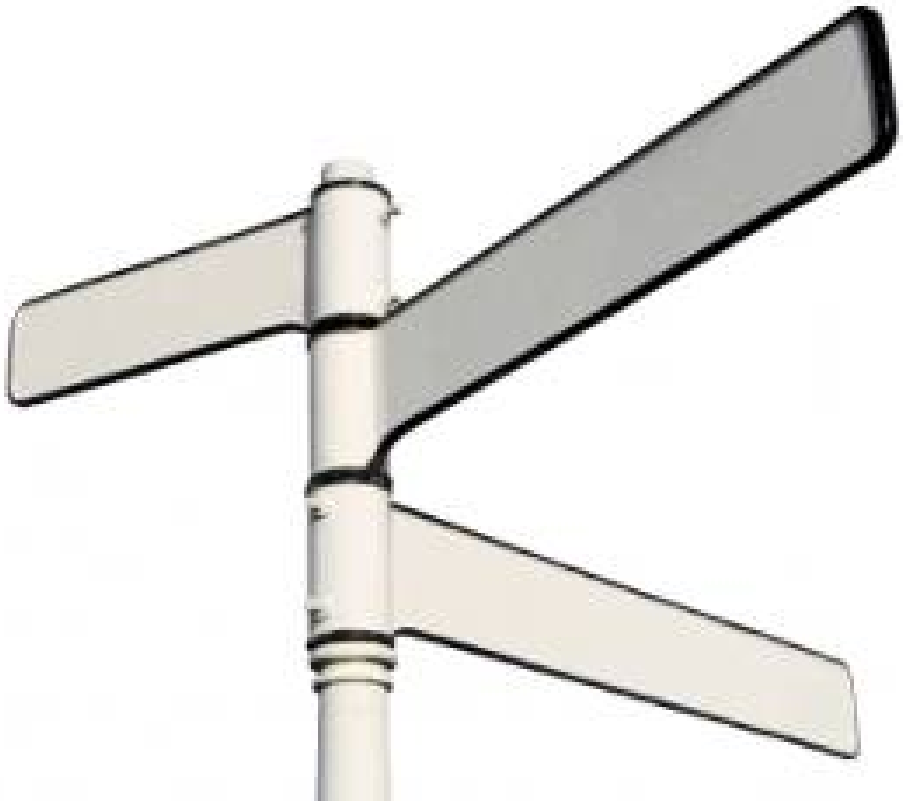
Fifth Version

Palliative Care



Salford Pain and Symptom Control Guidelines

Greater Manchester & Cheshire Cancer Network

Salford NHS
Primary Care Trust

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PAIN & SYMPTOM CONTROL GUIDELINES
5th Edition January 2009

NOTES

This is the fifth edition of the Salford Primary Care Trust *Pain and Symptom Control Guidelines* and the second of the Greater Manchester and Cheshire Cancer 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.

Many drugs are used in palliative care outside their licensed indication at the doctor's discretion. Details of these, together with "typical" doses and maximum doses are included, however, the inclusion of a drug or treatment in these guidelines does not absolve the doctors of their personal responsibility in providing treatment that they are confident with and can justify, and that is tailored to the individual patient's circumstances. For further information or advice please contact your local Specialist Palliative Care Team, Hospital and Primary Care Trust Pharmacy Service Advisers.

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Also available on the following websites:
Salford PCT and Salford Royal NHS Foundation Trust
Greater Manchester and Cheshire Cancer Network

CONTENTS

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 - "Controlled Drugs and Drug Dependence" section
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		gramme(s)
h		hour(s)
hrly		hourly
i/m		intramuscular
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
NSAID		Non - steroidal anti-inflammatory drug
o.d		once a day (omni die)
p.o		by mouth (per oris)
PPI		proton pump inhibitor
p.r		by rectum (per rectum)
p.r.n.		when required (pro re nata)
q4h		Every 4 hours (preferred to q.q.h - quarta quaque hora)
q.d.s		four times a day (quarter die sumendus)
®		Trade mark
SC		Subcutaneous
SL		Sublingual
SSRI		Selective serotonin re-uptake inhibitor
stat		Immediately
t.d.s		three times a day (ter die sumendus)
TENS		Transcutaneous electric nerve stimulator
UK		United Kingdom
UTI		urinary tract infection
WFI		water for injection
WHO		World Health Organization
≈		Is approximately equivalent to

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 – mood / relationship effects / sleep etc
  spiritual – fears / hopelessness / regrets / guilt

Assess physical aspects of the pain:

- cause of *each* pain - there may be more than one; may have non-cancer 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”

2. Table 1 - Common Pain Types

Pain	Examples	Character	Initial management	Adjuvants	Consider
Deep Somatic	Bone metastases	Gnawing, aching. Worse on moving or weight bearing.	WHO Ladder	NSAIDs	Radiotherapy Surgery Bisphosphonate
Visceral	Liver, lung, bowel	Sharp ache *or* deep, throbbing. Worse on bending or breathing.	WHO Ladder	Corticosteroid NSAIDs	Nerve Block Surgery
Neuro-pathic	Nerve compression Nerve damage	Burning, shooting; sensory disturbance in affected area	WHO Ladder	Tricyclic antidepressant Anticonvulsant Corticosteroid *See Table 3*	Radiotherapy TENS Nerve block
Smooth muscle spasm	Bowel obstruction Bladder spasm	Deep, twisting, colicky (waves)	May be sensitive to opioid - variable	Anticholinergic - e.g hyoscine butylbromide for bowel colic	Surgical relief of obstruction

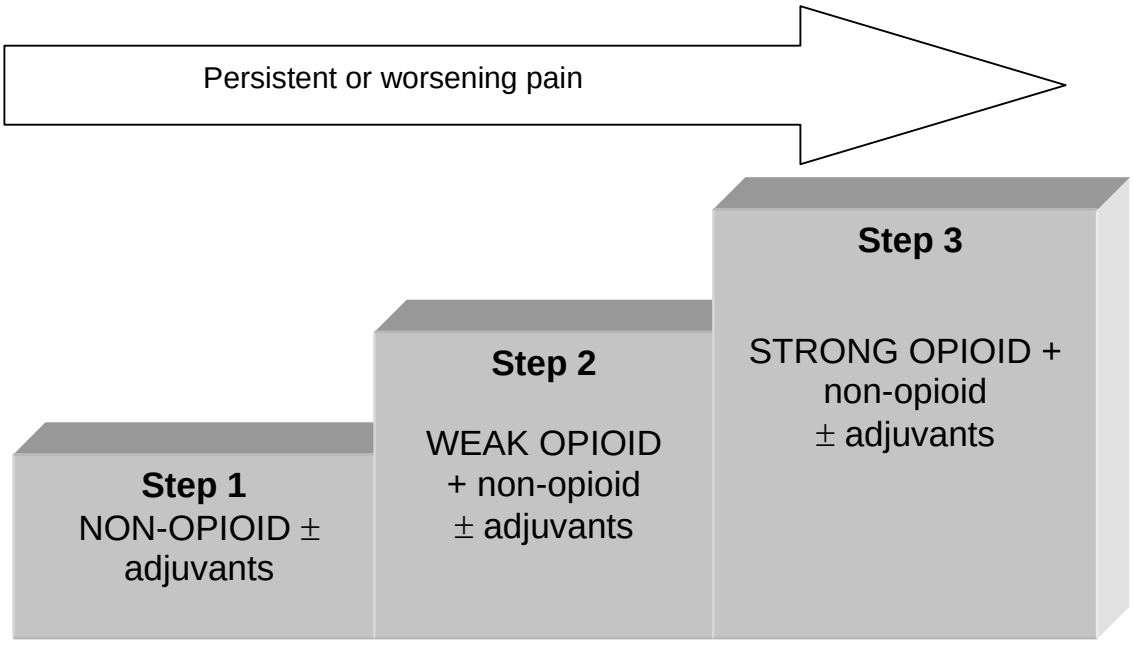
3. Pain Relief

- Set realistic goals, stage by stage: e.g. pain-free overnight; at rest; on movement.
- Prescribe analgesics regularly.
- Prescribe p.r.n. analgesic for breakthrough and/or incident pain (see section 5).
- Consider most appropriate route of administration – use oral route where possible.
- Prescribe by the WHO analgesic ladder (see section 4).
- Give patients and carers information and instruction about their pain and pain management. Encourage them to take an active role in their pain management.
- Review pain control regularly.

4. The WHO Analgesic Ladder

NOTE: MORPHINE IS STILL THE FIRST LINE STRONG OPIOID AT STEP 3 OF WHO LADDER (1996) AND EAPC GUIDELINES (2001)

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.

Adjuvant drugs contribute to pain relief and can be used alone or in conjunction with analgesics (see Table 3). They can be introduced at any step in the analgesic ladder.

Example use of analgesic ladder

Patient on no analgesics – mild pain:

Step 1 -	Start **regular** paracetamol 1g q.d.s
Step 2 -	Complaining of more pain - add codeine 30-60mg q.d.s. **regularly.**
Step 3 -	On maximum paracetamol and codeine, still in pain - <u>stop weak opioid</u>. Commence morphine: *Either* morphine m/r 10-30mg b.d *Or* short-acting morphine 5-10mg 4 hourly **regularly**; Or use alternative strong opioid if indicated (see below)

Notes

i. Tramadol is another weak opioid. However, the preparations available in the UK are more potent than codeine – e.g. tramadol 50mg is approximately as potent as 5-10mg of oral morphine. It is partly antagonized by ondansetron. See Table 32 for further details.

For dose conversion for weak opioids and buprenorphine to oral morphine see Appendix Table 33, p48.

5. Morphine

- Explanation and reassurance about morphine is essential to patients and carers.
- Reassure patients that they will not become psychologically dependent

Regular morphine

- See section 4 above for advice on commencing regular morphine.

- Be aware of dose conversions from weak opioids to oral morphine (see Appendix Table 33, p48.)
- In patients who are elderly, frail or have renal impairment, start with short acting morphine, using lower doses and/or increased dosage intervals
- Titrate morphine dose to achieve maximum analgesia and minimum side effects
    - typical steps as 30-50% increments (in mg per 4h); 5-10-15-20-30-40-60-90mg.
    - also prescribe "as needed" short-acting morphine for breakthrough pain (see below)
- If commenced on regular short-acting morphine, once pain control is achieved, consider conversion to modified release morphine at same 24h total dose.

** Note: it is recommended that strong modified release oral opioids are prescribed by brand rather than generically.*

Generic morphine	Morphine brand names *	Dose intervals
Short-acting morphine	Oramorph®, Sevredol®	4 hourly
Modified release morphine	Zomorph®, MST®, Morphgesic SR®	12 hourly (b.d.)

Note – an once daily morphine m/r capsule preparation called MXL is also available

"As needed" (p.r.n.) morphine

- ALWAYS prescribe short-acting morphine for breakthrough pain when prescribing regular morphine.

Calculate p.r.n. dose **= total daily dose of morphine ÷ 6 (**(e.g. Morphine m/r 30mg b.d. = Total oral morphine dose over 24hrs of 60mg, therefore breakthrough morphine oral dose = 60 ÷ 6 = 10mg p.r.n.). This may be given up to every two hours if 2 or more doses given in 24h seek specialist advice.

Management of breakthrough pain (pain occurring before the next regular dose of analgesic)

- Is the regular opioid dose adequate? Titrate dose as necessary.
- If on m/r strong opioid, prescribe short-acting opioid p.r.n. and administer when required.
- Review pain and analgesia regularly.

Management of incident pain (pain free at rest but pain occurs on movement, weight-bearing; procedures such as dressing changes)

- Exclude a surgically correctable lesion, e.g. bone fracture
- Give equivalent of 4 hourly dose of short-acting opioid 30 min before procedures.
- If ineffective seek specialist advice.

Parenteral morphine and diamorphine

- If a patient is unable to take morphine orally, then give morphine or diamorphine by CSCI via syringe driver and prescribe appropriate SC p.r.n doses.
- ***Dose equivalents:*** **Oral morphine 3mg ≈ SC morphine 1.5mg ≈ SC diamorphine 1mg**

(For other strong opioid conversions, see p[47] and Syringe Driver Guidelines on p[44])

- Opioid naive patients should be observed for at least ONE HOUR following the administration of the first dose of morphine or diamorphine injection (see National Patient Safety Agency, Safer Practice Notice 2006/012; ensuring safer practice with high dose ampoules of diamorphine and morphine) [1]
- Parenteral morphine and diamorphine should normally be stocked and used in 5mg and 10mg strength ampoules for stat and p.r.n. breakthrough dose administration, and 30mg strength ampoules reserved for use in patients on continuous subcutaneous infusions (syringe drivers) requiring higher daily doses, unless the patient requires larger doses (see National Patient Safety Alert 2006/012) **Error! Bookmark not defined.**

6. Management of Opioid Side Effects

If side effects are intractable and reducing the patient's quality of life or limiting pain relief, consider changing to an alternative opioid. **Seek specialist advice**.
Consider *renal impairment* as a cause if toxicity occurs on previously tolerated dose.

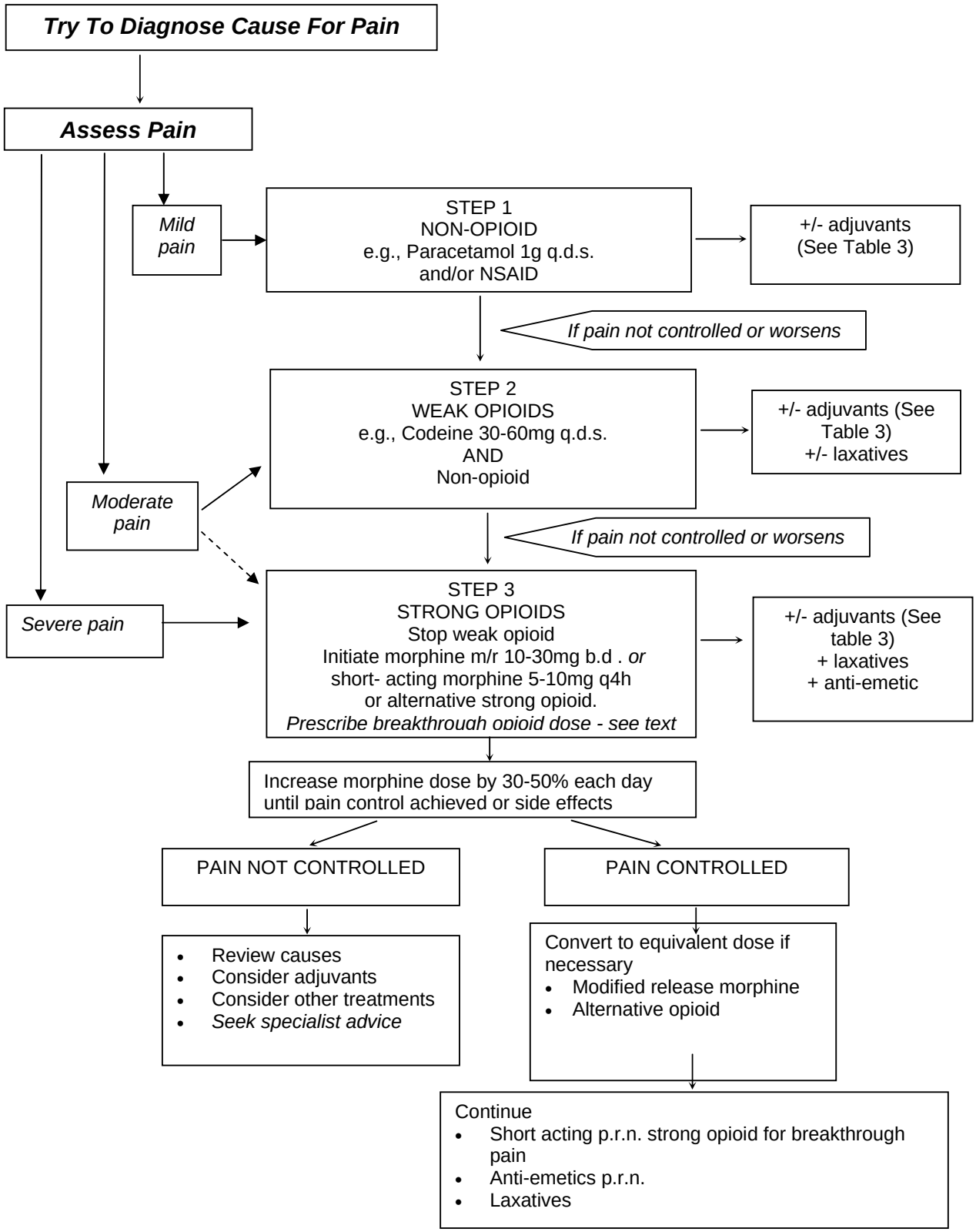
i. *Constipation (very common)* - prevent by prescribing concurrent stimulant laxative ± softener and titrate
ii. *Nausea and vomiting (c30%)* - prescribe haloperidol 1.5mg at night or metoclopramide 10mg t.d.s. for 5 days and then stop if asymptomatic;
iii *Drowsiness* - warn patients that drowsiness and poor concentration may occur at start of therapy, and when dose is increased, but will lessen after a few more days
iv *Delirium* - decrease dose if possible; consider adjuvant drug or alternative opioid; consider haloperidol 1.5 - 3mg orally or subcutaneously – see page 29
v *Myoclonus* - decrease dose if possible; if this dose of opioid is essential, add oral clonazepam 500 micrograms nocte or use SC midazolam 2.5mg 4h p.r.n.
vi *Hallucinations* - decrease dose if possible; consider adjuvant drug or alternative opioid
vii *Dry mouth (nearly all patients)* - inform patient and advise good oral hygiene (see p27)
viii *Respiratory depression* - very unlikely if opioids used correctly. Note - naloxone can provoke a severe withdrawal syndrome if used too rapidly and/or in too high a dose

- If respiration slow (<12/min), but patient easily rousable
  - Stop opioid and monitor carefully until improves
  - Resume opioids at lower dose - **seek specialist advice**
- If respiration slow (<12/min), difficult to rouse and cyanosed or hypoxic (SaO_2 <90%) ***or*** respiration <8/min - use **naloxone** (to use dilute 1:10 with 0.9% sodium chloride solution for injections) – (*see BNF section 15.1.7)*
  - intravenous naloxone 100-200 microgram
  - then 100 microgram i/v every 2 minutes until respiration is satisfactory
  - monitor carefully - further doses (i/m or i/v) may be needed - naloxone acts for 30- 60mins
  - If venous access is not possible, or there would be an appreciable delay, naloxone may be given i/m or SC (see BNF)

[1] http://www.npsa.nhs.uk/patientsafety/alerts-and-directives/notices/morphine-diamorphine/ (accessed 16/7/8)

7. Treatment Guidelines for Cancer Pain

Figure 2



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

8. Alternative Strong Opioids

Morphine is the usual first line strong opioid

Rationale for using alternative strong opioids:

- Pattern and severity of side-effects (when switching to another opioid of similar opioid-receptor affinity, improved pain relief should not be expected; but the pattern and severity of undesirable side-effects may be altered.)
- 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, the appropriate equivalent dose can be calculated by knowing the relative potency of the two drugs (see Table 31). However, this conversion is only an approximation as wide variations exist between individuals. Especially when converting high doses the initial dose may have to be reduced by 25-50% of the calculated equivalent dose to avoid undesirable side-effects or toxicity.

Seek specialist advice on the most appropriate alternative strong opioid and the appropriate conversion dose.

Fentanyl

- Similar analgesic properties to morphine.
- Lower incidence of sedation, delirium and hallucinations; constipation is less severe
- It is available as a transdermal preparation ("patch")

or oro -mucosal ("lozenge")or sub-lingual/buccal tablet or parenterally(seek specialist advice).

Fentanyl transdermal patches * are not suitable for rapidly changing pain due to the long half-life of the drug. They should be used for chronic stable pain only.

- The patient should have been taking an equivalent dose of strong opioid previously
- Note that there are two forms of fentanyl patch - matrix patches (Durogesic DTrans®) and forms with liquid reservoir (generic products and parallel imports of Durogesic TTS®).

Place in therapy - stable pain responding to strong opioids *and with* at least one of the following:

- Unacceptable level of side effects with morphine/diamorphine or alternative opioids
- 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)

* Note – it is recommended that fentanyl patches are prescribed by brand name due to small, significant differences in release rates between opioid patches for individuals (Royal Pharmaceutical Society of Great Britain – February 2006)

Dosing of Transdermal Fentanyl Patch

- Available as 12, 25, 50, 75, 100 micrograms/h.
- Changed every 72h (rarely every 48h, seek advice).
- Takes 12-24h to achieve therapeutic blood levels and on removal levels decrease by about 50% in 17h.
- Dose range is 25 -300 microgram/h; may be higher under specialist care

- In strong opioid –naïve patients the lowest 25 microgram/h fentanyl dose should be used as the initial dose - note: this is equivalent to 60mg/24h of oral morphine, which might be too strong for some patients. If smaller doses may be indicated, seek specialist advice.
- Note – the fentanyl 12 microgram patch is licensed for dose titration between steps 25 to 50, and 50 to 75 micrograms/h; thereafter dose adjustments should be made in increments of 25 micrograms/h.

Table 2. To convert from strong opioid regimens to fentanyl patches

1.	Short acting strong opioid (e.g. Oramorph®, OxyNorm®)	Apply patch – continue q4h strong opioid for first 12h until fentanyl reaches therapeutic level. Use q4h dose of short acting opioid p.r.n. for 'breakthrough' pain
2.	Twice daily strong opioid	Apply patch with last dose of twice daily strong opioid and give q4h short acting strong opioid p.r.n. for 'breakthrough' pain
3.	Once daily strong opioid	Apply patch 12h after last dose of once daily strong opioid and prescribe q4h strong opioid prn for 'breakthrough' pain
4.	Syringe driver	Apply patch; discontinue syringe driver after 12h. Give q4h strong opioid SC p.r.n. for 'breakthrough' pain.

Ensure correct breakthrough dose of short-acting strong opioid is prescribed (see Appendix Table 32 and 34, p47/49)

10% of patients may experience morphine withdrawal 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 short-acting strong opioid. **Seek specialist advice**.

When a change to fentanyl is made, halve the dose of laxatives and adjust according to need.

Breakthrough pain

Prescribe morphine, diamorphine or oxycodone unless previously causing unacceptable toxicity, in which case ask for specialist advice for alternative drugs.
The dose is 1/6 of the equivalent 24h total equivalent dose to the fentanyl patch – use Tables 31 and 33.

Management of patients with a fentanyl patch in the terminal phase

It is usual practice to leave the fentanyl patch in place - **seek specialist advice**

In the terminal phase, if a patient on a fentanyl patch develops unstable pain, a strong opioid continuous subcutaneous infusion (CSCI) given by syringe driver can be used **in addition** to the patch **:-**

- The total number of breakthrough doses of SC strong opioid (e.g. morphine, diamorphine) needed in a 24h period is converted to a 24h CSCI and run **alongside** the fentanyl patch. Be aware of doses used for incident pain. Usually up to a maximum of 3 doses should be added to the CSCI which is equivalent to an increase in the total opioid dose of 50%.
- Calculate the new p.r.n dose according to the fentanyl *and* the CSCI dose of strong opioid - see Appendix Tables 31 & 33 Opioid Conversion Charts. ***Seek specialist advice***

For other drugs needed for symptom control, e.g., anti-emetics/sedatives, again leave the patch in place and administer the drugs by the oral or subcutaneous route. A syringe driver can be used for anti-emetic/sedative medication. (see Table 32, p47)

Fentanyl Lozenge (Actiq)

Licensed for breakthrough pain in patients already on opioid therapy. Expensive.
Doses of 200, 400, 600, 800, 1200 and 1600 micrograms are available.
There is no direct dose equivalence with other opioids, including transdermal fentanyl, so it needs separate titration.
In order to achieve maximum mucosal exposure to the fentanyl, the lozenge should be placed in a cheek and moved constantly up and down, and changed at intervals from one cheek to the other. It should not be chewed. The aim is to consume the lozenge within 15min. If there is inadequate benefit after 15 minutes, then they should repeat the action with a second one. If this is inadequate, the next dose should be increased by 50-100%.
The manufacturers advise that the lozenges may be given up to 4 times a day.

Place in Therapy

- For breakthrough pain in patients on fentanyl patches who are intolerant of morphine, oxycodone, hydromorphone
- Should only be used in patients already on strong opioids
- Breakthrough pain that has a fast onset, but short duration of action.
- Seek specialist advice before use

For newer nasal or sub-lingual / buccal fentanyl preparations seek specialist advice

Oxycodone

Oxycodone is a strong opioid with similar properties to morphine.
It is licensed for moderate to severe pain in cancer and post-operative pain.

Place in therapy

- Tolerance to morphine or unacceptable level of side effects with oral morphine
- Breakthrough medication for patients using fentanyl patches but intolerant of morphine.
- Analgesic potency ratio of oral morphine to oral oxycodone 2:1 (e.g. 20mg oral morphine = 10mg oral oxycodone)

Dosing

It is available in short-acting or m/r (over 12h) oral and parenteral formulations.

- Short-acting (OxyNorm®):- 5mg, 10mg, 20mg caps; 5mg/5ml liquid, 10mg/ml concentrated liquid
- m/r (OxyContin®):- 5mg, 10mg, 20mg, 40mg, 80mg tablets
- Parenteral oxycodone (OxyNorm® injection):- 10mg/ml; 1ml and 2ml amps
  If no previous strong opioid, use oral short-acting 2.5mg q4h or m/r 5mg b.d. and titrate
- If already on strong opioid; convert dose according to Conversion Table 31
- In renal impairment the clearance of oxycodone and its metabolites is reduced. Lower doses and/or longer dose intervals may be required.
- Lower doses may also be required in the elderly
- Prescribe a p.r.n. dose as for morphine – 1/6 of the total 24h regular dosage, as needed up to every two hours.

Parenteral oxycodone should be reserved for those patients who are intolerant of morphine, or on oral oxycodone who are no longer able to tolerate oral medication.
Dose of SC oxycodone = Dose of oral oxycodone ÷ 1.5 (Table 31)
See Syringe Driver Guidelines (p44)

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

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.
- Analgesic potency ratio of oral morphine to hydromorphone is 5-10:1 (average of 7.5:1) e.g. 1.3mg oral hydromorphone is approximately equivalent to 10mg oral morphine.

Dosing
It is available in short-acting or m/r (12 hrly) forms. Both forms may be swallowed whole or opened and sprinkled onto cold soft food (not suitable via PEG or nasogastric (NG) tubes).
- If no previous strong opioids, prescribe short-acting 1.3mg q4h *or* m/r 2mg b.d and titrate
  If already on strong opioid convert dose according to Conversion Table (See Table 31)
- Hydromorphone is renally excreted. Monitoring for toxicity is required in renal impairment; decrease frequency of dosing in moderate renal impairment (creatinine 300-700mmol/L) e.g. 8hrly and severe renal impairment (creatinine > 700mmol/L) e.g. 12 hrly. **Seek specialist advice**.
- Consider dose reduction in the elderly
- Prescribe a p.r.n. dose as for morphine – 1/6 of the total 24h regular dosage, as needed up to every two hours.

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

Renal Failure and Opioid Prescription
If using weak or strong opioids in patients with acute or chronic renal disease and a reduced glomerular filtration rate (GFR)(<60 ml/min/1.73m^2), please seek specialist advice from the palliative care team or pharmacist.

9. Other approaches to pain (consider seeking specialist advice)

- Radiotherapy/chemotherapy/hormone therapy
- TENS
- Massage
- Relaxation
- Psychological support

- Neural blockade/epidural/intrathecal analgesia.

10. Use of Adjuvant Analgesics

Table 3

Drug	Use	Comments
Tricyclic antidepressant, e.g. • amitriptyline - 25mg at night (10mg in elderly); 25mg increments every 5 days, to 150mg as tolerated	Neuropathic pain.	Usually response in 5 days. Helps sleep. Monitor for side effects
Anticonvulsant drugs, e.g. • Gabapentin 300mg daily increased by 300mg each day to 600mg tds for higher doses seek specialist advice • Pregabalin 75mg b.d up to 150mg b.d after 3 to 7 days. Max 300mg b.d • Clonazepam 500 microgram to 2mg nocte • Carbamazepine 200mg nocte. Max 1600mg daily	Neuropathic pain	Increases in dose may be limited by sedation. May need slower titration – increase by 300mg every 3 days Titration may be limited by side effects, e.g. sedation Titration may be limited by side effects, e.g. sedation Titration may be limited by side effects, e.g. sedation
Ketamine Orally; continuous SC infusion	Neuropathic pain	**Seek specialist advice** • high incidence of hallucinations • contra-indicated in hypertension, raised intracranial pressure,epilepsy
Corticosteroid - e.g: dexamethasone 8-16mg a day in 1-2 doses. Give in the morning to avoid sleep disturbance	To decrease peri-tumour oedema. • Nerve compression. • Raised intracranial pressure • Spinal cord compression • Organ infiltration. • Bone pain	May increase appetite, mood. • consider gastro-protective agent (e.g. PPI) • monitor blood glucose • stop if no response after 7 days • review and reduce every 5-7 days to avoid side effects. • Dexamethasone is 7 times more potent than prednisolone.

NSAIDs • e.g. ibuprofen 400mg* -600mg q.d.s., naproxen* 250-500mg b.d. diclofenac 50mg t.d.s * patients lower risk of GI side-effe and thrombotic episodes COX-2 Inhibitors • see BNF 10.1.1 • **seek specialist advice** Diclofenac or Ketorolac by SC infusion • **seek specialist advice first**	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.

NAUSEA AND VOMITING

About 40% of patients with advanced cancer have nausea and 30% will vomit.
Note - nausea may occur without vomiting and vice versa.
Definitions:
Nausea - unpleasant feeling of the need to vomit. Distinguish from anorexia
Vomiting - forceful expulsion of gastric contents through the mouth. Distinguish from regurgitation and expectoration

Assessment

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

Table 4 - Management Of Reversible Causes

Cause	**Specific Management**
Drug Therapy	Stop or find alternative unless essential
Uncontrolled pain	Analgesia - non-oral route until vomiting settles
Cough	Cough suppressant
Urinary retention	Catheterize
Constipation	Laxatives; bowel intervention
Anxiety	Determine fears; explanation; anxiolytics
Raised intracranial pressure	Corticosteroids (e.g. dexamethasone)
Electrolyte disturbances	Correct if possible and appropriate
Hypercalcaemia	Rehydration and intravenous biphosphonate
Oral/oesophageal candidosis	Antifungal (fluconazole,nystatin; imidazole)
Infection (URTI, UTI)	Antibiotic
Gastritis	Stop irritant drug; add PPI

Management

- Assess cause(s) of symptom ; may be more than one
- Remove reversible causes if identified
- Treat according to underlying mechanisms
- If vomiting or severe nausea, use a non-oral route until controlled
- Avoid triggers (e.g. food smells); aim for small frequent meals

Anti-emetic Therapy

- Decide most likely cause, and choose first line treatment - Table 5
- Reassess daily - increase dose as **needed until** at maximum
- If no response, reassess likely cause
    - if **cause** changes, then use most appropriate medication
    - if same cause, go to second choice; combinations may be needed

If poor response to second choice, consider second line approach (see below) and seek specialist palliative care advice

TABLE 5

Drug	***Main Action of Drug***	***Suggested Dose & Route***	***Recommended Use***
		FIRST LINE	
Cyclizine‡	Inhibits vomiting centre Vestibular sedative	Oral – 25-50mg t.d.s. SC - 75-150 mg/24h by CSCI (higher doses under specialist advice)	Cerebral irritation; vertigo Visceral distortion/obstruction Oropharyngeal irritation *May be effectively added to haloperidol*
Haloperidol	Inhibits chemoreceptor trigger zone	Oral - 1.5mg - 5mg at night SC - 2.5 - 10mg o.d. or by CSCI	Biochemical disturbance (drug, metabolic, toxic) *May be effectively added to cyclizine*
Metoclopramide *	Pro-kinetic	Oral - 10-20mg t.d.s.-q.d.s. SC - 30-60 mg/24h by CSCI (higher doses under specialist advice)	Gastric stasis, reflux "Squashed stomach" - mass, ascites *Avoid in mechanical bowel obstruction*
		SECOND LINE	
Levomepromazine	Broad spectrum anti-emetic (not pro-kinetic) Also sedative - dose related	Oral – 6.25 -25mg nocte or in divided doses b.d 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 (usually in doses > 25mg/24h)
Ondansetron (or alternative equivalent)	$5HT_3$ antagonists	Oral - 8mg b.d. (may be 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 *Added to previous anti-emetic* *Note – profoundly constipating*
Dexamethasone	Reduces inflammatory response May have central effect	Oral/SC - 4-16mg o.d. or in 2 divided doses	Adjuvant anti-emetic Cerebral oedema; liver metastases *Added to previous anti-emetic*

** - In Parkinson's syndromes, domperidone may be used in place of metoclopramide. See BNF 4.6*
Note - avoid adding cyclizine or anti-muscarinic drugs to metoclopramide, as they inhibit its prokinetic action
‡ - Cyclizine, like other antimuscarinic drugs, may aggravate heart failure and should be avoided in those at risk

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 6. Common causes of intestinal obstruction

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

- Intestinal obstruction has a mechanical or functional cause, or both.
- 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).

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)

Assessment

- Clinical - see above
- 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.

Surgery - consider for every patient at initial assessment.

Consider if:	*Prognosis is poor if:*	*Contra-indicated if:*
• patient willing • discrete and easily reversible mechanical cause of obstruction • 'reasonable' prognosis (>12 weeks) if treated	• previous abdominal radiotherapy • obstruction in small intestine or at multiple sites • extensive disease, poor condition, cachexia, poor mobility	• ascites +/- carcinomatosis peritonei present • past findings suggest intervention is futile • poor physical condition • short prognosis (<12 weeks)

Table 7 . Medical management of gastro- intestinal obstruction

Nausea +/- vomiting	
Complete obstruction	1) Cyclizine 75-150mg/24h by CSCI (higher doses may be used – seek specialist advice) 2) Add haloperidol 2.5-5 mg/24h by CSCI 3) Substitute both with levomepromazine 5-25mg/24h Refer to Palliative Care team for advice
Functional or partial obstruction	Metoclopramide: 30 – 60 mg/24h by CSCI (may be increased up to 100mg/24h – seek 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, or hyoscine butylbromide (as for colic below). Give together if symptom resistant. Seek specialist advice
Other Symptoms	
Constipation precipitating obstruction	Sodium docusate 100-200mg b.d – t.d.s. orally (avoid stimulant, bulk or fermenting laxatives such as lactulose)
Abdominal pain	Follow pain control guidelines, using non-oral route
Abdominal colic	• Anti-cholinergic agent, e.g. hyoscine butylbromide 60-300mg/24h by CSCI • Stop: pro-kinetic drugs; bulk-forming, osmotic and stimulant laxatives.
Hydration	Assess need for i/v or SC fluids on *individual* patient basis. Many are *not* dehydrated • May still absorb oral fluid above level of obstruction. • SC fluid can be given up to 1-2 L/24h
Dietary intake	• Allow food and drink if wished. • Total Parenteral Nutrition (TPN) may be appropriate in selected cases - multidisciplinary team decision.

Naso- gastric intubation

Do **not** use nasogastric (NG) tube *routinely* for obstruction in the terminally ill.
Prolonged NG aspiration with i/v fluids is not recommended as it rarely gives sustained relief. Use medical measures described above.
May be considered for:

- decompression of upper gastrointestinal (GI) tract if surgery is being considered
- faeculent vomiting which is responding poorly to drug treatment

Venting percutaneous gastrostomy is occasionally useful for symptom relief.

Ongoing Management

Review treatment at least daily
Discharge to or management at home requires early planning.

ANOREXIA

Definition - reduced desire to eat. Distinguish from nausea

Causes include

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

Management of cancer-related anorexia

- Treat reversible causes
- 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;

Medication

Corticosteroid e.g.

- Dexamethasone - 4-6 mg once daily assess after one week
  - if beneficial, continue - reduce weekly to lowest effective dose
  - if no benefit after 1 week, stop

Megestrol acetate

- 160mg once daily; may be increased - refer for specialist palliative care advice
- If no benefit after two weeks, then stop
- Less side effects than dexamethasone *except* increased risk of leg dependent oedema and thromboembolic phenomena (5% excess risk)

Metoclopramide - if impaired gastric emptying suspected

- 10-20mg t.d.s. - q.d.s.

CONSTIPATION

Causes to consider

- Drug induced – review medication; consider prophylactic laxative
- Dehydration - encourage fluids; review diuretics
- Reduced mobility - ensure ready access to toilet; attention to privacy
- Altered dietary intake - review and advise as appropriate
- Hypercalcaemia – i/v fluids and biphosphonates (see Table 27)
- Neurological (e.g. spinal cord compression; autonomic neuropathy)
- Intestinal obstruction - see Table [8]

Assessment

- History - normal bowel habit; medication list; causative factors
- Abdominal palpation and auscultation; digital rectal examination
- Investigations - if needed for treatment; e.g. abdominal x-ray; calcium levels

For intractable constipation, seek specialist advice

Table 8 Medical Management - Laxative Therapy

Clinical Situation	Agent Type and examples	Comments
Soft bulky stools - low colonic activity	*Stimulant* Senna 2-4 tablets at night; bisacodyl 10mg suppositories 1-2 o.d.	Start with low dose and titrate. May cause abdominal cramp
Colon full, no colic	*Stimulant* ± *softening agent* – e.g. senna + docusate sodium, or co-danthramer	
Colon full and colic present.	*Macrogols* Movicol® 2-3 sachets per day	Encourage fluids
Hard dry faeces	*Softening agents* - docusate sodium up to 500mgs/day. Arachis oil enema	Useful in sub-acute obstruction. Higher doses may stimulate peristalsis.
Hard faeces in rectum	Glycerol (glycerin) suppository 4g	
Hard faeces - full rectum, colon	Stimulant plus softener, e.g. Co-danthramer strong 2.5-15ml or caps 1-3 at night and titrate	May cause red urine; peri-anal rash/irritation; colic
	2nd line -Movicol® 2-3 sachets/day	Encourage fluids
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 - Movicol® - 8 sachets dissolved in 1Litre 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

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, avoiding faecal incontinence on the one hand and impaction on the other.

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 constipation with overflow - a plain abdominal x-ray if overflow may help if suspected. Treat as for constipation (Table8).
Other investigations appropriate if will significantly affect treatment
If the patient is in the last days of life, treat symptomatically and do not investigate

Table 9 - 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; antibiotic uncommonly needed (seek microbiology advice)
Overflow (constipation, partial obstruction)	Identify. Treat underlying constipation. Soften stool if partial obstruction. Avoid constipating treatments.
Acute radiation enteritis	Absorbent (see below); seek specialist advice
Secretory diarrhoea (e.g. AIDS, tumour, fistula)	**Seek specialist advice**
Steatorrhoea	Pancreatin supplements

Table 10 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	Octreotide 300-1200 microgram/24h by CSCI (**seek specialist advice before use**)

For severe resistant diarrhoea – seek specialist advice

RESPIRATORY SYMPTOMS

BREATHLESSNESS (DYSPNOEA)

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

Dyspnoea is an unpleasant subjective sensation 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 11 – 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 Hb level
Pulmonary Embolism	Anti-coagulation
Anxiety	Psychological support, anxiolytics
Superior Vena Cava Obstruction	Consider high dose steroid see palliative care emergencies - Table 30 (p39) Refer to Oncologist for radiotherapy/ chemotherapy Stents
Tracheal/ Bronchial Obstruction from 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
- Physiotherapy – decrease respiratory secretions and breathing exercises
- Occupational Therapy- modify activities of daily living to work with symptoms
- Establish the meaning of the breathlessness for the patient and explore fears
- Psychological support – to reduce distress of anxiety and depression

Pharmacological Management

Oxygen therapy

- The evidence for efficacy is limited. Oxygen therapy may help dyspnoeic patients who are hypoxic ($Sa0_2$ < 90%) at rest or who become so on exertion. It may help other dyspnoeic patients due to facial or nasal cooling effect
- Consider a trial of oxygen for hypoxic patients ($Sa0_2$ <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 COPD who are chronically hypoxic – do not use >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 LTOT in COPD follow local guidelines.

Corticosteroids

May reduce inflammatory oedema.

Table 12

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

If patient is opioid naïve:

- Oral short acting morphine 2.5 – 5 mg p.r.n. for dyspnoea
- If patient requires > 2 doses in 24 h, consider long - acting opioid

If patient is already taking regular strong opioid for pain:

- For breathlessness use a 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

  E.g. If patient on morphine m/r 30mg b.d. oral short-acting morphine dose for dyspnoea = 2.5 – 10mg p.r.n titrated according to response,
  when experiencing both symptoms add to the dose for pain = 10mg p.r.n .
- Consider increasing the regular dose by 25-50%
- Titrate according to response

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

Benzodiazepines

- Decrease anxiety
- Muscle relaxant
- Panic attacks

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

Table 13

Drug	Dose	Comments
Diazepam	2 - 5 mg orally up to t.d.s.	Long acting. (Half life = 20-100h)
Lorazepam	500 micrograms– 1 mg sublingually p.r.n.	Short acting (half life = 12 – 15h), fast onset of action. Standard lorazepam tablets 1 mg are scored and can be used sublingually.
Midazolam	2.5 - 5 mg SC 4 hrly	Short acting (half life = 2-5h) Useful for intractable breathlessness

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

Nebulised medications
Table 14

Drug	Dose	Comments
Sodium chloride 0.9%	5 ml p.r.n. or 4 hrly	Mucolytic for viscous secretions
Salbutamol	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

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

Management

- Treat specific causes- see Table 15

Table 15: 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 750 mg b.d. can reduce sputum viscosity
Tumour Related Therapy	Refer to Oncologist for radiotherapy/ chemotherapy Laser Therapy
Infection	Physiotherapy/ nebulised saline/ antibiotics
Recurrent Laryngeal Nerve Palsy	Refer urgently to an Ear, Nose and Throat (ENT) specialist.
Pleural Effusion	Drainage procedures

Table 16: Pharmacological Management

Drug	Dose	Comments
Simple linctus	5-10 ml t.d.s.-q.d.s.	Locally soothing demulcent action Some anti - tussive effect
Codeine linctus 15mg/5ml	5-10 ml t.d.s.-q.d.s.	If patient is already taking strong opioid for pain there is no rationale for using codeine linctus. Use p.r.n. dose of strong opioid to treat cough (the p.r.n. dose is usually 1/6 of total daily dose of strong opioid).
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 patient has already been taking codeine linctus but 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

HAEMOPTYSIS – See Haemorrhage in emergencies section

Management

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

Table 17

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

- Etamsylate 500 mg orally q.d.s. (does not affect coagulation)
- Tranexamic acid 1 g orally t.d.s. – q.d.s
- Can be used in combination when symptoms difficult to control

Major life- threatening haemorrhage (see palliative care emergencies p 38)

- Ensure patient is not left alone
- Keep patient warm
- Have dark towels (e.g. green, blue – *not* red) available
- Midazolam 5-10 mg deep i/m or i/v (for control of anxiety and amnesia)
- Diamorphine / morphine 5-10 mg deep i/m or i/v (or an appropriate dose if already on opioids)

RESPIRATORY SECRETIONS

Refer to end of life care section page 43

ORAL PROBLEMS
Preventative management

- Teeth and tongue should be cleaned at least twice daily with a small medium head toothbrush and fluoride toothpaste. The mouth should be rinsed thoroughly with water after cleaning.
- Dentures should be removed twice daily, cleaned with a brush and rinsed with water. They should be soaked overnight in water or the patient's usual solution and cleaned with a brush.
- Adequate oral fluid intake should be encouraged.
- Lips should be moisturised sparingly with lip balm.

Table 18

Problem	Management
Aphthous ulcers	Local steroid – e.g. Adcortyl in Orabase, Corlan Antiseptic mouthwash – e.g. chlorhexidine gluconate Topical gels – anti-inflammatory (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 gels (see above)
Malignant ulcers	Consider antibiotic
Radiation stomatitis	Benzydamine (Difflam) mouthwash or spray Paracetamol mucilage (Christie formula) 1 g, 4-6 hrly (similar preparations may be available from local pharmacies) 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. povidone-iodine or chlorhexidine gluconate mouthwash
Dry mouth	Review medications (opioids, anti-muscarinics) Increase oral fluid intake Saliva substitutes - e.g. Saliva Orthana, for dry mouth (see BNF 12.3.5) Boiled sweets, ice cubes, sugar free chewing gum Pilocarpine tablets/eye drops- seek specialist advice
Coated tongue	Chewing pineapple chunks Brushing tongue with soft toothbrush
Fungal infection	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. Dentures should be soaked overnight in a weak chlorine solution (e.g. Milton) Review and reassess treatment after 5 – 7 days. If recurrent please seek specialist microbiological advice.

DELIRIUM AND CONFUSION

Definition

Delirium is characterised by 4 core features

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

It can be a great source of distress to patients and carers.
It can have an acute or sub-acute onset (sub-acute seen commonly in the elderly) and should be distinguished from dementia.

Causes of delirium can be multi-factorial so assessment is essential.

- Identification and treatment of the underlying cause is vital.

Table 19: Management of Confusion

Causes	Treatment
Drug related: • Opioids • Corticosteroids • Sedatives • Anti-muscarinics that cross the blood/brain barrier	Stop suspected medication if possible or change to suitable alternative
Withdrawal: e.g. alcohol, nicotine , benzodiazepines, opioids	Review drug regimen. It 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 breathlessness guideline p22) • See Hypercalcaemia guideline (Tables 28 & 29, p38)
Raised Intracranial Pressure:	Dexamethasone 16 mg daily p.o. /SC – review after 5 to 7 days; stop if ineffective; reduce in stages if helps
Circulatory: • Dehydration • Shock • Anaemia	Treat any reversible causes if possible
Other: • Pain • Constipation • Urinary retention	• See pain guideline p4-13 • See constipation guideline p20 • Catheterise if patient able to comply

Pharmacological management

- Only use if symptoms are marked, persistent, and causing distress to the patient.
- Regular review is imperative as sedative drugs may exacerbate symptoms.
- Use a step-wise approach to drug dosages and use only one drug.
- For dying patients, please refer to local symptom control algorithm for Integrated Care Pathway of the Dying.

Table 20

Delirium where sedation undesirable	Haloperidol 0.5–3 mg at night or b.d. orally or i/m or 2.5 mg – 5 mg by CSCI over 24h. Consider a benzodiazepine if alcohol withdrawal is suspected.
Agitated delirium where sedation would be beneficial	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 5 mg SC or IM repeated after 20-30 min - seek specialist advice

Non- Pharmacological management

- Provide environmental and personal orientation. This maybe helped by the presence of a family member or trusted friend.
- Manage patient in a quiet well-lit room.
- 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.

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

Table 21

Cause	Specific Management
Gastric distension – Vagus nerve Gastritis / gastro -oesphageal reflux Hepatic tumours Ascites / intestinal obstruction	Peppermint Water Metoclopramide 10 mg q.d.s. (not concurrently with peppermint water) Anti-flatulent e.g. Asilone 10mls q.d.s.
Diaphragmatic Irritation – tumour Phrenic Nerve Irritation – mediastinal tumour	Baclofen 5 mg orally t.d.s. Anticonvulsant – 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	Haloperidol 1-3 mg orally nocte Chlorpromazine 10-25 mg orally t.d.s **Caution: can be cause sedation and hypotension especially in elderly patients** Midazolam – Seek specialist advice
CNS tumour Meningeal : infiltration by cancer	Anticonvulsant – e.g. gabapentin Baclofen 5 mg orally t.d.s.

Sweating (hyperhidrosis)

Table 22

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

Non-pharmacological management

- Oral fluids
- Fan
- Tepid sponging
- Fewer bedclothes
- Cotton clothing
- Layered clothing

Pharmacological management

- Paracetamol 1 g q.d.s
- NSAID (standard doses)
- Anti - muscarinic (e.g. amitriptyline 10-25 mg nocte)
- Propranolol 10-40 mg t.d.s.

If symptom persists seek specialist advice.

PRURITUS (ITCH)
Pruritus is an unpleasant sensation that provokes the urge to scratch

Non-Pharmacological Measures
If skin becomes wet, dry the skin by patting gently
Keep finger nails 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 role in allowing a good nights sleep. Other measures need to be tried including treating the underlying cause if possible. In addition, stop any potentially causative drugs.

Table 23

Cause	Specific Management
Dry Skin	Emollients q.d.s. initially and b.d. long-term. e.g. Aqueous cream (+/- 1% menthol) Balneum Plus bath oil
Primary Skin Diseases e.g. Scabies Dermatitis Psoriasis	Appropriate treatment of underlying condition
Skin inflamed	Topical corticosteroids e.g. hydrocortisone 1-2% cream
Lymphoma	Prednisolone 10 –20 mg t.d.s. Cimetidine 400 mg b.d.
Opioid Induced Itch	Step 1. Consider switching to alternative opioid Step 2. Ondansetron 4 – 8 mg b.d. Step 3. Paroxetine 5 - 20 mg o.d. Step 4.Anti-histamines e.g. chlorphenamine 4 mg t.d.s.
Cholestasis	Step 1.Emolient cream +/- night sedation Step 2 Naltrexone 12.5 to 50 as a starting dose with effective doses up to 50-300 mg o.d. ***** Step 3 Rifampicin 75 mg o.d. – 150 mg b.d. or Colestyramine (but is poorly tolerated in patients with advanced cancer (unpalatable, can cause diarrhoea and is often ineffective) Paroxetine 5-20 mg o.d. Ondansetron 4 mg b.d. (increasing to 8 mg b.d. if required)
Uraemia	Naltrexone 50-100 mg o.d. * Ondansetron 4 mg b.d. (increasing to 8 mg b.d. if required) UVB phototherapy as a potential intervention when other options have been exhausted
Paraneoplastic Itch	Paroxetine 5 – 20 mg o.d. Mirtazepine 15 – 30 mg nocte
Unknown Cause	Antihistamines e.g. chlorphenamine 4 mg t.d.s. Paroxetine 5 – 20 mg o.d.

* Naltrexone - do not use in patients using opioids for analgesia. Seek specialist advice

ANXIETY IN ADVANCED ILLNESS

Anxiety is 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, job 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 24 – Pre-existing anxiety disorders

General anxiety disorder	Anxiety symptoms *most of the day*
Panic disorder	Episodic panic or severe 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 also be due to organic disorders:

- Hypoxia
- Sepsis
- Medications (e.g. Neuroleptics/ SSRIs/ steroids)
- Drug/ 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 25 – 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	Avoid situations/ discussions that provoke anxiety

Management
- The severity of the underlying disease and the overall prognosis guides treatment 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
- Hospice Day Care 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 (<c 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 26 – Pharmacological management of anxiety

Medications	Comment
Benzodiazepines e.g. Lorazepam 500 micrograms-2mg p.o or sublingually b.d. to t.d.s. Diazepam 2-15mg nocte or divided doses Midazolam 2.5-10mg SC p.r.n 4 hourly 10-60mg CSCI	Reduce anxiety Can cause physical and psychological dependence Short term use only Immediate acting/ rapid onset Long-acting If oral route not available Rapid onset/ short acting
Beta-Blockers E.g. propranolol 10mg – 40mg t.d.s. (See BNF 2.4)	For tachycardia/ tremor/ sweating Monitor BP/ heart rate. Avoid in asthma/ COPD
SSRIs licensed e.g.Escitalopram 5-20m o.d adjusted after 2 - 4 weeks Paroxetine 20mg o.d (See BNF 4.3.3) please see local guidelines for SSRI usage	Panic disorders 12 week course initially: Review within 2 weeks, then monthly from 4 weeks
Mirtazepine 15-45 mg nocte (See BNF 4.3.4)	Well-tolerated Rapid onset of action (less than a week) Increases appetite Does not cause nausea and vomiting For anxiety associated with agitation/ poor sleep
Venlafaxine m/r 75mg o.d	For generalised anxiety disorder if two previous interventions (psychological/ self-help/ pharmacological) have been tried Discontinue if no response after 8 weeks Contra-indicated in hypertension or with high risk of arrhythmia
Pregabalin	Has licence for anxiety – **Seek specialist advice**

DEPRESSION

Depression is persistent low mood or loss of interest, usually accompanied by one or more of:

- Low energy
- Changes in appetite, weight or sleep pattern
- Poor concentration
- Feelings of guilt/worthlessness
- Suicidal ideas

- Palliative care patients are at increased risk for depression
- Physical consequences of life - limiting illnesses can mimic symptoms of depression.
- Untreated depression increases suffering by increasing the impact of existing symptoms and reducing the effectiveness of 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 27 Pharmacological management for depression

Selective serotonin reuptake inhibitors (SSRIs) (See BNF 4.3.3) e.g. Citalopram 20-60mg o.d. Fluoxetine 20-60mg o.d Sertraline 50-200mg o.d (use if recent myocardial infarct or unstable angina) and refer to local guidelines for SSR1 use	• Recommended by NICE in routine care • As effective but better tolerated than tricyclic antidepressants TCAs • Useful for mixed anxiety and depressive disorders • May provoke anxiety "flare" (manage with benzodiazepines as needed)
Tricyclic anti-depressants (TCAs) (See BNF 4.3.1) e.g. Amitriptyline 25mg (10mg in elderly or frail patients)-150mg nocte	• Choice if the patient also has neuropathic pain or bladder spasms • Consider risks in cardiovascular disease • Cause weight gain, dry mouth, constipation and sedation • More likely than SSRIs to cause seizures
Mirtazepine 15-45 mg nocte (See BNF 4.3.4)	• Well-tolerated • Response rate equivalent to other antidepressants (70%) • Rapid onset of action (less than a week) • Increases appetite at low dose • Does not cause nausea and vomiting • Causes sedation at low dose • Not associated with cardiac toxicity or sexual dysfunction
Venlafaxine	• Restricted use if severely depressed or hospitalised requiring doses 300mg or greater /day

Antidepressants take time to work and maybe inappropriate if prognosis is short.
Seek advice from specialist palliative care team or mental health specialists.

PALLIATIVE CARE EMERGENCIES

HYPERCALCAEMIA

Presentation:

Corrected serum calcium >2.7mmol/L
In Primary Care seek specialist advice

Assessment:

- May develop insidiously
- Frequently missed, consider in unexplained nausea/vomiting or confusion
- Severity of symptoms related to speed of rise of serum calcium

Cause:

- Common tumour types (breast, myeloma, lung, kidney, cervix, bony metastases)
- Ectopic parathyroid hormone (PTH)secretion
- Can occur without bony metastases

Table 28 Symptoms and Signs:

General	Gastro Intestinal	Neurological	Cardiological
Dehydration Polydipsia Polyuria Pruritus	Anorexia Weight loss Nausea Vomiting Constipation Ileus	Fatigue Lethargy Confusion Myopathy Hyporeflexia Seizures Psychosis Coma	Arrhythmias Conduction defects

Management / Treatment:

- Check urea, electrolytes, creatinine
- Correct dehydration
- I/v Fluids 0.9% Sodium Chloride, 2-3 Litres/24hrs
- Potassium supplements

Table 29

Initial Corrected Serum Calcium mmol/Litre	Recommended total Pamidronate dose (mg)	Zoledronic Acid *
Up to 3.0	15 – 30	4mg
3.0 – 3.5	30 – 60	4mg
3.5 – 4.0	60 – 90	4mg
> 4.0	90	4mg
Infusion rate	< 60mg/hr	Not less than 15 minutes
Do not exceed concentration:-	60mg/250ml normal saline	Dilute in 100mls sodium chloride or 5% dextrose
Side Effects	Pyrexia, flu-like symptoms and fatigue Late effects: osteonecrosis of jaw	
Duration of effect	Onset 3-7 days Duration 3 weeks	Onset – 2-3 days Duration > 3 weeks

- seek specialist advice if impaired renal function and see (BNF Appendix 3)

Monitor for Recurrence:

Recurrence can be a poor prognostic sign, especially if resistant to treatment. Repeat i/v bisphosphonates or commence oral bisphosphonates (see BNF 6.6.2 for guidance)

SUPERIOR VENA CAVA OBSTRUCTION (SVCO)

- Compression /invasion or thrombosis of Superior Vena Cava due to tumour or nodal mass within mediastinum
- Commonest cause – Lung Cancer, consider lymphoma

Table 30 – Symptoms and signs of SVCO

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

Recurrence:

- I/v or oral steroids – reintroduce or increase dose
- Stent
- Thrombolysis if stent blocked by thrombus

Outcome:

Treatment often gives symptomatic relief

METASTATIC SPINAL CORD COMPRESSION

- 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 plantars
  - clonus may be present
- Altered sensation – look for a sensory level
- Distended bladder

Management / Treatment:

- High dose dexamethasone 16mg stat dose oral or i/v commence immediately even if diagnosis is not confirmed
- Urgent same day referral to Clinical Oncologist for advice re radiotherapy and/or chemotherapy
- Urgent MRI of whole spine scan
- Refer for specialist spinal opinion for possible surgical decompression if progressive weakness despite radiotherapy, evidence of spinal instability
- Immobilisation for patients with symptoms and signs suggestive of spinal instability and spinal cord compression until stability is confirmed.

Aim of Treatment:

The earlier treatment is commenced the greater chance of preventing permanent paralysis and disability.

- 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, sciatic pain, urinary hesitancy and perianal numbness.

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

Treatment:
As for spinal cord compression - using high dose dexamethasone 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.

Significant bleeding may occur from:

- Significant bleeding from Tumour or invasion of blood vessels
- ,Bleeding of oesophageal varices
- Gastrointestinal tract: may be associated with or use of non-steroidals, especially if steroids are used concomitantly
- Haemoptysis (see page 26)and may be a terminal event in both advanced cancer and non-malignant disease. It is a frightening experience for both patients and carers.

Presentation and treatment catastrophic haemorrhage:

Symptoms / Signs:

- Cold
- Hypotension
- Anxiety

Management:

- To 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 and communicate this to all team members
- Pre-prescribe sedation in case needed urgently - midazolam 5-10mg deep i/m or i/v which can be repeated as required
- Pre-prescribe Morphine 10mg i/m or i/v (or an appropriate increased dose if already on opioids)
- Provide dark coloured towel to disguise blood loss.

In the event of catastrophic bleed:

- Manage as per plan
- Ensure patient is not left alone
- Keep patient warm
- Use sedation appropriately if the patient is distressed
- Support the patient and family
- If at home and no doctor or nurse available, family can be instructed to give rectal diazepam solution 10mg or use of sublingual lorazepam 1-2mg / 5 –10mg buccal midazolam as an agreed management plan.

Further care:

- If bleeding temporarily stops further management will depend on overall clinical status and discussion with patient and family in relationship to further acute interventions.
- It may be necessary to commence and continue an infusion of midazolam and diamorphine or diamorphine in the terminal phase.

CARE OF THE DYING

Symptoms that may occur in the dying phase:

- 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.
- Pre-emptive prescribing via the SC route is advocated for symptoms of:
    1. Pain
    2. Nausea and vomiting
    3. Agitation
    4. Respiratory tract secretions
    5. Dyspnoea
- For guidance on symptom management for dying patients, see relevant symptom chapter, your local Care of the Dying Pathway prescribing algorithms and procedures (including any disease specific algorithms). Contact your local palliative care team if needed
- Explanation to patient and family vital with ongoing psychological support
- Identify and address wishes for location of care – liaison and management as appropriate
- Spiritual and religious needs of the patient and family should be assessed.
- Rites and rituals that are appropriate to the culture and beliefs of the patient should be discussed.
- Care after death for family/carers.

Staff Role and Needs

- To identify when patients are dying and explain the use of the Liverpool Care Pathway for the Care of the Dying.
- To provide information on the patient's physical and psychological needs to the informal carers.
- To ensure good communication within the team about the aims of care.
- To give mutual support in the patient's last few days and afterwards to the relatives and staff involved.

Syringe Drivers
SIMS Graseby MS26 or Mckinley T34/ Micrel MP101 *(delete as appropriate for each locality guidelines)* is recommended currently for use in palliative care in the following circumstances;

- Dysphagia
- Intractable nausea +/- vomiting;
- Malabsorption
- Inability to administer medication via oral route i.e. head/neck cancers
- Intestinal obstruction
- Profound weakness/cachexia
- Reduce numerous injections
- Patient choice e.g. aversion to oral medication; dislike of alternative routes (e.g. rectal)
- End of life

NB pain control is no better via the subcutaneous route than the oral route if the patient is able to swallow or absorb drug.

Consider alternatives:

- If SC route not available, can drug be given by another route?
    - Rectal (e.g. NSAID)
    - Sublingual (e.g. lorazepam)
    - Transdermal (e.g. fentanyl).
- Can drug be given effectively SC once a day? E.g. dexamethasone, haloperidol, levomepromazine

It is not recommended to give several 'once' daily injections SC. However, consider this as an alternative if syringe drivers are scarce or it is the patient's choice.

Contra-indications

- Poor pain control but none of above
- Some very restless patients
- Oedematous tissue.

Advantages of using a syringe driver

- Continuous infusion avoids peaks and troughs in plasma drug level

Disadvantages

- Patient may become psychologically dependent upon the driver
- Site problems
- May be seen as a 'terminal' event by the patients/carers

Drug compatibility
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

For more information on drugs used via this route access www.palliativedrugs.com or www.prodigy.nhs.uk

N.B. many are used off-licence, for further information www.palliative-medicine.org

The following drugs are NOT suitable for SC injection as they are irritant to the skin:

- Diazepam
- Prochlorperazine (Stemetil)
- Chlorpromazine

Good practice

- All new staff should ensure they are familiar with syringe driver before using.
- Follow local protocol for use
- All syringe drivers in use should be serviced regularly see local guidelines
- After use all syringe drivers should be cleaned and decontaminated as per local guidelines.

It is **not** recommended to use boost button where available on syringe driver. Ensure the correct SC breakthrough dose is prescribed (i.e. 1/6th of 24-hour opioid dose)

TABLE 31 Common syringe driver drugs

Drug	**24 hr range**	**Indication**	**Comments**
Haloperidol	2.5mg-10mg	Anti-emetic	Antipsychotic
Cyclizine	75-150mg	Anti-emetic	Irritant
Levomepromazine (Nozinan)	5-25mg 25-200mg	Anti-emetic Terminal restlessness	Sedating at higher doses
Metoclopramide	30-90mg	Anti-emetic	Irritation at site
Midazolam	10-120mg	Terminal restlessness Anticonvulsant Anxiolytic	
Glycopyrronium bromide	600-1200 micrograms	Anti- muscarinic for noisy secretions	Start asap for noisy secretions
Hyoscine butylbromide	60 – 180mg	Intestinal obstruction Noisy secretions	Non-sedative
Hyoscine hydrobromide	800 – 2400 micrograms	Noisy secretions	Can cause agitation

TABLE 31 (continued) Common syringe driver drugs

Drug	24 hr range	Indication	Comments
Diamorphine	No ceiling doses	Analgesic	
Morphine	No ceiling dose. Dose is limited by volume 510-540mg maximum quantity in mg for a 20ml syringe. Higher doses will require 2 syringe drivers or seek specialist advice	Analgesic	
Oxycodone	No ceiling dose. Dose is limited by volume 170-180mg maximum quantity in mg for a 20ml syringe. Higher doses will require 2 syringe drivers or seek specialist advice	Analgesic	Do not mix with cyclizine

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

Appendix

Table 32 Opioid Conversion Charts (note: – rounded to convenient doses)

	Morphine mg				Diamorphine mg		Oxycodone † mg				Hydromorphone mg	
Route	**Oral**		***SC** **		***SC** **		**Oral**		***SC** **		**Oral**	
	24h total	q4h 4 hrly	*CSCI 24h*	*q4h*	*CSCI 24h*	*q4h*	24h total	q4h	*CSCI 24h*	*q4h*	24h total	q4h
Dose	30	5	*15*	*2.5*	*10*	*2.5*	15	2.5	*10*	*2.5*	4	1.3
	60	10	*30*	*5*	*20*	*5*	30	5	*20*	*5*	8	1.3
	90	15	*45*	*7.5*	*30*	*5*	45	7.5	*30*	*5*	12	2.6
	120	20	*60*	*10*	*40*	*5*	60	10	*40*	*5*	16	2.6
	150	25	*75*	*12.5*	*50*	*7.5*	75	12.5	*50*	*7.5*	20	3.9
	180	30	*90*	*15*	*60*	*10*	90	15	*60*	*10*	24	3.9
	240	40	*120*	*20*	*80*	*15*	120	20	*80*	*15*	32	5.2
	360	60	*180*	*30*	*120*	*20*	180	30	*120*	*20*	48	7.8
	480	80	*240*	*40*	*160*	*25*	240	40	*160*	*25*†	64	10.4
	600	100	*300*	*50*	*200*	*30*	300	50	*200*	*30*†	80	13
	800	130	*400*	*65*	*260*	*40*	400	65	*260*	*40*†	106	16.9
	1000	160	*500*	*80*†	*330*	*60*	500	80	*330*	*60*†	132	22.1
	1200	200	*600*	*100*†	*400*	*70*	600	100	*400*	*70*†	160	26

This table does **not** indicate incremental steps. Increases are normally in 30-50% steps - more, if indicated by need for p.r.n. doses.

† SC volumes > 2ml are uncomfortable; oxycodone maximum concentration is 10mg/ml, and morphine is 30mg/ml; consider using **2 injection sites per p.r.n. dose**

Conversion factors:

Oral morphine to **SC morphine - divide by 2; oral morphine** to **SC diamorphine – divide by 3**

Oral morphine to **oral oxycodone – divide by 2**

Oral morphine to **oral hydromorphone – divide by 7.5**

Oral oxycodone to **SC oxycodone – divide by 1.5**

*** Parenteral use of morphine,diamorphine and equivalent doses of oxycodone see opioids page 7 and safety guidance NPSA 2006/012**

Table 33 Dose conversion for weak opioids and buprenorphine to oral morphine

Drug	To obtain equivalent oral morphine dose, multiply by:	For example if the patient is having:	Dose in 24h	Approximate oral morphine equivalent in 24h
Dihydrocodeine	1/10	30mg q.d.s	120mg	12mg
Codeine	1/12	30mg q.d.s.	120mg	10mg
Tramadol	1/5	100mg q.d.s.	400mg	80mg
Buprenorphine (sublingual)	80	200microgram t.d.s	600microgram	50mg
Buprenorphine (transdermal patch e.g. Transtec®, BuTrans®)	100	35microgram/h	840microgram	84mg

Table 34 Comparative doses of buprenorphine and morphine.

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 manufacturer's dose ratio range of 75–115:1 (see SPC; it is an approximation, and inevitably there will be individual variation.

Buprenorphine patch strength (microgram/h)	Equivalent codeine dose	Equivalent oral morphine dose (mg/24 h)	p.r.n dose of oral morphine (mg) *
Bu Trans®			
5**	30mg qds	12	2
10**	60mg qds	24	5
20	-	48	10
Transtec®			
35	-	84	15
52.5	-	126	20
70	-	168	30

* using traditional 1/6 of total daily dose as p.r.n. dose and rounded to a convenient dose

** At these doses p.r.n. codeine may suffice.

Table 35 Converting from Oral Morphine to Fentanyl Transdermal Patches

24-hrly morphine dose (mg)	Fentanyl Transdermal (microgram/h)	Oral short -acting morphine breakthrough dose
60 - 90	25	15
90 - 134	37	20
135 - 189	50	30
190 - 224	62	35
225 - 314	75	45
315 - 404	100	60
405 - 494	125	75
495 - 584	150	90
585 - 674	175	105
675 - 764	200	120
765 - 854	225	135
855 - 944	250	150
945 - 1034	275	165
1035 - 1124	300	180

Note: The Fentanyl 12 microgram/h patch is licensed for dose titration between the steps 25 - 50, 50 - 75 micrograms/h

For doses outside the ranges above, seek advice from the specialist palliative care team. For other opioids, calculate the equivalent morphine dose from Table 33 If in doubt, seek advice

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