



Northern England
Clinical Networks

Palliative and End of Life Care Guidelines

Symptom control for cancer
and non-cancer patients

Fourth edition: 2016
Next review date: 2021

FOREWORD

Welcome to the fourth edition of the Northern England Clinical Networks' Palliative and End of Life Care Guidelines. To ensure that the fourth edition continues to be useful, we surveyed clinical staff from primary and secondary care teams across the North East of England and North Cumbria who used the third edition. We received considerable valuable feedback and have taken this into consideration, removing sections which were thought to be repetitive or rarely used, and adding guidance which was felt to be more helpful.

It has always been the intention that this guidelines booklet should be small, simple and accessible, and present 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.

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

Please note that drug dose guidance – and especially the stated relative potencies of different opioid drugs – is drawn from the Palliative Care Formulary Fifth Edition (PCF5). 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 PCF5, pages xix-xxiv)

Guidelines are a place to begin. They cannot replace specialist advice from experienced clinicians. Fundamental to the practice of palliative care is an emphasis on individualised care for the patient.

If symptoms fail to respond to usual measures, or if you are concerned that the guidance given here may not be appropriate to the clinical situation, please contact your local specialist palliative care team.

We are immensely grateful to the effort and commitment made by section authors and editorial team. The contributors to this edition are medical, nursing and pharmacy colleagues working in primary and secondary care across our region. With their support, and the enormous assistance of the Northern England Clinical Networks, the fourth edition has been successfully accomplished.

Finally we welcome interest from other network groups who may consider adopting aspects of these guidelines with appropriate acknowledgment of authorship.

For further information, please visit www.nescn.nhs.uk

Dr Alexa Clark
Chair, NECN Guidelines Review Group

Dr Alex Nicholson
Co-chair, NECN Guidelines Review Group

INDEX

Palliative Care 1
 Pain 2
 Using Adjuvant Analgesic Drugs in Palliative Care..... 3
 Using Opioids for Pain in Palliative Care 4
 Opioid Dose Conversion Chart 8
 Nausea and Vomiting 9
 Constipation 11
 Emergencies - Bowel Obstruction 12
 Emergencies – Seizures 13
 Emergencies – Metastatic Spinal Cord Compression (MSCC) 14
 Emergencies – Malignant Hypercalcaemia 15
 Emergencies – Major Haemorrhage 16
 Emergencies – Malignant Superior Vena Cava Obstruction 17
 Emergencies - Opioid Toxicity 17
 Corticosteroids in Palliative Care 18
 Control of Glucose in Patients on Corticosteroids 19
 Care in the Last Days of Life 20
 Diabetes Management at the End of Life 21
 Pain at the End of Life 22
 Pain at the End of Life in Renal Impairment 23
 Pain at the End of Life – Supplementary Information 24
 Nausea and/or Vomiting at the End of Life 25
 Restlessness, Agitation and/or Delirium at the End of Life 26
 Respiratory Tract Secretions at the End of Life 27
 Breathlessness at the End of Life 28
 Syringe Drivers and Drug Compatibility Chart 29

KEY RESOURCES

- Twycross R, Wilcock A, Howard P (eds) (2014) Palliative Care Formulary. 5th Edition. Palliativedrugs.com Ltd., Nottingham.
- BNF 70 (September 2015) BMJ Group and Pharmaceutical Press, London.

FREQUENTLY USED ABBREVIATIONS

BD	-	twice daily	MR	-	modified release
eGFR	-	estimated glomerular filtration rate	NSAID	-	non-steroidal anti-inflammatory drug
EMA	-	European Medicines Agency	ON	-	at night
GI	-	gastrointestinal	PO	-	by mouth
GMC	-	General Medical Council	PPI	-	proton pump inhibitor
hr(s)	-	hour(s)	PRN	-	as required
hrly	-	hourly	QDS	-	four times daily
IR	-	immediate release	SC	-	subcutaneous
MCA	-	Mental Capacity Act	SPCT	-	specialist palliative care team
mg	-	milligrams	TENS	-	transcutaneous electrical nerve stimulation
MHRA	-	Medicines and Healthcare products Regulatory Agency	TDS	-	three times daily
min(s)	-	minute(s)	UTI	-	urinary tract infection
mL	-	millilitres	WHO	-	World Health Organisation
mmol/L	-	millimoles per litre	UTI	-	urinary tract infection

PALLIATIVE CARE

The World Health Organisation (WHO 1996) defined palliative care as:

“the active, holistic care of patients with advanced, progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families.”

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

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 www.nescn.nhs.uk/common-themes/deciding-right

Key aspects of ***Deciding Right***, reproduced directly from the web-site, 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

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is a highly subjective phenomenon.
Simple definition: *“pain is what the patient says hurts”*

The concept of TOTAL PAIN is commonly used in Palliative Care to prompt health professionals to consider all possible influences on the pain experience:



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

Careful initial assessment is very important and should include clear documentation of findings. This allows the assessing clinician, and others, to compare progress in management against the early features. Many pains change with time and frequent reassessment is necessary, especially during and after interventions. Multiple sites and/or types of pain are common. **EACH** pain should be assessed, documented, managed and reviewed.

Charts may be used to record site and radiation of pains, and associated clinical findings. Pain scores or scales, although subjective, allow the patient to rate the severity of pain and review effectiveness of analgesia.

Each pain should be assessed for:

- site, severity, radiation and characteristics of its timing/frequency/variation
- quality, using descriptive terms (e.g. burning, tingling, throbbing, etc)
- exacerbating and relieving factors including the effects of drug and non-drug interventions
- associated symptoms and features.

The patient's understanding, fears and concerns, previous experience of pain and expectations of treatment, and other aspects relevant to social, psychological and spiritual care, should be determined.

Clinical examination should be performed to assist in determining the likely type and cause of pain. Relevant investigation, appropriate to the patient's condition, should be considered. This might include biochemistry (which may influence drug choice) and X-rays/scans.

Prescribing guidance

- Use the oral route wherever possible.
- Use a non-oral route if necessary, e.g. dysphagia, vomiting, bowel obstruction, terminal phase.
- Prescribe regularly at a dosing interval appropriate to the formulation.
- Prescribe analgesia as required for breakthrough pain that may occur despite regular treatment.

“Review, review, review”

Success in pain management depends upon regular review of pain and its causes, the effectiveness of the treatment and its acceptability to the patient.

Guidance on seeking advice from the Specialist Palliative Care Team (SPCT)

SPCTs are experienced in the management of complex pain and will offer advice on the use of standard, adjuvant and non-drug measures to manage pain or will consult with the patient for assessment, treatment and review. The following situations warrant referral:

- complex or multiple pains where assessment is difficult
- pain that appears resistant to usual measures
- difficulty with management caused by adverse effects of medication
- pain associated with more than usual distress, particularly where non-physical factors are involved.

If in doubt, please ask your local SPCT for advice.

USING ADJUVANT ANALGESIC DRUGS IN PALLIATIVE CARE

A step-wise approach (e.g. **WHO analgesic ladder**) provides a framework for palliative pain management (see p4).

Adjuvant analgesic drugs may be used alongside any step. An adjuvant analgesic is a drug whose primary indication is for something other than pain, but which has analgesic effects in some painful conditions.

Common adjuvant analgesic drug groups	Indications
Corticosteroids – see p18 for dose guidance	Raised intracranial pressure, nerve compression, liver capsule pain, soft tissue infiltration
Antidepressants, Anticonvulsants	Neuropathic pain*, tenesmoid pain
Muscle relaxants (e.g. baclofen, benzodiazepines)	Muscle cramp/spasm, myofascial pain
Bisphosphonates	Bone pain
Antispasmodic (e.g. hyoscine butylbromide)	Bowel colic, bladder spasm

*See section below on neuropathic pain

Additional approaches to pain relief will be dictated by clinical circumstances:

- **Interventional methods** - spinal analgesia, nerve block, radiotherapy, surgical stabilisation.
- **Non-drug measures** - TENS, acupuncture, massage, complementary therapies, cognitive behavioural therapy
- **Rehabilitative support** - physiotherapy, occupational therapy

Adverse effects

Prescribers must know the adverse effects and contraindications of all medications that they prescribe and should consult the BNF if they are unsure. See p5 for common opioid adverse effects.

NB: Combinations of certain drugs (e.g. NSAIDs, corticosteroids, SSRIs and anticoagulants) substantially increase the risk of GI bleeding. Co-prescription of a PPI and close monitoring is essential.

Neuropathic pain (see NICE CG173: Neuropathic pain in adults. www.nice.org.uk/guidance/cg173)

First line drugs for neuropathic pain include **amitriptyline** and **gabapentin**. Local prescribing variations may include **pregabalin**, **duloxetine** and **nortriptyline**. All have comparable efficacy and tolerability, though the supporting evidence for amitriptyline, gabapentin and pregabalin is more extensive. Choice may be influenced by individual patient characteristics, drug characteristics and cost. Consider a step-wise approach.

Step 1: Gabapentin/Pregabalin OR Amitriptyline Step 2: Gabapentin/Pregabalin AND Amitriptyline

Step 3: SPCT advice

Drug	Cautions	Additional indications	Common side effects	Typical dosing schedule
Amitriptyline <i>Once daily - tablet / syrup</i>	Avoid in patients with arrhythmias, heart block, ischaemic heart disease, congestive heart failure. May reduce seizure threshold. Glaucoma, hepatic impairment.	Depression, anxiety, bladder spasm, urgency of micturition	Dry mouth, sedation, postural hypotension, hyponatraemia, urinary hesitancy	10mg ON, increased to 25mg ON after 3-7 days, then increased by 25mg every 1-2 weeks. Max 150mg ON (if successive increases are beneficial and tolerated).
Gabapentin <i>Three times daily - tablet, capsule (can be opened), solution</i>	Absence seizures, psychotic illness. Reduce dose in renal impairment.	Seizures, spasticity	Sedation, dizziness, ataxia	<i>(300mg ON, increased by 300mg every 2-3 days. Max 600mg TDS). Elderly / frail patients¹: 100mg ON, increased by 100mg every 2-3 days. Reduce dose/frequency in renal impairment.</i>
Pregabalin <i>Twice daily - capsule / solution</i>	Avoid in patients with congestive heart failure. Reduce dose in renal impairment.	Seizures, anxiety	Sedation, dizziness, ataxia	<i>(75mg BD increased by 75mg every 3-7 days. Max 300mg BD). Elderly / frail patients¹: start 25-50mg BD and titrate more slowly. Reduce dose/ frequency in renal impairment.</i>

¹ This is likely to be a more appropriate titration schedule in most palliative care patients.

USING OPIOIDS FOR PAIN IN PALLIATIVE CARE

Using opioid drugs safely

Morphine and other opioids are valuable drugs for the relief of severe pain in patients with advanced malignant and non-malignant disease. These drugs are safe, effective and appropriate provided that clinicians:

- start and titrate opioids cautiously
- remember different opioids have different properties and potencies (see p7 and 8)
- monitor and manage adverse effects caused by opioids
- remember that some types of pain do not respond well to opioids and require adjuvant analgesics (see p3).

The place for opioids in pain management may be guided by a step-wise approach (such as the traditional WHO "analgesic ladder"), moving up the steps if pain control is not achieved.

STEP 1 Non-opioid (Paracetamol and/or NSAID) +/- adjuvant
STEP 2 Opioid for mild to moderate pain* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant (* e.g. codeine, dihydrocodeine, tramadol)
STEP 3 Opioid for moderate to severe pain* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant (* e.g. morphine, oxycodone, fentanyl – see p7)

COMMON CONCERNS OVER THE USE OF MORPHINE AND OTHER OPIOIDS

Opioids and addiction - Psychological dependence is rare in patients with severe pain in whom opioids are titrated carefully. When caring for patients with history of substance misuse, liaise with that specialist team and do not withhold pain relief when there is clinical need. Physiological dependence will not prevent dose reduction/gradual withdrawal when pain has been addressed by other measures. Increasing doses without benefit may indicate tolerance or a pain that is poorly responsive to opioids requiring adjuvant analgesia – seek specialist advice.

Opioids and respiratory depression – Opioids may cause respiratory depression but this is usually counteracted by pain. Dose titration, clinical judgement and regular review allow safe use even in patients with cardio-respiratory disease.

Opioids and renal impairment – In acute kidney injury, and chronic and end-stage renal failure, opioids must be used cautiously because some have active metabolites that accumulate if renal clearance is reduced. Opioids differ in their potential to cause toxicity and this influences the choice. Some opioids are cleared by dialysis which may result in pain flare afterwards.

Mild-moderate renal impairment: reduce dose, lengthen dose interval and review regularly. Be cautious with codeine, dihydrocodeine, morphine and oxycodone.

Severe renal impairment (eGFR < 30ml/min): Avoid *regular* codeine, morphine and oxycodone; low dose *immediate release* (IR) oxycodone with increased dose intervals may be appropriate in some clinical situations. Consider fentanyl, buprenorphine or alfentanil depending on type of pain and preferred route of administration. You are strongly advised to seek specialist advice on use of alfentanil. Tramadol may be used cautiously and at reduced dose or increased dose interval in the short term. Methadone for pain may be continued under specialist supervision.

See BNF: 'prescribing in renal impairment' or 'The renal drug handbook' (Ashley & Dunleavy (eds) 4th edition; 2014; Radcliffe)

If in doubt, seek advice.

MANAGEMENT OF COMMON OPIOID ADVERSE EFFECTS

- **Constipation** – common, persists, worse with dose increase. Prescribe stimulant laxative (e.g. senna) adding a softener if needed (e.g. docusate). (See *Constipation* p11).
- **Nausea/vomiting** – common when starting, usually settles within days. Prescribe anti-emetic 'as required' (e.g. haloperidol 0.5-1.5mg nocte or metoclopramide 10mg tds) for the first week, titrating to response.
- **Sedation** – 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 saliva stimulants (e.g. pilocarpine) or artificial saliva (e.g. Biotene or Bioextra gel).

OPIOID TOXICITY (for Emergency Treatment see p17)

Features: myoclonic jerks, pin-point pupils, hallucination, confusion, reduced respiratory rate. Reduce opioid dose by 30-50%. Check renal function. Seek specialist advice on alternative analgesics or opioid switch.

OPIOID TITRATION**Morphine is the first line WHO step 3 opioid of choice**

- Initiation and titration may use Immediate Release (IR) or Modified Release (MR) formulations
- Ensure the breakthrough dose is 1/6th – 1/10th of the total daily opioid dose
- Prescribe regular laxative (ongoing), and regular or 'as required' anti-emetic (for 1 week)
- Monitor closely for efficacy, adverse effects and toxicity
- Make patients aware of driving regulations when on opioids (<https://www.gov.uk/drug-driving-law>)

**If the pain is severe and rapid dose titration seems necessary, seek specialist advice.
For safety, do not increase regular doses of MR opioid by more than 30-50% every 2 days.**

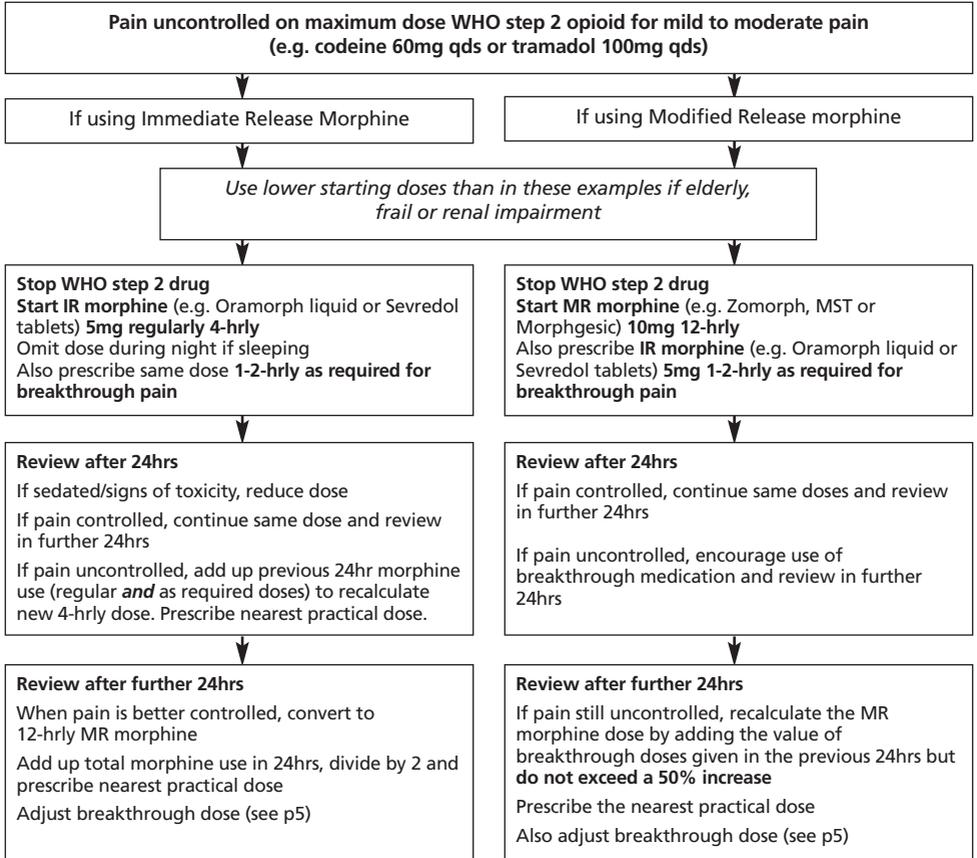
Breakthrough doses of opioids

Pain occurring despite regular opioid (breakthrough pain) is treated with an immediate release (IR) formulation of the same opioid where possible. The breakthrough dose is usually between 1/10th and 1/6th of the total 24hr dose. IR opioids usually have onset of action within 30 minutes and last 3-4hrs at most. A common starting point is to prescribe 1/6th of the total 24hr dose (using a practical dose, rounding down rather than up) to be given 2-hourly as required and adjusted according to benefit and tolerability. Setting a daily maximum number of breakthrough doses (e.g. 6 in 24hrs) should prompt review of a patient whose pain is out of control.

Severe, refractory or rapidly recurring pain may require higher doses than 1/6th of the daily amount, and/or repeating sooner than 2 hours. However it is best to avoid repeating within 1 hour in case delayed absorption results in rapidly accumulating doses. If frequent doses seem necessary, seek specialist advice and monitor the patient closely for opioid toxicity.

KEY POINT: Codeine 240mg/24hrs is equivalent to oral morphine 24mg/24hrs (except in the few patients who do not metabolise codeine) and tramadol 400mg/24hrs is considered equivalent to oral morphine 40mg/24hrs. The flowchart on the next page is deliberately cautious to allow safety in patients who do NOT metabolize codeine normally and are therefore less tolerant to strong opioid effects.

Flowchart for opioid titration using morphine



SWITCHING BETWEEN DIFFERENT ROUTES OF ADMINISTRATION

- When changing the route of administration and formulation, always use the opioid dose conversion chart guidance (on p8). Don't forget to cancel the previous prescription.
- If the opioid switch is because of opioid toxicity, check the eGFR and seek specialist advice on opioid choice and dose.
- Breakthrough doses may be needed to cover transition periods.

Oral to subcutaneous infusion

From IR opioid: start syringe driver immediately.

From 12-hrly MR opioid: start syringe driver 2 hours before next oral dose would have been due.

Subcutaneous infusion to oral

Switching to either IR or MR opioid, stop the syringe driver and give first oral dose at the same time.

Oral to patch

From IR opioid: apply patch when convenient and use oral IR opioid as required.

From twice daily MR opioid: apply patch at same time as last dose of MR oral opioid.

(From once daily MR opioid: apply patch 12 hours after last dose of MR opioid).

Patch to oral

Remove patch 6 hours before giving first dose of oral MR opioid.

For first 24 hours (i.e. first two doses) give HALF the calculated equivalent dose since the transdermal opioid will take time to be cleared from plasma and subcutaneous reservoir.

After 24 hours, increase to the calculated equivalent dose if clinically indicated by pain.

Patch to subcutaneous infusion

If the patient is thought to be in the last hours to days of life, leave the 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. (see p24)

In other situations where a change from patch is required, remove 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 the need for breakthrough analgesia.

Subcutaneous infusion to patch

Apply patch. Continue subcutaneous infusion for a further 6 hours then discontinue syringe driver.

INFORMATION ABOUT DIFFERENT OPIOIDS (NB drugs are listed in alphabetical order, not order of preference)**Morphine is the first line strong opioid of choice**

Alfentanil: Please seek specialist advice about the use of alfentanil. Synthetic injectable highly potent opioid. Thirty times as potent as oral morphine (1mg SC alfentanil is approximately equivalent to 30mg PO morphine). Used in preference to other SC opioids in renal failure because there is no accumulation of neurotoxic metabolites. Single SC doses (as required doses) are very short-lasting (<2hours) and this may make alfentanil unsuitable as an opioid for breakthrough analgesia even in the context of renal impairment. Reduce dose in liver failure. Opioid withdrawal symptoms (like 'gastric 'flu') may occur (rarely) when switching from other opioids. If so, give 'as required' dose of previous opioid for a few days.

Buprenorphine: Strong opioid used as sublingual tablets and transdermal patches (7-day range and 3-4 day range). Analgesic efficacy may be reviewed 24hrs after starting 3-4-day patch or 72hrs after starting 7-day patch.

Diamorphine: Di-acetylmorphine (diamorphine) is rapidly metabolised to morphine. It has no clinical advantage over morphine but is much more soluble, therefore recommended for use where opioid dose requirement exceeds morphine 360mg/24hours by SC infusion.

Fentanyl: Highly potent synthetic opioid. At least 100 times as potent as oral morphine. Potency often unappreciated resulting in serious adverse events. See MHRA warnings on accidental exposure.

Available as transdermal patches, injection, and transmucosal (buccal, sublingual and intranasal) formulations. A practical choice of opioid for use by transdermal or transmucosal route in severe and end stage renal failure. May be less constipating than morphine.

Transmucosal formulations: rapid onset, short acting. Licensed for breakthrough cancer pain. May be useful for procedure and movement-related pain (unlicensed indication).

Transdermal formulation (patches): useful when oral route not possible or in those with compliance/concordance problems. Not well suited to titration in unstable pain as takes 24 hours to achieve steady state after dose adjustment (increase OR decrease).

Hydromorphone: Semi-synthetic opioid. Oral and injectable preparation. Considered to be 5 to 7.5 times more potent than morphine. Less often used due to limited IR preparations. Despite its active metabolites being renally excreted, it is sometimes used as a preferred strong opioid in renal impairment.

Morphine: **First line strong opioid** for use by mouth and injection/infusion. When used by SC infusion, doses greater than 360mg/24hours are difficult to deliver because of the volume of the corresponding breakthrough dose. A morphine rescue dose greater than 60mg (i.e. 1/6th of 360mg/24hours) is 2mls in volume and will be a painful SC injection. In this situation seek specialist advice.

Oxycodone: Semi-synthetic oral and injectable opioid. Alternative opioid if morphine not tolerated or toxicity occurs. Considered to be 1.5 to 2 times as potent as morphine. When switching either way between morphine and oxycodone, start the new drug at the lowest dose based on the ratios and re-titrate as needed. Be careful not to confuse the MR formulation (usually tablets) with the IR form (usually capsules, liquid or injection).

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 clinical record.** To calculate appropriate breakthrough dose of opioid, see p5 and/or p24.

Opioid	Oral opioid Dose in <u>mg</u> per 24 hours		Subcutaneous opioid infusion Morphine is <i>first line</i> injectable opioid of choice Doses are for medication in syringe driver in <u>mg</u> given over 24hours			Opioid by <u>patch</u> (Dose in <u>micrograms</u> /hr patches)	
	Morphine	Oxycodone	Morphine	Oxycodone	Alfentanil	Fentanyl (72 hrly)	Buprenorphine (7 day and 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	

Note (a): PCF5 advises morphine = 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, PCF5 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 PCF5 which is morphine:fentanyl = 100:1 (BNF states 150:1).

Note (d): Data sourced by PCF5 suggests that TD buprenorphine is between 70 and 115 times more potent than PO morphine. PCF5 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).

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 p10 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 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 p12
F Raised intracranial pressure/intra-cerebral causes	Headache, visual disturbance, other neurological signs.	Cyclizine (Consider steroids)
G Psychological factors	Anxiety, fear, anticipation	Consider non-drug treatment options first. 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 next page for frequency.
- Levomepromazine can be considered in addition as required for refractory symptoms.

4. Review – reassess symptom control within 24 hours

- Review drug choice if symptoms persist or worsen.
- Review route: consider switch to oral if symptoms resolving or to SC if poor control.
- If cause/symptom resolves, consider whether anti-emetic can be discontinued.

Commonly used anti-emetic drugs (see PCF5 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/SC: 50mg TDS. Syringe Driver: 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. Illogical to combine with metoclopramide because both act by central dopamine antagonism. Contra-indicated in Parkinson's disease.

DOSE: PO/SC: 0.5-3mg ON. Syringe Driver: 0.5-3mg/24hrs. (5mg max dose if necessary).

LEVOMEPRMAZINE - broad spectrum anti-emetic. Consider for refractory/persistent symptoms. Risk of sedation and hypotension (even at low dose). Caution in Parkinson's disease. If prescribed regularly, give at night. Some specialists recommend very low doses (2.5-5mg) to avoid any risk of sedation.

DOSE: PO/SC: 6.25-25mg ON. 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.

Contraindicated in Parkinson's disease, complete obstruction and recent GI surgery.

DOSE: PO/SC: 10mg TDS to QDS. Syringe Driver: 30-40mg/24hrs. Higher doses and long term use under specialist supervision. Be aware of regulatory advice (MHRA/EMA) on dose and duration related to neurological side effects.

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 p18.

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.

DOSE: PO: 10mg TDS. Higher doses and long term use under specialist supervision as may prolong QT interval with risk of cardiac dysrhythmia. Be aware of regulatory advice (MHRA/EMA) on dose/duration related to cardiac side effects.

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

DOSE: SC: 20mg 1-hrly as required up to three doses. Syringe Driver: 60mg-120mg/24hrs.

OCTEOTIDE – somatostatin analogue. Reduces GI secretions.

DOSE: Syringe Driver 250-1000micrograms/24hrs.

OLANZAPINE – centrally active broad spectrum antiemetic. May be useful in those patients intolerant to haloperidol and/or levomepromazine.

DOSE: Seek specialist palliative care advice.

ONDANSETRON 5HT3 receptor antagonists. Only recommended post-op and in the acute phase of chemotherapy/radiotherapy treatment. Other indications only under specialist supervision. Can cause severe constipation.

DOSE: follow oncology guidelines. PO/SC: 4-8mg BD-TDS. Syringe Driver 16mg/24hrs.

CONSTIPATION

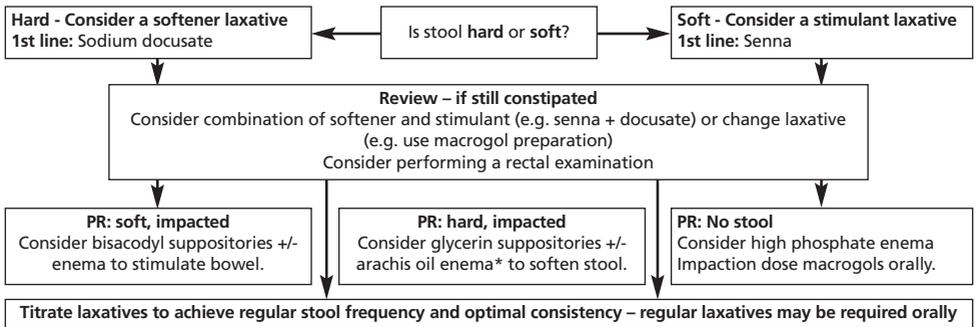
Common reversible causes to consider

- 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, anticholinergics, 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, see p12.



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

Class	Examples	Information	Dose
Stimulant laxatives	<i>Senna</i> <i>Bisacodyl</i>	Reduces bowel transit time. Think carefully before using if possibility of bowel obstruction.	15-30mg at night PO 5-10mg at night PO
Softeners	<i>Docusate</i>	Reduce surface tension and so improve water penetration of the stools.	100-200mg BD/TDS PO
Combination stimulant/softener laxatives	<i>Co-Danthramer</i> <i>Co-Dantrusate</i>	Dantron may cause orange 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.	Co-danthramer 10mls at night PO ('Strong' preparation available – approx. double strength) Co-dantrusate 2 capsules at night PO
Osmotic laxatives	<i>Macrogols (e.g. Movicol, Laxido)</i> <i>Lactulose</i>	Volumes may be difficult for some patients to manage. They retain water in the gut lumen which encourages peristalsis. Lactulose can cause flatulence, bloating and abdominal cramps, not generally used first line. Use in hepatic encephalopathy.	Start with 1-3 sachets daily (total volume 125mls per sachet) PO 15ml BD PO
Suppositories	<i>Bisacodyl</i> <i>Glycerin</i>	Stimulant (10mg per suppository) Softener (4g per suppository)	1-2 suppositories PR 1-2 suppositories PR
Enemas	<i>Arachis oil</i> <i>Microlox</i> <i>Phosphate</i>	Softener. *Contraindicated if nut allergy Softener Softener	1 PR 1 PR 1 PR

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 or other GI catastrophe.

Medication: opioids, anticholinergics (e.g. tricyclic antidepressants, hyoscine salts), diuretics, 5HT3-antagonists, phenothiazines, chemotherapy.

Clinical presentation:

Pattern and severity of symptom(s) depends on whether high or low obstruction, or multiple levels

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?

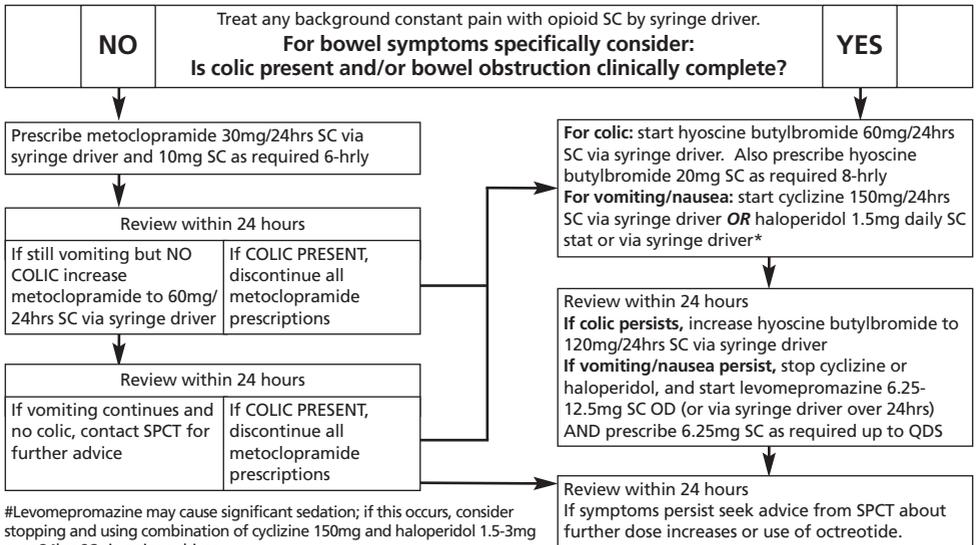
Consider patient's wishes, documented emergency health care plans or other records, and guidance from family/others.

If YES - admit as emergency. Give medication for symptom relief during transfer, i.e. stat dose **opioid analgesic** (appropriate to analgesic history) and stat 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 and supine abdominal X-ray; consider CT scan; seek urgent surgical opinion; start IV fluid resuscitation; consider decompression of distended gut with NG tube. **Exclude constipation** or manage appropriately.

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. 9.9mg injectable formulation SC or IV) alongside guidance below. Review effect after 5 days. Stop if no effect. Reduce gradually if benefit. Change to oral when possible.

3. ONGOING MANAGEMENT



#Levomepromazine may cause significant sedation; if this occurs, consider stopping and using combination of cyclizine 150mg and haloperidol 1.5-3mg over 24hrs SC via syringe driver

*Cyclizine and hyoscine butylbromide should not be mixed in syringe driver as incompatible

EMERGENCIES – SEIZURES

For any palliative patient at risk of having a seizure, it is helpful to ensure that an Emergency Health Care Plan is formulated (see *Deciding Right*).

1. RECOGNITION

- Seizures can be frightening for the patient and their family.
- 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.
- Seizures may become more severe or frequent at the end of life. If the patient is no longer able to take or absorb their oral anticonvulsants, subcutaneous antiepileptic medication should be prescribed using midazolam 20-30mgSC/24hr via syringe driver. Alternatively sodium valproate or levetiracetam may be given subcutaneously.

2. IMMEDIATE ACTION for treatment of status epilepticus

- Put the patient in the standard recovery position if appropriate. Ensure safety and protect airway.
- This assumes exclusion of other causes of loss of consciousness or abnormal limb/ facial movement. (e.g. vasovagal episode (faint), postural hypotension, arrhythmia, hypoglycaemia – check BM, extrapyramidal side effects from dopamine antagonists, alcohol).
- **Community/inpatient:** if seizure does not resolve spontaneously after 5 minutes, give midazolam 5-10mg via the buccal route (using oromucosal solution or injectable formulation) or SC/IM using injectable formulation. Repeat after 10-20 mins if seizure not resolved.

OR

- **Inpatient:** IV lorazepam 2mg/min up to 4mg. Repeat once after 10-20 mins if seizure not resolved.
- If further treatment needed, seek advice from Neurologists or SPCT. Drugs such as phenobarbital or phenytoin may need to be considered.

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.

Seek advice from local neurology team if needed

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

At this stage, it is usually inappropriate to investigate. To prevent further seizures, commence midazolam 20-30mg/24hrs subcutaneously via syringe driver over 24hrs. Prescribe midazolam 5-10mg buccal or 5-10mg SC/IM as required for further seizure control.

Alternatively or additionally, sodium valproate and levetiracetam can be given via the subcutaneous route. **Seek advice from Specialist Palliative Care Team if needed.**

EMERGENCIES – METASTATIC SPINAL CORD COMPRESSION (MSCC)

This guidance applies only to patients with a known cancer diagnosis

Patients with suspected MSCC must be assessed as a *priority*.

Community patient - admit as emergency.

Hospital/hospice inpatient - contact Acute Oncology Service (if your hospital has one) or seek advice from Cancer Centre on call Registrar/Consultant.

1. RECOGNITION

Consider this possible diagnosis in any cancer patient who goes 'off legs'

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

DO NOT WAIT FOR LATE SYMPTOMS/SIGNS TO APPEAR.

Pain – 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. Often precedes neurological signs. **The diagnosis of spinal cord compression should be considered in any cancer patient with severe back pain in a nerve root distribution.**

Late symptoms/signs include

- limb weakness, altered gait, unsteadiness, falls
- 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; Inpatients: 13.2mg IV (13.2mg of injectable dexamethasone is the closest dose using 3.3mg/mL injection strength. If given SC, volume needs to be divided into two sites, 2mls each).
- **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 acute receiving team will make arrangement for whole spine MRI.

Hospital/Hospice Inpatient

Contact Acute Oncology Service at your hospital (see <http://www.nescn.nhs.uk/wp-content/uploads/2015/02/NECN-AOS-Guidelines-v1.31.pdf>). There is 24hour advice from Oncology Consultant on call across the Network (NCCC for North of Tyne, South of Tyne and Wear, Durham; JCUH for Tees and Darlington).

This discussion will guide appropriate decisions and facilitate emergency virtual MDT discussion between radiologist, oncologist and spinal surgeon.

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.

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.

Commonest paraneoplastic syndrome in patients with advanced cancer.

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 Calcium' level in venous blood. Normal range 2.20 - 2.60 mmol/L
- If normal but clinical suspicion remains, recheck in 1 week. Also check renal function (U&E)

Management

- **Admit** to hospital/hospice unless it is agreed that intervention is not appropriate.
- Stop thiazide diuretics – may increase calcium levels
- **Rehydrate with IV 0.9% sodium chloride**. Aim for 2-4L/day. Caution if risk of fluid overload.
- After 1-2 litres sodium chloride (to prevent renal damage) give IV bisphosphonate

Bisphosphonate treatment (drug of choice may depend on local guidance)

(If eGFR less than 30mL/min seek advice on whether bisphosphonates are suitable)

Disodium pamidronate: stated dose in 500mL sodium chloride IV 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

Zoledronic acid: dose is 4mg in 100mL sodium chloride IV over 15 min. Reduce dose to 3mg if eGFR less than 40mL/min.

Adverse effects: 'Flu-like syndrome/pyrexia is common – treat with paracetamol. Osteonecrosis of jaw is a rare but significant side effect. Rebound *hypocalcaemia* may occur.

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 IV.

If no response, seek 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.

NOTE

Resistant/refractory hypercalcaemia may herald the end of life. If so, manage symptomatically. Consider use of an **Emergency Health Care Plan** to prepare for this situation.

EMERGENCIES – MAJOR HAEMORRHAGE

This guidance applies only to patients with a known cancer diagnosis

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.

2. ANTICIPATORY MANAGEMENT

- Massive haemorrhage is often preceded by smaller bleeds. Oral/topical treatment may help (see below). When planning ahead, agree an **Emergency Health Care Plan**.
- Review risk: benefit balance of anticoagulants. Correct any coagulation disorder if possible.
- Consider referral for radiotherapy or embolisation if patient has an erosive tumour.
- Review 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.

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 resuscitation measures.

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.

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.

4. FOLLOW UP

- Ensure support available for family and staff following experience of haemorrhage.
- If the patient survives the haemorrhage consider transfusion.
- To prevent rebleeding: **ORAL**: Tranexamic acid 1g 8-hourly (avoid in haematuria) **TOPICAL**: Sucralfate paste (2g/5mL aqueous gel) applied directly to ulcer under non-adherent dressing; Adrenaline 0.1% (1mg/ml) soaks (10ml on gauze); Tranexamic acid (500mg/5ml injectable formulation) soaked on gauze.
- Consider diathermy, radiotherapy or embolisation.

EMERGENCIES – MALIGNANT SUPERIOR VENA CAVAL 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.

Clinical Presentation:

- Facial swelling, redness, headache, periorbital oedema, engorged conjunctivae.
- Swelling of the arms, prominent distended veins on neck and chest wall.
- Breathlessness, cough, chest pain, stridor, cyanosis.
- Visual disturbance.

2. IMMEDIATE ACTION

- Steroids may be helpful. 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 p28 and agitation p26).
- 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:

- 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

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, OR
- RR < 12/min AND difficult to rouse AND oxygen saturation < 90% on pulse oximeter

Action (please follow local guidance where this exists)

Aim is to reverse respiratory compromise whilst maintaining adequate analgesia

- Stop opioid.
- 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.

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.

The National Poisons Information Service (0844 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).

Route and formulations: tablets (soluble), oral solution, injection. Dexamethasone should be prescribed in terms of the 'base' (*dexamethasone*) rather than the 'salt' (*dex phosphate* or *dex 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 tablet.

(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. Ensure daily dose 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. Judge response within 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: 6 - 16mg daily.

Spinal cord compression: 16mg daily for 5 days. Maintain on 8mg daily during radiotherapy, then reduce dose over 2 weeks. If symptoms recur, increase to previous effective dose for at least 2 weeks before reducing again.

Raised intracranial pressure: 8-16mg daily for one week, and then reduce over 2-4 weeks to lowest dose which maintains benefit. (If treated with radiotherapy, steroids should be continued until one week post treatment, and then reduced as above). Consider trial of dose increase if symptoms recur.

Prostate cancer: refractory to hormone control: consider prednisolone 10-20mg daily (seek Oncology advice).

Adverse effects

Glucose metabolism: Steroids can increase blood sugar levels. See detailed guidance on p19.

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 with Warfarin, LMWH or other agent.

Psychiatric disturbance: depression, mania, psychosis, delirium.

Change in appearance: moon face, truncal obesity, negative body image.

Musculoskeletal problems: proximal myopathy, osteoporosis, avascular bone necrosis.

Increased susceptibility to infection: especially oral/pharyngeal candidosis (examine mouth regularly).

Skin changes: thinning, bruising, acne, impaired wound healing.

Other: hypertension, oedema, pancreatitis.

Drug interactions: see BNF. **Anti-epileptics:** accelerate steroid metabolism so patients may require higher doses of steroids. **Warfarin:** steroids alter the metabolism of warfarin increasing INR. Monitor INR more regularly.

Safe use: monitoring and stopping treatment

Use the lowest effective dose for the shortest period of time. Close careful monitoring is essential.

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 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 SC dose. If recent and/or low dose prescription for appetite stimulation, discontinue. If long-term, continue at physiological dose 1mg dexamethasone base.

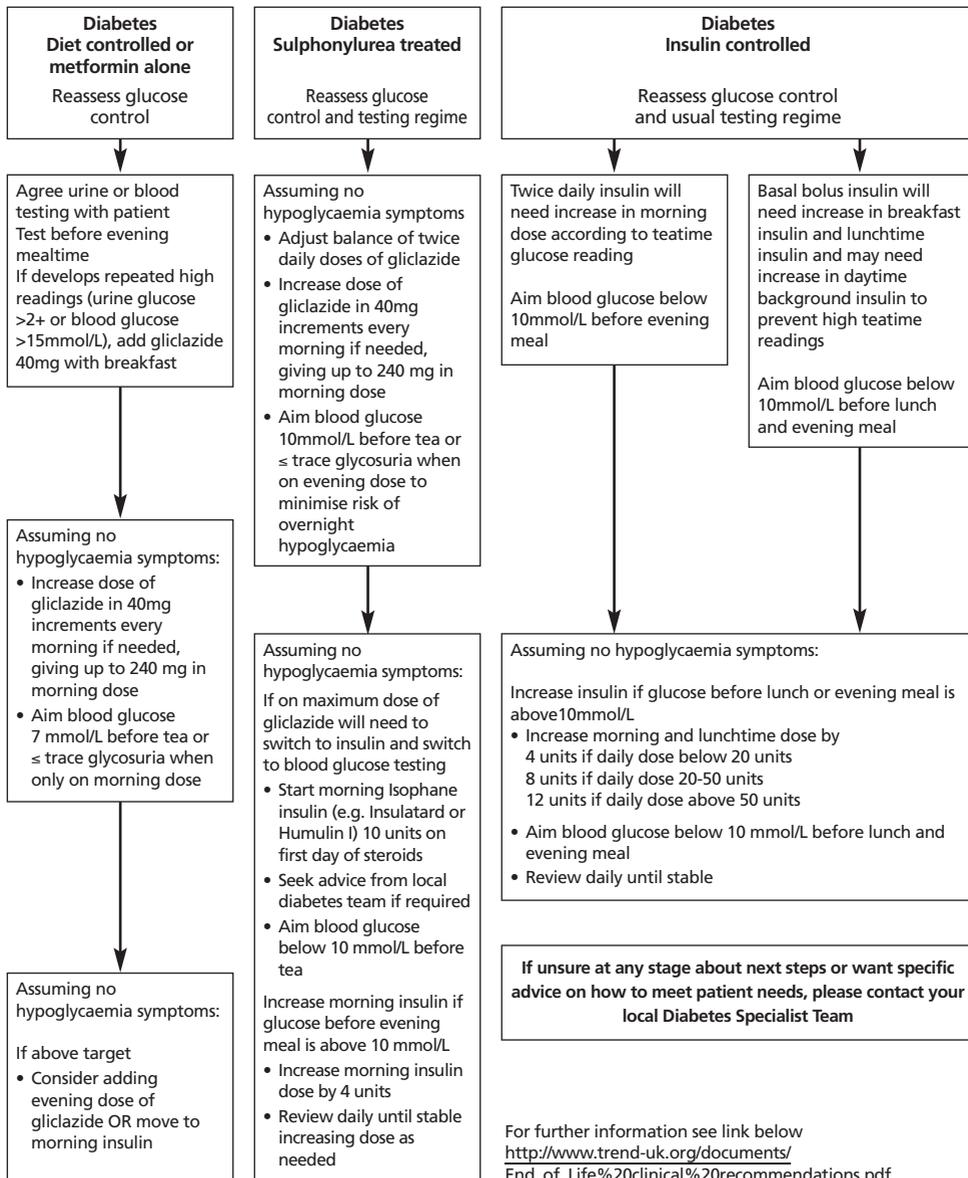
Steroid treatment card: Patients on systemic steroids for > 3 weeks must be given a steroid card.

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.

CONTROL OF GLUCOSE IN PATIENTS ON CORTICOSTEROIDS

No known diabetes

Check glucose before starting on steroids. Random capillary blood glucose over 8mmol/L needs further checking with venous blood samples for laboratory glucose to identify those at risk of new diabetes.
 Fasting laboratory glucose >6.1 OR random >7.8mmol/L means at risk of developing diabetes with steroids
 Fasting laboratory glucose ≥ 7 or random ≥ 11mmol/L needs second check to confirm pre-existing diabetes – contact Diabetes Specialist Team for advice



For further information see link below
http://www.trend-uk.org/documents/End_of_Life%20clinical%20recommendations.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 (reference at foot of page):

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
- facilitating or preventing change in place of care
- supporting oral food and fluid intake
- starting, continuing or stopping clinically assisted nutrition and/or hydration
- observations and investigations
- 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).

Document all plans - and all communication about them – 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 specialty advice if unsure)

Kidney disease: See p4 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' (p16).

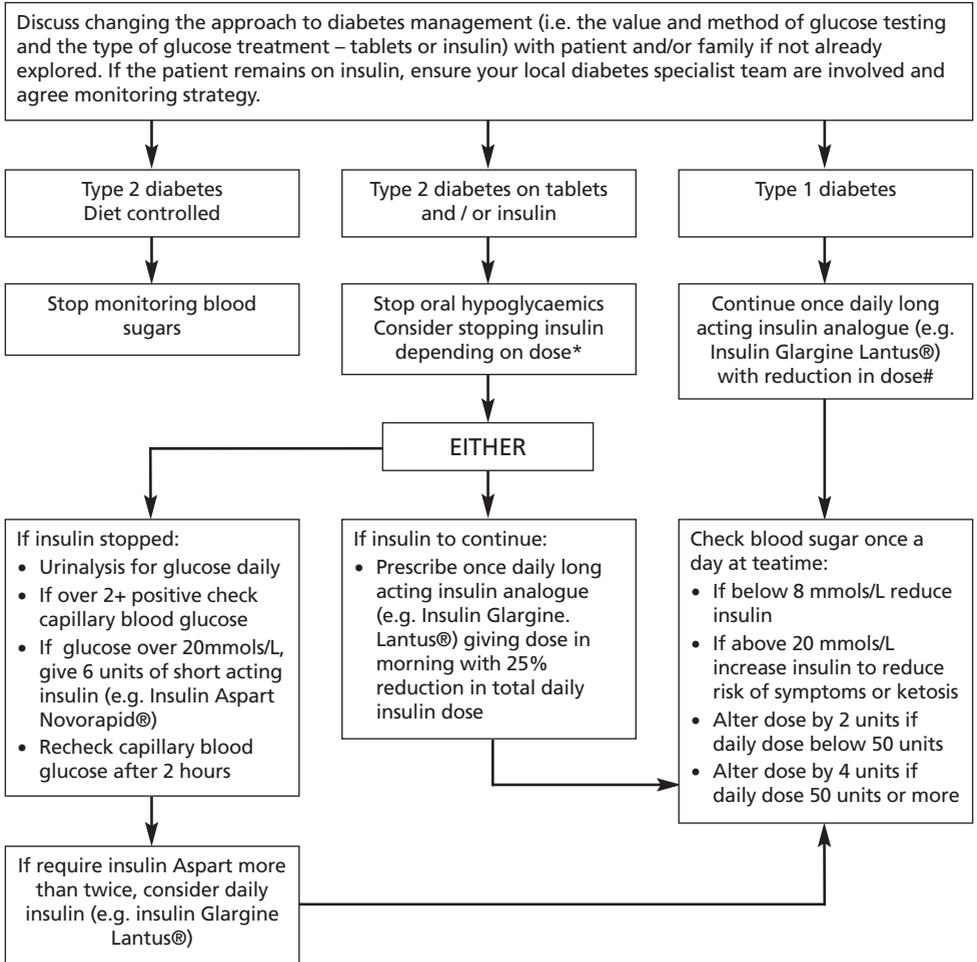
Parkinson's disease: dopamine agonist medication (e.g. levodopa) may need to be changed from oral to another route even in a dying patient unless death is expected within hours. For nausea/vomiting, use domperidone or ondansetron. Use levomepromazine cautiously. Avoid metoclopramide, haloperidol and 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. PEG in these patients – valuable route of administration; review feed/fluid need and volumes daily, reducing to balance burden/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 CG31: Care of Dying Adults in the Last Days of Life: www.nice.org.uk

DIABETES MANAGEMENT AT THE END OF LIFE



- Keep invasive tests to a minimum. It is necessary to perform some tests to ensure unpleasant symptoms do not occur due to low or high blood sugars.
- It is very difficult to identify symptoms due to hypo or hyperglycaemia in a dying patient. If observed symptoms could be due to blood glucose levels, a urine test should be performed if practical, followed by a blood glucose check if necessary.

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

Reduce insulin (e.g. Insulin Glargine Lantus®) 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 http://www.trend-uk.org/documents/End_of_Life%20clinical%20recommendations.pdf

PAIN AT THE END OF LIFE

(for acutely ill patients with rapidly deteriorating renal function, or patients with eGFR<30mL/min, consider advice on p23)

Unless specifically indicated, morphine is the injectable first-line 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 patients on morphine or oxycodone, follow guidance below. For patients on other opioids, seek advice

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

Patient on morphine or oxycodone

- Divide 24 hour total dose of regular oral opioid by 2 and prescribe this as morphine or oxycodone SC by syringe driver over 24 hrs
- 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 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 to 1-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 drive 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 hrly as required for breakthrough pain

Review regularly and adjust as above

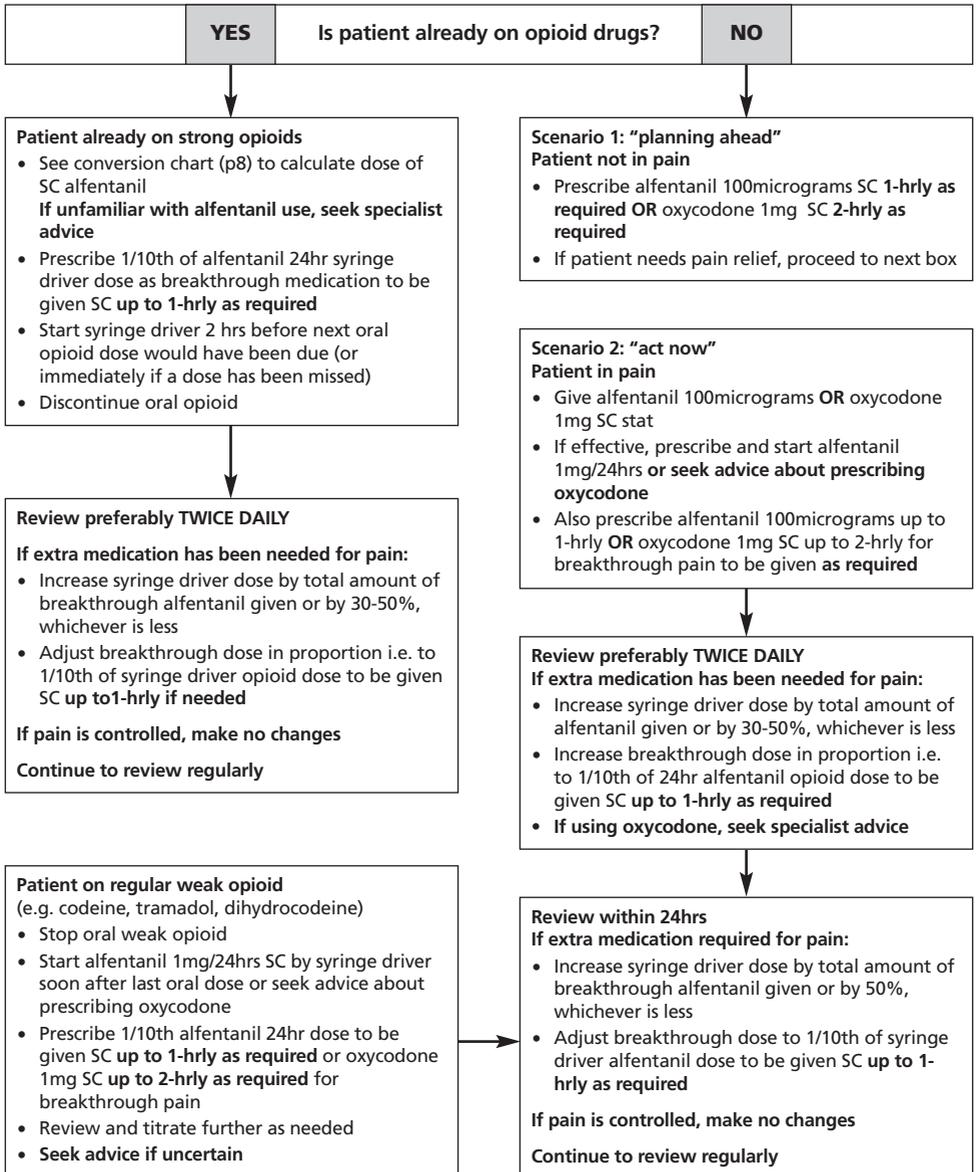
Patient with patches for pain relief (Fentanyl, Buprenorphine)

- See p7, 8 and 24 for guidance

PAIN AT THE END OF LIFE IN RENAL IMPAIRMENT

Key points

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



PAIN AT THE END 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) every 72 hours – this is sometimes forgotten.

If pain occurs, give breakthrough doses of morphine or whichever injectable opioid has been recommended by the Specialist Palliative Care Team.

Consult the chart on p8 to calculate the correct breakthrough dose.

If morphine is not appropriate, seek advice about an alternative injectable opioid.

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.

Continue to review. Do not increase dose by more than 50% (of patch and driver combined) each day.

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

IF YOU ARE IN ANY DOUBT ABOUT THESE CALCULATIONS, ASK FOR 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 $1/6^{\text{th}}$ 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 $1/10^{\text{th}}$ 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 p8 to calculate the appropriate dose. Keep the fentanyl patch in place and renew every 72hrs 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.

When 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 AT THE END 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 p9.

IN RENAL IMPAIRMENT (eGFR<10ml/min): AVOID CYCLIZINE. USE REDUCED DOSE HALOPERIDOL or LEVOMEPRMAZINE

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 24 hours**. This may require a change of drug if SC preparation not available (ie 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 develop

Prescribe cyclizine 50mg SC as required up to TDS, or haloperidol 1.5mg SC as required up to BD.
OR prescribe levomepromazine* 6.25mg (some areas prefer 2.5-5mg) SC as required up to QDS

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 50mg SC as required, maximum 150mg/24hrs

If **NO** prescribe cyclizine 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 two drugs, consider levomepromazine* prescribed as below. Some areas use levomepromazine as first line anti-emetic 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.

*Notes on levomepromazine

Levomepromazine has a broad spectrum of action.

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 p26). Where even slight sedation is an unacceptable side-effect, start at a dose of 2.5mg SC.

RESTLESSNESS, AGITATION AND/OR DELIRIUM AT THE END OF LIFE

Consider and treat common causes of restlessness: eg urinary retention, faecal impaction and pain. Support a calm environment, familiar voices and faces, gentle and usual routine.

Patients on regular or long term benzodiazepines should continue to receive a benzodiazepine. Give midazolam by SC infusion to prevent rebound agitation/withdrawal.

The doses given here are a guide. In complex situations seek specialist advice.

If patient is distressed or agitated, use midazolam.

Where there is delirium or to avoid excess sedation, use haloperidol.

Levomepromazine is an alternative for delirium, though more sedating.

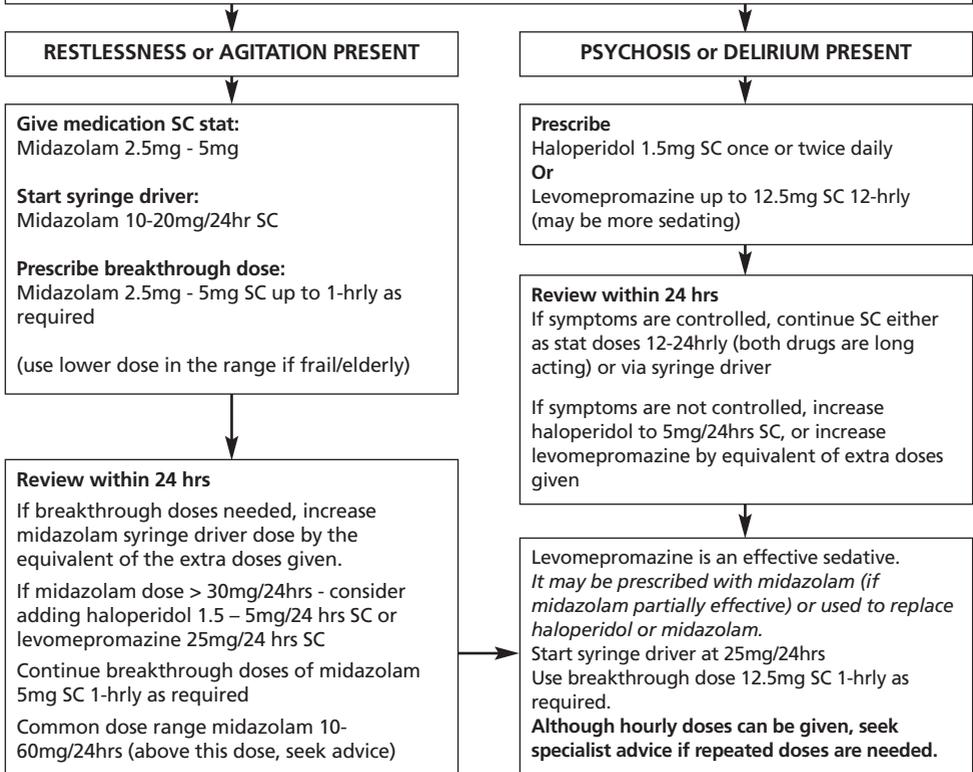
Renal failure: Midazolam is a good first choice, as toxin accumulation increases seizure risk.

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 2.5mg SC 1-hrly as required (up to QDS), or Haloperidol 1.5mg SC 1-hrly as required (up to BD)

Doses should be titrated or regular treatment prescribed as below if symptoms develop.



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 medicines. **Specialist advice should be sought.** It is vital that patients are not left in distress.

RESPIRATORY TRACT SECRETIONS AT THE END OF LIFE

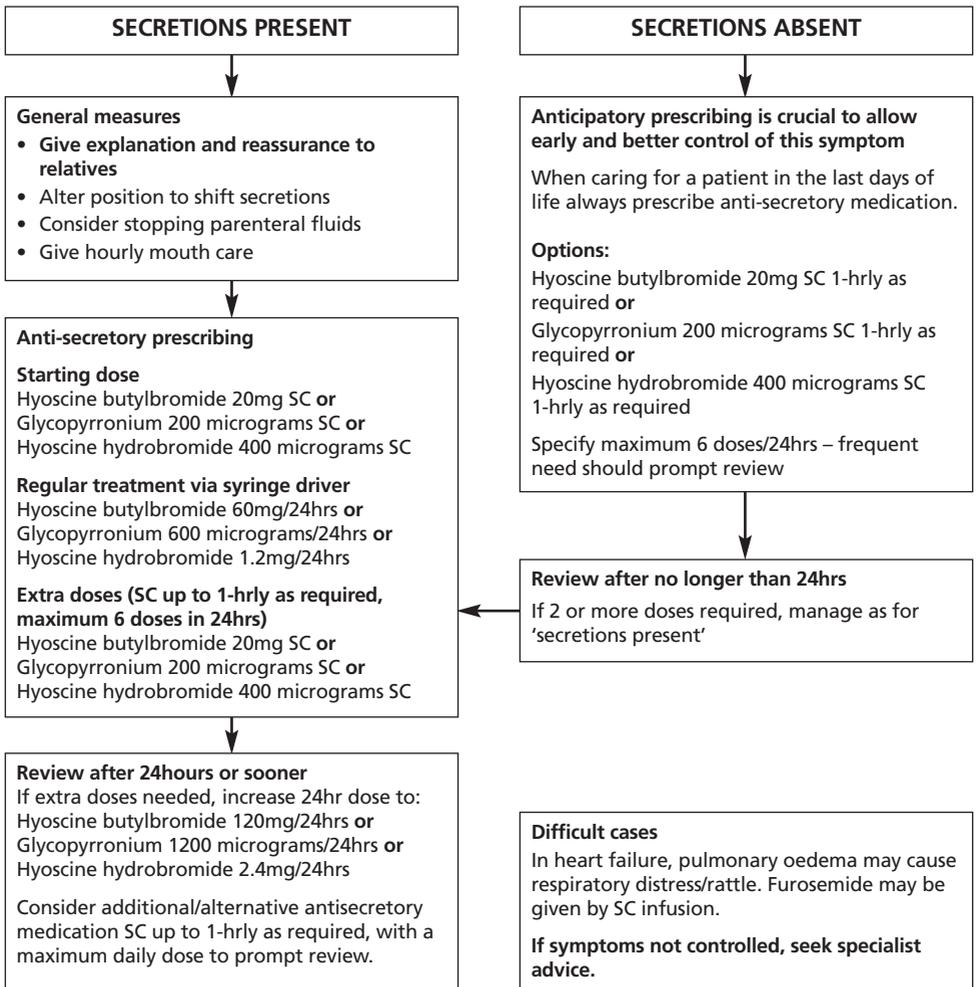
Secretions which have already accumulated will not be removed by medication. Early treatment improves the prospect of achieving symptom control.

Considerations when choosing an anti-secretory drug:

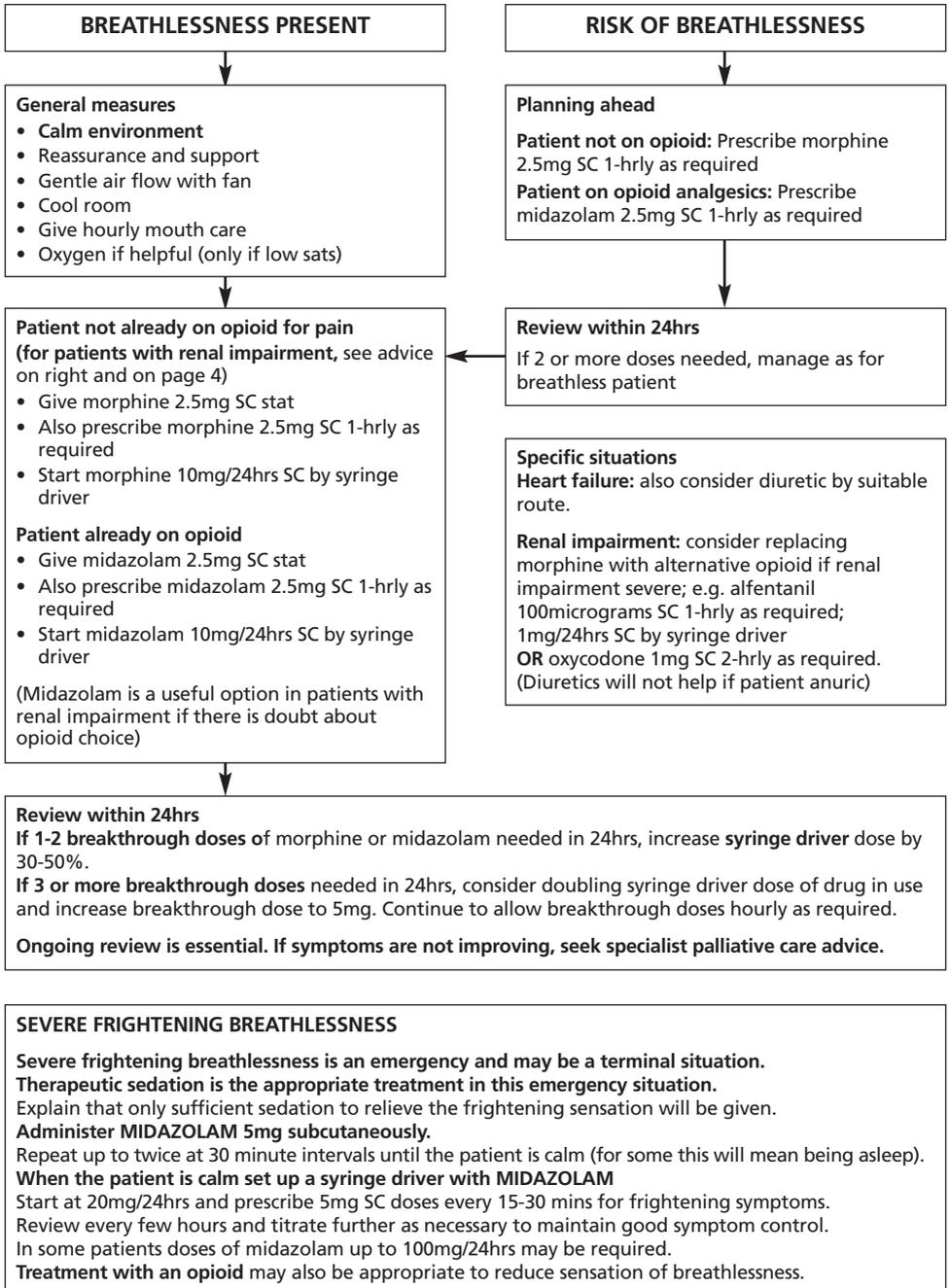
Hyoscine butylbromide and hyoscine hydrobromide are broadly similar in effectiveness, controlling secretions in up to 2/3rds of patients. Glycopyrronium is more potent and may work when a hyoscine salt has not. Hyoscine hydrobromide crosses the blood-brain barrier and may cause sedation; this may be a disadvantage and therefore a factor to influence the choice of drug.

In renal failure, use hyoscine butylbromide or half the stated glycopyrronium dose.

In cardiac disease, glycopyrronium may be preferred.



BREATHLESSNESS AT THE END OF LIFE



SYRINGE DRIVERS AND DRUG COMPATIBILITY CHART

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 <i>Diluent: water for injection</i>	DOSE		COMPATIBILITY - 2 MEDICINES	
	Per 24hrs Use conversion ratio if on regular opioids	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	5mg No upper limit (increase dose by 30-50% at a time)	2.5 - 5mg OR 1/6th (- 1/10th) of total daily dose of morphine	Cyclizine Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomopromazine Metoclopramide	Haloperidol <i>incompatible</i> at high concentrations of Haloperidol >1mg/mL Midazolam: generally regarded as <i>compatible</i> , microscopic precipitation may occur
OXYCODONE Pain / Dyspnoea	5mg No upper limit (increase dose by 30-50% at a time)	2.5 - 5mg OR 1/6th (- 1/10th) of total daily dose of oxycodone	Haloperidol Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomopromazine Metoclopramide Midazolam	Cyclizine <i>incompatible</i> at high concentrations *Cyclizine is 150mg/23mL, max Oxycodone ≤60mg Oxycodone + Cyclizine is a problematic combination, always dilute to maximum & monitor.
ALFENTANIL Pain / Dyspnoea	500micrograms No upper limit (increase dose by 30-50% at a time)	Minimum 100micrograms OR 1/10th of total daily dose of alfentanil	Haloperidol Hyoscine butylbromide Glycopyrronium Levomopromazine Metoclopramide Midazolam	Cyclizine <i>incompatible</i> at high concentrations *Cyclizine is 150mg/23mL, max Alfentanil 5.5mg *Cyclizine is 150mg/17mL, max Alfentanil 4mg Hyoscine hydrobromide <i>not known</i> , no data available
MIDAZOLAM Agitation	10mg No upper limit (Increase by 30- 50% at a time)	2.5 - 5mg	Alfentanil Haloperidol Hyoscine butylbromide Hyoscine hydrobromide Glycopyrronium Levomopromazine Metoclopramide Oxycodone	Cyclizine <i>incompatible</i> at some concentrations *Cyclizine is 200mg/23mL, max Midazolam 20mg *Cyclizine is 150mg/17mL, max Midazolam 15mg Diamorphine Morphine (see MORPHINE section)
MIDAZOLAM Seizures	> 30mg (Start at lower dose 10-20mg to avoid sedation)	5 - 10mg		
CYCLIZINE Nausea and vomiting	150mg (Always dilute as much as possible with water eg: up to 23mL for McKinley T34)	50mg	Haloperidol Hyoscine hydrobromide Morphine	Alfentanil (see ALFENTANIL section) Diamorphine Glycopyrronium <i>not known</i> , no data available Hyoscine butylbromide <i>incompatible</i> Levomopromazine <i>not recommended</i> Midazolam (see MIDAZOLAM section) Metoclopramide <i>not recommended</i> Oxycodone (see OXYCODONE section)
METOCLOPRAMIDE Nausea and vomiting	30 - 120mg (Note EMA/MHRA guidance on dose)	10mg	Alfentanil Diamorphine Glycopyrronium Haloperidol Midazolam Morphine Oxycodone	Cyclizine <i>not recommended</i> Hyoscine butylbromide <i>not recommended</i> Hyoscine hydrobromide <i>not recommended</i>

*= examples given of doses, assuming use of a McKinley T34 machine using either 17mL or 23mL (specified) as max total volume after dilution.

MEDICINE/ INDICATION <i>Diluent: water for injection</i>	DOSE		COMPATIBILITY - 2 MEDICINES	
	Per 24hrs Use conversion ratio if on regular opioids	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 0	0.5 - 5mg	0.5 - 1.5mg	Alfentanil Cyclizine Glycopyrronium Hyoscine hydrobromide	Diamorphine Levomepromazine <i>not recommended</i> Morphine (see MORPHINE section)
HALOPERIDOL Agitation	3 - 10mg	1.5mg	Hyoscine butylbromide Metoclopramide Midazolam Oxycodone	
LEVOMEPRMAZINE Nausea and vomiting	6.25 - 12.5mg	2.5 - 6.25mg	Alfentanil Diamorphine Glycopyrronium	Cyclizine <i>not recommended</i> Haloperidol <i>not recommended</i> Metoclopramide <i>not recommended</i>
LEVOMEPRMAZINE Agitation	12.5 - 200mg (Dilute high doses as much as possible)	12.5mg	Hyoscine butylbromide Hyoscine hydrobromide Midazolam Morphine Oxycodone	
HYOSCINE BUTYLBROMIDE Chest secretions / Colic pain	60 - 120mg	20mg	Alfentanil Diamorphine Haloperidol Levomepromazine Midazolam Morphine Oxycodone	Cyclizine <i>incompatible</i> Glycopyrronium <i>not recommended</i> Hyoscine Hydrobromide <i>not recommended</i> Metoclopramide <i>not recommended</i>
HYOSCINE HYDROBROMIDE Chest secretions	1.2 - 2.4mg	400 micrograms	Cyclizine Diamorphine Haloperidol Levomepromazine Midazolam Morphine Oxycodone	Alfentanil <i>not known</i> , no data available Glycopyrronium <i>not recommended</i> Hyoscine butylbromide <i>not recommended</i> Metoclopramide <i>not recommended</i>
GLYCOPYRRONIUM Chest secretions	600 micrograms – 1.2mg	200 micrograms	Alfentanil Diamorphine Haloperidol Levomepromazine Metoclopramide Midazolam Morphine Oxycodone	Cyclizine <i>not known</i> , no data available Hyoscine Hydrobromide <i>not recommended</i> Hyoscine butylbromide <i>not recommended</i>

*= examples given of doses, assuming use of a McKinley T34 machine using either 17mL or 23mL (specified) as max total volume after dilution.

Principles of medicines compatibility in a syringe driver

General points

Only mix two medicines per syringe.

- If considering using 3 or more medicines, 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 but seek specialist advice on compatibilities

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 the syringe driver.

Evidence

The information for the chart is taken from the Palliative Care Formulary 5th Edition and is based on clinical observations in palliative care services.

