PAIN & SYMPTOM CONTROL GUIDELINES

Palliative Care

Greater Manchester Strategic Clinical Network

Revised Final June 2015

Adapted for Eastern Cheshire use with permission

August 2015

GREATER MANCHESTER PAIN AND SYMPTOM CONTROL GUIDELINES 4TH EDITION (REVISED)

EASTERN CHESHIRE VERSION

This is the Eastern Cheshire version of the Greater Manchester Pain and Symptom Control Guidelines (GMCSCG), adapted for local use. The originating group of the guideline is happy to accept local adaptation. Where there is a significant change in the local advice from the original guideline, this is indicated by a footnote.

The main focus of these guidelines is the easing of pain and other symptoms in the patient with advanced cancer. Much of the symptom control advice here may be extrapolated to other terminal illnesses - with a degree of caution, bearing in mind the specific pathophysiological stresses that specific illnesses may cause.

This is a set of *guidelines* and not protocols. There are often alternative ways to manage symptoms that may be appropriate and advised by specialists.

If the situation is deteriorating, complex or the patient has problems with side effects of medication, then, unless already done so, refer to the appropriate local specialist palliative care team. Out of hours the local hospice (East Cheshire or St Luke's) can offer telephone advice – see below.

Progressive terminal illnesses are more likely with advancing age, and multiple comorbidities may be present, meaning that medication and supportive care needs review and tailoring to the individual. In particular, regular review of medication, especially in the individual on many drugs, is most important.

This guideline has been accepted by the East Cheshire Medicine Management Group, and may be accessed by the East Cheshire trust intranet; this, and much more advice help relevant to palliative and end of life care, may also be accessed via E-PAIGE (http://www.cheshire-epaige.nhs.uk/)

Further advice and support:

East Cheshire Clinical Commissioning Group area; Macclesfield DGH	*South & Vale Royal Clinical Commissioning Groups area; Leighton Hospital*
Macmillan Specialist Palliative Care Team (Mon-Fri 9-5) - Tel (01625) 663177 **Macmillan Lung Cancer Team (Mon-Fri 9-5) - Tel (01625) 661997** **East Cheshire Hospice Helpline (24 hour advice available) - Tel (01625) 666999**	**Macmillan Specialist Palliative Care Team (Mon-Fri 9-5) - Tel (01606) 544155** **St Luke's Hospice Helpline (24 hour advice available) - Tel (01606) 555489**

PAIN & SYMPTOM CONTROL GUIDELINES
4th Edition March 2015 - Revised June 2-15

[Introduction from the originating guideline]

NOTES

This is fourth edition of the Greater Manchester Strategic Clinical Network *Pain and Symptom Control Guidelines* in palliative care for multi-professional health care teams involved in prescribing, advising, and administering therapies across all care settings including primary care, hospital, hospice and nursing homes. The guidelines cover pain and symptom control in specific situations and end of life care in the management of patients with an advanced progressive illness.

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

Throughout the guidelines there are numerous recommendations to seek specialist advice. For further information or advice please contact your local Specialist Palliative Care Team, Hospital and Clinical Commissioning Group Pharmacy Service Advisers.

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Abbreviations

b.d		twice a day (bis die)
BNF		British National Formulary
caps		Capsules
CD		Controlled Drug - preparation subject to prescription requirements of the Misuse of Drugs Act (UK). (See BNF)
COPD		Chronic obstructive pulmonary disease
COX; COX2I		Cyclo-OXygenase; Cyclo-OXygenase type 2 Inhibitor
CSCI		Continuous SubCutaneous infusion
EAPC		European Association for Palliative Care
g		gram(s)
h; hrly		hour(s); hourly
i/m		Intramuscular
i/r		Instant release
i/v		Intravenous
L		Litre(s)
microgram		not abbreviated
mg		milligram
ml		millilitre
min		minute(s)
mmol		millimoles
m/r		modified release (used interchangeably with controlled release)
nocte		at night
LTOT		Long Term Oxygen Therapy
NSAID		Non - Steroidal Anti-Inflammatory drug
o.d		once a day
p.o		by mouth
PPI		proton pump inhibitor
p.r		by rectum
p.r.n.		when required
q4h; q.d.s		Every 4 hours; four times a day
®		Trade mark
SC		SubCutaneous
SL		SubLingual
SNRI		Serotonin-Noradrenaline Reuptake Inhibitor
SSRI		Selective Serotonin Reuptake Inhibitor
SPC		Summary of Product Characteristics. See www.medicines.org.uk/emc/
Stat		Abbreviation of “Statim”, Latin for “immediately”
TD		transdermal
t.d.s		three times a day
TENS		Transcutaneous electrical nerve stimulation
PENS		Percutaneous electrical nerve stimulation
UK		United Kingdom
UTI		urinary tract infection
WFI		water for injection
WHO		World Health Organization
≈		Is approximately equivalent to

Glossary

Breakthrough pain	Includes incident pain
Breakthrough pain relief	Also known as rescue dose
Immediate release	Also known as “short acting”
(Strong) opioid naive	Not previously having taken (strong) opioids

PAIN MANAGEMENT

1. Pain assessment

- Therapy must be tailored to each patient. Use a logical, stepwise approach.
- Consider: physical aspects
  functional aspects – effects on activities of daily living
  psychosocial aspects – mood / relationship effects / sleep etc
  spiritual aspects – fears / hopelessness / regrets / guilt

Assess and record physical aspects of the pain:

- cause of *each* pain - there may be more than one (in 66% of cases)
  - there may be a non-cancer related pain
- character, location, frequency, relieving and aggravating factors (see Table1)
- response to previous medication and treatment.
- severity, by asking the patient (if able to respond); e.g.
  - use of numerical score where 0 = no pain and 10 = severe, overwhelming
  - simple verbal rating “none”, “mild”, “moderate” or “severe”

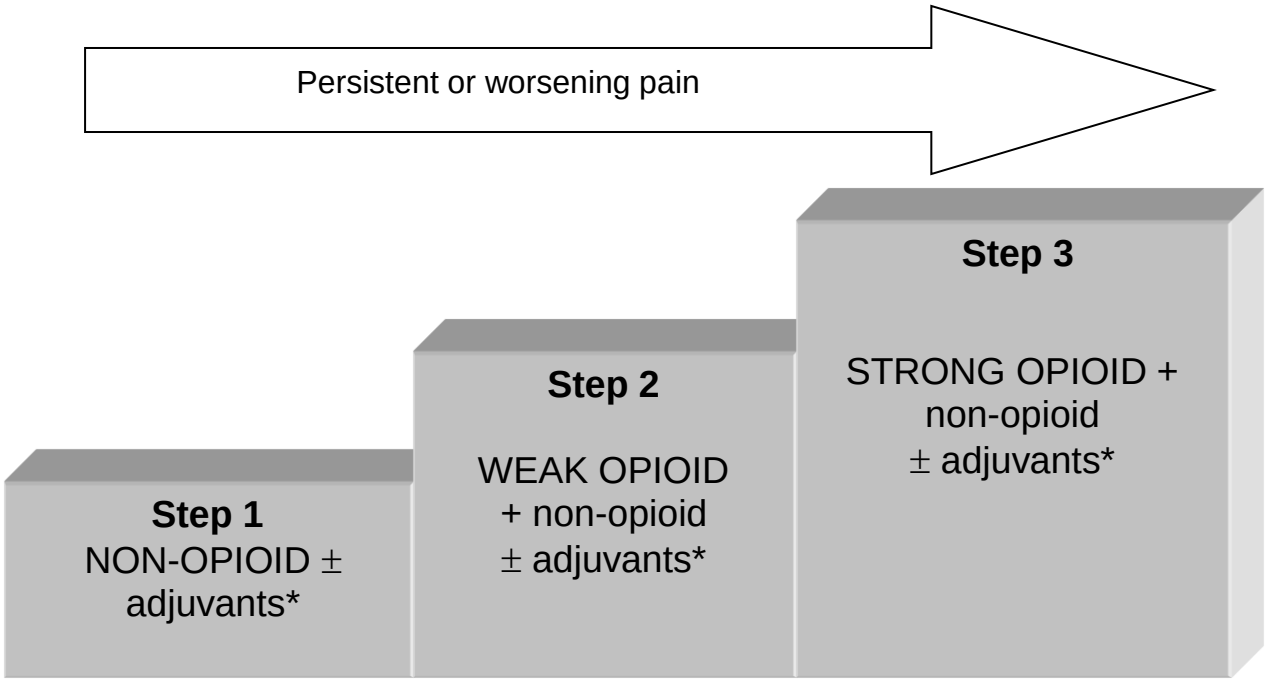
Table 1- Common Pain Types

Pain	Examples	Character	Initial manage-ment	Adjuvants	Consider
Deep somatic	Bone metastases	Gnawing, aching. Worse on moving or weight bearing.	WHO Ladder	NSAIDs gabapentin	Radiotherapy; surgery; bisphosphonate
Visceral	Liver, lung, bowel	Sharp ache *or* deep, throbbing. Worse on bending or breathing.	WHO Ladder	Corticosteroid NSAIDs	Nerve Block; Surgery
Neuro-pathic	Nerve Com-pression; Nerve damage; Bone metastases	Burning, shooting; sensory disturbance in affected area	WHO Ladder	Tricyclic antidepressant e.g. amitriptyline Anti-epileptic e.g. gabapentin/ pregabalin. SNRI - e.g. duloxetine Corticosteroid	Radiotherapy; TENS / PENS; Nerve block; Topical capsaicin
Smooth muscle spasm	Bowel obstruction; Bladder spasm	Deep, twisting, colicky (waves)	May respond to opioid - variable	Anticholinergic - e.g. hyoscine butylbromide for bowel colic	Surgical relief of obstruction

2. The WHO Analgesic Ladder

NOTE: MORPHINE IS STILL THE FIRST LINE STRONG OPIOID AT STEP 3 OF WHO LADDER (1996) AND EAPC GUIDELINES (2012)

Figure 1



Assess pain

- For *mild* pain start at step 1
- For *moderate* pain start at step 2
- For *moderate to severe* pain, start at step 3. If in doubt, give drug from step 2 and assess after 30-40 minutes.

By the clock – analgesics should be prescribed regularly in addition to breakthrough analgesia prescribed p.r.n.
By the mouth – the oral route is preferred for all steps of the ladder
By the ladder
Adjuvants - contribute to pain relief and can be used alone or in conjunction with analgesics (see Table 11.). They can be introduced at any step in the analgesic ladder.

Table 2 - Example of the use of the WHO analgesic ladder
Patient on no analgesics – mild pain:

Step 1	Start **regular** paracetamol 1g q.d.s
Step 2	Persistent or worsening pain - add codeine 30-60mg q.d.s. **regularly.**
Step 3	On maximum paracetamol and codeine, persistent or worsening pain - stop weak opioid and commence strong opioid e.g. morphine (see below)

** Adjuvants = adjuvant analgesic drugs – see section 9, table 11*

WHO ladder Step 2 - Weak Opioids

i. Codeine - in most people, about 10% is converted to morphine – BUT there is wide inter-individual variation.
   - "Slow metabolisers" produce little or no morphine, and obtain little or no pain relief from codeine. They act as if opioid naive when converting to Step 3
   - "Ultra- rapid metabolisers" produce greater than usual amounts of morphine which can lead to opioid toxicity.
   - Good Practice when titrating to a strong opioid is to prescribe small initial doses of morphine to account for this.

ii. Tramadol is an alternative weak opioid at Step 2. Tramadol 50mg is approximately equivalent to 5mg of oral morphine (see Table 42). The effect of tramadol may be *reduced* by concurrent use of ondansetron.

Pain Relief – General points

- Set realistic goals and steps - e.g. pain-free overnight; at rest; on movement.
- Give patients and carers information and instructions about their pain and pain management. Encourage them to take an active role in their pain management.
- Review pain control regularly.

WHO ladder Step 3 – Strong Opioids

Morphine

- Explanation and reassurance about morphine is essential to patients and carers.
- Explanation should include information about indications and side effects, and that patients will not become addicted
- Be aware of dose conversions from weak opioids to oral morphine (see Table 42)
- In elderly or frail patients, start with immediate release morphine, using small doses and longer "as required" dosage intervals (e.g. 4 hourly)
- Prescribe initially either:
  - regular morphine instant release (i/r – liquid or tablets) 2.5mg – 5mg 4 hourly and 2[a] hourly p.r.n for breakthrough pain *OR*
  - morphine m/r 10mg b.d. and morphine 2.5mg – 5mg 2-hourly p.r.n [a]
- If p.r.n. doses are needed more than 4 hourly SEEK SPECIALIST ADVICE.
- Check with the patient whether morphine is effective before increasing the dose.
- Titrate the morphine dose to achieve analgesia and minimum side effects using incremental steps of not more than 33-50%; e.g. 5 → 10 → 15 → 20 → 30 → 40mg 4 hourly morphine i/r or 10 →15 →20 →30 →40mg morphine m/r b.d. Adjust the breakthrough dose at each step.
- If commenced on regular immediate release (i/r) morphine, once pain control is achieved, consider conversion to modified release (m/r) morphine at same 24h total dose
- ALWAYS prescribe a morphine i/r breakthrough dose when prescribing regular morphine.
- Always consider prescribing laxatives alongside strong opioids. Most need this.

[a] Original Manchester document suggests 4hourly – however, this leaves insufficient time between regular doses if given 4 hourly; in normal renal function, 4 hours is too long an interval during morphine titration too enable reasonable pain control

Table 3 - Morphine preparations and recommended frequency

Generic morphine	Morphine brand names	Dose intervals
Immediate release morphin (liquid and tablets)	e.g. Oramorph®, Sevredol® Generic preparations are available	4 hourly
Modified release morphine (12 hourly preparations)	e.g. Zomorph®, MST®, Morphgesic SR®	12 hourly (b.d.)
Modified release morphine (24 hourly preparation)	e.g. MXL capsules	24 hourly (o.d.)

Breakthrough pain

Table 4 - Management of breakthrough pain (pain occurring before the next regular dose of opioid)

Type of breakthrough pain	Example	Suggested action
Incident pain	Pain free at rest, but pain occurs on movement, weight bearing, and procedures such as dressing changes.	Exclude a surgically correctable lesion, e.g. bone fracture. Give equivalent of 4 hourly dose of immediate release strong opioid 30 minutes before procedure. SEEK SPECIALIST ADVICE if considering use of trans-mucosal fentanyl preparations.
Spontaneous bouts of pain	No predictable or precipitating factors	Give equivalent of 4 hourly dose of immediate release strong opioid. SEEK SPECIALIST ADVICE if considering use of trans-mucosal fentanyl preparations.

Recommended management of breakthrough pain

- An immediate release strong opioid should be prescribed p.r.n. (4 hourly) at about 1/10th to 1/6th of the total daily regular dose
- The p.r.n dose should be increased as regular dosing is increased.
- The need for 2 or more p.r.n. doses per day should prompt a pain review.

Note that the recommendations within this document are a guide only. Individual variability needs to be taken in to account – such as the patient's age, weight, renal function and co-morbidities

For the purpose of this guide breakthrough pain analgesia will be calculated as a 1/6 of the regular 24 hour dose of strong opioid.

Example-

Morphine m/r capsules (e.g. Zomorph®) 30mg b.d. - the p.r.n dose = 60/6 = morphine i/r 10mg p.r.n 4 hourly

When the oral route is not available

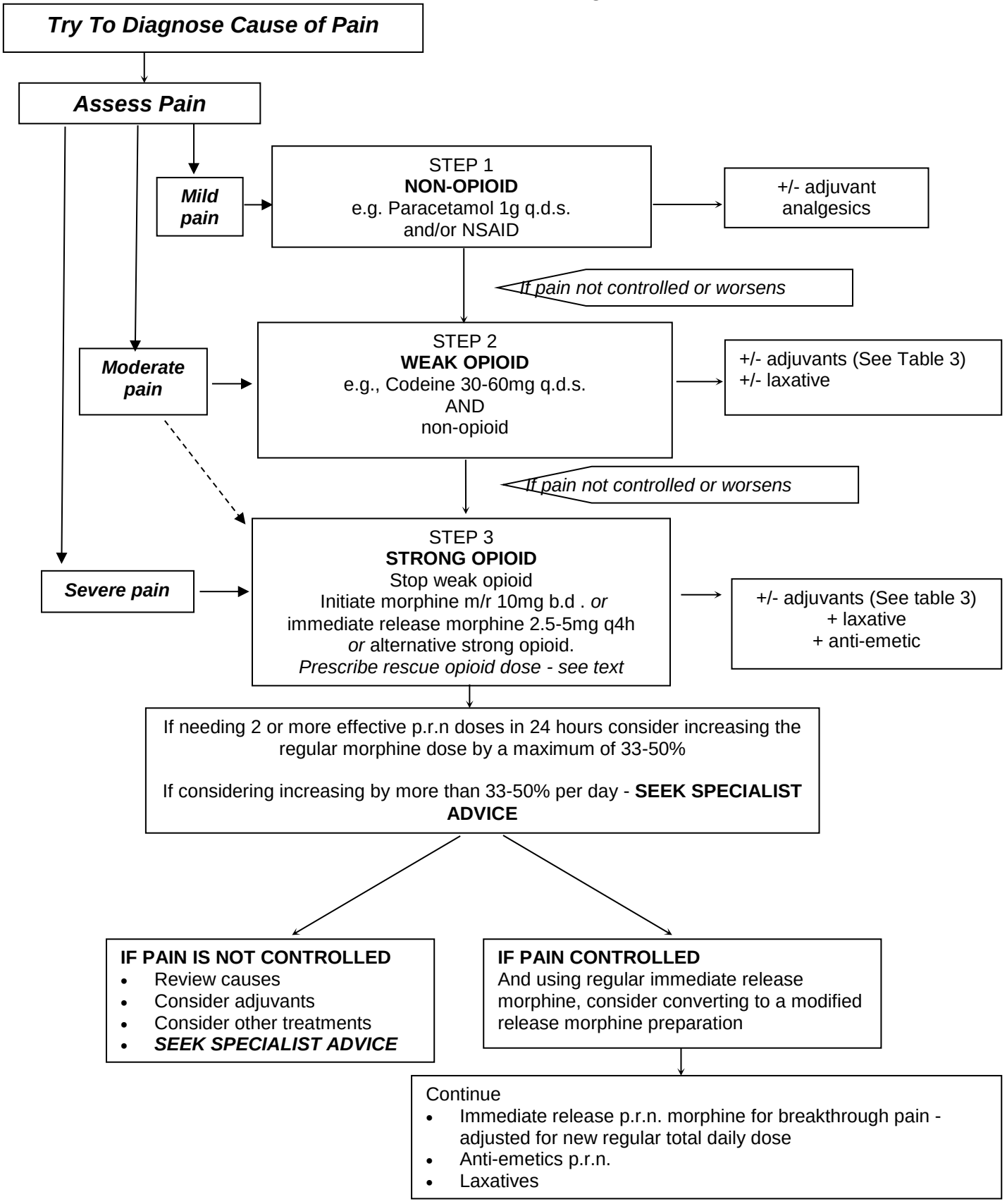
- Prescribe diamorphine[b] as regular 4 hourly SC injections *or* as a 24 hour continuous infusion via a syringe pump. ***Dose equivalents:*** **Oral morphine 3mg ≈ SC diamorphine 1mg**
- Breakthrough doses of 1/6th of the regular 24 hour dose of opioid should be prescribed 4 hourly SC p.r.n.
- See Table 43 for strong opioid conversion tables
- Opioid naive patients should be observed for at least ONE HOUR following the administration of the first dose of diamorphine injection (or morphine if used)

Table 5 - End of dose failure

Example	Suggested action
If taking morphine m/r capsules e.g. Zomorph, analgesia wears off after 10 hours, only requiring p.r.n analgesia in the 2 hours before next dose is due.	Increase morphine m/r dose based on p.r.n doses used. Do not increase regular dose by more than 30-50%. Continue with a 12 hourly dosage regime.
Fentanyl patches work well for 2 days but p.r.n. doses are used on the third day. This pattern of p.r.n use repeats itself.	The patient may be a fast metaboliser of fentanyl. Keep the fentanyl patch dose the same but change the patch every 48 hours – SEEK SPECIALIST ADVICE.

[b] In many other localities morphine may be used as the injectable strong opioid of choice. *Dose equivalents:* Oral morphine 3mg ≈ SC morphine 1.5mg ≈ SC diamorphine 1mg. The only advantages of diamorphine are that is more soluble, so the risk of crystallization in the syringe is less likely with high doses; also when high dose p.r.n injections are need, smaller volumes may be used.

3. Treatment Guidelines for Cancer Pain - Figure 2



Note: Adjuvant analgesics can be added on any step of the ladder.

4. Alternative Strong Opioids

- Morphine is the first line strong opioid
- Rationale for using alternative strong opioids:
  - Different pattern and severity of side-effects
  - Renal impairment leading to accumulation of drug/metabolites (especially codeine, morphine and diamorphine) causing side-effects/toxicity
  - Non-availability of oral route.

Equivalent dosage

- When switching from one opioid to another, an equivalent dose can be calculated by knowing the relative potency of the two drugs (Tables 45 and 47).
- *However*, this conversion is *only an approximation* as wide variations exist between individuals.
- Especially when converting high doses, the initial calculated equivalent dose may have to be reduced by 25-50% to avoid undesirable side-effects or toxicity.

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

Buprenorphine

- Buprenorphine has both opioid agonist and antagonist properties.
- Only transdermal preparations are recommended for routine use in chronic cancer pain.

Place in therapy

- Transdermal buprenorphine should not be used for acute or intermittent pain or when rapid dose titration is required
- It may be indicated where there are:
  - Intolerable undesirable effects with morphine
  - Renal failure
  - Tablet phobia or poor compliance with oral medication.

Dosing

Several preparations of transdermal buprenorphine are available varying in potency and length of action.

- A 7 day patch (BuTrans®) (5, 10 & 20 micrograms/h) is licensed for non-malignant pain of moderate intensity unresponsive to non-opioid analgesics. It is considered a WHO ladder Step 2 analgesic (see Table 2).
  - The same application site must not be used for at least three weeks.
- A 4 day patch (Transtec®) and a 3 day patch (Hapoctasin®) are available as 35, 52.5 & 70 micrograms/h, licensed for moderate to severe cancer pain and severe pain unresponsive to non-opioid analgesics. They are WHO ladder Step 3 analgesics (See Table 2).
  - Patients should have been titrated with a strong opioid prior to starting higher dose buprenorphine
  - The same application site must not be used for 1 week.
- Immediate release morphine or oxycodone can be used for the management of breakthrough pain (see conversion Table 44)

Fentanyl

- Similar analgesic properties to morphine.
- Constipation is less severe than with other strong opioids
- Better tolerated in renal impairment
- Available as transdermal patches.
- Other formulations are available e.g. trans-mucosal and parenteral preparations. Prescribe according to local formularies. SEEK SPECIALIST ADVICE.

Fentanyl transdermal patches

Place in therapy

- Not suitable for acute pain or rapidly changing pain because of the time it takes to reach therapeutic levels (12 – 24 h).
- Should be used only for chronic stable pain.
- Patient should have been taking an equivalent dose of strong opioid previously.

- **At least one of the following should apply:**
    - Unacceptable level of side effects with morphine or alternative opioid.
    - Oral route is inappropriate, e.g. dysphagia, vomiting
    - Patient with renal impairment
    - Patient with resistant morphine-induced constipation
    - Where use may improve compliance (e.g. unwilling to take morphine)

Dosing

- Available as 12, 25, (37.5), 50, 75, 100 micrograms/h patches.
    - *Note: 37.5 microgram/h strength is not available in all brands*
- The12 microgram/h patch is approximately equivalent to oral morphine 30-45mg /24 h.
- Consider buprenorphine patches as an alternative in strong opioid naïve patients.
- Patients that are converting from a weak opioid to fentanyl patches should start on 12 microgram/h fentanyl patch
- Use Table 45 to decide on a safe starting dose of fentanyl patch in relation to duration and dose of previous opioid.
- Change patch every 72 hours
- On removal significant blood concentrations of fentanyl persist for at least 24 hours. Therefore do not start an alternative long acting opioid medication for at least 12 hours.
- If any of the following apply then SEEK SPECIALIST ADVICE:
    - Ineffective pain relief
    - Rapid dose escalation of fentanyl patch
    - Dose exceeds fentanyl patch 100 micrograms/h

Table 6 - To convert from strong opioid regimens to fentanyl patches

1.	Immediate release strong opioid (e.g. morphine, oxycodone or hydromorphone)	Apply patch – continue regular q4h immediate release strong opioid for first 12h until fentanyl reaches therapeutic level. See conversion chart (tables 46 and 47, p74-6) for appropriate immediate release breakthrough dose & prescribe it 2 hourly p.r.n
2.	Twice daily strong opioid (e.g. Zomorph)	Apply patch with last dose of twice daily strong opioid and prescribe immediate release strong opioid for 'breakthrough' pain 2 hourly p.r.n
3.	Once daily strong opioid (e.g. MXL)	Apply patch 12h after last dose of once daily strong opioid and prescribe immediate release strong opioid for 'breakthrough' pain 2 hourly p.r.n
4.	24 hour SC syringe pump	Apply patch; discontinue syringe pump after 8-12h (morphine infusion). Prescribe strong opioid SC injection for 'breakthrough' pain 2 hourly p.r.n (see page 46)

- Approximately 10% of patients previously taking regular morphine may experience withdrawal symptoms after changing to fentanyl giving symptoms of shivering, restlessness and bowel cramps.
- Pain control is not affected and the symptoms can be managed initially with breakthrough doses of immediate release strong opioid. **SEEK SPECIALIST ADVICE**
- Fentanyl causes less constipation than morphine or oxycodone. If a switch to fentanyl is made, and laxatives have been controlling constipation, then halve the dose of laxatives and adjust according to need.

Management of breakthrough pain for patients on fentanyl patches.
Use Tables 45 and 46 to decide on an appropriate breakthrough dose of strong opioid for patients on fentanyl patches.

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

- It is usual practice to leave the fentanyl patch in place in the management of patients in the last days and hours of life – see Appendix 1 and **SEEK SPECIALIST ADVICE**

<u>Fentanyl trans-mucosal preparations</u>

- There are several rapidly acting fentanyl preparations, designed either for buccal or sublingual use, or as transmucosal nasal sprays.
- Their onset of action is between 10 and 30 minutes and maximum duration of analgesic effect is approximately one hour
- These products are expensive.
- Prescribers should be aware of the potential for fentanyl to be abused
- Prescribe according to local guidelines and **on specialist advice only**.
- They should **only** be used in patients who are:
    - on regular strong opioids, for chronic cancer pain, for at least a week at a dose equivalent to morphine 60mg/24 h orally
    - able to follow instructions regarding indication, administration and storage

Place in therapy

- Spontaneous, unpredictable, fast onset and short duration pain in patients who are already receiving and tolerant to opioids for cancer pain e.g. morphine, oxycodone, hydromorphone and fentanyl patches
- There is no direct dose equivalence with other opioids, including transdermal fentanyl, so they need separate titration.
- The formulations of trans-mucosal fentanyl preparations are not bioequivalent and so are not inter-changeable

Oxycodone

- Oxycodone is a strong opioid with similar properties to morphine.
- It is licensed for moderate to severe pain in patients with cancer and post-operative pain and for the treatment of severe pain requiring the use of a strong opioid.

Place in therapy

- Tolerance to morphine or unacceptable level of side effects with oral morphine
- Breakthrough medication for patients using fentanyl or buprenorphine patches but intolerant of morphine.
- A systematic review comparing efficacy and tolerability of oxycodone versus other opioids found no difference in the undesirable effect profile between oxycodone and either morphine or hydromorphone .

Dosing

- Preparations available- there are immediate release and modified release oral products available.
- Oral solution and concentrated oral solution are available.
- See current BNF.

Table 7 – Oxycodone products

Generic oxycodone	Oxycodone brand names	Dose intervals
Immediate release oral oxycodone (5mg/5ml liquid; 10mg/1ml concentrated liquid; and 5mg, 10mg & 20mg capsules)	e.g. OxyNorm®, Lynlor® Generic preparations are available	4-6 hourly regular dose; 2 hourly p.r.n. dose
Modified release oral oxycodor (12 hourly preparations 5mg,10mg,20mg,40mg, 80mg and 120mg)	e.g. OxyContin®, LongTec®	12 hourly (b.d.)
Parenteral oxycodone (10mg/1ml - 1ml & 2ml ampoules). (50mg/1ml as 1ml ampoules)	e.g. OxyNorm® injection	2 hourly breakthrough dose or over 24 hours subcutaneously via syringe pump (CSCI)

- If strong opioid naive, use regular oral immediate release liquid 1mg- 2.5mg 4 hourly or m/r tablets 5mg b.d. with an appropriate breakthrough dose (see conversion table 47) and titrate.
- Oxycodone is approximately twice as potent as morphine when given orally (e.g. 10mg oral oxycodone is equivalent to 20mg oral morphine)
- If switching from an alternative strong opioid to oxycodone consult the conversion tables Appendix 2 for advice.
- Immediate release oxycodone should be prescribed p.r.n (4 hourly) at 1/10th-1/6th of the total daily regular dose. The p.r.n dose should be increased as regular dosing is increased. The use of 2 or more p.r.n doses per day should prompt a pain review.
- *Example - oxycodone m/r tablets 45mg b.d, p.r.n dose = 90/6 = 15mg p.r.n 4 hourly (this is using the 1/6th factor as used in the conversion tables)*

Hydromorphone - *infrequently used in Cheshire*

Hydromorphone is a strong opioid, licensed for the relief of severe pain in cancer.

- it is metabolised in the liver; metabolites can accumulate in renal impairment.

Place in therapy

- Patient intolerant of morphine or experiencing unacceptable level of side effects with oral morphine, particularly sedation / hallucinations.
- Breakthrough medication for patients using fentanyl patches but intolerant of morphine.

Dosing

Available as i/r or m/r (12 hrly capsules). Either may be swallowed whole or opened and sprinkled on cold soft food (not suitable via feeding tubes).

- If strong opioid naïve , prescribe immediate release 1.3mg four hourly *or* modified release 2mg b.d with appropriate breakthrough dose and titrate.
- If already on strong opioid convert dose according to conversion table.
- Analgesic potency ratio of oral morphine to oral hydromorphone is 5-10:1 (average of 7.5:1); e.g. 10mg oral morphine is approximately equivalent to 1.3mg oral hydromorphone .
- Consider dose reduction in the elderly.

Recommended management of breakthrough pain

- Prescribe i/r hydromorphone capsule p.r.n (4 hourly) at 1/10th-1/6th of the total daily regular dose. Increase the p.r.n dose as regular dosing is increased. The use of 2 or more p.r.n doses per day should prompt a pain review.
  Example- Hydromorphone m/r capsules 12 mg b.d - p.r.n dose = 24 /6 = 3.9mg p.r.n 4 hourly (using 1/6th factor from conversion tables & the closest i/r capsule strength).

Methadone

Pharmacology of methadone is complex and its use as an alternative strong opioid should be under ***specialist supervision***, preferably as an inpatient.

Tapentadol

- Tapentadol is a centrally acting analgesic which is both a mu opioid agonist and an inhibitor of synaptic reuptake of noradrenaline.
- It is licensed for moderate-severe acute pain which can be managed only with opioid analgesics. It can be used off licence for severe chronic pain.
- It should only be used under specialist supervision,

6. Opioids in Renal Impairment (see Table 8)

Opioid naïve patients and patients taking regular weak opioids:

- SEEK SPECIALIST ADVICE if the patient has impaired renal function, i.e. eGFR < 50ml / min.

Patients already established on strong opioids

- Accumulation of opioid or active metabolite will lead to prolonged duration of action and increased toxicity – SEEK SPECIALIST ADVICE.
- Therefore for patients with renal impairment:
  - Optimise the use of adjuvants to reduce need for opioid.
  - Opioid dosage may need to be reduced.
  - Consider increasing intervals between opioid doses
  - Monitor closely for toxicity.

Table 8 - Recommended dose reductions for strong opioids in renal impairment

	Dose in renal impairment eGFR (ml/min)			
Drug	eGFR 20 - 50	eGFR 10 -20	eGFR < 10	Comments
Morphine	75% of normal dose	Use reduced doses 50% of dose, (2.5mg – 5mg) extended dosage intervals (6-8 hrly)	Use reduced doses 50% (1.25-2.5mg) extended dosage intervals	Active metabolites. Titrate to response.
Oxycodone	75% of normal dose	75% of normal dose	50% of normal dose.	Active metabolites can accumulate. Has been used in CKD 5 patients. Start with low dose and titrate to response.
Fentanyl Patches	75% of normal dose	75% of normal dose	50% of normal dose.	No active metabolite. Possible accumulation of parent drug. Titrate to response.
Hydromorphone	Dose as in normal renal function	Reduce dose – start low and titrate	Reduce dose – start low and titrate	Active metabolite

- Note: Some centres use alfentanil and fentanyl subcutaneously in severe renal failure. **ONLY with specialist advice.**

7. Management of Opioid Side Effects

If side effects are intractable and reducing the quality of life or limiting analgesic titration, consider changing to an alternative opioid, **SEEK SPECIALIST ADVICE**.
Consider renal impairment as cause, if toxicity occurs on previously tolerated dose.

- *Constipation* (very common) – prevent by prescribing concurrent stimulant laxative ± softener and titrate
- *Nausea and vomiting* (occurs in 30%) – prescribe p.r.n. antiemetic (see Nausea and Vomiting section) or a regular dose for 5 days (e.g. haloperidol 500 micrograms to 3mg at night; metoclopramide 10mg t.d.s) then stop if asymptomatic
- *Drowsiness* - warn that drowsiness and poor concentration may occur at start of therapy, and when dose is increased, but usually reduces after a few days
- *Delirium* - decrease dose if possible; consider adjuvant drug or alternative opioid; consider haloperidol 1.5 - 3mg orally or subcutaneously – (see Delirium section of guidance.)
- *Myoclonus* - decrease dose if possible; if this dose of opioid is essential use SC midazolam 2.5mg 4h p.r.n or clonazepam oral at night (see BNF, start with lowest dose)
- *Hallucinations* – may occur without delirium, usually visual; decrease dose if possible; consider adjuvant drug or alternative opioid
- *Dry mouth* (nearly all patients) - inform patient and advise good oral hygiene (see Oral Care section of guidance.)
- *Respiratory depression* - unlikely if opioids used and monitored correctly. See use of naloxone below

8. Naloxone – for reversal of respiratory depression caused by prescribed therapeutic opioids

- Clinical circumstances will vary. Therefore the following is a guide to naloxone use alongside an individual's professional clinical judgement – SEEK SPECIALIST ADVICE if needed
- The respiratory rate of the patient should be an important deciding factor as to whether naloxone is indicated. (See Table 9)
- **In patients receiving opioids for pain relief, naloxone should not be used for drowsiness and / or delirium <u>which is not life threatening,</u> because of the danger of reversing the opioid analgesia, precipitating a major physical withdrawal syndrome including severe increase in pain.**
- Pinpoint pupils can occur at any time in patients taking opioids. It is NOT an indication of opioid toxicity by itself

Table 9 - Management of respiratory depression with naloxone

Respiratory rate (RR) (breaths / min) and associated Conscious level and/ or cyanosis			Advice	Consider
RR ≥ 8	AND	Easily rousable and Oxygen saturations (SaO2) at baseline level	Monitor respiratory rate and SaO2 Watch and wait	Omitting or reducing the next regular dose
RR < 8	AND/OR	Comatose or unconscious and/ or cyanosed	Assess Airway/ Breathing/ Circulation **Give naloxone (see below)**	Rate of deterioration should inform dose. (option 1 or 2) Restart lower dose of regular opioid once conscious level has maintained improvement and respiratory rate satisfactory
If the combination of parameters of Respiratory Rate, conscious level or SaO_2 are not covered by advice above, then **use clinical judgement** – SEEK SPECIALIST ADVICE				

- Administration of naloxone is for reversal of <u>respiratory depression</u> caused by the medicinal use of opioids.
- Titrate the dose of naloxone against <u>respiratory function</u> and NOT the level of consciousness
- Caution: Total antagonism leading to severe pain and agitation is likely if a standard 400microgram naloxone ampoule is used.
- Therefore a reduced dose of naloxone is recommended. The dose regime (option 1 or 2) used will depend on clinical judgement and the rate of deterioration of respiratory function.

Option 1 – If respiratory rate and consciousness levels decreasing rapidly

- Administer naloxone 100 – 200micrograms IV stat.
- Administer repeated doses of 100 micrograms every 2 mins until the respiratory rate is satisfactory.(> 8 breaths/min).

Option 2 – if respiratory rate and consciousness levels decreasing at a slower rate.

- Dilute a standard 1ml ampoule of naloxone 400microgram /ml to 10ml with 0.9% sodium chloride for injection.
- Administer 0.5ml (20 microgram) IV every 2 mins until the respiratory rate is satisfactory (> 8 breaths / min).

- Titrate the dose of naloxone against respiratory function and not the level of consciousness.
- Naloxone is best given IV but, if this is not practical, may be given IM or SC
- Wait until a sustained improvement in consciousness is observed before restarting a lower dose of opioid
- Be aware of pharmacokinetics of naloxone in relation to strong opioids.(Table 10) .Repeated doses of naloxone may be required.

Table 10 - Pharmacokinetics of naloxone in relation to strong opioids.

Drug	**Duration of action**	**Half life**
Naloxone	15 – 90 mins	1 hour
Morphine or oxycodone m/r	12 hours	1.5 – 4.5 hour (longer for m/r)
Methadone	8-12 hours	8 – 75 hours

9. Adjuvant Analgesics (Co-analgesics)

Table 11 – Adjuvant analgesics

Drug	Use	Comments
Tricyclic antidepressants		
• Amitriptyline 10-75 mg at night. Start at 10mg; increase to 25mg ; then by 25mg increments every week, as tolerated and required	Neuropathic pain May be combined with antiepileptic if insufficiently effective alone.	**Onset of Action may be less than a week in neuropathic pain**. Helps sleep. Monitor for side effects (See BNF)
• Nortriptyline 10-70mg at night. Start at 10mg; increase by 10mg increments every week, as tolerated.		If amitriptyline too sedating for patient.
SNRIs (Serotonin-noradrenaline reuptake inhibitor)		
• **Duloxetine 30mg daily - increase by 30mg steps every 2 weeks; Max 120mg daily**	Neuropathic pain and/or anxiety disorder	Alternative to tricyclics if not tolerated
• Venlaflaxine m/r 75mg daily - increase by 75mg steps every 2 weeks • Max 300mg daily	Neuropathic pain and/or anxiety disorder	Alternative to duloxetine if not tolerated. **Under Specialist Advice only**
Anti-epileptics		
• Gabapentin 100mg or 300mg daily titrated to 300mg t.d.s .initially. • Then by 300mg steps every 3-7 days up to 1200mg t.d.s. maximum.	Neuropathic pain	Dose increases may be limited by side effects (e.g. sedation, dizziness). Slower titration and lower doses if in renal failure and frailer patients – use 100mg steps rather than 300mg; SEEK SPECIALIST ADVICE
• Pregabalin 75mg b.d, up to 150mg b.d. after 3 to 7 days. Max 300mg b.d. • Consider lower dose of 25mg b.d. (Comments right) - increase in 25mg b.d increments every 3-7 days.	If intolerant to gabapentin. As initial therapy if anxiolytic required in addition to analgesia	Titration may be limited by side effects (e.g. sedation, dizziness) Consider commencing lower doses in patients with renal failure, concurrent opioids and frailer patients.
• Clonazepam 500 microgram to 2mg nocte.	Neuropathic pain especially with sleep disturbance	Titration may be limited by side effects, e.g. sedation.
• Carbamazepine initially 50 -100mg b.d; titrate in 50 - 100mg steps every 1-2 weeks. Max 1600mg daily.	Second line Neuropathic pain	Limited by drowsiness, nausea side effects typically.
• Oxcarbazepine – On Specialist Advice only	Second line Neuropathic pain	Alterative to carbamazepine if not tolerated.

Drug	Use	Comments
Corticosteroids		
• Dexamethasone 8-16mg a day in 1-2 doses • **Give in the morning to avoid sleep disturbance** • Dexamethasone is 7 times more potent than prednisolone .	To decrease peri-tumour oedema e.g. • Nerve compression. • ↑ intracranial pressure • Spinal cord compression • Organ infiltration.	May increase appetite, affect mood. • add gastro-protective agent (e.g. PPI) • stop if no response after 7 days • review; reduce every 3-7 days to avoid side effects. • check blood glucose daily for 3 days, then twice weekly.
NSAIDs		
• Ibuprofen 400mg -600mg q.d.s. or naproxen 250-500mg b.d. • COX-2 Inhibitors (see BNF) • Ketorolac by CSCI - **Seek specialist advice .**	Bone pain / soft tissue infiltration	Should respond within 1 week - stop if no improvement. • monitor for side effects • add gastric protection (e.g. PPI) unless contra-indicated. **GI side effects and thrombosis risk is less with ibuprofen and naproxen in lower doses.**
OTHER		
Ketamine Oral or continuous SC infusion **ONLY TO BE USED ON SPECIALIST ADVICE**	Neuropathic pain	**Dose related** drowsiness, dysphoria side effects common Consider prophylactic use of benzodiazepine or haloperidol **AVOID in hypertension, raised intracranial pressure, epilepsy and cerebrovascular disease.**

<u>Other approaches to pain (consider seeking specialist advice)</u>

- Radiotherapy/chemotherapy/hormone therapy
- TENS
- Massage
- Relaxation
- Psychological support
- Neural blockade/epidural/intrathecal analgesia
  Neuro-destructive blocks e.g. intrathecal, cordotomy

NAUSEA AND VOMITING

About 40% of patients with advanced cancer have nausea and 30% will vomit.

Definitions:

Nausea - unpleasant feeling of the need to vomit. Distinguish from anorexia

Vomiting - forceful expulsion of gastric contents through mouth. Distinguish from regurgitation and expectoration.

Retching is physiologically similar to vomiting, but without expulsion of gastric contents

Note *- nausea may occur without vomiting and vice versa.*

Assessment

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

Table 12 - Management of Reversible / Treatable Causes of Nausea/ Vomiting.

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

Management

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

Anti-emetic Therapy

- Decide most likely *cause*, and choose first line treatment (See **Table 13)**
- Reassess daily
- Titrate dose as needed
- If no response, reassess cause
    - if **cause** changes, then use most appropriate medication
    - if same cause, try second choice; may need combinations of anti-emetic therapy
- If poor response to second *choice*, consider second line approach (see below) and **SEEK SPECIALIST ADVICE**

Table 13 - Management of nausea and vomiting.

Drug	*Main action of drug*	*Suggested dose & route*	*Recommended use/comments*
FIRST LINE			
Cyclizine † ‡	Inhibits vomiting centre Vestibular sedative	Oral – 25-50mg t.d.s. SC - 75-150 mg/24h by CSCI	Cerebral irritation; vertigo; visceral distortion/obstruction; oropharyngeal irritation *May be **added to** haloperidol* *Constipating; delays gastric emptying*
Haloperidol*	Inhibits chemoreceptor trigger zone	Oral – 500 micrograms - 3mg at night. (higher doses under specialist advice) SC -– 500microgram – 3mg od or 1.5 - 5mg by CSCI	Biochemical disturbance (drug, metabolic, toxic) *May be **added to** cyclizine*
Metoclopramide* †	Pro-kinetic	Oral - 10mg t.d.s.(higher doses under specialist advice) SC - 30mg/24h by CSCI (higher doses under specialist advice)	Gastric stasis, reflux "Squashed stomach" - mass, ascites *Avoid in mechanical bowel obstruction, colic*
SECOND LINE			
Levomepromazine	Broad spectrum anti-emetic (not pro-kinetic) Sedative - dose related	Oral – 6 -12.5mg nocte or in divided doses b.d. Note can be sedative in higher doses; seek specialist advice SC - 5-25mg o.d. or by CSCI	***Replaces** previous anti-emetic* Second choice - may be used earlier if sedation is not a problem or is desirable (**more likely** in doses ≥ 25mg/24h)"
Ondansetron (or other $5HT_3$ antagonist, doses differ)	$5HT_3$ antagonists	Oral - 8mg b.d. (up to t.d.s. – seek specialist advice) Rectal - 16mg o.d. SC - 16mg/24h by CSCI (higher doses may be used – seek specialist advice)	Mainly in chemotherapy, post-operatively Adjuvant in renal failure, gastric irritation or biochemical stimulus ***Add to** previous anti-emetic* *Note – profoundly constipating*
Dexamethasone	Reduces inflammatory response. ? central effect	Oral 4mg o.d. or SC – 3.3-16mg o.d. or in 2 divided doses	Adjuvant anti-emetic Cerebral oedema; liver metastases ***Add to** previous anti-emetic*

**** - In Parkinson's syndromes, domperidone may be used in place of dopamine antagonists (e.g. metoclopramide, haloperidol) which cross the blood brain barrier. See BNF***

† Note - avoid adding cyclizine or anti-muscarinic drugs to metoclopramide, as they inhibit its pro-kinetic action

‡ - Cyclizine, like other anti-muscarinic drugs, may aggravate heart failure and should be avoided in those at risk

GASTRO-INTESTINAL OBSTRUCTION

Definition

- It occurs in 3% of all cancer patients; more frequent complication if advanced intra-abdominal cancer (e.g. colon -10%; ovary -25%)
- Site of obstruction is small bowel in 50%; large bowel in 30%; both in 20%

Table 14 - Common causes of intestinal obstruction

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

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

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

Assessment/ Signs and symptoms of bowel obstruction

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

Table 15 - Surgery - consider for every patient at initial assessment

Consider if:	*Poor surgical outcome likely if:*	*Surgery is likely contra-indicated if:*
• patient willing • discrete and easily reversible mechanical cause of obstruction • prognosis >12 weeks if treated	• previous abdominal radiotherapy • small intestinal obstruction; multiple sites • extensive disease • poor condition • cachexia • poor mobility	• ascites present • carcinomatosis peritonei • findings suggest intervention is futile • poor physical condition • short prognosis <12 weeks

- Bowel obstruction may be temporarily reversible
- Consider high dose steroid by non-oral route if there are no contraindications– e.g. dexamethasone 12-16mg per day.
- Reassess, if no improvement after 5-7 days, or adverse side effects present, then stop steroids.
- If improvement shown, reduce steroid dose gradually as symptoms allow.

Table 16 - Medical management of gastro- intestinal obstruction symptoms[3]
SEEK SPECIALIST ADVICE if patient is not responding or the situation is complex.

Nausea +/- vomiting	
Complete obstruction	*Try in sequence until effective:* 1) Cyclizine 75mg-150mg/24h by CSCI 2) Add haloperidol 1.5mg-5 mg/24h by CSCI **3) Substitute both with levomepromazine 5-25mg/24h**
Functional or partial obstruction	• Metoclopramide: 30mg/24h by CSCI (higher doses may be used on specialist advice) • Contraindicated in complete bowel obstruction • Stop if precipitates colic; use anti-emetics above.
Persistent/high volume vomiting	• Octreotide 300-1200 micrograms/24h by CSCI • Hyoscine butylbromide (as for colic below) may be added • Consider i/v PPI or i/v or SC ranitidine if resistant vomiting due to proximal obstruction **under specialist guidance**.
Other Symptoms	
Constipation precipitating obstruction	• Sodium docusate 200mg t.d.s. orally • Consider macrogols if impaction • Laxatives risk inducing colic – ensure hyoscine butylbromide injection is available if needed • Avoid stimulant, bulk or fermenting laxatives e.g. lactulose
Abdominal pain	• Follow pain control guidelines, using non-oral route
Abdominal colic	• Anti-cholinergic agent, e.g. hyoscine butylbromide 60-120mg/24h by CSCI then SEEK SPECIALIST ADVICE • Stop: pro-kinetic drugs; bulk-forming/osmotic/stimulant laxatives
Hydration	• Assess need for i/v or SC fluids on individual basis. Many are not dehydrated, absorbing oral fluid above level of obstruction. • SC fluid can be given up to 1-2L/24h
Dietary intake	• Allow food and drink if desired. Warn - may vomit. • Total Parenteral Nutrition may be appropriate in selected cases with longer prognosis - multidisciplinary team decision.

Note - higher doses of some drugs above may be used – SEEK SPECIALIST ADVICE

Nasogastric (NG) intubation

- Do **not** *routinely* use NG tube for obstruction in patients with advanced illness.
- Prolonged NG aspiration plus i/v fluids is not recommended as it rarely gives sustained relief. Use medical measures described above.
  - Consider for decompression of upper gastrointestinal (GI) tract if surgery is being considered *OR* faeculent vomiting if responding poorly to drug treatment.

Venting percutaneous gastrostomy

- May be considered for symptom relief in patients whose vomiting is not relieved by pharmacological means.

Ongoing Management

- Review treatment at least daily

Discharge to, or management at home requires early planning.

FATIGUE

Causes of fatigue

- Fatigue may be a consequence of underlying disease process (e.g. cancer) or as a consequence of treatment (e.g. chemotherapy , radiotherapy) or an intercurrent illness.
- Other causes of fatigue include:
    - Anaemia – consider blood transfusion if appropriate
    - Dehydration – consider IV/SC hydration
    - Pain – optimise pain control
    - Iatrogenic: drugs with sedative effects, such as opioids, benzodiazepines, antidepressant medication
    - Poor nutrition: consider dietician referral, build up drinks
    - Depression – consider antidepressants
    - Endocrine abnormalities: Addison's disease (consider steroid replacement) and hypogonadism (consider testosterone replacement where appropriate. Consult with an endocrinologist)
- Fatigue is often a combination of reversible and irreversible causes.

Management

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

Non-pharmacological management

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

Pharmacological management

- Corticosteroids: Reduces effect of pro-inflammatory cytokines and improves general feeling of wellbeing
    - Doses: dexamethasone 4-8 mg each morning for a maximum of 14 days
    - Please note that use can result in steroid induced diabetes and fluid retention, on long term use proximal myopathy.

- Psycho-stimulants - e.g. methylphenidate, modafinil
    - Can be considered for fatigue or fatigue secondary to opioid induced sedation – seek specialist advice
    - Psychostimulants should be used with caution in patients with cardiovascular conditions, psychiatric illness and epilepsy.

ANOREXIA

Definition

- Reduced desire to eat
- Loss or absence of appetite

Causes

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

Management of cancer-related anorexia

- Treat reversible causes
- Explanation - an effect of the cancer itself
- Listen to fears and anxieties of patient and family/carers - failure to eat can cause fear and conflict
- Consider asking for dietician advice unless prognosis is short
- Food or supplements may be more easily taken by snacking through the day; smaller portions more often
- Avoid offering excessive food.

Pharmacological management

- Corticosteroid e.g. Short-term improvement of appetite. Rapid effect but tends to decrease after 3–4 weeks. May also help to reduce nausea, improve energy and general feeling of wellbeing
    - Consider need for gastric protection
- Dexamethasone - 2-6 mg once daily; assess after one week
    - if beneficial, continue - reduce weekly to lowest effective dose
    - if no benefit after 1 week, then stop
    - side effects: fluid retention, candidiasis, myopathy, insomnia, gastritis and steroid-induced diabetes.

<u>Megestrol acetate</u>

- 160mg once daily; titrate if needed to maximum 800mg/day
- For appetite stimulation, lower doses are as effective as higher doses *but* for weight gain there is a dose-response relationship.
- Reduce dose gradually if it has been used for more than 3 weeks (adrenal suppression).
- If no benefit after two weeks, then stop.
- Less side effects than dexamethasone *except* nausea, increased risk of leg dependent oedema and thromboembolic phenomena (5% excess risk).

<u>Pro-kinetic</u>

- If impaired gastric emptying suspected, metoclopramide 10mg t.d.s.

CACHEXIA

- A multi-factorial syndrome characterised by an on-going muscle loss (with or without fat loss) that cannot be fully reversed by nutritional support and leads to progressive functional impairment.
- The pathophysiology is characterized by a negative protein and energy balance driven by a variable combination of reduced nutritional intake and abnormal metabolism.
- Anorexia/cachexia as a syndrome is a complex metabolic process found in many end stage illnesses.
- This syndrome impacts significantly on quality of life and can cause anxiety and distress for patients, and often even more so for carers.

CONSTIPATION

Causes to consider

- Drug induced – review medication;
- Dehydration - review diuretics and fluid intake
- Reduced mobility – e.g. patient may not be able to get to the toilet; lack of privacy
- Altered dietary intake - review
- Hypercalcaemia – (see Palliative Care Emergencies section of guidance)
- Neurological (e.g. spinal cord compression; autonomic neuropathy)
- Intestinal obstruction – (see Table 16)

Assessment

- History - normal bowel habit, medicines, other causative factors
- Abdominal palpation and auscultation, digital rectal examination
- Investigations - if needed for treatment, e.g. abdominal x-ray; check calcium levels
- ***For intractable constipation, SEEK SPECIALIST ADVICE***

- **Management**
- Prevention is the best management of constipation
- Patients on opioids usually require regular oral laxatives
- Encourage a good oral fluid & dietary intake
- Use oral laxatives first line.

See Table 17 on next page

Table 17 – Pharmacological Management

Clinical Situation	Agent Type and examples	Comments
Soft bulky stools - low colonic activity	*Stimulants – e.g.* Senna 15mg at night increasing to 30mg b.d. Bisacodyl 5mg at night increasing to 10mg b.d. Sodium picosulfate 5-10mg at night to 30mg daily	Start with low dose and titrate. May cause abdominal cramp Suppositories also available
Colon full, no colic	*Stimulant* ± *softening agent* – e.g. senna + docusate sodium, or co-danthrusate 50/60 capsules/suspension [4]	
Colon full and colic present.	*Macrogols* (e.g. Movicol, Laxido) 2-3 sachets per day	Require adequate oral fluids to be effective
Hard dry faeces	*Softening agents* - docusate sodium up to 500mgs/day - capsules or oral solution Arachis oil enema **(avoid if known nut allergy)**	Useful in sub-acute obstruction. Higher doses may stimulate peristalsis.
Hard faeces - full rectum, colon	Stimulant plus softener, e.g. co-danthrusate 50/60 - 1-3 capsules or 5-15 ml at night and titrate	Codanthrusate may cause red urine; peri-anal rash/irritation; colic
	2nd line –Macrogols (e.g. Movicol® or Laxido) 2-3 sachets/day.	Requires adequate oral fluids to be effective
Faecal impaction	Arachis oil retention enema **(avoid if known nut allergy)** ± phosphate enema	Warm before use Give arachis oil at night, followed by phosphate enema in the morning
	2nd line – Macrogols (e.g. Movicol® or Laxido) 8 sachets dissolved in 1 Litre of water over 6h p.o. Repeat for up to 3 days.	Keep dissolved solution in a refrigerator. Limit to 2 sachets/h in heart failure
Opioid-induced constipation resistant to the above methods	SC methylnaltrexone may be used.	SEEK SPECIALIST ADVICE.

N.B. – in paraplegic patients it is *essential* that a regular bowel regimen is established. A common pattern is use of a stimulant laxative with defaecation assisted by suppositories or enema. This avoids faecal incontinence on the one hand and impaction on the other.

[4] N.B. - codanthramer capsules advised in the original document are now no longer available. The suspension is available in ordinary and strong forms.

DIARRHOEA

Increase in the frequency of defecation and/or fluidity of the faeces.
Prevalence: 4% of patients with advanced cancer.

Assessment and management

- Establish cause - usually evident from history
- Review diet
- Review medication (including laxatives) – uncommon side effect of some drugs (e.g. PPIs)
- Clinical assessment includes a rectal examination and inspection of the stool
- Exclude:
  - Infective cause
  - Constipation with overflow - a plain abdominal x-ray if overflow may help if suspected. Treat as for constipation (Table 17).
- Other investigations may be appropriate if the results will significantly affect management.
- If the patient is in the last days of life, treat symptomatically but do not investigate.

Table 18 – Management

Cause	Management
Drugs - e.g. laxatives, magnesium antacids, PPIs	Review medication
Antibiotics - altered bowel flora	Stop antibiotic if possible Exclude Clostridium difficile (use local guidelines)
Infection	Fluid and electrolyte support; seek microbiology advice
Overflow (constipation, partial obstruction)	Identify. Treat underlying constipation. Soften stool if partial obstruction. Avoid **specifically** constipating treatments
Acute radiation enteritis	Absorbent (see below); seek specialist advice
Chemotherapy	Seek oncology advice
Secretory diarrhoea (e.g. AIDS, tumour, fistula)	Seek specialist advice
Steatorrhoea	Pancreatin supplements

Table 19 - Pharmacological Management

Medication type	Example and dose
Opioid drugs	Loperamide 4-32mg/day in 2-4 divided doses Codeine 30-60mg 4-6 hrly
Absorbents - hydrophilic bulking agents	Ispaghula husk 1 sachet b.d. - avoid fluids for 1h after taking
Intestinal secretion inhibition; fistula	Hyoscine butylbromide (e.g. Buscopan) 80-160mg by CSCI as first line. SEEK SPECIALIST ADVICE for use of octreotide Octreotide 300-1200 microgram/24h by CSCI

For severe resistant diarrhoea – seek specialist advice

RESPIRATORY SYMPTOMS

Respiratory symptoms are frequent in patients with advanced disease, and tend to become more common and severe in the last few weeks of life.

Breathlessness/ Dyspnoea definition

- An unpleasant subjective sensation of inadequate ventilation that does not always correlate with the clinical pathology.
- The patient's distress indicates the severity.

The causes of breathlessness are usually multi-factorial: physical, psychological, social and spiritual factors all contribute to this subjective sensation. It is important to recognise and treat potentially reversible causes of breathlessness.

Assessment

- History and clinical examination
- Investigations e.g. chest x-ray
- Management will be dependent on clinical diagnosis.

Management

- Treat reversible causes
- Non-pharmacological measures
- Drug treatments

Table 20 – Potentially treatable causes of breathlessness

Cause	Consider
Cardiac failure and pulmonary Oedema	Diuretics / ACE inhibitors /nitrates /opioids
Pneumonia	Antibiotics where appropriate
Bronchospasm	Bronchodilators ± steroids
Anaemia	Transfusion – treat symptoms rather than haemoglobin level
Pulmonary embolism	Anticoagulation
Anxiety	Psychological support, anxiolytics
Superior vena cava obstruction	Consider high dose steroid see palliative care emergencies - Table 40 Refer to oncologist for radiotherapy/ chemotherapy Vascular stents
Tracheal or bronchial obstruction due to malignancy	Refer to oncologist for radiotherapy Or refer for stenting
Lung metastases	Refer to oncologist for radiotherapy/ chemotherapy
Pleural effusion Pericardial effusion Ascites	Drainage procedures

Non-Pharmacological Management

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

Pharmacological Symptomatic Management

Oxygen therapy

- Oxygen therapy may help dyspnoeic patients who are hypoxic (SaO_2 < 90%) at rest or who become so on exertion. There is no evidence that oxygen therapy is helpful in breathless patients who are not hypoxic.
- Consider a trial of oxygen for hypoxic patients (SaO_2 <90%) and those where saturation measurements not available. If of no benefit then discontinue.
- Oxygen therapy may lead to limited mobility, barrier to communication, inconvenience and cost implications; alternative therapies should be offered.
- For patients with chronic obstructive pulmonary disease who are chronically hypoxic – do not use more than 28% oxygen**.** Seek guidance from respiratory physicians and follow local guidelines
- Domiciliary oxygen for continuous or p.r.n use should be prescribed according to local guidelines using a home oxygen order form (HOOF).
- For patients meeting the requirement for long term oxygen therapy in COPD follow local guidelines.
- Guidance for the management of COPD in adults in primary and secondary care has been produced by the National Institute for Clinical Excellence (NICE) (2004) and by the British Thoracic Society (BTS) (available at www.brit-thoracic.org.uk).
- Local and national guidelines are available for the management of other diseases such as asthma and diffuse parenchymal disease (BTS Guidelines available at www.brit-thoracic.org.uk).
- Guidance includes how many hours per day the oxygen should be used for

Oxygen flow rates (L/minute)

- There are no strict criteria to be met as far as the flow rate is concerned.
- In COPD patients, care must be taken to avoid carbon dioxide retention if at all possible, although in patients who are terminally ill this consideration is balanced by the need to palliate symptoms.
- If pulse oximetry is available, it is reasonable to provide oxygen at a flow rate sufficient to keep the SaO_2 at around 92% (88-92% in patients who retain CO_2), or as near to this as possible without causing significant side effects (such as dry upper airways due to high flow rates, or headaches due to carbon dioxide retention).
- Patients with pulmonary fibrosis often have very low oxygen saturations and de-saturate still further on exertion. They frequently require high flows of oxygen.

Corticosteroids
May reduce inflammatory oedema.

Table 21 – Steroid management

Indication	Dexamethasone dose
• Superior vena cava obstruction	16 mg
• Stridor	8-16 mg
• Lymphangitis carcinomatosis • Post-radiotherapy • Bronchospasm	8 mg

- **Review treatment with corticosteroids after 5 days**.
- If symptoms have improved, reduce dose gradually to the lowest effective dose.
- If no improvement in symptoms, steroid should be stopped or reduced to previous maintenance dose.
- If patient has taken steroids for less than 14 days this can be done abruptly.
- If taken for more than 14 days reduce dose gradually and stop.

Opioids
- Decrease perception of dyspnoea, decrease anxiety and decrease pain

Opioid naïve patient
- Oral immediate release morphine 2.5 – 5 mg four hourly p.r.n. for dyspnoea
- Titrate according to response
- If patient requires > 2 doses in 24 h, consider use of a long-acting opioid

Patient already taking regular strong opioid for pain
- For breathlessness use an additional p.r.n. dose of strong opioid which is in the range of 25-100% of the 4 hourly strong opioid dose depending on severity of breathlessness.
- For example, if patient is on morphine m/r 30mg b.d. for pain . – the additional range for oral immediate release morphine dose for dyspnoea is 2.5 -10mg p.r.n titrated according to response.
- Titrate according to response.
- Consider increasing the regular dose by maximum of 25-50% if p.r.n doses are beneficial.

Note: Use with caution in patients with type 2 respiratory failure

Benzodiazepines

- Decrease anxiety
- Act as muscle relaxants
- Reduce anxiety and panic attacks

Note: Use with caution in patients with type 2 respiratory failure

Table 22 – Benzodiazepine management

Drug	Dose	Comments	Pharmacokinetics
Diazepam	2 - 5 mg orally up to t.d.s.	• Long acting. • Reduce dosage in frail and elderly.	Onset of action Oral = 15 min Half-life = 25-50h; active metabolite <200h
Lorazepam	500 micrograms -1 mg sublingually ***/*** PO 8hrly p.r.n.	• Some brands of lorazepam tablet dissolve easily when placed under the tongue. • 1mg tablets are scored • This is an unlicensed use that results in a fast onset of action.	Onset of action Sublingual = 5min Oral = 10-15 min Duration of action 6-72 h Half-life = 10 – 20h
Midazolam	2.5 - 5 mg SC 4 hrly p.r.n.	• Short acting • Useful for intractable breathlessness • If patient is too unwell to take oral medication, midazolam 2.5mg SC four hourly p.r.n. can be used as an alternative. • If multiple doses are required, consider giving via 24 hour CSCI at a starting dose of 5-10mg.	Onset of action 5-10 mins SC Duration of action 5mg < 4 h Half-life = 1-4 h

Review treatment with benzodiazepines after one week and reduce dose if the drug Is accumulating and causing drowsiness.

Table 23 - Nebulised medications

Drug	Dose	Comments
Sodium chloride 0.9% nebuliser solution	5 ml p.r.n. or 4 hrly	Hydrating agent for viscous secretions
Salbutamol nebules	2.5 - 5 mg p.r.n. or 4 hrly	Bronchodilator

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

COUGH

- Assess the likely causes(s) for the cough
- May be cancer related / treatment related or due to other diseases.
- Cough may serve a physiological purpose for clearing bronchial secretions. Where possible, expectoration/ physiotherapy should be encouraged

Management

Table 24: Some causes of cough and their management

Cause	Management
Malignancy related	Refer to oncologist for radiotherapy Consider corticosteroids
Treatment related	Medication review e.g. ACE inhibitor induced cough
Cardiac failure and pulmonary oedema	Diuretics/ACE inhibitors
Pneumonia	Antibiotics if appropriate
Asthma	Bronchodilators +/- steroids
COPD	Bronchodilators/ steroids. Carbocisteine - start 750mg t.d.s. and reduce to 750 mg b.d. can reduce sputum viscosity. Review maintenance after 4 to 6 weeks.
Tumour related therapy	Refer to oncologist for radiotherapy/ chemotherapy Laser Therapy
Infection	Physiotherapy/ nebulised saline/ antibiotics. Maintain hydration.
Recurrent laryngeal nerve palsy	Refer *urgently* to an Ear, Nose and Throat (ENT) specialist.
Pleural effusion	Drainage procedures

Table 25 - Pharmacological Management

Drug	Dose	Comments
Simple linctus	5ml t.d.s.- q.d.s.	Locally soothing demulcent action Some antitussive effect
Codeine linctus 15mg/5ml	15- 30 mg t.d.s. - q.d.s.	If taking strong opioid for pain there is no rationale for adding codeine linctus. Use p.r.n. dose of strong opioid to treat cough
Morphine oral solution	2.5-5 mg q.d.s – 4 hrly	Use if opioid naive
Morphine oral solution	5 –10 mg 4 hrly	Use this dose if previously taking codeine linctus found it to be ineffective
Carbocisteine	750 mg b.d.	Reduces sputum viscosity
Sodium chloride 0.9%	2.5 ml nebulised 4 hrly p.r.n	Helps expectoration, useful if it is a wet cough

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

HAEMOPTYSIS – See also Haemorrhage in Palliative Care Emergencies section

Management

- Reassurance/ explanation
- Consider whether there is a treatable cause:

Table 26 – Management of haemoptysis

Cause	Management
Infection	Antibiotics
Pulmonary embolus	Consider investigation
Underlying malignant disease	Palliative radiotherapy
Medications	Review need & doses of anticoagulants/ aspirin/ NSAIDs
Thrombocytopenia/ haematological cause	Consult local guidelines

Pharmacological Management

- Tranexamic acid 1 g orally t.d.s. – q.d.s

RESPIRATORY SECRETIONS

- See Care of Dying section of guidance for management of troublesome respiratory tract secretions in the dying patient.

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ORAL PROBLEMS

Prevention Management

- Teeth and tongue should be cleaned at least twice daily with a small/ medium head toothbrush and fluoride toothpaste. Rinse mouth thoroughly after cleaning.
- Remove dentures twice daily, clean with a brush and rinse with water. Soak overnight in water or patient's usual solution and cleaned with a brush.
- Adequate oral fluid intake should be encouraged.
- Moisturize lips sparingly with lip balm or tasteless oil, e.g. olive oil
- Consider if any medications can be stopped or an alternative prescribed.
- Diagnose and manage secondary oral infection.

Table 27 - Management

Problem	Management
Aphthous ulcers	• Hydrocortisone oromucosal tablet 2.5mg q.d.s. Allow tablet to dissolve at site of ulcer. • Antiseptic mouthwash – e.g. chlorhexidine gluconate • Topical analgesic gels –choline salicylate 8.7% oral gel (e.g. Bonjela) or local anaesthetic (e.g. lidocaine) – see BNF 12.3.1
Viral ulcers	• Aciclovir 200 mg 5 times a day for 5 days • Topical analgesic gel (see above)
Malignant ulcers	• Consider antibiotic
Radiation stomatitis	• Benzydamine mouthwash or spray (Difflam) • Paracetamol 1g/10ml mucilage (use Christie formulation) 1 g, 4-6 hrly (similar preparations may be available from local pharmacies) • Consider Caphosol (4-10 times a day) • Consider applying a coating protectant e.g. Gelclair • Opioid analgesics if above inadequate
Gingivitis	• Metronidazole 200 mg t.d.s. orally for 3 days • Consider metronidazole suspension topically (400 mg (10 ml) rinsed around the mouth then spat out) or rectal administration if not tolerated orally • Antiseptic mouthwash – e.g. chlorhexidine gluconate
Dry mouth	• Review medications (opioids, anti-muscarinics) • Increase oral fluid intake • Saliva substitutes - e.g. AS Saliva Orthana, for dry mouth (see BNF 12.3.5), Glandosane, BioXtra o avoid acidic saliva products in dentate patients o note - some saliva substitutes are porcine in origin • Boiled sweets, ice cubes, sugar free chewing gum • Consider saline mouthwashes/sprays/nebulisers • Pilocarpine tablets/eye drops- seek specialist advice o Avoided in those with a lack of salivary function
Coated tongue	• Chewing pineapple chunks • Brushing tongue with soft toothbrush

Problem	Management
Fungal infection – *note: on occasion bacteriological infection may mimic candida – e.g. Staphylococcus, Klebsiella. If in doubt, take sample for culture and indicate suspicion to lab*	• Nystatin oral suspension 100,000 units/ml 1 ml – 5 ml q.d.s. held in the mouth for 1 min and then swallowed after meals and at bedtime or • Fluconazole 50-100mg daily for 7 days (14 days if dentures worn). Fluconazole 150mg stat can be used if prognosis is short. (note - reduce dose by 50% if eGFR < 50 ml/min) • Consider the use of an alternative antifungal agent, e.g. amphotericin B, itraconazole, voriconazole or posacanazole. Seek microbiologist advice. • Dentures should be soaked overnight in a weak chlorine solution (e.g. Milton® Sterilising Fluid) • Review and reassess treatment after 5 – 7 days. If recurrent please seek specialist microbiological advice.
Bacterial Infection	• Consider the use of antibiotics
Dry Lips	• Yellow/ white soft paraffin or normal lip salve ○ Contraindicated if patient having radiotherapy to head and neck • If oxygen therapy in place then water soluble lubricant should be used

DELIRIUM AND CONFUSION

Definition - Delirium is characterised by four core features:

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

- Delirium can have an acute or sub-acute onset (sub-acute seen commonly in the elderly) and should be distinguished from dementia.
- Some patients may have significant cognitive disorder, but be quiet and withdrawn – in this situation the delirium may be overlooked
- It can be a great source of distress to patients and carers.
- Delirium is associated with higher mortality.
- Causes of delirium can be multi-factorial so assessment is essential.
- Identification and treatment of the underlying cause is vital.

Table 28 – Pharmacological Management of Underlying Causes of Delirium

Causes	**Treatment**
Drug related, e.g. • Opioids • Corticosteroids • Sedatives Anti-muscarinics that cross the blood/brain barrier	Reduce or stop suspected medication as appropriate or switch to suitable alternative. *Many other drugs may cause delirium – if in doubt, review patient's medication list with the aid of the BNF*
Withdrawal: e.g. alcohol, nicotine, benzodiazepines, opioids	May be appropriate to allow the patient to continue to use responsible agent. Nicotine patches may be useful.
Metabolic: • Respiratory failure • Liver failure • Renal failure • Hypoglycaemia/ hyperglycaemia • Hypercalcaemia • Adrenal, thyroid or pituitary dysfunction • Infection	Treat any reversible causes if possible Consider oxygen (see Respiratory Symptoms section of guidance) See Palliative Care Emergencies section of guidance for hypercalcaemia
Raised Intracranial Pressure:	Dexamethasone 16 mg daily p.o /SC – review after 5 to 7 days; If not effective then stop. If effective, then gradually reduce dose
Other: • Circulatory (dehydration, shock, anaemia) • Pain • Constipation • Urinary retention	Treat reversible causes if possible and appropriate (e.g. IV fluids, transfusion) · See Pain section of guidance · See Constipation section of guidance Catheterise if patient able to comply

Non- Pharmacological management

- Provide environmental and personal orientation. This may be helped by the presence of a family member or trusted friend.
- Manage patient in a quiet well-lit room.
- Support and correct any sensory deprivation.
- Ensure continuity of care by avoiding any potential disruptive interventions – e.g. moving patient to different bed or ward
- Maintain hydration.
- Hallucinations, vivid dreams and misperceptions may reflect unresolved fears and anxieties: facilitated discussion maybe necessary
- Reassure relatives and carers that the patient's confusion is secondary to a physical condition.

Pharmacological management of symptoms

- Only use if symptoms are marked, persistent, and causing distress to the patient and non-pharmacological interventions have not worked.
- Regular review is imperative as sedative drugs may exacerbate symptoms.
- Use a step-wise approach to drug dosages.

Table 29 – Pharmacological management of delirium symptoms

Delirium where sedation undesirable	Start with haloperidol 500 micrograms at night or b.d. orally or s/c; this can be increased as needed. 1.5 mg – 5 mg by CSCI over 24h. Consider a benzodiazepine if alcohol withdrawal is suspected.
Agitated delirium where sedation would be beneficial	Olanzapine 2.5mg -5mg once or twice daily (less sedating than levomepromazine) Levomepromazine 12.5 – 25 mg 6-8 hourly orally or SC. If two or more doses given in 24 h, please SEEK SPECIALIST ADVICE
Acutely disturbed, violent or aggressive; at risk to themselves or others	Haloperidol 1.5- 5 mg SC or IM repeat as needed after 20-30 min - SEEK SPECIALIST ADVICE

HICCUPS

A pathological respiratory reflex characterised by spasm of the diaphragm resulting in sudden inspiration and abrupt closure of the epiglottis.

Management of Hiccups
Treat if causing patient discomfort and distress
Treat gastro-oesophageal reflux with proton-pump inhibitor

Table 30 – Management of Hiccups

Cause	**Specific Management**
Gastric distension – vagus nerve Gastritis / gastro - oesophageal reflux Hepatic tumours Ascites / intestinal obstruction	Peppermint Water 10ml b.d Metoclopramide 10 mg t.d.s. (not concurrently with peppermint water) Anti-flatulent e.g. Altacite plus
Muscle relaxant Diaphragmatic Irritation – tumour Phrenic Nerve Irritation – mediastinal tumour	Baclofen 5 mg orally t.d.s. Antiepileptic – e.g. gabapentin – in usual doses (see BNF 4.8) Nifedipine m/r 10 mg b.d. Midazolam – seek specialist advice
Systemic: • Uraemia • Hyponatraemia • Hypokalaemia • Hypocalcaemia • Hyperglycaemia • Infection	1st line Haloperidol 500 micrograms-3 mg orally nocte 2nd line Chlorpromazine 10-25 mg orally t.d.s or Levomepromazine 2.5 - 5 mg at night **Caution: can cause sedation and hypotension especially in elderly patients** Midazolam – Seek specialist advice
CNS tumour Meningeal : infiltration by cancer	Antiepileptic – e.g. gabapentin Baclofen 5 mg orally t.d.s. higher dose SEEK ADVICE
Hepatic, mediastinal or cerebral compression/irritation by disease/tumour	Dexamethasone oral 4 -8mg in the morning may reduce compression/irritation. Stop if no benefit after a week. If beneficial gradually reduce dose.

SWEATING (hyperhidrosis)
Excessive sweating occurs in 10 to 20% of patients with advanced cancer, occurs more at night and may require a change of clothes, bedding or both.

Table 31 – Assessment and Management

Cause	Treatment
Room temperature Excessive bedding	Lower ambient temperature Adjust bedding
Infection Hypoxia Pain Anxiety	Treat underlying cause where possible
Drugs (alcohol, opioids, SSRI antidepressants etc.)	Review medication
Endocrine Hormonal treatment for cancer, e.g.: • Tamoxifen • Gonadorelin analogues (e.g. goserelin, leuprorelin) • Menopause due to radiotherapy, chemotherapy. • Hypoglycaemia • Hyperthyroidism • Autonomic neuropathy	Seek specialist advice
Paraneoplastic (± pyrexia), e.g.: • lymphoma • solid tumour (e.g. renal carcinoma) Liver metastasis (often with no pyrexia).	See pharmacological management

Non-pharmacological management
- Oral fluids
- Fan
- Tepid sponging
- Fewer bedclothes
- Cotton clothing
- Layered clothing

Pharmacological management
- Paracetamol 1g q.d.s
- NSAID (standard doses)
- Anti-muscarinic (e.g. amitriptyline 10-25 mg nocte)
- Propranolol 10-20 mg b.d - t.d.s.
- Cimetidine 400 – 800mg b.d
- Olanzapine 5mg b.d.

If symptoms persists SEEK SPECIALIST ADVICE.

PRURITUS (ITCH)

Pruritus is an unpleasant sensation that provokes the urge to scratch.
It causes discomfort, frustration, poor sleep, anxiety and depression.
Itch may be localised or due to systemic disease. Pruritus in systemic disease is often worse at night.
Persistent scratching, and the 'itch-scratch-itch' cycle leads to skin damage excoriation and thickening.
Patients with itch usually have dry skin.

Common drug causes include - opioids in particular morphine and diamorphine, SSRIs, ACE inhibitors, statins, chemotherapeutic drugs

Non-pharmacological measures:
If skin becomes wet, dry the skin by patting gently
Keep fingernails cut short
Keep skin cool and hydrated
Keep creams and lotions in fridge
Rub with ice cubes and leave wet to evaporate
Avoid hot baths
Distraction techniques
Avoid rough clothing.

Pharmacological Measures
The evidence of the treatment of pruritus is limited. Many causes of pruritus are *not* histamine related. Antihistamines may have a sedative role in allowing a good night's sleep. Other measures need to be tried including treating the underlying cause if possible. In addition, stop any potentially causative drugs.

See table 32 below.

Seek specialist advice.

Table 32 - Suggested management of pruritus

Cause	Specific Management
Dry Skin	Emollients q.d.s. initially and b.d. long-term. e.g. Aqueous cream (+/- 1% menthol) and emollient bath additive.
Primary Skin Diseases e.g. Scabies, dermatitis, psoriasis	Appropriate treatment of underlying condition.
Skin inflamed	Topical corticosteroids e.g. hydrocortisone 1% cream b.d.
Hodgkin's lymphoma	Prednisolone 10 –20 mg t.d.s. Cimetidine 400 mg b.d.
Opioid Induced Itch	Step 1. Antihistamine e.g. chlorphenamine 4mg t.d.s. or non-sedating antihistamine (see BNF). Step 2. Switch opioid. Step 3. Ondansetron 8 mg PO b.d.
Cholestasis	1st line - sertraline 50-100mg o.d. 2nd line - rifampicin 150-600mg o.d.
Uraemia	Options: - if localized, capsaicin cream 0.025-0.075% o.d. – q.d.s. - Doxepin 10mg b.d. - Gabapentin 100 – 400mg after haemodialysis - Sertraline 50mg o.d.
Paraneoplastic Itch	Sertraline 50 – 100mg o.d. Mirtazapine 15 – 30 mg nocte
Unknown Cause	Antihistamines e.g. chlorphenamine 4 mg t.d.s. Paroxetine 5 – 20 mg o.d.

ANXIETY IN ADVANCED ILLNESS

Definition

- A state of apprehension or fear, which may be appropriate to a particular situation.
- Morbid anxiety occurs when individuals are unable to banish their worries.
- Anxiety tends to aggravate severity of other symptoms
- People with life-limiting illnesses may suffer general anxiety or panic for a number of reasons including uncertainty about the future, separation from loved ones, financial, work and social worries as well as unrelieved pain or other symptoms
- Anxiety may be new to the individual, but is commoner in patients with pre-existing anxiety disorders

Table 33 – Pre-existing anxiety disorders.

General anxiety disorder	Anxiety symptoms *most of the day*
Panic disorder	Episodic panic or severe episodic anxiety; avoidance; anticipatory anxiety between attacks
Agoraphobia, social phobia, simple phobia	Episodes of panic or anxiety triggered by external stimuli or specific situations

- Symptoms and signs of anxiety may be due to or exaggerated by organic disorders:
  - Hypoxia
  - Sepsis
  - Medications (e.g. antipsychotics; SSRIs; steroids)
  - Drug or substance withdrawal (e.g. benzodiazepines/ opioids/ nicotine/ alcohol)
  - Metabolic causes (e.g. hypoglycaemia/ thyrotoxicosis)
  - Poorly controlled pain / other symptoms
  - Dementia

Assessment

- Full medical history and examination
- Recognition of organic causes
- Elicit patient's specific fears and understanding
- Note language, cultural or other characteristics that may be important
- Information from those close to the patient may help (e.g. family, GP)

Symptoms and Signs

Symptoms may be due to anxiety or to physical causes or both.

Table 34 – Symptoms and signs of anxiety

	Symptoms and Signs
Cardiovascular	Palpitations/ chest pain/ tachycardia/ hypertension
Respiratory	Breathlessness/ hyperventilation
Neurological	Dizziness/ paraesthesia/ weakness/ headache/ tremor
Gastro-Intestinal	Anorexia/ nausea/ diarrhoea/ dysphagia/ dry mouth
General	Sweating/ fatigue
Cognitive/ hypervigilance	Insomnia/ fearfulness/ poor concentration/ irritability
Avoidance behaviour	Avoiding situations or discussions that provoke anxiety

Management

- The severity of the underlying disease and the overall prognosis guides management decisions.
- Share decision making with the patient in developing management plan.
- Treat reversible causes for anxiety if possible
- Offer appropriate reassurance

Non-pharmacological measures

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

Pharmacological Management

- Indications:
    - Non-pharmacological measures are not effective
    - Situation is acute and severe or disabling
    - Unacceptable distress
    - Short prognosis (< 4-6 weeks)
    - Patient has cognitive impairment
- Advise patients about the side effects of medication prescribed
- Warn of side effects due to discontinuation (e.g. antidepressants).

Table 35 – Pharmacological management of anxiety

Medications	Comment
Prognosis of days to weeks	
Benzodiazepines e.g. • Lorazepam 500 micrograms -1mg p.o. or sublingually as required or in 2-3 daily divided doses. Max 4mg in 24hours.	Can cause physical and psychological dependence. Short term use only for 2-4 weeks Rapid onset when used sublingually.
• Diazepam - see BNF for dose	Long acting
• Midazolam 2.5-5mg SC p.r.n 4 hourly. If symptoms persist seek specialist advice.	If oral route not available Rapid onset/ immediate release
Prognosis of > 2 weeks SSRI +/- benzodiazepine initially e.g. • Citalopram 10mg o.d. (see BNF for titration). Maximum dose 20mg if over 65 years. • Sertraline 25mg (see BNF for titration)	Citalopram and sertraline are licensed for panic disorder
• If SSRI ineffective switch to alternative antidepressant ○ e.g. mirtazapine15-45mg nocte	Sedative, often on first dose. Normally rapid tolerance develops. Onset of antidepressant action 1-2 weeks. May help appetite Does not cause nausea and vomiting
• Duloxetine 30mg-60mg o.d. up to a maximum of 120mg o.d.	
Beta-Blockers e.g. • propranolol 40mg o.d. increased to 40mg t.d.s. if necessary (See BNF)	For tachycardia/ tremor/ sweating Monitor BP/ heart rate. Avoid in asthma/ COPD cardiac disorders or peripheral vascular disorders. Not recommended for panic disorder
Pregabalin (See BNF)	Has licence for anxiety – SEEK SPECIALIST ADVICE

DEPRESSION

Definition

- Persistent low mood or loss of interest
- Usually accompanied by one or more of:
    - Sustained low energy
    - Loss of interest in activities
    - Changes in appetite, weight or sleep pattern
    - Poor concentration
    - Feelings of guilt/ worthlessness
    - Suicidal ideas
- Depression is 2-3 times more common in people with a chronic physical health problem.
- Physical consequences of life - limiting illnesses can mimic symptoms of depression.
- Untreated depression may increase the impact of existing symptoms and reducing the effectiveness of usual interventions.

Assessment

Screening should be undertaken in all settings using screening questions such as:

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

Management

- Explore the patient’s understanding of his/her illness
- Explain the management plan
- Address and treat current causes of physical and psychological distress
- Watchful waiting, with reassessment within 2 weeks, for patients who do not want an intervention, or who may recover without
- Refer to a mental health specialist if treatment-resistant, recurrent symptoms, atypical and psychotic depression and or at significant risk

Non-Pharmacological Management

- Distraction
- Relaxation
- Sleep and anxiety management advice
- Complementary therapies
- Day Care
- Guided self-help
- Specific psychological treatments including cognitive behavioural therapy (CBT)
- Exercise.

Table 36 – Pharmacological management for depression if prognosis is > 4 weeks

Selective serotonin reuptake inhibitors (SSRIs) (See BNF) e.g. Sertraline 50-200mg o.d Citalopram 10-40mg o.d. (20mg maximum in patients over 65 years	• Recommended by NICE in routine care • Useful for mixed anxiety and depressive disorders • May provoke anxiety "flare" (manage with benzodiazepines as needed) • Be aware of side effect of SSRIs (See BNF) • Incidence of sexual dysfunction <10%
Mirtazapine 15-45 mg nocte (See BNF 4.3.4)	• Response rate equivalent to other antidepressants (70%) • Rapid onset of action (possibly less than a week) • May increase appetite • Does not cause nausea and vomiting • Causes sedation at low dose so given at night. • Not associated with cardiac toxicity or sexual dysfunction
Duloxetine 60-120mg o.d.	• May be beneficial if also has neuropathic pain. • Incidence of sexual dysfunction (30%)
Venlafaxine Reserved for refractory depression	• Seek specialist advice

Please be aware that SSRIs have many interactions with commonly used medication. See BNF

If prognosis is less than 4 weeks psychostimulants may be appropriate - seek specialist advice.

PALLIATIVE CARE EMERGENCIES

HYPERCALCAEMIA

Presentation:

- Corrected serum calcium >2.7mmol/L (some variation between laboratories)
- In Primary Care seek specialist advice

Incidence

- Hypercalcaemia is common in cancer of breast, myeloma, lung, head and neck, kidney, thyroid and cervix.
- 80% of cancer related hypercalcaemia is associated with skeletal metastasis.
- 20% are related to ectopic PTH secretion
- Primary hyperparathyroidism should be considered as a possible cause (6% of cancer patients)

Table 37: Symptoms of hypercalcaemia:

General	Gastro Intestinal	Neurological	Cardiological
Dehydration Polydipsia (thirst) Polyuria Malaise Weakness	Anorexia Nausea Vomiting Constipation Ileus	Fatigue Lethargy Confusion Myopathy Hyporeflexia Seizures Psychosis Coma	Arrhythmias Conduction defects

- Common symptoms include malaise, weakness, anorexia, thirst, nausea, constipation and polyuria
- Severe symptoms include nausea, vomiting, ileus, delirium, seizures, drowsiness and coma
- Pain can be precipitated or exacerbated by hypercalcaemia
- Onset of symptoms raising clinical suspicion should be investigated. Check urea and electrolytes, eGFR, liver function tests and corrected calcium.

Assessment:

Hypercalcaemia is frequently missed, consider in unexplained nausea/ vomiting and confusion

- May develop insidiously
- Severity of symptoms is related to speed of rise of calcium.

Points to consider prior to active treatment

- First episode or long interval since previous episode
- Patient reports good quality of life prior to episode
- Expectation is that treatment will have durable effect
- Patient is willing and able to have intravenous treatment and blood tests
- Treat in context – may not be appropriate if prognosis is very poor.
- Treatment **may not** be appropriate in a patient at the end of life – **seek advice.**
- Is it mild hypercalcaemia (serum adjusted calcium < 3.0 mmol/L)
- Active management requires in-patient or day therapy care if patient is symptomatic with a corrected[5] calcium < 3.0 mmol/L, or any corrected calcium > 3.0 mmol / L

Management / Treatment:

- **If calcium < 3mmol / L and patient truly <u>asymptomatic</u>:**
  - Review medications e.g. those that impact on renal function especially diuretics (especially thiazide)/ vitamins (specifically vitamin D)/ medications or supplements containing calcium/ ACE inhibitors
  - Correct dehydration - IV fluids 0.9% sodium chloride, 2-3 Litres/24h or ensure equivalent adequate oral fluid intake
  - Recheck after 24 hours and treat if calcium level rising
  - Requires regular monitoring of calcium and renal function, as there is a high risk that the patient's calcium may continue to rise and/or patient becomes symptomatic. Initially consider checking weekly for a month, if active treatment would be indicated, then review[6]

- **If patient symptomatic and adjusted calcium <3.0 mmol/L, *or any* adjusted calcium >3mmol /L**
  - Review medications e.g. those that impact on renal function especially diuretics / vitamins / supplements containing calcium
  - Treat with IV fluids 0.9% sodium chloride 2-4 L / 24h. The amount and rate of hydration depends on renal function, calcium level and cardiovascular status.
  - After initial rehydration, administer IV bisphosphonate: pamidronate disodium or zoledronic acid (according to local guidelines / formulary) (See Table 38)
  - If renal impairment (see table 39)
  - If eGFR <30mmol/L do not give bisphosphonate **seek specialist advice**

[5] Specified **corrected** calcium – or **adjusted** calcium if preferred.

[6] This line has been added – if the patient does not have active treatment, the risks of becoming symptomatic are indeed high, requiring a further admission.

Table 38 - Use of bisphosphonates in patients with normal renal function (eGFR >60)

	Pamidronate disodium	Zoledronic acid
Corrected serum calcium up to 3 mmol/L	Dose = 30mg *	Dose = 4mg
Corrected serum calcium 3.1 – 3.5 mmol/L	Dose = 30 – 60mg	Dose = 4mg
Corrected serum calcium 3.6 – 4 mmol/L	Dose = 60 – 90mg	Dose = 4mg
Corrected serum calcium > 4.0mmol/L	Dose = 90mg	Dose = 4mg
Maximum concentration	60mg/250ml	4mg / 100ml
Infusion fluid	0.9% sodium chloride	0.9% sodium chloride or 5% glucose
Infusion rate	1mg / minute (reduce rate in renal impairment see SPC at www.medicines.org.uk)	Not less than 15 minutes
Onset of effect	Up to 3 days	Up to 4 days
Maximum effect	5-7 days	4-7 days
Duration of effect	2.5 weeks	4 weeks

*** The SPC recommends a dose related to corrected serum calcium concentration (www.medicines.org.uk). PCF5 suggests the higher dose (90mg) is given irrespective of calcium level to increase response and duration of effect.**

Table 39 Renal impairment and dosage of bisphosphonates

eGFR (ml/min)	Recommended dose (mg) pamidronate disodium	Recommended dose (mg) zoledronic acid
>60	Dose of pamidronate unchanged in *mild to moderate* renal impairment (creatinine clearance>30 ml/min) but infusion rate should not exceed 90mg over 4 hours.	4.0
50–60		3.5
40–49		3.3
30–39		3.0

Monitor for Recurrence:

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

Side effects of bisphosphonates include pyrexia, flu-like symptoms and fatigue, Late effects include osteonecrosis of jaw, especially if poor dental hygiene. For full list of side effects see SPC

SUPERIOR VENA CAVA OBSTRUCTION (SVCO)

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

Table 40 – Symptoms and signs of SVCO

Symptoms / Signs	Management
• Swelling of face, neck, arms • Headache • Dizziness • CNS depression • Fits • Dyspnoea • Dilated veins – neck, trunk, arms • Hoarse voice • Stridor	• Sit patient up • 60% oxygen • Dexamethasone 16mg/day SC or p.o. • Consider Furosemide 40mg i/v or p.o. • Seek specialist oncological advice • Endovenous stent • Radiotherapy • Chemotherapy (Small Cell Lung Cancer or Lymphoma)

Recurrence:

- I/v or oral steroids – reintroduce as or increase dose to 16mg once a day
- Stent
- Thrombolysis if stent blocked by thrombus

Outcome:

Placement of an endovenous stent offers the most rapid and effective initial symptomatic relief – *this is performed locally in the University Hospital of South Manchester at Wythenshawe*

Radiotherapy and / or chemotherapy may be offered depending on primary tumour site/histology.

METASTATIC SPINAL CORD COMPRESSION (MSCC)

The Greater Manchester Cancer Services MSCC pathway and Network Guidance on the assessment and management of MSCC is available at:
http://www.christie.nhs.uk/MSCC

- Affects 5-10% of patients with cancer
- Spinal metastases: most common in prostate, lung, and breast cancer and myeloma
- Catastrophic event – aim is to prevent establishment of paresis
- Symptoms may be vague, there should be a high index of suspicion
- Patients with cancer and neurological signs or symptoms of spinal cord compression should be treated as an oncological emergency

Symptoms

- Back/ Spinal Pain:
    - may radiate in a radicular 'band-like' pattern
    - progressive or unremitting
    - may be worse on coughing or straining
    - may be nocturnal pain preventing sleep
    - may not be present
- Nerve root pain in limbs
- Weakness of limbs (out of proportion to general condition of patient)
- Difficulty walking
- Sensory changes – tingling, numbness, "my legs don't belong to me"
- Difficulty passing urine – usually a late presentation
- Constipation or faecal incontinence

Signs

- Localised spinal tenderness
- Weakness of limbs
- Reflexes -absent / increased
    - extensor plantar reflexes
    - clonus may be present
- Altered sensation – look for a sensory level
- Distended bladder.

Management / Treatment:

- High dose dexamethasone 16mg stat dose oral, i/v or SC - commence immediately even if diagnosis is not confirmed and continue 16mg daily.
- Consider starting a PPI alongside high dose steroid treatment.
- Urgent MRI of whole spine scan (within 24 hours)
- Urgent same day referral to the Network MSCC coordinator or out of hours contact the Christie Hotline (Christie Hospital, 0161 446 3658) for advice re. radiotherapy and/or chemotherapy
- The Network MSCC coordinator (or oncology team out of hours) may advise referral for specialist spinal opinion for possible surgical decompression if:
    - No underlying diagnosis has been made
    - There are limited levels of spinal cord compression on imaging
    - Minor neurological impairment is present
    - There is progressive weakness despite previous radiotherapy at this level
    - Evidence of spinal instability and estimated life expectancy of at least six months with general condition suitable for general anaesthesia and surgery
- Immobilisation is recommended for patients with symptoms and signs suggestive of spinal instability and spinal cord compression until stability is confirmed.

Aims of Treatment:

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

CAUDA EQUINA COMPRESSION – Lumbar Spine below L1

Presentation

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

Symptoms / Signs

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

Cause

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

Treatment

As for spinal cord compression - using high dose dexamethasone 16mg stat dose oral, i/v or followed by radiotherapy.

Recurrence:

Consider steroids as above.

CATASTROPHIC HAEMORRHAGE

- It is a frightening experience for both patients and carers.
- It may be a terminal event in both advanced cancer and non-malignant disease.

Sites of haemorrhage

- Haemoptysis
- Haematemesis
- Rectal / vaginal haemorrhage
- Melaena
- Haematuria
- Surface bleeding

Nose bleed

Signs and symptoms

- Cold
- Hypotension
- Anxiety

Management:

- Plan ahead where possible
- Consider appropriateness of admission, urgent blood transfusion, i/v fluids
- If there are warning signs or high anticipated risk of bleeding have a proposed management plan ideally discussed with patient and/or family and staff
- Record management plan in case notes; communicate this to all team members
- Provide dark coloured towel to disguise blood loss.

Pharmacological Management

- Anticipatory prescribing - anxiolytic (midazolam) and analgesic (opioid)
- Midazolam naïve patients: midazolam 10mg i/v, i/m, buccal or sublingual
  - Regular midazolam use: equivalent breakthrough dose
  - In the community, train family member in the use of buccal or sublingual midazolam
- Opioid naïve: diamorphine/morphine 10mg i/v, i/m or equivalent alternative opioid
  - Regular opioid use: equivalent breakthrough dose using i/v, i/m route
- The subcutaneous route should not be used in catastrophic bleeds due to peripheral shut down and therefore unpredictable absorption of the medication

Catastrophic bleed

- Manage as per plan
- **Ensure patient is not left alone**
- Keep patient warm
- Use anxiolytic or analgesics as needed if the patient is distressed
- Support the patient and family

Further care

- If bleeding temporarily stops further management depends on overall clinical status and discussion with patient and family in relation to further acute interventions
- It may be necessary to commence an infusion of anxiolytic (midazolam) and/or analgesic (morphine or diamorphine) in the last hours of life

CARE OF THE DYING

Priorities of Care for the Dying Person

- Recognition that the person may be dying, entering the last days and hours of life
- Sensitive communication between staff and the dying person and those identified as important to them
- Involve the person and those identified as important to them in decisions about treatment and care to the extent that the dying person wants
- Support the needs of families and others identified as important to the person including any questions or concerns they may have
- Senior responsible clinician to agree an holistic individual plan of care including symptom control to be delivered
- Individualised care should be supported by the NHS England Leadership Alliance Priorities for Care of the Dying.

Symptoms that may occur in the last days and hours of life

- Pain
- Nausea and vomiting
- Respiratory – secretions, dyspnoea, stridor
- Psycho-neurological – anxiety, panic, convulsions, delirium and terminal restlessness/ agitation
- Urinary incontinence/ retention
- Sweating
- Haemorrhage

Management

- Identification and regular review of symptoms is essential
- Anticipatory prescribing via the SC route is advocated for symptoms of:
    - Pain
    - Nausea and vomiting
    - Agitation
    - Respiratory tract secretions
    - Dyspnoea
- For guidance on symptom management for dying patients, see relevant symptom chapter, and individualised last days of life prescribing algorithms (Appendix 1) and procedures (including any disease specific algorithms).

SYRINGE DRIVERS or Syringe Pumps

Recommendation – refer to the East Cheshire "Policy / Procedure for the Use of the McKinley T34 Syringe Driver" – available on-line at:

- *East Cheshire Trust website under policies (look under "S") - http://www.eastcheshire.nhs.uk/About-The-Trust/policies or*
- *E-PAIGE web - http://www.cheshire-epaige.nhs.uk/Stages/Syringe%20Driver.aspx*

Definition

The syringe driver (or syringe pump) is a portable battery operated devise used to give medication continuously via the subcutaneous route over a pre-set time, usually over a 24 hour period. A number of drivers are available. That used in Eastern Cheshire is the T34 ambulatory syringe pump. Previously this has been referred to as the **McKinley T34**; this is now part of CME Medical and is referred to as the T34 ambulatory syringe pump.

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

- Dysphagia
- Intractable nausea +/or vomiting
- Malabsorption
- Inability to administer medication via oral route i.e. head/neck cancers
- Intestinal obstruction
- Profound weakness/cachexia
- Unconsciousness
- Patient choice e.g. aversion to oral medication; dislike of alternative routes (e.g. rectal)
- Care in the last days and hours of life

For most drugs, this method of administration is unlicensed.

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

It is important to consider the following:

- If the subcutaneous route in not available, can the drug(s) be given by another route
  - Rectal (e.g. NSAID)
  - Sublingual (e.g. lorazepam)
  - Transdermal (e.g. fentanyl).
- May the drug be given as a once daily injection (e.g. dexamethasone, haloperidol, levomepromazine, octreotide)?
- It is best to avoid giving several 'once' daily injections subcutaneously. However, consider this as an alternative or if this is the patient's choice.
- Drugs are generally more bioavailable by injection than orally. This means that the dose of drug given via the syringe pump is likely to be lower that the dose previously given orally.

- Syringe drivers can take a variety of syringe sizes. The minimum recommended size is 20ml. Dilute the mixture to the maximum volume the syringe driver will take to minimise problems with site irritation. See local policy for recommendations relating to the volumes that can be accommodated in different size syringes.
- It takes a few hours before the drugs are sufficiently absorbed for an effect to be seen. If symptoms are controlled start the syringe pump 1-2hr before the effect of medications are due to wear off. If symptoms are uncontrolled, set up the syringe pump immediately. It may be necessary to cover the 'lag time' with a stat subcutaneous dose of the relevant drug if a delay would be unacceptable for symptom control.
- Protect the contents of the syringe from light with a holster.

Care in the last days or hours of life

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

Advantages of using a syringe pump

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

Disadvantages

- Patient may become psychologically dependent on the syringe pump.
- Irritation or erythema and swelling at the cannula site which may interfere with the rate and absorption.
- May be seen as a 'terminal' event by the patient and carers.
- Lack of reliable compatibility data for some mixtures.
- Possible infection.

Drug compatibility

- It is common practice to administer 2 – 3 drugs in the same syringe. It is not recommended to mix more than 3 drugs without specialist palliative care advice.
- One predictor of drug compatibility is pH. The majority of drugs given by syringe pump are acidic, with only dexamethasone, diclofenac, ketorolac and phenobarbitone being alkaline. Consequently, combinations involving these drugs tend to be incompatible and separate infusions are usually recommended.

- For most drug combinations, water for injection is the suggested diluent, as there is less chance of precipitation.
- Generally, incompatible drugs cause precipitation and thus cloudiness in the syringe. *Do not use* if this happens. Change both the syringe and the giving set.
- Some drugs are not suitable for subcutaneous injection as they are irritant to the skin; e.g. diazepam, prochlorperazine, chlorpromazine.

For more information on drugs used via this route access:
www.palliativedrugs.com (requires registration and subscription) *or*
http://www.pallcare.info/mod.php?mod=sdrivers&menu=14

Good practice re: Syringe Pump

- Before setting up the syringe pump explain to the patient and carer/family:
    - The reason for using this route and method
    - How the device works
    - Advantages and possible disadvantages.
- Qualified nursing staff should receive training and be familiar with their local syringe pump before using.
- Follow local protocol for use (links at the top of this Syringe Driver section, p60)
- All syringe pumps in use should be serviced regularly; see local guidelines.
- After use all syringe pumps should be cleaned and decontaminated as per local guidelines.
- When prescribing the drugs to be placed in the syringe pump, ensure that the correct subcutaneous breakthrough doses are prescribed (i.e. for analgesia this would be c 1/6th of the total 24 hour dose of opioid).
- Label the syringe with the list of drugs, date and time the syringe pump is commenced.
- Use of a syringe pump chart can prompt checks that the syringe pump is functioning properly.
- Checks should include the remaining volume, site condition, rate setting and appearance of the contents of the syringe.
- If the site becomes inflamed or painful re-site using a fresh cannula.
- Site irritation may be reduced by diluting the drugs in a greater volume of diluent; or using sodium chloride 0.9% as the diluent; or substituting a plastic cannula.
- Assess symptom control and adjust the prescription at appropriate intervals.
- Some patients are able to revert from a syringe pump to oral/transdermal medication. When this seems possible, convert the drugs sequentially rather than all at once.

- See Table 41 on next page

TABLE 41 - Common syringe driver drugs

Drug	24hr range	Indication	Comments
Haloperidol	1.5-5mg	Anti-emetic	Antipsychotic with less sedative effects than levomepromazine. *Higher doses may be used on specialist advice*
Cyclizine	75 – 150mg	Anti-emetic	Irritant Mild sedative
Levomepromazine	6.25 – 12.5mg 6.25 – 25mg	Broad spectrum anti-emetic Terminal restlessness	Higher doses may be used on specialist advice (more sedating)
Metoclopramide	30mg	Anti-emetic	Irritation at site Extrapyramidal effects Less sedating Avoid in bowel obstruction
Midazolam	5 – 30mg	Terminal restlessness Antiepileptic Anxiolytic	Higher doses may be used on specialist advice
Glycopyrronium	600 – 1200 microgram	Terminal secretions Intestinal obstruction	Non-sedative
Hyoscine hydrobromide	800 – 2400 microgram	Terminal secretions Intestinal obstruction Anti-emetic	Although sedative, it may cause agitation and confusion at the higher doses
Hyoscine butylbromide (Buscopan)	40 – 120mg	Terminal secretions Intestinal obstruction	Non-sedative
Diamorphine	Seek specialist advice for doses above 100mg	Analgesic	May precipitate with cyclizine at concentrations >15mg/ml
Morphine *(note – diamorphine generally preferred in this locality)*	Seek specialist advice for doses above 150mg	Analgesic	Volume of injection may be dose limiting. (maximum solubility is 30mg/ml)
Oxycodone	Seek specialist advice for doses above 100mg	Analgesic	Avoid using cyclizine with oxycodone doses >150mg in 24 hour

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

APPENDIX 1

LAST DAYS OF LIFE - SYMPTOM CONTROL GUIDANCE

- The following algorithms outline symptom control in **the last days of life**
- They have been adapted to match the Local Guidelines, which are part of the Care Plan for the End of Life document in Eastern Cheshire and Mid Cheshire Hospitals Trusts. *The Greater Manchester guidelines, which have been adapted for this locality, state "They are intended as a general guide/ Local guidelines should be followed where available."*
- Anticipatory prescribing should be encouraged in the last days of life, as it can avoid delays in obtaining medication to treat distressing symptoms. In the Community, it is recommended that this should be done on the "Blue Booklet" – Controlled Drug / Syringe Driver and Administration Record.
- Symptom control must be tailored for the individual. Reversible causes for any symptom must be assessed and managed effectively when considering prescribing or administering symptom specific medications.
- All medications, including the prescribing of anticipatory medications must:
    - Be targeted at specific symptoms
    - Be prescribed with a clinical rationale for the starting dose
    - Have their purpose, use and side effects explained to the dying person and (with the consent of the patient) those close to them if possible

- Syringe Drivers:
    - This should be obtained as soon as it is anticipated that it will be needed
    - Always explain the purpose of the syringe driver to the dying person where possible and those close to them. This should be done **before** setting the pump up other than in exceptional circumstances
- Symptom control using prescribed medications should be reviewed regularly and adjusted as needed for the individual person.

SYMPTOM: PAIN

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

If the patient is known to be intolerant to diamorphine/morphine, or it has not been effective, ***SEEK SPECIALIST ADVICE***

Is the patient in pain?
If pain is controlled by regular opioid, see pages following this.

YES

PRN S/C diamorphine
- Give diamorphine 2.5 – 5mg SC 4 hourly p.r.n
- If repeat doses are required and effective, review and consider continuous SC diamorphine

Continuous SC diamorphine
Start a CSCI via a syringe pump over 24 hours
- Start at 10-20mg over 24 hours
- Calculate p.r.n. 'breakthrough' dose by dividing total 24 hour dose of SC diamorphine by 6
- Prescribe p.r.n dose of diamorphine ~~4~~ 2 hourly p.r.n

NO

Pre-Emptive Prescribing
Prescribe diamorphine 2.5 - 5mgs SC 2hly p.r.n **in case** pain occurs

Review Pain At Each Visit
- Is diamorphine effective?
- If more than 2 p.r.n doses in 24 hours needed consider increasing the 24 hour CSCI dose -
  - Recalculate CSCI dose by adding total p.r.n doses to amount in CSCI
    - **(Do not increase CSCI dose by more than 50% without specialist advice)**
- If patient needs more that 3 p.r.n doses, or diamorphine not effective, **seek specialist advice**

KEY MESSAGES – PAIN

- Alternative strong opioids may be prescribed according to guidelines in other localities, e.g. morphine
- Consider and eliminate reversible causes for pain (constipation, urinary retention, spiritual and psychological causes)
- Consider whether a pain chart would be of benefit
- Refer to the opioid conversion charts in Appendix 2 below for information
- When calculating CSCI increase from p.r.n use, exclude doses used for incident pain

SYMPTOM: PAIN

WHEN PATIENT TAKING REGULAR ORAL MORPHINE BECOMES UNABLE TO SWALLOW

*If the patient is taking oral **oxycodone** seek specialist advice when commencing a continuous subcutaneous infusion. Principles are similar, conversions differ.*

Is pain controlled on current dose?

NO

Commence CSCI via a Syringe Pump

- Convert the 24h dose of oral morphine to the SC equivalent (see key messages below)
- Consider increasing calculated total 24 hour dose of SC diamorphine by 33-50%.
- Give the total 24 hour dose of SC diamorphine via syringe pump over 24 hours
- Calculate new breakthrough dose (see key messages below) – normally 1/6 x 24h dose in CSCI

YES

Commence CSCI via a Syringe Pump

- Convert the dose of oral morphine to the SC diamorphine equivalent (see key messages below)
- Calculate breakthrough dose in case required (see key messages below) – normally 1/6 x 24h dose in CSCI

Review Pain at Each Visit

- Is the diamorphine effective?
- If the patient needed more than 2 p.r.n. doses in 24 hours consider increasing the 24 hour CSCI dose
- Recalculate CSCI dose by adding p.r.n. doses to amount in CSCI **(Do not increase by more than 50% without specialist advice)**
- If patient needs more that 3 p.r.n. doses in 24h, or diamorphine is not effective **seek specialist advice**

KEY MESSAGES - PRESCRIBING SUBCUTANEOUS MORPHINE

- To calculate the dose of SC diamorphine, divide total dose of oral morphine by 3
- To calculate the breakthrough dose of diamorphine divide total 24 hour dose of SC diamorphine by 6 and prescribe this dose 2 hourly SC p.r.n.
- Alternative strong opioids may be prescribed according to local guidelines, e.g. morphine. See opioid conversion charts section in Appendix 2 for information.

SYMPTOM: PAIN

PATIENT USING FENTANYL PATCHES WHO BECOMES UNABLE TO SWALLOW

IMPORTANT

CONTINUE TO USE AND CHANGE PATCH EVERY 72 HOURS AS PREVIOUSLY PRESCRIBED

Anticipatory Prescribing

- Use SC diamorphine for breakthrough pain.
- Calculate or consult conversion chart (Appendix 2) as a guide for the p.r.n. dose of SC diamorphine that is relevant for the strength of patch
- If diamorphine or morphine not previously tolerated, consider use of oxycodone – seek specialist advice
- Alternative strong opioids may be prescribed according to local guidelines.
- Prescribe the breakthrough pain dose 2 hourly p.r.n. in case pain occurs

If pain is not controlled, or if needing more than 3 p.r.n doses over 24 hours seek specialist advice

TERMINAL RESTLESSNESS AND / OR AGITATION

YES

Look for and treat any reversible causes (see key messages below*)

AND

Consider whether the patient has delirium?

Has restlessness been resolved?

NO

YES

SEEK SPECIALIST ADVICE

NO

Anticipatory Prescribing For Terminal Restlessness / Agitation
Prescribe midazolam 2.5 to 10mg SC 3 hourly p.r.n. (for frail patients, may use lower range 2.5-5mg); start with lower dose

- **Give midazolam 2.5mg-5mg SC Review after 1 hour (30 minutes if severe) – if restlessness not resolve, give a second dose of 2.5mg and review after a further 1 hour**
- Prescribe midazolam 2.5 – 10mg/24h by CSCI

Has restlessness been eased?

NO

Prescribe levomepromazine 12.5-25mg SC stat and p.r.n 3hly
If effective, consider adding levomepromazine 25-50mg/24h to midazolam in CSCI

Seek Specialist Advice

YES

If recurs - reassess
Increase p.r.n midazolam to 5-10mg SC
Consider increasing CSCI midazolam dose

Has restlessness been resolved?

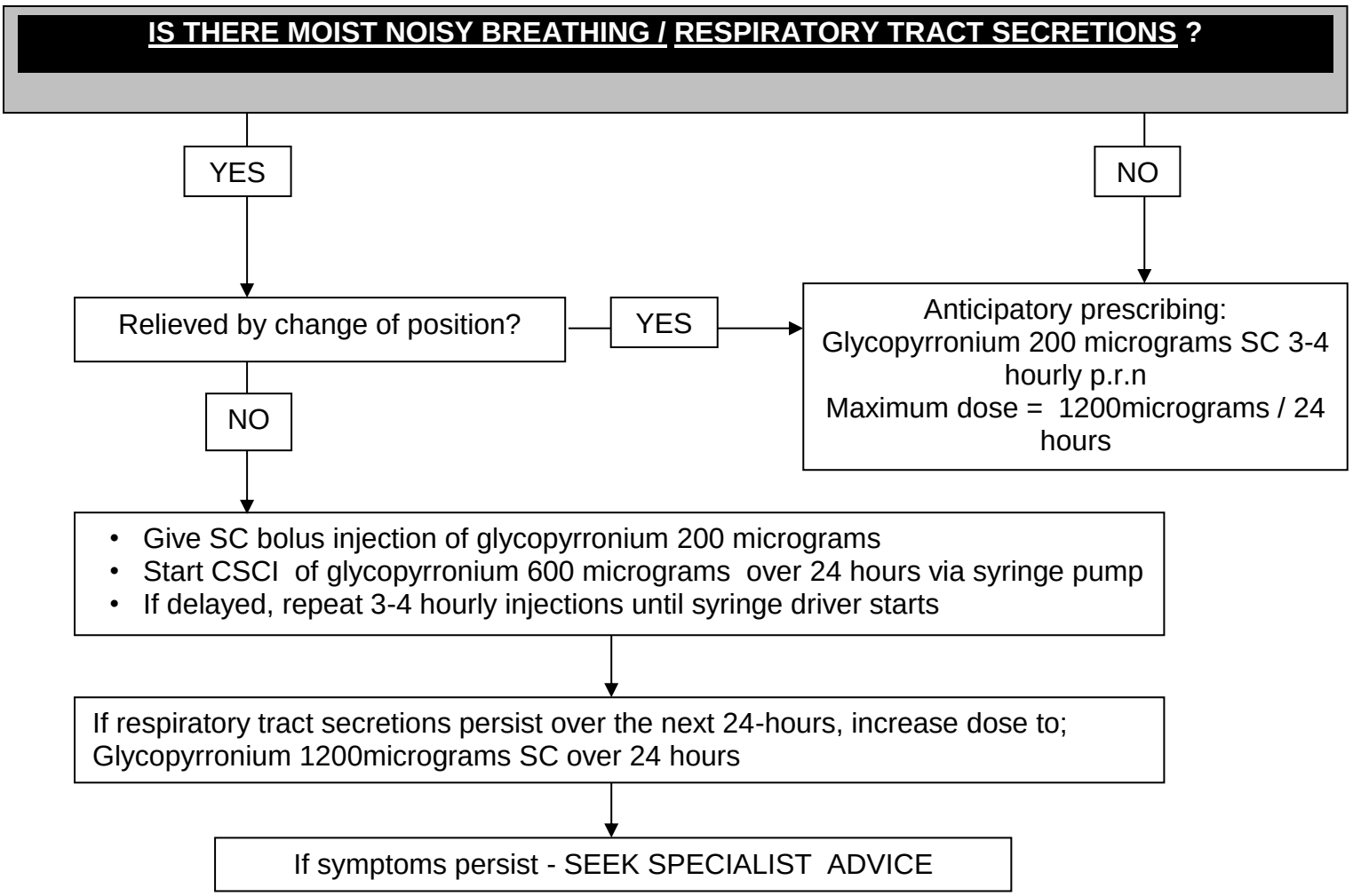
NO

YES

Monitor Continuous SC Infusion (CSCI) of midazolam
If 2 or more p.r.n. doses are required in a *24*-hour period consider increase in CSCI dose
If insufficient, consider levomepromazine as above

KEY MESSAGES – TERMINAL RESTLESSNESS AND AGITATION

- * Look for & document review of potentially reversible causes of agitation (e.g. pain, constipation, urinary retention, overheating, infection, nicotine withdrawal, hypercalcaemia)
- If requiring 3 or more p.r.n doses within 8 hours seek urgent specialist advice
- Consider adding any p.r.n doses given in previous 24 hours to syringe pump dose
- P.r.n dose of midazolam should approximate the amount in the syringe pump divided by 6



Mechanical forms of removing secretions, including suction, may be used if tolerated by the patient at any time.

KEY MESSAGES – RESPIRATORY TRACT SECRETIONS

- The advice above refers to moist noisy secretions in a dying person who is **unconscious.**
- Antimuscarinic drugs cause reduced saliva flow, and sputum to become reduced in volume and stickier. If the patient is conscious, this causes a dry mouth and increased difficulty in expectoration.
- Treatment should preferably start at **onset** of secretions. Medication will prevent *new* secretions being produced but will not remove secretions already present
- Glycopyrronium dose advice varies from different sources. The 400mcg dose is more effective but may have more side effects, including on circulation. Evidence is limited and based to a large extent on experience.
- If there is a delay in starting a syringe driver when appropriate, administer regular glycopyrronium 200micrograms 3-4 hourly until available.
- Alternative antimuscarinic drugs can be used e.g. hyoscine butylbromide (Buscopan®) 20mg SC 4 hourly p.r.n., 60-120mg CSCI or hyoscine hydrobromide 400micrograms SC 4 hourly p.r.n, 1.2mg – 2.4mg CSCI over 24 hours. The latter can rarely cause agitated delirium.
- Terminal respiratory secretions may be most upsetting for family and those close to the patient. Discussion of these symptoms with them is important.

IS THE PATIENT BREATHLESS?

YES

General Measures

- Explanation
- Companionship
- Fan / open window
- Oxygen if hypoxic and symptomatically beneficial
- Nurse in upright position

Is there a reversible cause that can be managed given likely limited time?

YES

Treat the cause –

e.g. nebulised bronchodilators for bronchospasm; diuretics for heart failure,

If still symptomatic, aim to relieve symptoms of breathlessness

NO

Pre-Emptive prescribing of PRN medication

- If **not currently** taking regular strong opioid prescribe morphine 2.5mg SC 4 hourly p.r.n in case patient becomes breathless
- If **currently** taking strong opioid ensure correct p.r.n dose is prescribed for pain and use this dose for breathlessness.
- If a dose is given for breathlessness follow the pathway for the patient who is breathless

If patient is unable to take morphine *SEEK SPECIALIST ADVICE*

NO

If **not** currently on regular strong opioid - start morphine 2.5mg SC 4 hrly p.r.n

- If **unable to take oral** morphine, use diamorphine 1.25-2.5mg SC 4 hrly p.r.n.
- If 3 or more p.r.n doses are required, prescribe regular oral morphine or assess need for CSCI via syringe driver
- If currently taking strong opioid increase dose by 33% to cover the dyspnoea

If the patient is also agitated consider adding midazolam 2.5mg SC hourly p.r.n

- If 3 or more doses of midazolam are required, consider CSCI

If symptoms persist **SEEK SPECIALIST ADVICE**

KEY MESSAGES – BREATHLESSNESS

- Treatments for reversible causes include; bronchodilators, diuretics, and antibiotics
- Simple measures such as a calm environment, a fan or open window can be just as effective as medication
- If 3 or more p.r.n doses are required within 8 hours **seek specialist advice**

IS THE PATIENT EXPERIENCING NAUSEA AND / OR VOMITING?
Note – this algorithm differs from the GMSCN, which recommends metoclopramide as first choice

YES

Give cyclizine 50mg SC stat **and** start cyclizine 100-150mg/24h by CSCI

or

Give haloperidol 1.5-5mg stat **and** start haloperidol 2.5-10mg/24h by CSCI

and

Prescribe p.r.n. doses:

- Cyclizine – 50mg SC 4-6 hrly (max total 200mg/24h including CSCI) ***and/or***
- Haloperidol 1.5-5mg 4-6 hrly q.d.s (max 10mg/24h)

If symptoms persist, see box below

NO

If on established effective antiemetic, assess whether this can be converted to a CSCI, and if it is compatible with other medications in use

Prescribe p.r.n. drugs, indicate which is first line and which 2nd:

- Cyclizine – 50mg SC 4-6 hrly (max total 200mg/24h) ***and/or***
- Haloperidol 1.5-5mg 4-6 hrly q.d.s (max 10mg/24h)

If 2 or more p.r.n doses required, consider starting CSCI

IF SYMPTOMS PERSIST

Combine cyclizine and haloperidol together in CSCI ***or***

Convert to levomepromazine 6.25mg stat, then start CSCI with 6.25-12.5mg/24h

- Prescribe p.r.n. levomepromazine 6.25-12.5mg SC 4-6 hrly and titrate
- If dose needed exceeds 50mg/24h or there is uncertainty, SEEK SPECIALIST ADVICE

KEY MESSAGES – NAUSEA AND VOMITING

- Where dose ranges are given, start at the lower end of the dose range give. Total p.r.n doses may advise the starting dose of a CSCI if needed
- Patients with complete bowel obstruction should not receive metoclopramide
- Alternative antiemetics may be prescribed in specific circumstances, e.g. metoclopramide if a prokinetic effect on the stomach and/or bowel is required
- Metoclopramide and cyclizine should not be prescribed simultaneously
- *For patients with Parkinsonism or Parkinson's Disease seek specialist advice*
- Simple measures such as treating constipation and keeping the patient away from strong food smells may also help
- Maximum doses above are given as a guide. Specialist advice may suggest doses higher than this in specific circumstances.

APPENDIX 2

Drug Conversion Charts

- Breakthrough p.r.n doses within these charts are based on 1/6 of total regular daily dose of opioid.
- Each patient should be assessed on an individual basis.
- Some variation in the dose required will exist between patients as outlined in the above sections.
- Be cautious when converting between different opioids.
- The conversion tables below act as a guide but consideration should be given to wide inter-individual variation that exists in both patients and drugs.
- Consider a dose reduction when switching opioids.

Table 42 - Dose conversions of weak opioids to oral morphine with examples

Drug	Conversion	E.g. dose in 24 hours (mg)	Approximate oral morphine equivalent in 24 hours (mg)
Codeine	To obtain equivalent oral morphine dose divide by 10	240	24
Dihydrocodeine		240	24
Tramadol		400	40

Table 43 - Recommended strong opioid dose conversions

Convert from	**Convert to**	**Calculation**
Oral morphine	SC diamorphine	Divide by 3
	SC morphine	Divide by 2
	Oral oxycodone	Divide by 2
	Oral hydromorphone	Divide by 7.5
	SC oxycodone	Divide by 3
Oral oxycodone	SC oxycodone	Divide by 1.5
	SC morphine	Equivalent
	SC diamorphine	Divide by 1.5
SC morphine	SC diamorphine	Divide by 1.5
	SC oxycodone	Divide by 1.5
SC diamorphine	SC oxycodone	Equivalent

E.g. an equivalent switch from oral morphine m/r 120mg b.d to oral oxycodone m/r – total oral 240mg a day; divide by 2, gives oxycodone m/r 120mg/24h, or 60mg b.d.

Table 44 - Recommended starting dose for buprenorphine patch

Oral codeine dose (mg / 24 hours)	Oral morphine dose (mg / 24 hours)	Buprenorphine patch strength (microgram/hr)	P.r.n dose of oral morphine (mg)	Fentanyl patch strength approximate equivalent (microgram/hr)
		BuTrans® Change patch ONCE a week		
120mg	12	5 *	2	-
240mg	24	10	5	-
	48	20	7.5 - 10	12
		Transtec® Change patch twice a week		
	84	35	15	25
	126	52.5	20	37
	168	70	30	50

* For patients on BuTrans 5 microgram/h patch, p.r.n codeine may be adequate

These recommendations are based on a PO morphine:TD buprenorphine dose ratio of 100:1 derived from published data, which is in keeping with the buprenorphine manufacturer's dose ratio range of 75–115:1 (see SPC; it is an approximation, so be aware of individual variation).

Commencing fentanyl patches and conversion charts

- Fentanyl patches are not recommended for patients who are strong opioid naïve.
- Consider buprenorphine patches for opioid naïve patients requiring transdermal strong opioid (Table 44)
- Before commencing fentanyl patches consider how long the patient has been taking strong opioids.
- The recommended starting dose depends on the patient's level of opioid tolerance, estimated from the duration of previous treatment (see Skip M. UK Medicines Information (UKMi) Q&A 302.4 – full reference at end of document).
- If a patient has been taking morphine for no more than "several weeks" then opioid tolerance may be limited and still developing – table 45 below.
- If a patient has been taking morphine for months or longer – a "long time" as mentioned in this guidance and the BNF - then it likely that a degree of opioid tolerance has developed – table 46 below.

The difference between "up to several weeks" and "for a long time" is blurred. If in doubt, use Table 45 as the equivalent fentanyl patch doses are lower.

To convert a strong opioid other than morphine

- First use the tables above to calculate equivalent oral morphine dose
- Then use either table 45 or 46

On occasion, a patient is switched from transdermal fentanyl to an alternative strong opioid. In this case seek specialist advice – the tables are less reliable calculating from left to right.

If in any doubt about potential tolerance, then use a conservative dose – consider 25-30% below the calculated dose and assess over 48h, using p.r.n doses as a guide.

*"These are approximate guides only as comprehensive data are lacking and there is inter-individual variation. Patients who are taking a daily dose of morphine that falls between fentanyl patch strengths will need to be changed to a patch which is either slightly less or slightly more potent than the morphine dose (**Error! Bookmark not defined.**2). This will be a clinical decision which must take into account all individual patient factors. The Summary of Product Characteristics (SPC) for the specific fentanyl patch being used should also be consulted as guidance may vary between individual products." (Skip, 2015)*

Table 45 – If patient on strong opioid for no more than several weeks - conversion from strong opioid to fentanyl patch

- Dose ratio PO morphine to TD fentanyl 150:1 when calculating conversion from strong opioid to fentanyl patch
- This includes patients who have difficulty tolerating side effects of morphine or oxycodone.

Table 46 – If patient has been stabilised on strong opioids for a long time (months or more), they may be thought to be highly opioid tolerant

- Dose ratio PO morphine to TD fentanyl 100:1 when calculating conversion from strong opioid to fentanyl patch
- This includes patients who have been on the same dose of morphine or oxycodone for a long time.

Table 45 - Starting dose for fentanyl patches based on previous opioid regime.

FOR THOSE TAKING STRONG OPIOIDS FOR NO MORE THAN SEVERAL WEEKS.

- Based on dose ratio PO morphine to TD fentanyl 150:1

OPIOIDS FOR SEVERAL WEEKS AT MOST		**FENTANYL DOSE**	**AS REQUIRED (p.r.n) RESCUE DOSES**		
Oral morphine total 24 h dose (mg / day)		**Dose (microgram/h)**	**Oral morphine** immediate release 2 hourly rescue dose (mg)*	**Oral oxycodone** immediate release 2 hourly rescue dose (mg) *	**Diamorphine or oxycodone SC injection** 2 hourly rescue dose
Mid-point dose	**Range**				
45	< 70	12	7.5	3.5	2.5
90	70 - 111	25	15	7.5	5
135	112 - 157	37	20	10	7.5
180	157 - 201	50	30	15	10
225	202 - 246	62	35	15	12.5
270	247 - 314	75	45	20	15
360	315 - 404	100	60	30	20
450	405 - 494	125	75	35	25
540	495 - 584	150	90	45	30
630	585 - 674	175	100	50	35
720	675 - 764	200	120	60	40
810	765 - 854	225	130	70	45
900	855 - 944	250	150	75	50
990	945 - 1034	275	165	80	55
1080	1035 -1124	300	180	90	60

** Dose rounded to nearest convenient dose as appropriate. Calculated from 1/6 x equivalent mid-point dose of morphine; then for oral oxycodone divided by 2; and for SC diamorphine and oxycodone divided by 3.*

For patients on oral hydromorphone for breakthrough pain seek specialist advice. (PCF5)

Table 46 - Starting dose for fentanyl patches based on previous opioid regime.

FOR THOSE TAKING STABLE DOSE OF STRONG OPIOIDS FOR A LONG TIME

- Based on dose ratio PO morphine to TD fentanyl 100:1

OPIOIDS FOR A LONG TIME		**FENTANYL DOSE**	**AS REQUIRED (p.r.n) RESCUE DOSES**		
Oral morphine total 24 h dose (mg / day)		**Dose (microgram/h)**	**Oral morphine** immediate release 2 hourly rescue dose (mg)	**Oral oxycodone** immediate release 2 hourly rescue dose (mg)	**Diamorphine or oxycodone SC injection** 2 hourly rescue dose †
Mid-point dose	**Range**				
30	< 44	12	5	2.5	2
60	45 - 74	25	10	5	3.5
90	75 - 104	37	15	7.5	5
120	105 - 134	50	20	10	7
150	150 - 175	62	25	12.5	8
180	175 - 209	75	30	15	10
240	210 – 269	100	40	20	12.5
300	270 - 329	125	50	25	15
360	330 - 389	150	60	30	20
420	390 - 449	175	70	35	20
480	450 - 509	200	80	40	25
540	510 - 569	225	90	45	30
600	570 - 629	250	100	50	30
660	630 - 689	275	110	55	35
720	690 - 749	300	120	60	40

† - rounded to nearest convenient dose - nearest 5mg for doses > 20mg

For patients on oral hydromorphone for breakthrough pain seek specialist advice. (PCF5)

Table 47 - Opioid Conversion Chart (note: – rounded to convenient doses)

	Morphine (mg)				Diamorphine (mg)		Oxycodone (mg)			
Route	**Oral**		**SC**		**SC**		**Oral**		**SC**	
Dose	24h total	4 hourly	CSCI 24h	4 hourly	CSCI 24h	4 hourly	24h total	4 hourly	CSCI 24h	4 hourly
	30	5	15	2.5	10	2.5	15	2.5	10	2.5
	60	10	30	5	20	5	30	5	20	5
	90	15	45	7.5	30	5	45	7.5	30	5
	120	20	60	10	40	5	60	10	40	5
	150	25	75	12.5	50	7.5	75	12.5	50	7.5
	180	30	90	15	60	10	90	15	60	10
	240	40	120	20	80	15	120	20	80	15
	360	60	180	30	120	20	180	30	120	20
	480	80	240	40	160	25	240	40	160	25
	600	100	300	50	200	30	300	50	200	30
	800	130	400	65	260	40	400	65	260	40
	1000	160	500	80*	330	60	500	80	330	60
	1200	200	600	100*	400	70	600	100	400	70

This table does **not** indicate incremental steps. **Dose increases are normally in 30-50% steps**.

* SC volumes more than 2ml are uncomfortable; note: oxycodone injection is available as 10mg/ml or 50mg/ml; morphine is 30mg/ml; consider using alternative opioid or 2 injection sites per p.r.n. dose if injection volume is more than 2ml

APPENDIX 3

Pharmacokinetics of strong opioids

Preparation	*Onset of action*	*Time to peak plasma concentration*	*Duration of action*
Oral Immediate release morphine		15 – 60 mins	3-6 h
Oral Immediate release oxycodone	20 – 30 mins	60 – 90 mins	4 – 6 h
Oromucosal fentanyl products	10 – 15 mins	20 - 480mins	Greater than 1 hour
Modified release morphine			12 – 24 h *
Modified release oxycodone		3 hours	12 h
Transdermal buprenorphine	4 – 24 h	29 – 72 h	3 – 7 days *
Transdermal fentanyl	3 – 23h	24 – 72 h	72 h
SC morphine / oxycodone / diamorphine		15 mins	

** Depends on product used.*

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