) is a large volume when given SC, so is often given in divided doses; some centres give via CSCI over 4 hours. Ensure the daily dose(s) is administered before noon in order to minimise insomnia. Clinical response must be reviewed within 7 days. Titrate down to minimum effective dose.

Anorexia: 2 - 6mg daily. Review the response within 1- 2 weeks. Although enhanced effect can still be present at 4 weeks, short courses are recommended to reduce risk of side effects.

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

Anti-emetic: for chemotherapy, follow oncology guidelines. Refractory nausea and vomiting: 8 - 16mg daily.

Obstructive syndromes e.g. bowel obstruction, upper airways compression, SVCO, lymphangitis carcinomatosis: 8 - 16mg daily.

Spinal cord compression: 16mg daily until surgery or radiotherapy if appropriate. Maintain on 8mg daily 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 and stop. 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 daily 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 23.**

Insomnia: Give single or divided daily dose before noon to prevent insomnia.

Dyspepsia: Give after food. Co-prescribe PPI if history of peptic ulcer disease or patient also taking aspirin, NSAIDs, SSRIs or is anti-coagulated (e.g. with Warfarin, LMWH, DOAC or other agent).

Increased susceptibility to infection: especially oral/pharyngeal candidiasis – treat with anti-fungal.

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 of time. 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: is necessary if any of the following: 3 or more weeks treatment, daily dose of more than 6mg dexamethasone, 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 serious symptom control, continue at the most convenient subcutaneous dose. If recent and/or low dose prescription for appetite stimulation, discontinue. If long-term, consider low maintenance dose to prevent adrenal crisis.

Steroid Treatment Card (blue): Patients on systemic steroids for > 3 weeks must be given a steroid card.

Steroid Emergency Card (red): Patients at risk of adrenal crisis if steroids are stopped abruptly (see under gradual dose reduction criteria above) must be issued with a RED steroid emergency card by the prescriber.
(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 od (am) 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. Insulatard or 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 glucose before lunch or evening meal is above15 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 – 15 mmol/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 visit: https://trenddiabetes.online/wp-content/uploads/2021/11/EoL_TREND_FINAL4.pdf

CARE IN THE LAST DAYS OF LIFE

FIVE KEY PRIORITIES have been defined by the Leadership Alliance for the Care of Dying People (2014) and are supported by the NICE guidance*:

Recognise the possibility that a person may die within the next few days or hours and communicate this clearly; consider and address reversible causes where appropriate/possible; make decisions and act in accordance with person's needs and wishes; review these regularly and revise plans accordingly.

Communicate sensitively with the dying person and those close to them.

Involve all in making decisions as far as they indicate they want to be.

Support the family and other people important to the dying person by exploring, respecting and meeting their needs where possible.

Plan individualised care including attention to nutrition/hydration, physical observations and investigations, regular medication and anticipatory symptom control prescribing, and holistic needs that are psychological and emotional, social and cultural, spiritual and faith-based. The plan should include specific decisions about:

- cardiopulmonary resuscitation
- supporting oral food and fluid intake
- starting, continuing or stopping clinically assisted nutrition and/or hydration
- observations and investigations
- facilitating or preventing change in place of care
- review of regular long-term medication; stop those which are no longer needed and switch others to a route which ensures they continue to provide benefit
- anticipatory prescribing of medication for ALL five common end of life symptoms (i.e. pain, breathlessness, respiratory secretions, agitation, nausea/vomiting) and other problems specific to the patient (e.g. seizures, bleeding).

The plan should be discussed with patient (if able) and family/carers, and documented in careful detail. **Review** the dying person, those close to them and the associated care plans on regular and agreed occasions each day, *once daily being the absolute minimum*.

CONDITION SPECIFIC PROMPTS (seek advice from Specialist Team if needed)

Renal disease: See page 8 for guidance on opioid choice. Use haloperidol or levomepromazine for nausea/vomiting likely caused by chemical stimuli. Use midazolam for agitation, but lower doses may be effective as metabolites accumulate. Use hyoscine butylbromide or reduced dose glycopyrronium for secretions.

Heart disease: Arrange deactivation of implanted defibrillator (not pacemaker). Consider management of pulmonary oedema with subcutaneous furosemide. Co-existing renal impairment influences drug choices.

Respiratory failure: Severe breathlessness in a dying patient demands effective management; opioids or benzodiazepines used carefully may be valuable symptom management treatments. Consider SC physiological dose of dexamethasone (equivalent to 1mg dexamethasone base) for patients on long term corticosteroids.

Liver failure: Anticipate management of agitation from hepatic encephalopathy; if severe may require combination of midazolam with levomepromazine. Manage variceal bleeding as 'major haemorrhage' (page 20).

Parkinson's disease: dopamine agonist medication (e.g. levodopa) may need to be changed from oral to another route in a dying patient unless death is expected within hours. For nausea/vomiting, use domperidone or ondansetron; use levomepromazine cautiously; avoid metoclopramide, haloperidol and cyclizine unless death is imminent and/or no alternative antiemetic is effective for persistent symptoms.

MND: respiratory distress may be severe – anticipate with prescribing for breathlessness and assertive management of secretions. A PEG tube is a valuable route of administration; review feed / fluid need and volumes daily, reducing to balance burden vs benefit.

Frail / elderly: drug doses should be reduced. Depending on rate of decline and any stated/recorded wishes, patients deteriorating and dying slowly (e.g. from dementia) require careful consideration of risks and benefits of clinically assisted hydration and nutrition (in particular the role of subcutaneous fluids). See GMC guidance *Treatment and care towards the end of life* (2010) www.gmc.org.uk .

***See NICE NG31: Care of Dying Adults in the Last Days of Life:** www.nice.org.uk

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.

Type 1 diabetes always on insulin[1]

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

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.

Key to Insulins

Short Acting Insulins (mealtime or corrective dose)- e.g. NovoRapid (ASPART®) /Humalog (LISPRO®)
Long acting (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 Flash Glucose Monitoring Systems. 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 https://trenddiabetes.online/wp-content/uploads/2018/04/EoL_Guidance_2018_Final.pdf

PAIN IN THE LAST DAYS OF LIFE

(for acutely ill patients with rapidly deteriorating renal function, or patients with eGFR<30mL/min, consider advice on page 27)

Unless specifically indicated, morphine is the first line injectable opioid of choice.
Other opioids are indicated in renal failure and previous morphine intolerance.
Seek specialist advice if you consider that an alternative may be indicated.

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

For patient on morphine or oxycodone, follow guidance below. For patients on other opioids, seek advice.

Patient on morphine or oxycodone:

- Divide 24 hour total dose of oral opioid ***(regular + prn)*** by 2 and prescribe this as morphine or oxycodone SC by syringe driver over 24 hrs (Do not increase 24hr opioid dose equivalent by more than 50%).
- Prescribe 1/6th opioid syringe driver dose as breakthrough medication to be given SC **up to 1-hrly as required.**
- Start syringe driver 2 hours before next oral opioid dose would have been due (or immediately if a dose has been missed).
- Discontinue oral opioid.

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

- Prescribe morphine 2.5mg SC **up to 1-hrly as required.**
- 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/24hour by syringe driver.
- Prescribe morphine 2.5mg SC for breakthrough pain to be given **up to1-hrly as required.**

Review within 24hrs
If extra medication has been needed for pain:
- increase syringe driver dose by total amount of breakthrough opioid given or by 30-50%, whichever is less.
- adjust breakthrough dose to 1/6th of syringe driver opioid dose to be given SC up to 1-hrly as required.

If pain is controlled, make no changes.

Continue to review regularly.

Patient on regular weak opioid:
(Codeine, Tramadol, Dihydrocodeine)
- Stop oral weak opioid.
- Start morphine 10-20mg/24hrs by syringe driver soon after last oral dose *(use 20mg/24hrs if previous weak opioid was at maximum daily dose).*
- Prescribe morphine 2.5-5mg SC hourly as required for breakthrough pain.

Review regularly and adjust as above.

Patient with patches for pain relief (Fentanyl, Buprenorphine)
- See pages 2, 8, 9, 27 for guidance.

PAIN IN THE LAST DAYS OF LIFE IN RENAL IMPAIRMENT

Key points

- This guidance applies to the acutely ill patient with renal impairment and/or eGFR<30mL/min.
- Whilst alfentanil may be preferable, oxycodone may offer a more practical option.
- **These can be complex situations – do not hesitate to seek specialist advice.**

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

Patient already on strong opioids:

- See conversion chart (p2) to calculate dose of SC alfentanil.
- **If unfamiliar with alfentanil use or patient has signs of opioid toxicity, seek specialist advice.**
- Prescribe 1/10th of alfentanil 24hr syringe driver dose as breakthrough medication to be given SC **up to 1-hrly as required.**
- Start syringe driver 2 hrs before next oral opioid dose would have been due (or immediately if a dose has been missed).
- Discontinue oral opioid.

Review preferably TWICE DAILY

If extra medication has been needed for pain:

- Increase syringe driver dose by total amount of breakthrough alfentanil given or by 30-50%, whichever is less.
- Adjust breakthrough dose in proportion i.e. to 1/10th of syringe driver opioid dose to be given SC **up to1-hrly if needed.**

If pain is controlled, make no changes.

Continue to review regularly.

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

- Stop oral weak opioid.
- Start alfentanil 1mg/24hrs SC by syringe driver soon after last oral dose or seek advice about prescribing oxycodone.
- Prescribe 1/10th alfentanil 24hr dose to be given SC **up to 1-hrly as required** or oxycodone 1mg SC **up to 2-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 alfentanil 100micrograms* SC **1-hrly as required** OR oxycodone 1mg SC **2-hrly as required.**
- If patient needs pain relief, proceed to next box.

Scenario 2: "act now"
Patient in pain:

- Give alfentanil 100micrograms* **OR** oxycodone 1mg SC stat.
- If effective, prescribe and start alfentanil 1mg/24hrs **or seek advice about prescribing oxycodone.**
- Also prescribe alfentanil 100micrograms* up to 1-hrly **OR** oxycodone 1mg SC up to 2-hrly for breakthrough pain to be given **as required.**

Review preferably TWICE DAILY
If extra medication has been needed for pain:

- Increase syringe driver dose by total amount of alfentanil given or by 30-50%, whichever is less.
- Increase breakthrough dose in proportion i.e. to 1/10th of 24hr alfentanil opioid dose to be given SC **up to 1-hrly as required.**
- **If using oxycodone, seek specialist advice.**

Review within 24hrs
If extra medication required for pain:

- Increase syringe driver dose by total amount of breakthrough alfentanil given or by 50%, whichever is less.
- Adjust breakthrough dose to 1/10th of syringe driver alfentanil dose to be given SC **up to 1-hrly as required.**

If pain is controlled, make no changes.

Continue to review regularly.

*Some clinicians prescribe Alfentanil 250micrograms SC 1-hrly.

For further information on Alfentanil, refer to PAIN section page 8.

PAIN IN THE LAST DAYS OF LIFE – SUPPLEMENTARY INFORMATION

Fentanyl patches for a patient in the last days of life:

It is recommended to continue fentanyl patches in these patients. Remember to carry on changing the patch(es) regularly as previously (usually 72hourly) – this is sometimes forgotten.

If pain occurs, give breakthrough doses of morphine; if morphine is not appropriate, seek specialist advice about an alternative injectable opioid.

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

Adding a syringe driver to a patch:

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

The morphine (or other opioid) dose in the syringe driver should equal the total breakthrough doses given in previous 24 hours up to a maximum of 50% of the existing regular (patch) opioid dose equivalent.

Continue to apply this rule when reviewing pain control daily.

Remember to combine the dose of the patch and the dose in the syringe driver to work out the new breakthrough dose ($1/6^{th}$ – $1/10^{th}$ of the opioid total daily dose) each time a change is made.

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

Breakthrough dose calculation for patients in last days of life requiring subcutaneous medication.

Patients on morphine, oxycodone or hydromorphone via syringe driver:
A common starting point is to prescribe a breakthrough dose of 1/6th of the total 24 hour dose (using a practical dose, rounding down rather than up to be given 1-hrly as required, and adjusted according to benefit and tolerability).

Patients on alfentanil via syringe driver:
Calculate the breakthrough dose as 1/10th of the opioid total daily dose. These may need to be given more frequently than hourly. Single breakthrough doses of alfentanil are very short-lasting so there may be situations when an alternative such as oxycodone may be appropriate; seek specialist advice.

Patients with a fentanyl patch:
Decide on injectable opioid to be used for breakthrough pain, using the opioid dose conversion chart on page 2 to calculate the appropriate dose. Keep the fentanyl patch in place and renew regularly as usual.

Breakthrough doses may be given hourly up to the maximum defined by the prescriber.
A defined maximum number of doses will prompt early review if pain is uncontrolled.

Patients on other opioids: please seek specialist advice.

If managing a patient with renal failure and alfentanil is unavailable, please seek specialist advice. Oxycodone or hydromorphone may be alternative options.

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 page 12.

In **RENAL IMPAIRMENT (eGFR<10ml/min):** avoid CYCLIZINE. Use reduced dose HALOPERIDOL or LEVOMEPROMAZINE.

In **HEART FAILURE:** avoid CYCLIZINE.

In **HEPATIC FAILURE:** use reduced dose HALOPERIDOL.

In **PARKINSON'S DISEASE:** avoid METOCLOPRAMIDE and HALOPERIDOL. Consider using DOMPERIDONE (only oral preparation)) or ONDANSETRON (providing not on apomorphine), or seek specialist advice.

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 syringe driver over 24hours.** This may require a change of drug if SC preparation not available (i.e. domperidone should be replaced by SC metoclopramide; prochlorperazine should be replaced by SC cyclizine).

Also prescribe 'as required' dose of the same drug, or Levomepromazine* 6.25mg (some areas prefer 2.5-5mg) SC as required up to 4 doses/24hours.

Planning ahead - in case nausea/vomiting develops

Prescribe cyclizine 25-50mg SC as required up to t.d.s, or haloperidol 1.5mg SC up to b.d.
OR prescribe levomepromazine* 6.25mg (some areas prefer 2.5-5mg) SC as required up to q.d.s.

New nausea/vomiting in a patient not currently treated with an anti-emetic
ASK: Is a chemical cause likely?

If **YES** prescribe haloperidol 1.5-3mg daily SC stat or over 24hrs via syringe driver.
Also prescribe cyclizine 25-50mg SC as required, maximum 150mg/24hrs.

If **NO** prescribe cyclizine 75mg or 150mg/24hrs SC via syringe driver.
Also prescribe haloperidol 1.5mg SC, maximum 3 doses in 24hrs.

If anxiolytic/sedative effects likely to be helpful, or to avoid using 2 drugs, consider levomepromazine at dose of 6.25mg (some areas prefer 2.5-5mg) SC as required (up to 4 doses in 24hrs).

REVIEW AFTER 24 hours:
If symptoms are controlled, continue as before.
If either nausea or vomiting persists, change anti-emetic to levomepromazine as below and/or contact the Specialist Palliative Care Team.

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 combination of cyclizine and haloperidol fails to control nausea/vomiting, replace them with levomepromazine 12.5mg/24hrs SC via syringe driver. Also prescribe *levomepromazine 6.25mg (some areas prefer 2.5-5mg) SC as required up to 4 doses/24hrs.

Consider octreotide for large volume vomits - 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 q.d.s. PRN dose.

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

The maximum anti-emetic effect may be achieved at doses of 25-50mg/24hrs. Doses above 25mg/24hrs (or lower in patients who are sensitive) 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 30). 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

Consider and treat reversible common causes of restlessness e.g. urinary retention, faecal impaction and pain.
Support a calm environment, familiar voices and faces, gentle and usual routine.
The doses given here are a guide. In complex situations, seek specialist advice.

BENZODIAZEPINES: Patients on regular or long-term benzodiazepines should continue to receive a benzodiazepine. Give midazolam by SC infusion to prevent rebound agitation/withdrawal.
Benzodiazepine ORAL dosage equivalents *(these are approximations. Note that all drugs have differing half-lives. Appropriate caution and monitoring are required if switching between drugs; seek specialist advice if needed. If switching at a high dose, consider reducing by 30-40%).*
Diazepam 5mg = lorazepam 0.5mg = temazepam 10mg = midazolam 5mg (oral).
Note: midazolam 5mg oral = midazolam 2.5mg SC.

In **RENAL FAILURE:** MIDAZOLAM is a good first choice as toxin accumulation increases seizure risk.
In **HEPATIC FAILURE**: use reduced dose MIDAZOLAM and/or HALOPERIDOL.

ANTICIPATORY (*Just in case*) PRESCRIBING

Planning ahead is important even if a patient is not currently symptomatic: it is a risk in the dying phase.

Prescribe **either** midazolam 2.5-5mg SC 1-hrly as required (up to q.d.s.) **or** haloperidol 1.5mg SC 1-hrly as required (up to b.d.).
Doses should be titrated or regular treatment prescribed as below if symptoms develop.

RESTLESSNESS or AGITATION PRESENT

Give medication SC stat:
Midazolam 2.5mg - 5mg.

If stat dose effective, start syringe driver:
Midazolam 10-20mg/24hr SC.

Prescribe breakthrough dose:
Midazolam 2.5mg - 5mg SC up to 1-hrly as required.

(Use lower dose in the range if frail/elderly)

Review within 24 hrs

If breakthrough doses needed, increase midazolam syringe driver dose by the equivalent of the extra doses given.

If midazolam dose > 30mg/24hrs - consider adding haloperidol 1.5 – 5mg/24 hrs SC **or** levomepromazine 25mg/24 hrs SC.

Continue breakthrough doses of midazolam 5mg SC 1-hrly as required.

Common dose range midazolam 10-60mg/24hrs (above this dose, seek advice).

PSYCHOSIS or DELIRIUM PRESENT

Prescribe
Haloperidol 1.5mg SC once or twice daily
Or
Levomepromazine up to 12.5mg SC 12-hrly (may be more sedating).

Review within 24 hrs
If symptoms are controlled, continue SC either as stat doses 12-24hrly (both drugs are long acting) or via syringe driver.

If symptoms are not controlled, increase haloperidol to 5mg/24hrs SC, or increase levomepromazine by equivalent of extra doses given.

Levomepromazine is an effective sedative.

It may be prescribed with midazolam *(if midazolam partially effective) or used to replace haloperidol or midazolam.*

Start syringe driver at 25mg/24hrs.

Use breakthrough dose 12.5mg SC 1-hrly as required.

Although hourly doses can be given, seek specialist advice if more than 4 PRN doses in 24 hours are needed.

Unresolved or severe symptoms
A few patients become extremely agitated when they are dying. This can be a very difficult situation and may require very high doses of drugs. **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.

Considerations when choosing an anti-secretory drug:
Hyoscine butylbromide, hyoscine hydrobromide and glycopyrronium are broadly similar in effectiveness, controlling secretions in up to 2/3rds of patients. Glycopyrronium may work when a hyoscine salt has not. Consider that secretions may continue to accumulate despite choice of medication. Hyoscine hydrobromide crosses the blood-brain barrier and may cause sedation.

In RENAL FAILURE and HEPATIC FAILURE: avoid hyoscine hydrobromide; use HYOSCINE BUTYLBROMIDE or half the stated GLYCOPYRRONIUM dose.

**In some areas, hyoscine butylbromide is the preferred first line anti-secretory drug, and hyoscine hydrobromide is restricted for prescribing under specialist guidance only.*

SECRETIONS PRESENT

General measures
- Assess if 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.**
- Give hourly mouth care.

Any potentially reversible causes?

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

Chest infection – consider antibiotics for palliation of symptoms.

Anti-secretory prescribing

Starting dose:
Hyoscine butylbromide 20mg SC **or**
Glycopyrronium 200 micrograms SC **or**
*Hyoscine hydrobromide 400 micrograms SC.

Regular treatment via syringe driver:
Hyoscine butylbromide 60mg/24hrs **or**
Glycopyrronium 600micrograms/24hrs **or**
*Hyoscine hydrobromide 1.2mg/24hrs.

Extra doses: (SC up to 1-hrly as required, maximum 6 doses in 24hrs)
Hyoscine butylbromide 20mg SC **or**
Glycopyrronium 200 micrograms SC **or**
*Hyoscine hydrobromide 400 micrograms SC.

SECRETIONS ABSENT

Pre-emptive discussion with relatives that noisy secretions may occur, but may not distress patient.
Anticipatory prescribing is crucial to allow early and better control of this symptom.

Options:
Hyoscine butylbromide 20mg SC 1-hrly as required **or**
Glycopyrronium 200micrograms SC 1-hrly as required **or**
*Hyoscine hydrobromide 400micrograms SC 1-hrly as required.

Specify maximum 6 doses/24hrs – frequent need should prompt review.

Review within 24hrs
If 2 or more doses required, manage as for 'secretions present'.

Review after 24hours, or sooner if indicated

If extra doses needed, increase 24hr dose:
Hyoscine butylbromide 120mg/24hrs or
Glycopyrronium 1200micrograms/24hrs or
*Hyoscine hydrobromide 2.4mg/24hrs

Consider additional / alternative antisecretory medication SC up to 1-hrly as required, with a maximum daily dose to prompt review.

If symptoms not controlled, seek specialist advice.

BREATHLESSNESS IN THE LAST DAYS OF LIFE

BREATHLESSNESS PRESENT

General measures:
- **Calm environment**
- Reassurance and support.
- Cool room.
- Gentle air flow with fan.
- Give hourly mouth care.
- Oxygen if helpful (only if low saturations).

Patient not already on opioid for pain
(for patients with renal impairment, see advice on right and on page 8)
- Give morphine 2.5mg SC stat.
- Also prescribe morphine 2.5mg SC 1-hrly as required.
- Start morphine 10mg SC/24hours by syringe driver.

Patient already on opioid
- Give midazolam 2.5mg SC stat.
- Also prescribe midazolam 2.5mg SC 1-hrly as required.
- Start midazolam 10mg SC/24hrs by syringe driver.

(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 1-hrly as required.

Patient on opioid analgesics: Prescribe midazolam 2.5mg SC 1-hrly as required.

Review within 24hours

If 2 or more doses needed, manage as for breathless patient.

Specific situations
Heart failure: consider furosemide by continuous subcutaneous infusion.

Renal impairment: consider replacing morphine with alternative opioid if renal impairment severe e.g. alfentanil 100micrograms SC 1-hrly as required, 1mg SC/24hrs by syringe driver.

NB Diuretics will not help if patient anuric.

Review within 24hours
If 1-2 breakthrough doses of morphine or midazolam needed in 24hours, increase **syringe driver** dose by 30-50%.
If 3 or more breakthrough doses needed in 24hours, consider doubling syringe driver dose of drug in use and increase breakthrough dose to 5mg. Continue to allow breakthrough doses hourly as required.
Usually, the dose of morphine should not need to exceed 15mg SC/24hrs via syringe driver for breathlessness.
Ongoing review is essential. If symptoms are not improving, seek specialist palliative care advice.

SEVERE FRIGHTENING BREATHLESSNESS
Severe frightening breathlessness is an emergency and may be a terminal situation.
Therapeutic sedation is the appropriate treatment in this emergency situation.
Explain that only sufficient sedation to relieve the frightening sensation will be given.
Administer midazolam 5mg subcutaneously.
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 SC/24hrs and prescribe 5mg SC doses every 15-30 mins for frightening symptoms.
Review every few hours and titrate further as necessary to maintain good symptom control.
In some patients doses of midazolam up to 100mg SC/24hours may be required; seek specialist advice as needed.

Treatment with an opioid may also be appropriate to reduce sensation of breathlessness.

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

SYRINGE DRIVERS AND DRUG COMPATIBILITIES

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 QUERY compatible 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 QUERY COMPATIBLE
MORPHINE Pain / Dyspnoea	*5-10mg No upper limit for pain; if used for dyspnoea, see p28 (increase dose by 30-50% at a time)	2.5 - 5mg OR 1/10th-1/6th of total daily dose of morphine	Cyclizine Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomepromazine Metoclopramide	-Haloperidol *incompatible* at high concentrations of haloperidol >1mg/mL and,morphine>10mg/ml -Midazolam: generally regarded as *compatible*, microscopic precipitation may occur
OXYCODONE Pain / Dyspnoea *If using high strength oxycodone (50mg/ml), compatibilities may vary - seek specialist advice*	*5mg No upper limit (increase dose by 30-50% at a time)	2.5 - 5mg OR 1/10th–1/6th of total daily dose of oxycodone	Haloperidol Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomepromazine Metoclopramide Midazolam	-Cyclizine *incompatible* at high concentrations # If cyclizine is 150mg/**23mL**, max oxycodone **≤70mg** -Oxycodone + cyclizine is a problematic combination, always dilute to maximum & monitor.
ALFENTANIL Pain / Dyspnoea *Often not practical for PRN use due to short half-life, especially in community. Seek specialist advice for alternatives*	*500microg-1mg No upper limit (increase dose by 30-50% at a time)	100 micrograms OR 1/10th of total daily dose of alfentanil (Some areas use 250 micrograms)	Haloperidol Hyoscine butylbromide Glycopyrronium Levomepromazine Metoclopramide Midazolam	-Cyclizine *incompatible* at high concentrations # If cyclizine is 150mg/**23mL**, max alfentanil dose is **5.5mg** # If cyclizine is 150mg/**17mL**, max alfentanil dose is **4mg** -Hyoscine hydroromide *not known*, no data available
MIDAZOLAM Agitation / Dyspnoea (10mg/2ml)	10mg No upper limit, but consider seeking specialist advice if not responding to 30mg (Increase by 30-50% at a time)	2.5 - 5mg	Alfentanil Haloperidol Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomepromazine Metoclopramide Oxycodone	-Cyclizine *incompatible* at some concentrations # If Cyclizine is 150mg/**23mL**, max Midazolam **20mg** # If Cyclizine is 150mg/**17mL**, max Midazolam **15mg** -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)	Haloperidol Hyoscine hydrobromide 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* -Hyoscine hydrobromide *not recommended* -Levomepromazine *not recommended*
# examples given of doses, assuming use of a syringe driver using either 17mL or 23mL (specified) as max total volume after dilution.				

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 QUERY COMPATIBLE
HALOPERIDOL Nausea and vomiting (5mg/ml)	0.5 - 5mg	0.5 - 1.5mg	Alfentanil Cyclizine Glycopyrronium Hyoscine butlybromide Hyoscine hydrobromide 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)	3-10mg	1.5mg		
LEVOMEPROMAZINE Nausea and vomiting (25mg/ml)	6.25 - 12.5mg	2.5 - 6.25mg	Alfentanil Glycopyrronium Hyoscine butylbromide Hyoscine hydrobromide 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* -Hyoscine hydrobromide *not recommended* -Metoclopramide *not recommended*
HYOSCINE HYDROBROMIDE Chest secretions (400microg/ml) *(In some areas, under specialist advice only)*	1.2 - 2.4mg	400microg	Cyclizine Haloperidol Levomepromazine Midazolam Morphine Oxycodone	Alfentanil *not known*, no data available -Glycopyrronium *not recommended* -Hyoscine butylbromide *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* -Hyoscine hydrobromide *not recommended*
LEVETIRACETAM Seizures (100mg/ml)	Oral **:** SC conversion 1:1	Use midazolam inj	Limited compatibility information suggests that it is compatible with haloperidol, hyoscine *butylbromide*, levomepromazine, metoclopramide, midazolam, morphine, oxycodone ***using 0.9% sodium chloride as diluent***	

Principles of medicines compatibility in a syringe driver

The compatibility information above 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.

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
- Consider switch to using 0.9% sodium chloride as diluent; however seek specialist advice on compatibilities
- If site irritation continues, seek specialist advice. Consider the addition of low dose dexamethasone to CSCI, if compatibility data permits.

Legal considerations – Changes in the law state that the instruction / direction to mix medicines must be in writing; therefore, the prescriber must indicate which medicines to mix in each syringe driver.

Evidence – The information for the chart is taken from the Palliative Care Formulary 7th Edition and is based on clinical observations in palliative care services.

INDEX

KEY RESOURCES

- Wilcock A, Howard P, Charlesworth S (eds) (2020) Palliative Care Formulary - seventh edition (PCF7), Pharmaceutical Press, London.
- BNF 82 (September 2021) BMJ Group and Pharmaceutical Press, London.

FREQUENTLY USED ABBREVIATIONS

b.d.	twice daily
CSCI	continuous subcutaneous infusion
eGFR	estimated glomerular filtration rate
GI	gastrointestinal
GMC	General Medical Council
hr(s)	hour(s)
hrly	hourly
IR	immediate release
IV	intravenous
LMWH	low molecular weight heparin
MCA	Mental Capacity Act
mg	Milligrams
min(s)	minute(s)
mL	Millilitres
mmol/L	millimoles per litre
MR	modified release
NSAID	non-steroidal anti-inflammatory drug
o.n.	at night
o.d	once daily
PO	by mouth
PPI	proton pump inhibitor
PRN	as required
q.d.s.	four times daily
SC	subcutaneous
SPCT	specialist palliative care team
TD	transdermal
t.d.s	three times daily
TENS	transcutaneous electrical nerve stimulation
UTI	urinary tract infection
WHO	World Health Organisation