

# PALLIATIVE CARE PRESCRIBING

LANCASHIRE AND SOUTH CUMBRIA  
SPECIALIST PALLIATIVE CARE SERVICES 2010

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## NAVIGATIONAL INSTRUCTIONS

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## ABBREVIATIONS

BNF	British National Formulary
bd	twice daily
COPD	chronic obstructive pulmonary disease
csci	continuous subcutaneous infusion
DS	Data Sheet
E.O.L	end of life
g	grams
HOOF	Home Oxygen Order Form
iv	intravenous
LAB	long-acting bronchodilator
LTOT	long term oxygen therapy
MAOI	mono-amine oxidase inhibitor
mg	milligrams
ml	millilitres
NICE	National Institute for Clinical Excellence
NSAID's	non-steroidal anti-inflammatory drugs
od	once daily
PEG	percutaneous endoscopic gastrostomy
po	oral
pr	per rectum
prn	as required
qds	4 times a day
s/c	subcutaneous
sl	sub-lingually
SPC	Summary of Product Characteristics
SSRI	selective serotonin re-uptake inhibitor
stat	immediately
TCA	tricyclic antidepressant
TD	transdermal
tds	3 times a day

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## 1 : INTRODUCTION

This booklet is limited to prescribing issues in adult palliative care. Unlicensed use of drugs is common in palliative care. Some doses exceed those on the Data Sheet (DS) or Summary of Product Characteristics (SPC). See DS or SPC for full prescribing information. Whilst every care has been taken to ensure accuracy, prescribers are still required to exercise clinical judgement. It is the prescriber's personal responsibility to decide how far to apply the information in this booklet.

Consult BNF for cautions, contraindications, advice in renal, liver impairment etc as usual. Further information may be obtained from the specialist sources listed at the back of this guide.

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## 2 : GENERAL PRESCRIBING POINTS

Polypharmacy may be unavoidable; key points are to:

1. Use simple medication regimens, such as once or twice daily.
2. Use a suitable preparation. Does the patient prefer tablets, capsules, liquids?
3. Give clear instructions for use and the purpose of each medicine.
4. Warn of likely side effects and how to minimise them. Patients may become anxious after reading patient information leaflets.
5. Explore fears, e.g. addiction.
6. Troubleshoot: What to do if treatment doesn't work or side effects persist.  
Make sure patients have a contact number.

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## 3 : PAIN

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### PITFALLS IN THERAPY

Pain is common in advanced cancer, and patients may have more than one type. Pain management must take into account not only physical pain but also emotional, psychological and spiritual needs. If these are overlooked analgesic failure may result.

It is vital to diagnose the cause or mechanism of each pain before choosing therapy. This is because some pains respond only partially or poorly to oral opioids alone, e.g. bone or nerve pain. See Table 1, Common Pain Types, page 7. Others respond to non-analgesics e.g. painful swallowing from candida infection will need an antifungal. Relief of insomnia, anxiety, depression and breathlessness may also raise pain tolerance. In some cases non-drug treatments may be the first choice.

Take a good pain history. Identify character, location, frequency, relieving and aggravating factors. Assess severity e.g. numerical analogue scale 0-10 or verbal rating scale (mild, moderate or severe). Seek specialist advice if pain is not controlled.

TABLE 1. COMMON PAIN TYPES

Pain	Examples	Character	Initial Management	Adjuvants	Consider a
Deep somatic	Bone metastases	Gnawing, aching. Worse on moving or weight bearing	WHO ladder	NSAID's	Radiotherapy Surgery Bisphosphonate
Visceral	Liver, lung, bowel	Sharp ache or deep throbbing Worse on bending or breathing	WHO ladder	Corticosteroid NSAID's	Nerve block Surgery
Neuropathic	Nerve compression, Nerve damage	Burning, shooting Sensory disturbance in affected area	WHO ladder	Tricyclic antidepressant Anticonvulsant Corticosteroid	Radiotherapy TENS Nerve block
Smooth muscle spasm	Bowel obstruction, Bladder spasm	Deep, twisting, colicky in waves	May be sensitive to opioid - variable	Anticholinergic e.g. hyoscine butylbromide	Surgical relief of obstruction

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## ANALGESICS

Oral therapy is the route of choice. Other routes are only used if there are specific problems e.g. vomiting or swallowing difficulties (see section on Syringe Driver, page ). The WHO analgesic ladder provides a rational basis for prescribing in cancer pain, advocating analgesia "by mouth, by clock, by ladder".

### Key points include:

1. Continuous pain warrants continuous analgesia.
2. Combinations of analgesics are more effective than single agents.
3. When mild analgesics fail, change to a stronger one up the ladder, not to one of similar potency.

Adjuvants are those drugs not normally considered to be classical analgesics. They relieve pain in specific situations due to their mode of action or effect. They are used with or without conventional analgesics, at any step of the WHO analgesic ladder. Examples include anticonvulsants, tricyclic antidepressants, corticosteroids, antibiotics and antifungals.

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## THE WHO ANALGESIC LADDER

**There are three steps on the ladder.**

### Step 1: Non-opioids for mild pain, with or without adjuvants

Step 1 uses simple non-opioids e.g. paracetamol and NSAIDs.

**Paracetamol** 1g four times daily.

**Non steroidal anti-inflammatory drugs (NSAIDs)** have a role at all stages of the analgesic ladder if there is an inflammatory component e.g. pleuritic chest pain, soft tissue injury, bone pain. Differences between NSAIDs relate more to side effects than efficacy. Ibuprofen has the safest gastrointestinal and cardiovascular profile.

**The following is suggested:**

- 1) Ibuprofen 400mg tds

**if ineffective:**

- 2) Naproxen 500mg bd
- 3) If above ineffective or alternative route required, e.g. PR, then consider:  
Diclofenac 50mg tds orally or a maximum of 150mg in suppositories in divided doses daily. Note diclofenac has increased cardiovascular risk.

**For all of the above:**

Add gastric protection with a PPI if risk factor for peptic ulcer (age greater than 65 years old, smoker, previous gastric ulcer, on steroids or anti-coagulants).

*Move to Step 2 if maximum dose of non-opioids +/- adjuvants becomes ineffective.*

### Step 2: Weak opioids plus non-opioids, with or without adjuvants, for mild to moderate pain

If non-opioids fail to relieve pain at maximum tolerated dosage, add a weak opioid.



Codeine 30mg-60mg every four to six hours, maximum 240mg in 24 hours.

Or

Dihydrocodeine 30mg – 60mg every four to six hours. However, higher doses are associated with significant increase in side effects. Maximum 240mg per 24 hours. Slow release and immediate release preparations are available. Oral codeine and dihydrocodeine are approximately one-tenth as potent as oral morphine, i.e. 60mg orally of Codeine is the equivalent to approximately 6mg of morphine orally. See opioid conversion chart page 24.

Tramadol is also listed as a step 2 weak opioid analgesic. It has opioid and non-opioid properties, which are only partially reversed by naloxone.

Tramadol dose: 50mg-100mg four to six hourly, maximum dose 400mg per 24 hours. Slow release and immediate release preparations are available.

Tramadol is approximately one-fifth as potent as oral morphine, i.e. 50mg of oral Tramadol is approximately equivalent to 10mg of oral morphine.

Caution in epilepsy or patients with susceptibility to seizures. Convulsions reported at therapeutic doses. Risk increases if tramadol prescribed with other drugs lowering seizure threshold. Also an increased risk of CNS toxicity when given with SSRIs and TCA's, caution with MAOI's.

**Move to Step 3 if maximum dose weak opioid +/- adjuvants become ineffective.**

**Step 3: Strong opioids plus non-opioid, with or without adjuvants, for severe pain**

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## STRONG OPIOIDS

### MORPHINE

Morphine is recommended as the oral strong opioid of choice. If a pain is opioid responsive, oral morphine will be effective. However, pain poorly responsive to opioids should be suspected if escalating doses of morphine fail to bring relief.

#### **Morphine: Unfounded fears**

- 1) Respiratory depression is not a problem as long as the opioid has been started appropriately and titrated correctly against the patient's pain. Pain prevents respiratory depression by stimulating the respiratory centre. If pain is relieved by other methods e.g. nerve block, respiratory depression may occur. If this occurs, reduce the dose or stop the opioid as necessary - seek specialist advice.
- 2) Addiction (i.e. psychological dependence and craving) is not a problem in the palliative care setting. Abrupt withdrawal may cause an escalation of pain and an abstinence syndrome. These are not signs of addiction, which is characterised by loss of self control, compulsive behaviour and use of the drug despite potential harm to self or others.
- 3) There is evidence that the appropriate use of opioids for symptom control in this setting does not shorten life (see references, Thorns & Sykes). Adequate pain relief can only enhance quality of life.
- 4) There is no evidence to suggest that tolerance to the analgesic effect of opioids is clinically significant. Requests for more analgesia reflect progressive disease and require reassessment of the pain syndromes.

## Morphine Side Effects

Consider renal impairment if toxicity occurs on a previously tolerated dose. Alternative opioids e.g. oxycodone or fentanyl, may be more appropriate in renal impairment. Seek specialist advice.

- 1) Mild drowsiness is common and may occur at the start of therapy and when the dose is increased. Usually diminishes after a few days. If persistent, consider alternative.
- 2) Constipation is very common. Prescribe concurrent laxative, see constipation guidelines, page 37.
- 3) Nausea and vomiting occurs in approximately 30% of patients. Consider metoclopramide 10mg tds for five days or haloperidol 1.5mg at night. Nausea often settles and anti-emetics may be discontinued, but may recur when dose increased.
- 4) Dry mouth is very common and occurs in most patients. Advise good oral hygiene. See dry mouth guidelines, page 46.
- 5) Delirium, myoclonus and hallucinations are signs of toxicity and should prompt a review of the dose. Decrease or stop. Also review patient's renal function.
- 6) Usually well tolerated in hepatic impairment. If severe e.g. prolonged prothrombin time, metabolism may be reduced and require dose reduction or less frequent dosing.
- 7) Respiratory depression and coma – unlikely if opioids used correctly. If occurs, may require naloxone. See BNF or contact National Poisons Information Service. Also see severe opioid toxicity guidelines page 19. Specialist Palliative Care advice may be required for subsequent pain management.

## Writing prescriptions for morphine and other Controlled Drugs

When writing an outpatient or take-home prescription for a controlled drug, the total quantity to be supplied should be written in both words and figures. If more than one strength of a preparation is needed to achieve a dose, these details are required for each strength (e.g. 40mg MST can only be achieved by using a combination of 30mg and 10mg tablets). For the principal legal requirements see BNF: Guidance on prescribing /Controlled Drugs and drug dependence. If unsure, seek advice from a pharmacist.

Prescribe the dose in milligrams. Do not prescribe liquid preparations by volume alone because serious errors may result.

When prescribing strong opioids use brand names, e.g. MST, OxyContin, Durogesic D-Trans. Changing between brands may affect pain control and lead to altered uptake or absorption.

## TITRATION WITH ORAL MORPHINE

In moderate to severe renal failure consider alternative opioids - seek advice from specialist palliative care team.

### Conventional method

If regular weak opioid not controlling pain, start immediate release morphine e.g. oramorph solution or sevredol tablets.

- 1) Usual starting dose is 5mg-10mg orally every four hours.  
Remember that 60mg of oral codeine or dihydrocodeine is **approximately** equivalent to 6mg oral morphine, therefore 60mg codeine four times daily is 240mg in total and **approximately** equivalent to 24mg of oral morphine in 24 hours.
- 2) In addition prescribe the same dose of oral morphine for “as required” use to treat breakthrough pain. Usually start at 4hrly but in some situations may be required more frequently up to hourly.

- 3) Review analgesic requirements daily. After 24-48hrs convert to modified release preparation eg MST. Add the total daily dose of morphine given and divide by 2 to calculate the 12 hourly dose. Calculate the new "as required" dose for breakthrough pain which is one sixth of the total daily dose.

### Example

Patient started taking oramorph solution 10mg, 4 hourly 2 days ago. The "as required" dose = 10mg.

On review patient has taken two extra "as required" doses of 10mg oramorph in last 24 hours.

Total oramorph solution in last 24 hours =  $8 \times 10\text{mg} = 80\text{mg}$

Start MST dose =  $80\text{mg}$  divided by 2 =  $40\text{mg}$  12 hourly. Stop regular oramorph solution.

Make available the new dose of oramorph solution for breakthrough pain which will be  $80\text{mg}$  divided by 6 =  $10\text{mg} - 15\text{mg}$  "as required".

This is usually 4 hourly but in some situations may be needed more frequently up to hourly.

### Alternative method

- 1) Note: Some clinicians use modified release morphine plus rescue doses of immediate release morphine, at the titration stage. This is because they are concerned that on a busy ward or in the community the regular four-hourly dose cannot be guaranteed. The pharmacokinetics of modified release morphine preparations make it more difficult to assess adequacy of analgesia, to adjust the dose, and to make rapid dose changes.
- 2) If regular weak opioid not controlling pain, initiate modified release preparation e.g. MST at a starting dose of 10mg – 20mg orally 12 hourly. Remember 60mg of oral codeine four times a day is approximately equivalent to 24mg of oral morphine per 24 hours.
- 3) At the same time prescribe the appropriate dose of immediate release morphine e.g. oramorph solution for "as required" use, usually 4 hourly but in some situations may be required more frequently, up to hourly. The dose is one sixth the total daily dose of morphine.
- 4) Review pain control daily. After 24 – 48 hours add up total daily dose of morphine given and recalculate the 12 hourly and "as required" doses to reflect daily requirement.

### Example

Patient started on MST 10mg 12 hourly 2 days ago. The "as required dose" =  $20\text{mg}$  divided by 6 =  $2.5\text{mg}$ .

On review patient has taken 4 extra doses of oramorph solution in last 24hours in addition to MST.

Total dose in last 24 hours is MST  $10\text{mg} + \text{MST } 10\text{mg} + (4 \times 2.5\text{mg oramorph}) = 30\text{mg}$  in total.

New dose MST is  $30\text{mg}$  divided by 2 =  $15\text{mg}$  12 hourly

New dose of oramorph "as required" is  $30\text{mg}$  divided by 6 =  $5\text{mg}$ , 4 hourly.

**\*If rescue doses are required very frequently, seek specialist palliative care advice urgently. If the background pain worsens with time and a higher MR dose is needed, increase the daily dose according to breakthrough requirements.**

However if use of breakthrough analgesia has been particularly high it is advised to increase the background MR dose by 30% - 50% at most rather than incorporating all the breakthrough doses. Do not increase the frequency. It is important to review the total daily dose of morphine regularly whilst titrating. Titrate the dose until pain is relieved.

There is no maximum morphine dose, as long as increased doses continue to give increased pain relief without uncontrollable or unacceptable side effects (see also Strong Opioid Substitution, page 13).

Poor response may require the use of other drugs in combination. Re-assess the cause of pain if a dose of 200mg/day or more is needed.

## PREPARATIONS

### 12hrly Modified release (MR) morphine for twice daily use

- 1 MST Continus tablets are commonly prescribed.
- 2 MST Continus suspension is available as granules for reconstitution to a suspension, for those who can only cope with liquids.
- 3 Zomorph capsules can be opened and the contents sprinkled on soft food or mixed with liquid. They are used in the same way as 12 hrly MR tablets and can be given via gastrostomy tubes. When giving via a percutaneous endoscopic gastrostomy(PEG) tube, do not give with oral rehydration therapies, concentrated lactate solutions or similar treatments.

### 24 hrly Modified Release (MR) morphine for once daily use.

Do not confuse these with 12 hrly MR products - see above.

MXL capsules are used locally.

- 1 To convert to once daily morphine from immediate release oral morphine.  
Add up the total oral morphine dose given over the previous 24 hours. Prescribe the nearest strength of MXL capsules once daily. Patients must also be written up for treatment of breakthrough pain - see below. Give the first dose of MXL four hours after the last dose of immediate release oral morphine – there is no need to overlap.  
The capsule contents may be sprinkled onto a small\* amount of soft cold food but not chewed (\*ensures full dose taken).  
The capsule contents may be given via a PEG tube. The inner diameter of the tube needs to be about 3.6mm. The dry granules are introduced into the tube and the system rinsed with about 50ml of liquid intragastric diet from a syringe. Do not rinse with water, because this may block the tube due to the lipophilicity of the granules.
- 2 To convert to 24 hrly MXL morphine from 12 hrly MST morphine.  
Do not overlap. Give the first once daily MXL dose when the next MST dose would have been due, then once every 24 hours. See page 22 for dose conversions.
- 3 To change from MXL or MST to the syringe driver.  
See under "Pain" in Syringe Driver Section, page 60.

## DIAMORPHINE / MORPHINE BY INJECTION

Very few patients need injections. If the pain type is poorly responsive to opioids, simply changing the route to injections will not relieve it - use alternative therapy.

For those who cannot swallow and are either opioid naive or on oral morphine, diamorphine or morphine are the opioid of choice for injection. Diamorphine's high solubility in water means that only small volumes of injection are needed, even for high doses and so it is often preferred. Morphine is less soluble and so the volume of injection is larger and may be more painful in higher doses. The subcutaneous route is preferred over the intramuscular route in chronic cancer pain as it is less painful.

When other drugs are needed for subcutaneous injection at the same time as diamorphine (e.g. hyoscine or midazolam) they may be used as the diluent for diamorphine.

As a rough guide, the equivalent dose of diamorphine subcutaneously is about one-third of the oral morphine dose.

e.g. 15mg immediate release oral morphine e.g. (oramorph) = 5mg subcutaneous diamorphine.

The equivalent dose of morphine subcutaneously is about one-half of the oral morphine dose.

e.g. 15mg immediate release oral morphine = 7.5mg subcutaneous morphine.

If a patient is opioid naive a suggested starting dose would be diamorphine 2.5mg subcutaneously as required four hourly or morphine 5mg as required subcutaneously four hourly (in some situations may be required more frequently).

**If regular parenteral analgesia is necessary, see section on syringe driver page 59.**

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## STRONG OPIOID SUBSTITUTION

If contemplating substitution to control unacceptable side effects or achieve analgesia, first consider simple measures e.g.

- dose reduction
- adjuvant medication, e.g. haloperidol, laxatives etc.
- rehydration if appropriate
- co-analgesics
- use of techniques appropriate to the pain syndrome.

On present evidence, alternative opioids are no more powerful than morphine as analgesics, but may be better tolerated in some circumstances. "Dose equivalents" are only approximate and can be unpredictable. When substituting opioids close monitoring for side effects and efficacy is mandatory, especially at higher doses.

### Indications for choosing alternatives to morphine

1. When dose limiting side effects prevent titration to effective analgesic doses.
2. When intolerable central nervous system side effects develop during continuous use (e.g. agitation, delirium, myoclonic jerks, hallucinations and in extreme cases hyperalgesia and allodynia) which are unresponsive to dose reduction, or when dose reduction leads to increased pain.
3. When the patient is unable to swallow, and parenteral or rectal routes are inappropriate in that individual.

#### **If pain is uncontrolled /escalating.**

Oral oxycodone may permit dose titration.

#### **If pain is stable.**

In patients with malabsorption, dysphagia, poor compliance, renal impairment or resistant severe constipation, fentanyl patches maybe indicated.

Although comments on use in renal impairment are made in the following sections, always seek specialist advice before use.

The following alternative strong opioids are not in order of preference. Selection depends on the profile of the individual drug and suitability of available presentations.

Seek specialist palliative care advice.

## OXYCODONE (OXYNORM AND OXYCONTIN)

Oxycodone is a strong opioid. It provides another Step 3 alternative to morphine. As a guide oral oxycodone is approximately twice as potent as oral morphine. Ten milligrams of oral oxycodone is approximately equivalent to 20mg of oral morphine. See opioid conversion chart, page 22.

### Titration with oral oxycodone

If converting a patient from oral morphine to oral oxycodone, take the total daily dose of morphine and divide by 2.

#### **Example**

- 1) Patient taking MST 60mg bd. Total dose per 24hrs = 120mg
- 2) Oxycodone dose = 120mg divided by 2 = 60mg per 24 hrs = Oxycodone 30mg bd.
- 3) Stop MST and "as required" oramorph.
- 4) Calculate and prescribe new "as required" dose of oxynorm. The dose is one sixth the total daily dose of Oxycodone. Oxycodone 30mg bd = 60mg per 24hrs = 60mg divided by 6 = 10mg oxynorm "as required" usually 4 hourly, but in some situations may be required more frequently up to hourly.

If converting from a weak opioid eg codeine to oxycodone remember that oxycodone is twice as potent as oral morphine. Sixty milligrams of codeine is approximately equivalent to 3mg of oral oxycodone.

Use the same process as titrating oral morphine see page 10 but the starting doses will be lower.

### **Conventional method**

- 1) Starting dose of immediate release oral oxycodone is 2.5 - 5mg every 4 hours
- 2) "As required" dose to treat breakthrough pain is also 2.5mg - 5mg.

### **Alternative method**

- 1) Starting dose of modified release Oxycontin is 5mg – 10mg orally 12 hourly
- 2) "As required" dose of Oxynorm for breakthrough pain is one sixth the total daily dose of Oxycontin.

### **Modified release oxycodone preparations (Oxycontin)**

The modified release preparation is suitable for dose titration and maintenance. It is given 12hourly, reaching steady state plasma levels in about one day. The makers advise that these tablets must not be divided, because this destroys the controlled release matrix and could lead to an increase in oxycodone release.

Presentation: OxyContin tablets 10mg, 20mg, 40mg and 80mg. Further presentations will become available in 2009.

### **Immediate release oxycodone preparations (Oxynorm)**

The immediate release capsules are suitable for breakthrough pain, usually given 4hourly at one sixth of the total daily dose. In some situations may be required more frequently up to hourly. Presentation: OxyNorm capsules 5mg, 10mg, 20mg.

There are also immediate release liquid preparations.

Presentations: OxyNorm liquid 5mg/5ml.

OxyNorm liquid concentrate 10mg per ml.

Although the breakdown products are not clinically active, the plasma concentration of oxycodone itself may increase in certain patient populations. The SPC advises conservative, reduced-dose initiation in mild-moderate renal impairment and mild hepatic impairment. It is contraindicated in severe renal impairment and moderate to severe hepatic impairment. **Seek specialist advice if there is renal or hepatic impairment.**

Oxycodone suppositories are longer acting than morphine suppositories, so are preferred. Manufactured by the Boots Company as a "special". Supplied by them to their own retail outlets and hospital pharmacies. Independent community pharmacists may obtain supplies by contacting a Boots branch.

Presentation: Slow release suppository 30mg, given every eight hours.

## OXYCODONE (OXYNORM) BY INJECTION

If a patient is unable to swallow oral oxycodone then it is available by injection either intravenously or subcutaneously as a bolus or by infusion. As a guide, the subcutaneous dose of oxycodone is approximately half the oral dose.

### Example

OxyContin modified release 40mg bd = Oxynorm injection 40mg over 24 hrs via continuous subcutaneous infusion in syringe driver. (see opioid conversion chart page 22).

Presentation: Oxycodone injection 10mg per ml. Further presentations to become available in 2009.

If the patient is opioid naive a possible starting dose would be OxyNorm 2.5mg subcutaneously, as required, 4 hourly (in some situations may be required more frequently).

## FENTANYL PATCH

The fentanyl patch provides a transdermal strong opioid. Fentanyl patches will not help if oral morphine has failed, unless there is an absorption problem, or adverse effects prevented adequate doses from being given. Absorption of oral morphine is not usually a problem with the immediate release presentations.

Patients using these patches require an immediate release oral opioid preparation for breakthrough pain. The patches are suitable only when pain is stable, not if rapidly changing.

### Titration with fentanyl

See opioid conversion chart for dose conversion scheme, page 22.

Note: these are only approximate. Patients must be titrated and monitored.

- 1) It is recommended that patients have been titrated with opioids prior to starting a fentanyl patch. The dose equivalent of a fentanyl 25microgram patch is oral morphine 90mg per 24 hours. Fentanyl patches are now available in a 12microgram strength but these are not licensed as an initiating dose but as a titrating dose. If a patient has not been on the equivalent of 60mg to 90mg of oral morphine per 24 hours, seek specialist advice before commencing Fentanyl patches.
- 2) Onset is gradual, so evaluate the initial effect only after the first 24 hours. Phase out previous analgesic therapy gradually during this time e.g. continue 4 hourly oral morphine for about 6-12 hours, or apply patch at same time as the last 12 hourly MR morphine dose, or 12 hours after the last once daily MR morphine.
- 3) Carry out dose adjustments in 72-hour steps of 12 to 25 micrograms/hour. Many patients need a higher strength patch after the first three days. Remember to adjust the individual rescue dose if this occurs. If more than one patch needs to be used, apply at the same time to avoid error. Vary the site to rest the skin.



- 4) If pain relief does not last three days, some practitioners have found that occasionally, patients do better changing the patch every two days. However, others prefer to increase to the next patch strength and assess response, and only try changing every two days if pain is still poorly controlled. If pain relief does not last for the full three days seek specialist palliative care advice. Sudden escalation of pain always warrants reassessment of the pain syndrome.
- 5) Opioid withdrawal symptoms (such as colic, diarrhoea, nausea, sweating and restlessness) may occur for a few days on switching to the fentanyl patch, even though pain is relieved. Treat with rescue doses of oral morphine (see previous advice on Rescue Doses under MR morphine section page 11).

At doses above 300 micrograms/hour, consider additional or alternative analgesia.

Fentanyl is an option in renal impairment because there are no active metabolites. However dose reduction may still be required and depends on renal function. Seek specialist advice.

Fentanyl patch presentations: 25micrograms/hour, 50mmicrograms/hour, 75micrograms/hour, 100micrograms/hour. Patches are also available in 12micrograms/hour for titration between above patch doses.

### **To convert from fentanyl patches to MR oral morphine**

Remove the patch about 12 hours before the first dose of MR oral morphine, to give time for residual levels in the skin to drop. Make sure immediate release oral morphine in a sufficient rescue dose is prescribed and available to be given during this time, if required.

### **Fentanyl patches and subcutaneous diamorphine infusion**

1. If the patient is dying, continue using fentanyl patches as before. Use subcutaneous diamorphine when required as rescue medication. If this is needed regularly over 24 hours, give it by subcutaneous infusion using a syringe driver, in addition to the patch. See guidelines on terminal stage page 63.
2. If the patient is not dying and there is some reason to remove the patch and convert to a syringe driver:
  - The conversion from the patch, to diamorphine by subcutaneous infusion over 24hours, requires an intermediate step of calculating the patch equivalent in terms of oral morphine/24hours. However, if the publicised dose conversion scheme is applied when switching in the direction from the patch to oral morphine, this may result in a larger dose than is actually required, even if the lower end of the morphine range is selected. Individual titration is essential. Seek specialist palliative care advice. The following points are only intended to indicate the general approach.
  - Using the conversion scheme, convert the fentanyl patch dose to the equivalent 24 hour oral morphine dose. Use the lower end (or less) of the suggested equivalent range, as advised by the palliative care specialist.
  - Divide this oral morphine dose by three to give the equivalent diamorphine dose for subcutaneous infusion over 24 hours.
  - Start the syringe driver 12-18 hours after removing the patch.
  - Make sure appropriate breakthrough analgesia is prescribed and available for the period of patch removal and after the syringe driver is set up.

## PRESCRIBING FENTANYL PATCHES

In addition to the usual Controlled Drug prescribing requirements, this is an example of the specific fentanyl details required for the prescription:

**Fentanyl patch 25 microgram per hour**  
**Supply 10 (ten) patches**  
**One patch to be applied every 72 hours**

Remember to prescribe by brand name as changing between brands may affect pain control and lead to altered uptake and absorption.

### Other fentanyl preparations

Oral transmucosal fentanyl lozenges (Actiq), fentanyl sublingual tablets (Abstral ) and fentanyl buccal tablets (Effentora) are available for breakthrough pain in patient's receiving opioid therapy for chronic cancer pain. Seek specialist advice on their use.

Fentanyl is also available for injection. Only use with specialist advice or in conjunction with the "Liverpool Care Pathway for the dying patient with Chronic Kidney Disease."

## OTHER STRONG OPIOIDS

### Buprenorphine

Sub-lingual and injectable forms of Buprenorphine are not recommended for routine use in chronic cancer pain.

Transdermal patches are licensed for severe opioid responsive pain (Transtec, BuTrans) or for moderate severe cancer pain not responding to non-opioid analgesics (Transtec) or when there is intolerance to other strong opioids. Transdermal Buprenorphine should not be used for acute e.g. post-operative or intermittent pain or when there is need for rapid dose titration for severe uncontrolled pain.

Transdermal Buprenorphine is 100 times more potent than oral morphine. Transdermal Buprenorphine and transdermal Fentanyl are essentially equi-potent. See opioid conversion chart, page 22.

Not currently recommended locally, seek Specialist Palliative Care advice.

### Cyclomorph

This contains morphine plus cyclizine. Dose increases eventually cause unacceptable sedation due to cyclizine. AVOID.

### Methadone

Methadone is a third-line strong opioid substitute with complex properties, only initiated with specialist advice.

## Pethidine

Shorter duration of action and less potent than morphine. Toxic potentially fatal metabolite accumulates with regular use. AVOID. (Used in those countries where first line choices not available).

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## SEVERE OPIOID TOXICITY

Opioids can cause respiratory depression and coma. The specific antidote is naloxone. It has a shorter duration of action than many opioids around 30-60 minutes. Close monitoring and repeated injections or an iv infusion may be required. Some opioids e.g. buprenorphine are only partially reversed by naloxone.

See BNF or contact National Poisons Information Centre.

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## INCIDENT PAIN

When patients are on a stable background dose of analgesia, pain may also occur in relation to specific issues such as dressing changes or on movement. This is termed incident pain. If incident pain is predictable, then providing a dose of immediate release morphine eg oramorph 10 to 20 minutes before the incident (such as a dressing change) is appropriate. The dose of immediate release morphine for incident pain would be the same as the breakthrough dose, i.e. one-sixth of the total daily dose.

# PALLIATIVE CARE GUIDANCE ON OPIOID CONVERSION

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## VERSION 13, MAY 2009

### General Points:

1. Ratios are for guidance only. Considerable variation may occur between patients.  
Seek advice if concerned.
2. If converting from a less sedating opioid (e.g. fentanyl) to more sedating one (e.g. morphine/ diamorphine/oxycodone) consider reducing the dose.  
At higher doses (e.g. the equivalent of 180mgs oral morphine per 24 hours) consider reducing the dose by 30 - 50%. The sedative effects of an 'equianalgesic' dose may be much greater.
3. Please do not compare doses between charts. They are not interchangeable.
4. References for conversion ratios: Palliative Care Formulary (Third Edition).

**Conversion between oral morphine, oral oxycodone and fentanyl patches**

Morphine			Oxycodone		Fentanyl
4 hrly oral (oramorph)	MR b.d. oral (MST)	MR o.d. oral (MXL)	4hly oral (Oxynorm)	M.R. b.d. oral (Oxycontin)	3 day patch (topical)
10mg	30mg	60mg	5mg	15mg	
15mg	45mg	90mg	7.5mg	20mg	25microgram
20mg	60mg	120mg	10mg	30mg	37microgram
30mg	90mg	180mg	15mg	45mg	50microgram
40mg	120mg	240mg	20mg	60mg	75microgram
50mg	150mg	300mg	25mg	75mg	75microgram
60mg	180mg	360mg	30mg	90mg	100microgram
70mg	210mg	420mg	35mg	105mg	100microgram
80mg	240mg	480mg	40mg	120mg	125microgram
90mg	270mg	540mg	45mg	135mg	150microgram
100mg	300mg	600mg	50mg	150mg	175microgram
110mg	330mg	660mg	55mg	165mg	175microgram
120mg	360mg	720mg	60mg	180mg	200microgram
140mg	420mg	840mg	70mg	210mg	225microgram
160mg	480mg	960mg	80mg	240mg	275microgram
180mg	540mg	1080mg	90mg	270mg	300microgram

**Notes:** 1. Fentanyl 12 microgram per hour patch is licensed for dose titration between 25-50-75 microgram patches but not as a starting dose.

**Conversion between oral morphine, s/c morphine and s/c diamorphine.**

MST bd (oral morphine)	Morphine syringe driver s/c in 24 hours	Diamorphine syringe driver s/c in 24 hours
15mg	15mg	10mg
30mg	30mg	20mg
45mg	45mg	30mg
60mg	60mg	40mg
90mg	90mg	60mg
120mg	120mg*	80mg
135mg	135mg*	90mg
150mg	150mg*	100mg
180mg	180mg*	120mg

**Conversion factors:**

1. Oral morphine to s/c morphine – divide by 2
2. Oral morphine to s/c diamorphine – divide by 3

**Conversion between oral oxycodone and s/c oxycodone**

Oxycodone 4hly oral (Oxynorm)	Oxycodone bd oral (Oxycontin)	Oxycodone injection s/c 4hly (Oxynorm)	Oxycodone syringe driver s/c in 24 hours (Oxynorm)
5mg	15mg	2.5mg	15mg
10mg	30mg	5mg	30mg
15mg	45mg	7.5mg	45mg
20mg	60mg	10mg	60mg
25mg	75mg	10mg-15mg	75mg
30mg	90mg	15mg	90mg
40mg	120mg	20mg	120mg*
50mg	150mg	25mg	150mg*
60mg	180mg	30mg	180mg*
70mg	210mg	35mg	210mg*
80mg	240mg	40mg	240mg*
90mg	270mg	45mg	270mg*

**Conversion Factors**

1. Oral morphine to oral oxycodone – divide by 2
2. Oral oxycodone to s/c oxycodone – divide by 2  
(note some guidelines suggest divide by 1.5)

\* Oxycodone or morphine in doses above 100mg given s/c via a syringe driver when mixed with other drugs may result in a volume unsuitable for administration in a 20ml syringe. Seek advice from Specialist Palliative Care Team.

**Dose conversion for weak opioids 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 24 h
Dihydrocodeine	1/10	30mg q.d.s	120mg	10mg
Codeine	1/10	30mg q.d.s	120mg	10mg
Tramadol	1/5	100mg q.d.s	400mg	80mg

**Conversion from transdermal buprenorphine**

Transdermal buprenorphine is 100 times more potent than oral morphine

**BuTrans®** lower dose buprenorphine formulation patch designed to deliver 5, 10, or 20 microgram per hour changed every seven days, and approximately equivalent to the doses of morphine listed below:

BuTrans	5Microgram/hour	10Microgram/hour	20Microgram/hour
Oral Morphine	12mg per 24 hour	24mg per 24 hour	48mg per 24 hour

**Transtec®** higher dose buprenorphine formulation patch designed to deliver 35, 52.5 or 70 microgram per hour changed every four days.

Transtec	35microgram/hour	52.5microgram/hour	70microgram/hour
Oral Morphine	80mg per 24 hour	120mg per 24 hour	160mg per 24hour



**Dose sizes available: modified release preparations**

Tramadol SR bd capsules 50, 100, 150, 200mg  
Tramadol XL od – capsules 150, 200, 300, 400mg

Oxycodone bd (Oxycontin) tabs 5, 10, 20, 40, 80mg

Fentanyl –3 day patch 12, 25, 50, 75, 100microgram/h

MXL od – capsules 30, 60, 90, 120, 150, 200mg  
MST bd – tablets 5, 10, 15, 30, 60, 100, 200mg  
MST bd – sachets 20, 30, 60, 100, 200mg

Transec - 4 day patch 35, 52.5 and 70 microgram/h

BuTrans – 7 day patch 5, 10 and 20 microgram/h

**Dose sizes available: immediate release preparations**

Morphine (oramorph) – liquid 10mg/5ml, 100mg/5ml  
Morphine(Sevredol) – tablets 10, 20, 50mg

Morphine-injection – 10mg/ml, 15mg/ml, 20mg/ml, 30mg/ml amps

Oxycodone (Oxynorm) – capsules 5, 10, 20mgs, – liquid 5mg/5ml,10mg/ml

Oxycodone (Oxynorm) – injection 10mg/ml amps

Diamorphine – injection - 5, 10, 30, 100, 500mg amps

Tramadol – capsules, sachets – 50, 100mg – soluble tablets – 50mg



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## 4. BONE PAIN

Local bone pain from secondaries is a common pain syndrome in advanced cancer. It may be a dull ache or intense, often worse on movement and weight bearing. A combination of opioid and NSAID is often used. Prophylactic orthopaedic fixation and radiotherapy have important roles in palliation. Following radiotherapy it may be 2-3 weeks before full benefit occurs. Other techniques include hormone manipulation and chemotherapy. If other measures reduce pain, reduce the opioid dose to avoid opioid side effects.

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### OPIOIDS

Morphine relieves continuous dull aching pain, but not pain on movement (incident pain), when other techniques may be appropriate. Also see page 19 "Incident pain".

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### NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

Their precise mechanism in this situation is not fully understood, but prostaglandin synthesis inhibition is important. They are widely used for bone pain, although views differ on their efficacy. They are often used with opioids. NSAIDs should be started while awaiting radiotherapy, then if possible discontinued. If one NSAID fails to work after about 5-7 days it is worth trying one from another NSAID class.

See section on Pain: Step 1 of the Analgesic ladder, page 8 for details of NSAIDs.

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### BISPHOSPHONATES AS ADJUVANT ANALGESICS

Bisphosphonates have been used for metastatic bone pain and several regimes have been recommended for use when more conventional methods have been exhausted. An effect is generally seen within two weeks. The evidence suggest that benefit is more likely in patients with breast cancer or myeloma and with an IV bisphosphonate. Seek specialist advice.

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## 5. NEUROPATHIC PAIN

Pure non-cancer nerve injury pain e.g. post operative scar pain, post-herpetic neuralgia and diabetic neuropathy may respond to treatment with anti-depressants and anti-convulsants. Cancer related nerve pain may be associated with nerve root/trunk compression or infiltration. Paracetamol, non-steroidal anti-inflammatory drugs and morphine may be tried. Anti-depressants and anti-convulsants may be helpful. Steroids may be helpful in nerve root compression and are required for spinal cord compression.

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### SPECIALIST REFERRAL

Refer early if any of these apply:

1. If the guidelines below do not help.
2. If urgent control is required for severe uncontrolled pain.
3. If clinical features of “wind up” (magnified pain response) are present e.g. allodynia, hyperalgesia, hyperpathia.
4. If dose-limiting side effects of opioid preclude further dose escalation.

There are other drugs and routes available to pain specialists, including ketamine; methadone; spinal analgesia with bupivacaine, opioids, clonidine; mexiletine; plus a wide range of techniques and procedures.

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### OPIOIDS

Opioids may be continued, but be prepared to add or change drugs at an earlier stage if there is lack of response or toxicity.

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### PARACETAMOL

Regular paracetamol may be beneficial.

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### DEXAMETHASONE

Tumour pressure on a peripheral nerve can cause nerve compression pain and loss of function. Dexamethasone is particularly useful in nerve compression pain. Corticosteroids relieve pain within 48 hours, probably through reduction of oedema around the tumour. If there are no contraindications, prescribe dexamethasone 8mg as a single morning dose with food. If ineffective after 5 days, stop. There is no need to taper the dose; it is usually safe to stop abruptly after this length of course. If there is a response, decrease gradually to the minimum effective maintenance dose e.g. by one quarter of the dose per week (if there is a good response to steroids, local experience suggests that as a rule of thumb, radiotherapy, if indicated, would be effective.) In the emergency situation of spinal cord compression, refer urgently for an oncology opinion. Most protocols include the use of high dose dexamethasone (16mg) daily. Corticosteroids may cause gastric irritation, particularly if an NSAID is also being used. Gastroprotection may be provided by a proton pump inhibitor such as lansoprazole. Candida and diabetes mellitus are treatable corticosteroid side effects, so warn the patient of these, and the possible symptoms.

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## ANTIDEPRESSANTS

Tricyclic antidepressants such as amitriptyline or imipramine are used, which are mixed serotonin/noradrenaline re-uptake inhibitors (selective SSRIs lack useful analgesia). Pain relief may begin after about 1-7 days, but a trial of several weeks may be needed. There is usually a favourable effect after one week on an effective dose. The maximum effect may evolve over days/weeks.

Start with 25mg amitriptyline (10mg in elderly) taken in the early evening to avoid a hangover effect. The rate of increase depends on pain level and degree of supervision. If tolerated, the dose may be increased by about 25mg every three days to 100mg at night. In the elderly the rate of increase may need to be slower e.g. 25mg per week. The final dose may be lower than that for depression e.g. amitriptyline 25-75mg at night. The maximum dose is a balance between efficacy and side effects.

If there is no response after a reasonable trial, stop the drug. Some clinicians would only stop if the pain was no better or there were intolerable side effects, after 2-3 weeks on 75mg/day. If there is a partial response, continue the amitriptyline and add an anticonvulsant if there is no contraindication (see anticonvulsants below).

### Antidepressants:-

- must be taken regularly.
- side effects precede analgesic effects.
- are not addictive.
- benefit is independent of effect on mood.
- the standard patient information leaflets do not discuss this indication.  
Inform the patient of the reason for its use.

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## ANTICONVULSANTS

There is little comparative evidence between anticonvulsants, so the choice depends on the clinician's experience and preference. If unsure, seek specialist advice.

### Gabapentin

This is now licensed for neuropathic pain. The SPC advises rapid dose titration, but palliative care patients may tolerate the following regimen better:

Start with 300mg at night.

After three days increase to 300mg twice daily.

After another three days, increase to 300mg three times daily. Increase by 300mg as tolerated every third day, until pain relief is achieved up to a maximum of 3.6g daily in divided doses.

Generally well tolerated, although high doses may cause dizziness and sedation. Few interactions.

Dose adjustment is required in renal impairment and with haemodialysis. See BNF.

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### **Pregabalin**

Pregabalin is also licensed for neuropathic pain. It is no more effective than Gabapentin. Patients who fail to respond to Gabapentin or are unable to tolerate it, may tolerate Pregabalin and vice versa. In addition, dose administration is twice daily, which may be simpler for certain patients for titration purposes.

#### **The following regime is suggested:**

Start with 75mg twice daily.

After one week increase to 150mg twice daily if not effective enough.

After one further week increase to 300mg twice daily if required. Maximum dose 300mg twice daily.

If patient is frail or elderly, you may wish to consider a lower starting dose e.g. 25mg bd and titrating up at lower increments. Pregabalin is generally well tolerated but can cause dizziness and sedation.

Dose adjustment is required in renal impairment and with haemodialysis. See BNF.

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## **6. NAUSEA AND VOMITING**

### **This section covers:**

- Causes
- Antiemetic therapy
- Hypercalcaemia
- Raised intracranial pressure
- Intestinal obstruction

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### **CAUSES**

There are many causes of nausea and vomiting in advanced cancer, sometimes present in combination:

- Constipation
- Gastric stasis e.g. opioids, antimuscarinics
- 'squashed stomach syndrome'
- Hepatic metastases
- Drugs e.g. opioids, NSAIDs, aspirin, corticosteroids, SSRIs, antibiotics, iron, digoxin, proton pump inhibitors
- Metabolic e.g. uraemia, hypercalcaemia
- Severe pain
- Pharyngeal stimulation e.g. thrush, tenacious sputum
- Raised intracranial pressure
- Intestinal obstruction
- Severe anxiety

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## ANTIEMETIC THERAPY

Non-drug measures are very important.

The vomiting reflex is complex, with many neurotransmitters and pathways. There is no single antiemetic panacea. The choice depends on the cause of vomiting and site of drug action (see Table 2 page 32).

### Key Points

- Look for possible causes (including medication review) and pathways.
- Treat reversible underlying causes if possible (and if appropriate).  
Cover with most specific antiemetic whilst awaiting response.
- If not reversible, look for most likely causes and target with specific antiemetic.
- Check which antiemetics have already been tried, and by which dose and route.
- Choose appropriate antiemetic drug, dose and route. The oral route is only suitable for mild nausea or prophylaxis. In established nausea, gastric stasis interferes with oral absorption, so suppositories are useful.
- Subcutaneous administration is possible for many antiemetics. This route is usually preferred, with subcutaneous infusion in severe cases. Consider a syringe driver if vomiting for more than one day, or moderate/severe nausea unresponsive for more than 48 hours. (see section on Syringe Driver).
- Give antiemetics regularly, not just “when required” or before meals.
- Review often. If symptoms persist, are there any new or overlooked causes?
- If an optimal dose of an appropriate drug is ineffective, switch to an alternative.
- About a third of patients may need more than one antiemetic, with different sites of action, but do not persist with an ineffective drug. To reduce side effects, avoid combining drugs of the same class.
- Consider adjuvants: Antisecretory drugs (e.g. antimuscarinics or octreotide) may be used to reduce the volume of gut secretions. Corticosteroids such as dexamethasone may enhance anti-emetic effect.
- Set realistic goals, e.g. suppression of nausea with intermittent vomits may be acceptable to the patient.
- After 72hrs of good control with the subcutaneous route, consider converting to oral. If the patient is anxious when switching back to oral, phase out the subcutaneous drugs one at a time and replace with oral.
- Unless the cause is self-limiting, continue antiemetics indefinitely.

TABLE 2: ANTIEMETIC THERAPY

SITE OF ACTION / CAUSES	RECEPTOR / ANTIEMETIC DRUG
<p><b>Vomiting Centre</b> Raised intracranial pressure, intestinal obstruction, pharyngeal stimulation e.g. candida, tenacious sputum</p>	<p><b>H1 Antihistamine</b> Cyclizine, levomepromazine</p> <p><b>Antimuscarinic</b> Cyclizine, levomepromazine, (hyoscine hydrobromide)</p> <p><b>Corticosteroids</b> Dexamethasone</p> <p><b>5HT2 antagonist</b> Levomepromazine</p>
<p><b>Chemoreceptor Trigger Zone (Area Postrema)</b> Drugs, uraemia, hypercalcaemia, ketosis, radiotherapy, chemotherapy, toxins.</p>	<p><b>Dopamine D2 antagonist</b> Haloperidol, levomepromazine, metoclopramide, domperidone</p> <p><b>5HT3 antagonist</b> Ondansetron, granisetron, tropisetron, metoclopramide high dose.</p>
<p><b>Gastrointestinal tract</b> <b>Prokinetic</b> Oesophageal reflux, gastric stasis, squashed stomach, gastric irritation</p> <p><b>Antisecretory</b> Intestinal obstruction</p> <p><b>Vagal 5HT3 –receptor blockade</b> Chemotherapy, radiotherapy, intestinal obstruction</p>	<p><b>5HT4 agonist</b> Metoclopramide Dopamine D2 antagonist Metoclopramide, domperidone</p> <p><b>Antimuscarinic</b> Hyoscine butylbromide, glycopyrronium</p> <p><b>Somatostatin Analogues</b> Octreotide, lanreotide</p> <p><b>5HT3 antagonist</b> As above</p>
<p><b>Broad Spectrum</b> Intractable nausea and vomiting. Uncertain cause</p>	<p><b>Broad spectrum</b> Levomepromazine</p>
<p><b>Cerebral cortex</b> Anxiety, anticipatory nausea</p>	<p><b>Benzodiazepine</b> Lorazepam, diazepam</p>
<p><b>Vestibular</b> Motion, positional stimuli</p>	<p><b>H1 Antihistamine</b> Cyclizine</p> <p><b>Antimuscarinic</b> Hyoscine hydrobromide</p>
<p><b>Other</b> Tumour mass, liver metastases</p>	<p><b>Corticosteroid</b> Dexamethasone</p>



## ANTI-HISTAMINES

### Cyclizine

50mg three times daily PO or S/C. 75-150mg by 24 hour CSCI.

## DOPAMINE ANTAGONISTS

Beware of combining two of these - may increase risk of extrapyramidal side effects.

### Haloperidol

Anti-emetic of choice for opioid induced nausea and vomiting, hypercalcaemia and renal failure. More potent at chemoreceptor trigger zone than phenothiazines 1.5mg at night, PO or SC. Up to a maximum of 5mg by 24 hour CSCI. Side effects infrequent at this low dosage. Commonly used in combination with cyclizine.

### Levomepromazine (Nozinan)

This powerful broad spectrum antiemetic acts at several sites. This means greater potential for side effects (sedation, postural hypotension, antimuscarinic effects). Low doses retain antiemetic activity with less sedation. It is useful in intractable nausea and vomiting, including that of unknown aetiology. It is used to replace previous drugs, not as an addition (but hyoscine butylbromide can be retained if antisecretory needed). Levomepromazine is twice as potent subcutaneously as orally.

### Regimens include:

Often reserved for second or third line use some units use as first-line:

Tablets 3-6mg PO once – twice daily and PRN 8hrly.  
Titrated up to a maximum dose 25mg over 24 hours.

Liquid 2.5-5mg PO once – twice daily and PRN 8hrly.  
Titrated up to a maximum dose 25mg over 24 hours.

Injection 2.5-5mg S/C once – twice daily and 8hrly PRN.  
Titrated up to a maximum of 12.5mg over 24 hours.

CSCI 5mg – 12.5mg over 24 hours. Some units use up to 18.75mg over 24hours.

Use the lowest effective dose. If Symptoms are not controlled at these doses contact the Specialist Palliative Care Team. Levomepromazine is available in the UK as a 6mg tablet which is scored and available on a named patient basis. A liquid formulation is available from a number of 'Special Manufacturers'.

### Domperidone

10-20mg 4-8 hourly orally or 30-60mg every 4-8hrs rectally. Will not control severe nausea. Domperidone and metoclopramide improve gastric and small bowel motility. Domperidone is less likely to cause sedation and dystonia than phenothiazines or metoclopramide as it does not cross the blood-brain barrier.

### Metoclopramide

10mg three or four times daily PO or S/C; 30-60mg by 24 hour CSCI. S/C boluses may be uncomfortable due to the volume required (10mg/2ml). The action of prokinetic drugs such as metoclopramide or domperidone is antagonised by the gut-motility reducing effects of antimuscarinics such as hyoscine or cyclizine. Avoid such combinations if possible.

## ANTIMUSCARINICS

In this context they tend to be used as adjuvants for their antispasmodic effect in bowel colic, and antisecretory effect which reduces the volume of vomits (see section on Intestinal Obstruction for specific details). They are also used to reduce respiratory secretions and drooling.

### **Hyoscine butylbromide** (“Buscopan”)

This has no central antiemetic action because it does not cross the blood-brain barrier. For the same reason, it does not cause drowsiness. Poor oral absorption limits the use of the tablets to mild/moderate colic. The S/C route is preferred. Antisecretory drug of choice in inoperable intestinal obstruction.

### **Hyoscine hydrobromide**

This also has a central action which provides an antiemetic effect, but may cause side effects such as drowsiness, hallucinations, excitement and ataxia.

Not routinely used as an antiemetic in palliative care.

A transdermal patch delivering hyoscine 1mg over 72 hours (Scopoderm TTS) is available, but plasma levels are low. In practice, its use as an antiemetic is limited to motion sickness.

### **Glycopyrronium bromide**

This is a more powerful antisecretory agent than hyoscine hydrobromide, and may help where this has failed. It has no central effects because it does not cross the blood-brain barrier, so may be better tolerated.

### **5HT<sub>3</sub> Receptor Antagonists**

These are mainly useful in situations where excessive amounts of 5HT are released, such as chemotherapy, radiotherapy, renal failure or gastro-intestinal obstruction. They do not reverse opioid-induced nausea. Side effects include constipation. In practice there may be little to choose between them.

The doses in palliative care are:

Granisetron 1-2mg PO or S/C once daily.

Ondansetron 8mg twice daily PO or S/C or 8-24mg by 24 hour CSCI.

If there is no benefit after three days, discontinue. In intractable vomiting, additional haloperidol may be needed. Their action is potentiated by dexamethasone.

## OTHERS

### **Octreotide**

Seek advice from the Specialist Palliative care Team.

### **Dexamethasone**

May enhance the action of other antiemetics.

Dose range 8-16mg once daily PO or S/C (divide sites if the volume is too large).

If effective, consider decreasing the dose after 5-7 days. May be given by 24 hour CSCI e.g. if high plasma concentrations after individual injections are thought to have caused psychosis. In practice, oral and parenteral doses are equivalent. A licensed oral solution is available, 2mg in 5ml. Remember potential for raised glucose on steroids.

## HYPERCALCAEMIA

This is defined as a serum corrected calcium above 2.63mmol/L. It is a common complication of advanced cancer, which may be associated with nausea, vomiting, constipation, anorexia, confusion, drowsiness, polyuria, polydipsia and dehydration. Symptoms may be mistaken for the underlying malignancy.

### Treatment

If asymptomatic and corrected calcium less than 3mmol/L:

Check U&E and albumin.

Ensure adequate fluid intake, 2-3L per day and stop thiazide diuretics, Vitamins A, D and calcium supplements if taking.

Monitor fluid balance, corrected calcium levels and symptoms. Rehydration alone is often insufficient and most patients also need bisphosphonates. Treatment, where appropriate, should start as soon as possible, at least within 24 hours of diagnosis.

If symptomatic or corrected calcium above 3mmol/L:

Rehydrate with intravenous fluid. May require 2-4L per 24 hours. The amount and rate of rehydration depend on severity of symptoms, calcium level, cardiovascular status, urea and electrolytes.

If fluid overload give furosemide 20mg-40mg 12 hourly.

Give IV bisphosphonates. First choice is Zoledronate 4mg IV in 100mls sodium chloride 0.9% over 15 mins, then continue with rehydration. Disodium pamidronate is an alternative used in some centres. Refer to local guidelines.

Ensure adequate oral fluid intake when intravenous rehydration stops.

**Note:** Bisphosphonates are first line treatment for hypercalcaemia of solid tumours. Since they do not alter parathyroid hormone-related protein or renal calcium reabsorption, they may fail to control humoral hypercalcaemia of malignancy without bone metastases.

Calcium level monitoring:

Calcium levels start to fall after 48 hours with normalisation in 90% of patients in 5-10 days. Levels may respond faster than symptoms.

Urea and electrolytes should be checked regularly. When re-checking calcium levels, be aware of response time to treatment.

Once normalised check calcium two weeks after infusion, then every two weeks.

Asymptomatic hypocalcaemia may occur, but symptomatic hypocalcaemia is rare.

Treat the other symptoms associated with hypercalcaemia, e.g. bone pain, abdominal pain, constipation and nausea.

After symptoms have settled, and if appropriate, treat or review the treatment of the underlying problem causing the hypercalcaemia.

In recurrent hypercalcaemia, may be appropriate to consider regular treatment orally or intravenously. Seek specialist advice.

### Others

Calcitonin (salmon) / salcatonin acts within a few hours, but the effect lasts only a couple of days. It may be helpful as an adjunct if rapid control is needed in the early treatment of severe cases, or as an option in resistant cases. Side effects include nausea, vomiting and flushing.

Dose: 100 units every 6-8 hours increasing to a maximum of 400 units every 6-8 hours, according to response.

Corticosteroids are usually ineffective in hypercalcaemia of solid tumours, but may help in steroid responsive malignancies e.g. myeloma and lymphoma. They take several days to work.

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## RAISED INTRACRANIAL PRESSURE

This may be due to direct tumour pressure or surrounding cerebral inflammation. Headache, vomiting, confusion and blurred vision may occur. Steroids reduce oedema around the tumour. Dexamethasone 8mg bd may give a response within 24 hours. Apart from hydrocortisone, give oral corticosteroids no later than midday to reduce insomnia. In those with a history of gastrointestinal problems, or already on an NSAID for other reasons, provide gastroprotection with a proton pump inhibitor. After 4-5 days, reduce dose by one quarter per week to the minimum effective maintenance dose, to minimise side effects. Benefit may persist for 1-2 months. If no response after 7 days, reassess.

Patients on maintenance treatment should have a steroid card. There is no set maximum maintenance dose; some patients may progress to higher maintenance doses if symptoms return. Oral candida is common and treatable, so warn patients of possible symptoms. In practice, the oral and parenteral doses of dexamethasone are equivalent. Corticosteroid therapy should be reviewed constantly, but do not discontinue in the dying phase if it has relieved these symptoms.

If dexamethasone is contraindicated or ineffective, cyclizine is the preferred antiemetic. Positional emesis may respond to cyclizine or hyoscine hydrobromide. Headache may require analgesics in addition, e.g. codeine or strong opioids. NSAIDs increase the risk of corticosteroid gastrointestinal toxicity, so may be best avoided. Anticonvulsants may be needed for seizure control. Phenytoin or carbamazepine may reduce the effect of corticosteroids due to increased metabolism - retitrate steroid dose if necessary.

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## INTESTINAL OBSTRUCTION

This may be mechanical or functional or both. It can be managed medically even at home, if surgery is not indicated. Symptoms include vomiting, constant aching abdominal pain, and colic, usually occurring together, so combination therapy is required. See below for management of individual symptoms.

### COLIC

In complete obstruction, stop stimulant, osmotic and bulking laxatives, and gastrokinetic antiemetics, e.g. metoclopramide, domperidone. Prescribe hyoscine butylbromide (Buscopan) 40-60mg by 24 hour CSCI. This also reduces the volume of secretions and frequency of vomits. If there is no response after one day, increase in 40mg increments to 120mg over 24 hours. Glycopyrronium by 24 hour CSCI is an alternative. If symptoms are not controlled contact the Specialist Palliative Care Team for further advice.

### ABDOMINAL PAIN

Give morphine, at one half of the 24 hour oral morphine dose, or diamorphine at one third of the 24 hour oral morphine dose by 24 hour CSCI. Titrate dose if necessary.

## NAUSEA AND VOMITING

Cyclizine is often regarded as first line, and is given at 150mg by 24 hour CSCI. Some centres combine it with haloperidol 1.5-5mg (levomepromazine is an alternative to cyclizine, particularly if cyclizine would precipitate in combination with other drugs.). Partial obstruction of the large bowel without colic may benefit from a softening agent, e.g. docusate sodium 200mg twice daily. It may be difficult to distinguish between complete and partial obstruction. Severe constipation may mimic obstruction.

In resistant cases seek specialist advice. Levomepromazine may be of benefit. Octreotide 500 micrograms daily S/C may be required to reduce the volume and frequency of vomits. The dose may be increased over several days to 1mg subcutaneously daily if symptoms persist. Dexamethasone 8mg daily for five days may help, by decreasing tumour oedema. In high obstruction, other measures may be needed if these fail, e.g. nasogastric tube or venting gastrostomy. Seek specialist advice.

If symptoms remain stable for 48hrs review medications and decrease to the lowest effective dose. Oral therapy may be resumed in some patients. If the patient is anxious about stopping the syringe driver, phase in oral replacement of each component one at a time. It may not be possible to prevent all vomiting, but occasional vomiting may be tolerated.

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## 7. CONSTIPATION

Constipation is a major problem in patients with advanced illness and bowel management should be a routine aspect of their care. Factors which predispose to constipation in this patient group include reduced mobility, reduced fluid intake, medication including opioids and anti-muscarinics.

It is better to prevent constipation than to wait until treatment is needed. For existing constipation, assessment should rule out hypercalcaemia, ileus and intestinal obstruction. PR examination is essential, as is taking an accurate history. Passing soft stool less frequently or passing hard stool daily will both be described as constipation by some patients and clarifying what the patient sees as the problem will help in your choice of management. Patients who have hard stool in the rectum on PR examination will require either a suppository or enema to clear this.

TABLE 3: ORAL LAXATIVES

STIMULANT	
Bisacodyl	Available as tablets (suppositories also available) Starting dose 5–10mg at night - Can be increased to 10mg bd
Senna	Available as tablets, granules or syrup Starting dose 15mg at night - Can be increased to 30mg bd
SOFTENER	
Docusate	Available as capsules or oral solution Starting dose 200mg at night - Can be increased to 200mg tds
Movicol	Available as sachet for reconstitution Starting dose 1-2 sachets at night Can be titrated incrementally to 8 sachets a day
COMBINED STIMULANT/SOFTENER	
Co-dantrusate (50/60) Co-danthrimer (25/200) Co-danthrimer strong (75/1000)	Available as capsules or suspension Starting dose 2 caps/10mls at night Can be increased to twice daily  Strong formulation can be used if this is insufficient

Stimulants should be avoided if there is a tendency towards bowel obstruction or there is impacted stool that has not been cleared, as colic will be provoked. Movicol can be highly effective, but its use can be limited by the volume of liquid the patient has to take. Patients taking movicol do not usually require a stimulant laxative as well.

Combination preparations containing dantron will turn the urine red and can also cause peri-anal irritation which can be very severe, particularly in bed bound, incontinent patients. Dantron containing preparations are only licensed for use in patients with malignant disease of limited life expectancy.

Lactulose should be avoided as it is often unpalatable, and causes bloating and flatulence.

Bulking agents such as Fybogel are not recommended for use in palliative care patients.

Rectal interventions in the form of suppositories or enemas are important in the management of established constipation. All patients who have not opened their bowels for a number of days should have a PR examination to exclude stool impacted in the rectum. Simple glycerine suppositories can be tried first before moving on to docusate, arachis oil (beware of peanut allergy) or phosphate enema in this order.

A number of opioid antagonists are coming on to the market, either as stand alone products or in combination with opioid analgesics. These should only be used by palliative care specialists, as in most cases, the cause of constipation is multifactorial.

## 8. DIARRHOEA

As with all cases of diarrhoea, an infective cause should be excluded first, including testing for clostridium difficile. 'Overflow' diarrhoea, where there is impacted faeces higher up in the bowel allowing liquid stool to bypass needs to be treated as the constipation guidelines indicate.

If 'overflow' and infection have been excluded, then either codeine or loperamide can be used to try and reduce the frequency of stool.

**Loperamide 2mg tabs.** Up to 16mg/24hrs. In acute diarrhoea, 2mg can be given after each loose stool but for chronic diarrhoea, patients may require maintenance therapy.

**Codeine** 30-60 mg up to qds

Some specific causes of diarrhoea may require different management.

Pancreatic insufficiency usually requires treatment with creon supplements.

Some bowel tumours will produce copious secretions which will manifest as diarrhoea. Anti-secretory agents such as hyoscine butylbromide or octreotide can be used for these cases, but their management should be under specialist palliative care advice.

## 9. ANOREXIA

Explanations and practical solutions can be more important than drug treatment. Dietitians can help. The family must be involved. Listen to fears of patient and family/carers; failure to eat can cause fear and conflict. Food or supplements may be more easily taken by snacking through the day.

Avoid offering excessive food and portions look less daunting on a larger plate. Exclude treatable causes e.g. nausea, infection, sore mouth, constipation, drugs, anxiety, dyspepsia, gastric stasis, pain, malodorous tumours, hypercalcaemia, uraemia, depression. If drugs are appropriate, and there are no major contraindications, try a short course of prednisolone 15-30mg daily, or dexamethasone 2-4mg daily. They may be effective within a few days.

If there is no response after a week, stop the steroid (tapering not necessary). Corticosteroids help only some patients, and only for a few weeks. Best used as a short-term measure for symptomatic benefit. Patients with multiple complex symptoms and limited life expectancy are more likely to benefit from them.

Watch for sore mouth from oral candida, which may contribute to anorexia, and monitor capillary blood glucose in known diabetics on insulin and oral hypoglycaemics. Alternatively, if there is a prognosis of over three months, try megestrol acetate 160mg bd.

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## 10. BREATHLESSNESS

Breathlessness is a common symptom encountered in palliative care. When managing a patient with breathlessness consider the following underlying causes and treat where appropriate:

- Infection
- Anaemia
- Bronchospasm
- Pleural effusion
- Heart failure
- Pulmonary embolus

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### GENERAL PRINCIPLES

#### Non-pharmacological Management

The use of strategies that do not involve drugs can have a significant impact on the management of breathlessness:

- Avoiding claustrophobic environments
- Well ventilated rooms
- The use of a fan on the side of the face
- Breathing control management
- Occupational therapy – adaptations, lifestyle adjustments
- Physiotherapy – breathing recovery strategies, maintaining mobility/walking aids
- Complementary therapies, including relaxation, aromatherapy, acupuncture, visualisation
- Psychological support
- Anxiety management

#### Pharmacological Management

##### Benzodiazepines

These drugs can be very effective for breathlessness, especially if there is associated fear and anxiety:

- Lorazepam 500 microgrammes – 1 mg orally or sublingually PRN, up to a maximum dose of 2mg in 24 hours. Although not licensed to be taken sublingually, the oral tablet formulation can be administered by this route to achieve more rapid symptomatic relief.
- Alternatively, diazepam 2 mg PRN, increased if necessary up to a maximum total dose of 15 mg over 24 hours in divided doses. These doses should be halved in elderly and debilitated patients.
- If the patient is too unwell to take oral medication, midazolam 2.5mg S/C four hourly PRN can be used as an alternative. If multiple doses are required then consider administration via 24 hour CSCI at a starting dose of 5-10mg.



## Opioids

- Oral morphine sulphate solution (10 mg/ 5 ml) at a starting dose of 2.5 mg four hourly PRN, titrating upwards every 48 hours according to response.
- If PRN medication is required more frequently it would be advisable to seek advice from the Specialist Palliative Care Team.
- Immediate release morphine is often more effective for control of dyspnoea than modified release morphine.
- In patients who are already taking strong opioids, such low doses of oral morphine can still be effective for dyspnoea. Some patients may need to take different doses for dyspnoea and breakthrough pain.
- Morphine is excreted renally. In renal impairment use a lower dose initially & reduce the frequency of administration. In established renal failure alternative opioids may be more appropriate – seek specialist palliative care advice.

## Oxygen

The use of oxygen in hypoxic patients should be under specialist supervision (for use in end-stage chronic respiratory disease see following section). In exceptional circumstances, some patients do get benefit from having oxygen available at home but this should follow discussion with a palliative care specialist.

## Other agents

Nebulised bronchodilators can be useful if there is an element of reversible airways obstruction. Nebulised sodium chloride can also be useful if thick secretions are present. Dexamethasone may be beneficial in certain situations including large airway obstruction, SVCO and lymphangitis. Specialist advice should be sought in these situations.

For cough see page 45.

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## MANAGEMENT OF END-STAGE CHRONIC RESPIRATORY DISEASE

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](http://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](http://www.brit-thoracic.org.uk)).

- Regardless of the underlying diagnosis, by the time end-stage is reached, symptom control will be essentially the same. Where appropriate, disease-specific treatment should continue alongside symptom control. In the case of the less common respiratory diseases, close liaison with Specialist Respiratory teams is recommended, to ensure that, whilst appropriate, active management is optimised.

## Referral to Specialist palliative care services

Appropriate timing of referrals to palliative care services for patients with non-malignant disease can be harder to judge than for cancer patients. Referral criteria vary so check with local services before referring the patient.

The following guidelines may be helpful:

- The patient has had a diagnosis of chronic respiratory disease confirmed at some stage of their disease trajectory by a specialist respiratory physician, and attempts to optimise therapy, including pulmonary rehabilitation where appropriate, have been made.
- The patient has knowledge and understanding of their disease, is aware of the reason for referral to Specialist Palliative Care and agrees to this.
- Two or more of the following should also apply:
  - The patient has uncontrolled physical or psychological symptoms despite optimal tolerated therapy.
  - The patient makes increasing use of emergency treatment for infection and/or respiratory failure.
  - The patient has an anticipated life expectancy of 12 months or less.

Ideally, if a patient is being referred to hospice services, they should be aware that, dependent on local policy, resuscitation facilities are limited and such treatments as intravenous aminophylline, intravenous antibiotics and blood gas interpretation are generally not provided within the hospice setting.

## SYMPTOM CONTROL

The management of specific symptoms e.g. constipation, nausea and vomiting is applicable to both cancer and non-cancer patients. Please see relevant chapters for details. The information covered in the 'Breathlessness' chapter regarding non-pharmacological interventions, benzodiazepines and opioids is equally appropriate in the management of end-stage respiratory disease. The use of bronchodilators and oxygen specific to end-stage chronic respiratory disease will now be covered in more detail. Advice on cough and sputum management may be applicable to palliative care patients without end-stage respiratory disease.

## BRONCHODILATORS

- Inhaled or nebulised
- $\beta$ agonists e.g. salbutamol, terbutaline
- Antimuscarinic bronchodilators e.g. ipratropium bromide, tiotropium bromide
- Combination preparations

Bronchodilator therapy should be optimised in accordance with NICE guidance. Optimal doses include:

	Inhaled	Nebulised
<b>Salbutamol</b>	100 – 200 micrograms QDS +/- or PRN	2.5 – 5 mg QDS +/- or PRN
<b>Terbutaline</b>	500 micrograms QDS +/- or PRN	5 - 10 mg QDS +/- or PRN
<b>Ipratropium*</b>	20 – 40 micrograms 3 - 4 times daily Max QDS	250 – 500 micrograms 3 -4 times daily Max QDS
<b>Tiotropium*</b>	18 micrograms OD (Handihaler) 5micrograms OD (Respimat)	Not available
<b>Combivent*</b>	No longer available.	1 nebule 3 – 4 times daily

**Please note:** Tiotropium should be discontinued if patients are commenced on Combivent® or ipratropium. British National Formulary Volume 55, March 2009

- Higher doses can be used out of licence.
- See also local guidelines for management of COPD.
- Bronchodilators may not be effective in some diseases, eg pulmonary fibrosis. However a trial of inhaled, or occasionally nebulised, bronchodilators may be still be worthwhile in such conditions.
- Prescriptions for inhaled long-acting 2 bronchodilators (LAB) eg. Formoterol or Salmeterol or combination LAB/ corticosteroid inhalers should be continued. Use of a spacer device should be advised also.

Consider possible causes of breathlessness other than end-stage respiratory disease such as coexistent heart failure, pleural effusion, pneumothorax, pulmonary embolus.

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## OXYGEN IN END-STAGE RESPIRATORY DISEASE

Almost all patients with end stage respiratory disease will previously have been assessed, and been found to require long-term oxygen therapy (LTOT). The guidelines for requirement for LTOT are well documented for both COPD and pulmonary fibrosis.

However, oxygen can also be used for the palliation of disabling dyspnoea, not relieved by other treatments, in those patients who do not meet the requirements for LTOT. Oxygen for palliation can be ordered from primary or secondary care. Formal assessment, including measurement of blood gases, or follow up, may not be required in patients who are in the terminal phase of their illness. When ordering oxygen (using a Home Oxygen Order Form – HOOF), two decisions need to be made:

### **1. For how many hours per day does the oxygen need to be used?**

Patients who do not meet the criteria for LTOT may use oxygen on an 'as required' basis. Initially they will be supplied with oxygen cylinders. However, if they regularly use more than 180 litres of oxygen per day, the oxygen company will provide them with an oxygen concentrator and a cylinder as 'back up'.

### **2. What flow rate (Litres/minute) is required?**

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 overridden 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<sub>2</sub> is around 92% (88-92% in patients who retain CO<sub>2</sub>), 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 desaturate still further on exertion. They frequently require high flows of oxygen.

Across Lancashire all home oxygen is supplied by Air Products. Their fax number, to where completed HOOFs should be sent, is 0800 214709; telephone number is 0800 373580.

The response times for the company are set as follows:-

**Within 24 hours for patients awaiting hospital discharge**

**Within 3 working days for all other patients.**

However, oxygen can be ordered as an emergency request when it will be delivered within 4 hours (including weekends and Bank Holidays). The tariff for emergency oxygen delivery is 9 times higher than that for non-emergency supply.

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## COUGH AND SPUTUM MANAGEMENT

If sputum increases in amount or changes colour, exclude infection and consider antibiotics. Ensure adequate oral fluid intake, where appropriate, to liquefy secretions.

### Mucolytics

- Carbocisteine capsules at starting dose of 750 mg tds reducing to maintenance dose of 750mg bd or carbocisteine oral liquid (250 mg/5 ml) at initial dose of 750 mg tds reducing to 750mg bd.
- Mecysteine hydrochloride 200mg qds for 2 days then 200mg tds for 6 weeks, then 200mg twice daily.

These should both be reviewed 4 to 8 weeks after initiation and reduced to the maintenance dose. If the patient feels no benefit, then it should be stopped.

**Sodium Chloride 0.9% nebulas 2.5–5 ml PRN, which anecdotally may ease expectoration.**

**Symptomatic relief of tickly cough Simple linctus 5-10 ml PRN up to qds.**

### Antitussives

Codeine linctus 5-10 ml PRN up to qds.

Oral morphine solution (10 mg/5 ml) starting dose 2.5 mg 4 hourly PRN. This may also help dyspnoea & pain.

Methadone linctus (2 mg/5 ml) 2 mg initially nocte, increasing to bd if necessary.

In the event of acute infection it may not be advisable to use cough suppressants (see NICE guidance).

**Physiotherapy, positioning and acupuncture.**

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## TERMINAL RESPIRATORY FAILURE – THE LAST FEW DAYS OF LIFE

- There needs to be agreement within the team about the patient`s condition.
- It is important to recognise patients who appear to be approaching the terminal phase of their illness. It is often more difficult to diagnose the dying phase in patients with end-stage respiratory disease than in terminal cancer patients.
- In patients with end-stage respiratory disease, improvement may be achieved with medication – a reversible precipitant such as a chest infection may be present.
- If recovery is uncertain, this needs to be shared with patient & family.
- It is important to establish the inappropriateness of ventilation, including non-invasive ventilation, & cardiopulmonary resuscitation.
- Once the dying phase has been identified management should follow the guidance for the terminal stage (chapter 23), including the use of the end of life tools.

Adapted from: The Merseyside and Cheshire cancer network palliative care clinical network group.

## 11. MOUTH PROBLEMS

### DRY MOUTH

Mouth problems are common among palliative care patients. Many patients will admit that they have a sensation of dryness in the mouth if asked; they rarely volunteer this symptom spontaneously.

It can cause problems with discomfort, impaired taste and difficulties with chewing, swallowing and speaking. This may lead to secondary complications of poor oral hygiene, caries and infection.

These symptoms can adversely affect appetite and mood.

Drug therapy is a major cause of dry mouth and saliva production is affected. The saliva produced is of very poor quality and quantity.

Management is focused on treating the cause, using saliva stimulants and the use of saliva substitutes.

Saliva stimulants are more effective than substitutes and patients prefer them.

Prevention of secondary complications is often easier than treating them.

Poorly fitting dentures can aggravate the problem.

#### **Preventative treatment:**

Teeth and tongue should be cleaned at least twice daily with a small or 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 in the patient's usual solution and cleaned with a brush.

Adequate oral fluid intake should be encouraged.

Lips should be moisturised with lip balm or tasteless oil, e.g. olive oil.

#### **Management:**

Consider if drug therapy can be stopped or an alternative prescribed.

Diagnose and manage secondary oral infection.

Temporary relief can be provided by stimulating saliva production with regular small drinks, sucking boiled sweets or chewing sugar-free gum.

Artificial saliva sprays, pastilles or tablets are also useful. Many artificial saliva products are acidic and can accelerate the development of dental caries. Some patients benefit from the use of parasympathomimetics and are prepared to use them despite side effects as the sensation of dry mouth is so unacceptable. Side effects include blurred vision and sweating. Topical pilocarpine 4% eyedrops to the oral cavity is the cheapest option. Topical administration is most likely to increase lacrimation compared with PO administration. Bethanechol 25mg PO tds or pilocarpine tablet PO 5mg tds are alternatives.

## ORAL MUCOSITIS

Oral mucositis refers to inflammation of the oral mucous membrane. This is a common side effect of chemotherapy and local radiotherapy.

The amount of damage varies from the absence of symptoms and signs, through the presence of ulcers, causing pain and requiring soft diet, to marked haemorrhage and necrosis with a need for parenteral or enteral nutritional support.

Management is focused on improving comfort and maintaining good oral hygiene. A stepwise approach can be adopted, initially using a topical anti-inflammatory. If this provides inadequate relief try a topical anaesthetic. In some cases topical morphine is required.

TABLE 4: MANAGEMENT OF SPECIFIC ORAL PROBLEMS

Problem	Management
apthous ulcers	local steroid – adcortyl in orabase, corlan pellets antiseptic - mouthwash chlorhexidine - topical gels – anti-inflammatory (bonjela) local anaesthetic (lidocaine), see BNF 12.3.1 aloe vera toothpaste can be soothing
viral ulcers	aciclovir 200mg 5 times a day for 5 days topical gels (see above)
malignant ulcers	consider antibiotic
mucositis	benzydamine (Difflam) mouthwash or spray paracetamol mucilage 1gm 4-6 hourly opioid analgesics if above inadequate. Gelclair sachets
gingivitis	metronidazole 200mg PO tds for 3 days Consider metronidazole suspension topically or rectal administration if not tolerated orally Antiseptic mouthwash – e.g povidone-iodine or chlorhexidine gluconate mouthwash
dry mouth	review medications (opioids, antimuscarinics) increase oral intake saliva stimulants saliva substitutes – saliva orthana, glandosane spray, oralbalance gel, see BNF 12.3.5 pilocarpine tablets / eye drops – seek specialist advice
coated tongue	chewing pineapple chunks brushing tongue with a soft toothbrush
fungal infection	nystatin suspension 5ml qds fluconazole 50-100mg daily for minimum of 7 days or 150mg stat if appropriate soak dentures overnight in weak chlorine solution (Milton) use a new toothbrush and have 2 brushes in use so that the heads can dry out

## 12. HICCUP

May be due to gastric distension, toxicity from metabolic disorders or infection, or CNS tumour.

If due to gastric distension, try an antacid with a defoaming antifatulent (dimethicone), e.g. Asilone suspension 10 ml qds.

Metoclopramide or Domperidone will reduce gastric distension. Peppermint water may help, but less desirable than a defoamer. These should not be used concurrently because of their opposing actions.

If due to diaphragmatic or phrenic nerve irritation Baclofen 5-10 mg b.d. or t.d.s. (effective within 48 hours, but may be side-effects), Nifedipine 10-20 mg t.d.s. or an anticonvulsant such as Gabapentin 300 mg t.d.s. may help.

If due to toxicity, consider Haloperidol 1.5-3 mg b.d. or Chlorpromazine 10-25 mg t.d.s. If due to CNS tumour, an anticonvulsant such as Gabapentin or Sodium Valproate may help. In intractable cases or in the terminal stages Midazolam can be used 5 mg SC initially then by continuous subcutaneous infusion over 24 hours in a syringe driver, titrated as necessary, range 10-60 mg. Sedation is likely, so this may not be appropriate in non-terminal patients.

**An acute episode may respond to nebulised saline 2-5 mls over 5 minutes using mouthpiece. Its onset of effect is within minutes and may last 3-4- hours. It acts by causing pharyngeal stimulation and may be used every 2 hours for prophylaxis.**

## 13. DEPRESSION

### Definition

Depression is low mood or loss of interest, usually accompanied by one or more of the following:-

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

Patients with chronic health problems are at increased risk of depression.

### Assessment

In primary care and general hospital setting, screen patients with questions such as:-

- During the last month, have you often been bothered by feeling down, depressed or hopeless and
- During the last month, have you often been bothered by having little interest or pleasure in doing things.
- Explore further, patient's mood disorder and any relationship to their illness. Explore family, social issues.
- Always ask patients with depression sensitively about suicidal ideas and intent.



## Management

- Address and treat underlying causes of physical and psychological distress, where possible.
- Explain possible management plan.
- Watchful waiting, with reassessment within two weeks for patients who may recover or for patients who do not want an intervention.
- Referral to specialist mental health team if immediate risk of harm to self or others, treatment resistant depression, recurrent symptoms, atypical psychotic depression.

## Non-Pharmacological Management

- Sleep and anxiety management.
- Exercise.
- Guided self-help.
- Cognitive behavioural therapy.
- Short-term psychological interventions.

## Pharmacological Management

- Where mild depression persists after other interventions, consider use of an antidepressant.
- In moderate depression, offer antidepressant medication to patients before psychological interventions.
- Discuss patient's fears of addiction or other concerns about medication.
- When starting treatment, tell patients of the risk of discontinuation/withdrawal symptoms and potential side effects.
- Inform patients about delay in onset on action.
- Review patients every one to two weeks at the start of antidepressant therapy.
- Treatment should be continued for four weeks before considering whether to switch antidepressant due to lack of efficacy.
- In cases of partial response continue for a further two weeks (elderly patients may take longer to respond).
- For routine care use an SSRI e.g. Fluoxetine or Citalopram.
- If increased agitation develops early in treatment with an SSRI provide appropriate support and consider changing to a different antidepressant or offering concomitant treatment with a benzodiazepine for a brief period.
- St John's Wort may be of benefit in mild or moderate depression but its use is not advised because of uncertainty about appropriate doses and potential serious interactions with other drugs.
- If the first antidepressant fails, consider gradual increase in dose in line with the summary of product characteristics.
- If an antidepressant remains ineffective or is poorly tolerated, consider a switch to another single antidepressant. Choices for a second antidepressant include a different SSRI or Mirtazapine. Consult BNF and NICE guidelines for consideration when switching antidepressant.

## References:

National Institute of Clinical Excellence CG23 Depression:  
Quick Reference Guide (amended) 27 April 2007.

## 14. ANXIETY IN ADVANCED ILLNESS

**Anxiety** is a state of apprehension or fear, which may be appropriate to a particular situation. Morbid anxiety occurs with individuals who are unable to banish their worries.

- In addition to panic attacks, spontaneous panic attacks, irritability, poor sleeping, avoidance and poor concentration may all be symptoms.
- Anxiety tends to aggravate the severity of other symptoms.
- In life-limiting illnesses, anxiety or panic may be associated with uncertainty about the future, job and social worries, future separation from loved ones; as well as unrelieved symptoms.
- Co-existing depression is common.

Anxiety disorders can be divided into the following:-

### **Generalised anxiety disorder**

- Over arousal, irritability, poor concentration, poor sleeping and worry about several areas, most of the time.

### **Panic disorder**

- Intermittent episodes of panic or anxiety and taking avoiding action to prevent these feelings.
- Agoraphobia or social phobia – not covered by this guideline.

### **Assessment**

- Full medical history and examination.
- Signs and symptoms of anxiety may also be due to organic disorders such as hypoxia, sepsis, medication, metabolic causes, poorly controlled pain.
- Elicit patient's specific fears and understanding.
- Note language, culture or other characteristics that may be important.
- Gather information from those close to the patient, e.g. family, GP.
- Assess for depression.

### **General Management**

The severity of the underlying disease and the overall prognosis guides treatment decisions.

- Treat organic disorders.
- Acknowledge and discuss anxiety and specific fears.
- Share decision making with patient. Involve family.
- Consider referral to Specialist Palliative Care services for additional psychological support and access to therapy such as Hospice Day Care, relaxation techniques, etc.

### **Specific Management**

Generalised anxiety disorder.

- As for general management.
- In addition, consider referral for psychological therapy or pharmacological therapy.
- Benzodiazepines are only recommended for short-term use of not more than two to four weeks. Sedative antihistamines may be helpful.
- SSRI's may be considered.

### **Management of Panic Disorder**

- As for general management.
- Consider referral for psychological therapy.
- SSRI's may be considered.
- Benzodiazepines, sedating anti-histamines or anti-psychotics are not recommended for the treatment of panic disorder.

## 15. CONFUSION

Confusion is common in patients with advanced illness, particularly in older people and those with chronic cognitive impairment.

**Principles of Management:**

- Treat reversible causes
- Manage the patient in a suitable, quiet environment
- Make the patient safe
- Acknowledge the distress and fears of the patient and carers and give clear explanations and reassurances where possible.

### Potentially reversible causes of confusion:

Biochemical	Hypercalcaemia Hyponatraemia Uraemia Hyper- and hypoglycaemia
Infection	Urine Chest
Drugs	Opioids Benzodiazepines Antidepressants Anticonvulsants Steroids Antimuscarinics/anticholinergics (chlorpheniramine, cyclizine, hyoscine, glycopyrrrolate, levomepromazine)
Deficiency or Drug withdrawal	Thiamine Alcohol Benzodiazepine Opioid Adrenal steroid
Hypoxia	
Hypotension	
Extreme anxiety	
Severe pain	
Constipation	
GI bleed in patient with liver failure	
Brain metastases	

## Management

Consider the role of investigation to identify reversible causes.

If drug induced, reduce dose or stop as appropriate.

Medication should only be part of the treatment plan, and may not be needed in those who are “happily muddled” without distress. It will not reverse confusion and may sometimes worsen it.

If specific treatment does not help consider one of the following:

Haloperidol – drug of choice. Parenteral doses are twice as potent as oral.

Use low doses (0.5mg PO bd) in the elderly. Start at 1.5mg PO nocte in other patients and titrate to a maximum of 10mg daily. Higher starting doses may be used patients who are hallucinating.

Haloperidol can also be given subcutaneously in a syringe driver or as a stat injection.

Levomepromazine – powerful sedative. 6-12mg PO daily or 5-25mg via a syringe driver over 24 hours.

Admission to hospital or hospice may be required.

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## 16. CONVULSIONS

May occur with primary or secondary brain tumours, uraemia or other metabolic disorders e.g. hypercalcaemia. The following advice refers to palliative care patients with a diagnosed cause for fitting.

Dexamethasone is used to reduce oedema around brain tumours (See Nausea & Vomiting: Raised Intracranial Pressure, page 36). Anticonvulsants are used for prophylaxis: consider oral phenytoin, sodium valproate, carbamazepine or levetiracetam but seek specialist advice and check interactions.

Patients with a history of epilepsy and receiving treatment for it, will still need prophylaxis when the oral route is not possible.

Various emergency and prophylactic doses of benzodiazepines including diazepam, midazolam and lorazepam are cited in the literature. Caution is suggested with Diazepam because of its prolonged sedative effect. Typical ranges are quoted below.

Midazolam:

Emergency: 5-15mg, subcutaneously, intravenously or intramuscularly, repeated after 5-15 minutes if necessary.

Prophylaxis: 10-60mg by 24 hour subcutaneous infusion.

Midazolam is 3 times more potent than Diazepam in single doses for sedation but as an anti-epileptic it is twice as potent as Diazepam.

Diazepam:

Emergency: 5-10mg as rectal solution, repeated if not settled after 5-15 minutes .

Prophylaxis: 20mg orally at night or in two divided doses, or rectally. **Never give subcutaneously.**

Lorazepam:

Emergency: 4mg intravenously (diluted 1:1 with sodium chloride 0.9%) as a single bolus into a large vein.

When oral therapy is not possible, an alternative prophylaxis is phenobarbital (phenobarbitone) 200-400 mg by subcutaneous infusion over 24hrs in a separate driver but only on the advice of a palliative care specialist (See section on Syringe Driver: Compatibilities, page 58). A loading dose of 100-200mg by intramuscular injection can be given if necessary. It is not first line - for difficult cases only.

## 17. MUSCLE SPASM AND MYOCLONIC JERKS

### Muscle spasm

Usually due to pressure on, or irritation of, a nerve. The pain is not helped by opioids.

Diazepam:	Oral, 5-10mg up to three times daily.
Baclofen:	Oral. Increase slowly from 5mg every 8 hours after food. Max 100mg daily. Nausea and sedation common.

### Myoclonic jerks

Exacerbated by escalating doses of opioids, sepsis and metabolic disorders e.g. renal failure, hepatic failure. Common in the last 48hrs of life. Multifocal myoclonic jerks are considered pre-epileptiform.

Midazolam:	5-10mg by subcutaneous injection. 10-60mg by subcutaneous infusion over 24 hours.
Diazepam:	Orally or rectal solution, 5-10mg repeated every hour if necessary. <b>Do not use in syringe driver.</b>

## 18. PRURITIS

Diagnose and treat reversible causes of pruritis, e.g. skin disorders (scabies, fungal infection), obstructive jaundice, uraemia, lymphoma, iron deficiency anaemia, drugs (opioids). Good skin care is an essential component of any treatment. Avoid hot baths, rough underclothing and rough drying after bath and wear loose-fitting cotton clothing. The skin is often dry, so correct with emollients, e.g. alternatives to soap such as emulsifying ointment, bath emollients, and topical emollients to dry, itchy areas. Calamine is often too drying but Menthol 0.25-1% in aqueous cream is cooling. Crotaamin lotion/ointment and preparations including phenol or camphor may be helpful.

Use 1% hydrocortisone cream for inflamed skin. Creams and lotions can be kept in the fridge. Avoid topical antihistamines.

Antihistamines at full dosage may help, particularly if pruritis associated with probable histamine release and cutaneous causes. Antipruritic and sedative actions may be linked, so use the sedating antihistamines, e.g. Chlorphenamine, Trimeprazine or Promethazine. If one antihistamine doesn't work, it may be worth trying a different one or augmented with H<sub>2</sub> antagonists, e.g. Cimetidine 400 mg b.d. They may not be particularly effective in obstructive jaundice, uraemia, opioid-induced pruritis and lymphoma.

## 19. FUNGATING TUMOURS

### BLEEDING

These tumours may be friable and bleed during dressing change. Soak dressings with sodium chloride to ease removal. If the wound needs cleansing, irrigation with sodium chloride or water is preferred, because some antiseptics interfere with healing, and mechanical cleansing with swabs may be painful and disturb granulation tissue. Tranexamic acid can be used orally as prophylaxis against but should be used with caution in those patients with a history of thromboembolic disease. To avoid this it can be used topically by either dissolving the tablets in normal saline and applying directly with cover of non-adherent dressing or use gauze soaked in this solution, or use gauze soaked in Tranexamic acid for injection.

Other options include alginate dressings (e.g. Kaltostat) or topical adrenaline (epinephrine) 1 in 1000 to bleeding points.

An alternative is to use Sucralfate paste; crush a 1g tablet and mix with 5 ml KY jelly to appropriate consistency. Gauze soaked in Sucralfate suspension has also been used. These topical applications may be used as often as necessary and they are more effective and longer lasting than adrenaline.

If the tumour is near a major blood vessel, make plans to deal with major haemorrhage (see section on Major Haemorrhage, page 56)

### TUMOUR BULK

Discuss reduction of tumour bulk with a clinical oncologist.

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## ODOURS

Anaerobic organisms cause offensive smells which distress the patient and may cause nausea. Oral metronidazole, 400mg 8 hourly, can be used and may sometimes work at a “subtherapeutic dose” which the patient may tolerate better, e.g. 200mg twice daily. There are also gel formulations, e.g. Metronidazole gels for topical application, for topical application. Charcoal cloth dressing placed over the main dressing may help. Not all dressings are available on prescription in the community.

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## WOUND CARE

For further advice on wound care, contact your Tissue Viability Nurse or other specialist nurse, e.g. community/hospital Clinical Nurse Specialist in Palliative Care or Hospice Inpatient Unit. Useful dressings include hydrophilic foam sheets or cavity dressings, alginates, and semi-permeable films (to contain odour and exudate).

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## PAIN

This may be difficult to control, requiring regular drugs for neuropathic pain as well as opioids and NSAIDs\* (\*these may also control itch). Dressings changes may require a short-acting analgesic 30 minutes prior to changing the dressing, or irrigation with 20ml of 1% topical lidocaine (lignocaine) solution.

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## 20. SWEATING AND FLUSHING

Profuse sweating, often worse at night, may occur in malignancies such as lymphoma and other cancers, carcinoid syndrome and liver secondaries. Fluid loss may be significant. Exclude treatable causes such as infection, anxiety, thyrotoxicosis, menopause. Drug causes include tricyclic antidepressants, opioids, anti-oestrogens, anti-androgens and alcohol. Reduce or stop unnecessary diuretics.

General measures are most important, including skin cooling, attention to clothing and environment, and oral fluids. Drugs alone may be insufficient.

Regular paracetamol 1g qds or prn may help. NSAIDs, e.g. ibuprofen 200-400mg tds or naproxen 250-500mg bd may be effective, even in afebrile patients.

If paracetamol and/or NSAIDs are ineffective try an antimuscarinic drug e.g. amitriptyline 25-50mg nocte or hyoscine hydrobromide patch 1mg/72hours.

If antimuscarinics are ineffective other potential treatments include propranolol 10-20mg tds which may reduce sweating, but observe usual contraindications, e.g. asthma history. For hot flushes as a result of hormonal manipulation venlafaxine, gabapentin and clonidine have all been used with varying degrees of success. Megestrol acetate has been used successfully for treatment of hot flushes following surgical or chemical castration. Seek specialist advice.

For sweating related to strong opioids Cimetidine 400 mg od or bd can be helpful. For carcinoid syndrome sweats octreotide has a specific action. Seek specialist advice. For localised sweating of palms, soles, axillae, apply an aluminium chloride 20% antiperspirant preparation.

## 21. MAJOR HAEMORRHAGE

**This section deals only with prescribing for major haemorrhage occurring as a terminal event, when death may result within minutes. The management of chronic bleeding is not covered here. Please seek specialist advice.**

If there have been warning bleeds or there is a strong likelihood of major haemorrhage, ensure staff are aware of the management plan. Make sure that appropriate drugs have been prescribed "as required" on the community drug prescription sheet, and are available in the patient's home.

The intravenous route is best, otherwise give by deep intramuscular injection (subcutaneous drugs will be poorly absorbed in circulatory shut down). Red or green towels will mask the evidence of a bleed. Stay with the patient.

The intention is to relieve anxiety and distress, creating amnesia if necessary. Midazolam provides prompt relief of distress.

### Options:

- Midazolam up to 10mg intravenously, titrated to desired effect. Repeat if necessary. OR 10mg by deep intramuscular injection. Avoid oedematous sites. Repeat if necessary after 5 minutes if inadequate control.
- OR Diazepam rectal solution 10mg.
- Hypotension arising from these drugs or the bleeding itself, may arrest the bleeding temporarily. If blood pressure rises again, bleeding may re-start, so do not leave the patient alone.

In the event of survival, reassess and institute appropriate symptom management.

## 22. SYRINGE DRIVERS

### GENERAL GUIDANCE

The syringe driver is an infusion pump used to give medication subcutaneously, usually over 24 hours. The most common one in use is the Graseby MS26 syringe driver. Other machines are available, please refer to local policies.

For most drugs, this method of administration is unlicensed.

Other routes of administration may be useful and limit the need for a syringe driver, e.g. rectal, transdermal and sublingual.

Some drugs may be given as a once daily injection (dexamethasone, haloperidol, levomepromazine and octreotide). It is best to avoid giving several 'once daily' injections S/C. However, consider this as an alternative or if it is the patients choice.

Drugs are generally more bioavailable by injection than PO. This means that the dose of drug given by syringe driver is likely to be lower than the dose previously given PO.



Dilute the mixture to the maximum volume the syringe will take to minimise problems with site irritation; 16mls in a 20ml syringe, and 21mls in a 30ml syringe. 10, 20 and 30ml syringes will fit in the Graseby MS26 syringe driver. See local policies for other manufacturers.

It takes a few hours before the drugs are sufficiently absorbed for an effect to be seen. If symptoms are controlled start the syringe driver 1-2hr before the effect of medications are due to wear off. If symptoms are uncontrolled, set up the syringe driver 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 from light with a holster.

Pain control is no better via the subcutaneous route than the oral route if the patient is able to swallow or absorb the drugs.

If a patient is well symptom controlled using other routes of administration and these can be maintained in the dying phase, a syringe driver does not have to be set up as a matter of routine.

As a general rule TD fentanyl patches should be continued when the need for a syringe driver is short term, e.g. in the last days of life. It is more straight forward to supplement the patch with injected opioids PRN than to convert to a single alternative opioid.

## **USES**

The syringe driver is a useful method of administration when other routes are inappropriate; e.g. persistent nausea, vomiting, malabsorption, dysphagia and unconsciousness.

## **CAUTIONS**

Avoid oedematous tissue.  
Care in restless/confused patient.  
Bleeding diathesis.

## **ADVANTAGES**

Round the clock comfort because plasma concentrations are maintained, avoiding peaks and troughs.  
Avoids repeated injections.  
Generally needs to be loaded once daily.  
Independence and mobility maintained because device is light-weight and can be worn in a holster.  
Control of multiple symptoms with a combination of drugs.

## **DISADVANTAGES**

Irritation or erythema and swelling at the site interferes with rate and absorption.  
May be seen as a terminal care event by the patient and carers.  
Training necessary for staff.  
Lack of flexibility.  
Lack of reliable compatibility data for some mixtures.  
Infection.  
Psychological.

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## DRUG COMPATABILITY

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.

A predictor of drug compatibility is pH. The majority of drugs given by syringe driver 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.

Equianalgesic doses are difficult to ascertain due to wide interpatient variation. Initial dose conversion should be conservative; it is preferable to underdose the patient and use rescue medication for any shortfalls.

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 the syringe and the giving set. For more information on drugs used via this route access [www.palliativedrugs.com](http://www.palliativedrugs.com) or [www.prodigy.nhs.uk](http://www.prodigy.nhs.uk)

For more information on the use of drugs 'off licence' see [www.palliative-medicine.org](http://www.palliative-medicine.org)

Some drugs are not suitable for SC injection as they are irritant to the skin; e.g. diazepam, prochlorperazine, chlorpromazine.

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## GOOD PRACTICE

### **Before setting up the syringe driver explain to the patient and family:**

- The reason for using this route and method
- How the device works
- Advantages and possible disadvantages

When prescribing the drugs to be placed in the syringe driver ensure that the correct S/C breakthrough doses are prescribed (i.e. 1/6th of the total 24hour dose of opioid).

All staff should ensure they are familiar with the Graesby MS26 syringe driver or their local driver before using.

Follow local protocol for use.

All syringe drivers in use should be serviced regularly.  
After use all syringe drivers should be cleaned and decontaminated as per local guidelines.

Although the Graesby MS 26 has a boost button its use is not recommended.

Label the syringe with the list of drugs, date and time.

Use of a syringe driver chart can prompt checks that the syringe driver 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 resite 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 driver to PO medication. When this seems possible, convert the drugs sequentially rather than all at once.

TABLE 5: COMMON SYRINGE DRIVER DRUGS

DRUG	24HR RANGE	INDICATION	COMMENTS
Haloperidol	2.5 – 5mg	antiemetic	antipsychotic
Cyclizine	75 – 150mg	antiemetic	irritant
Levomepromazine	5 – 12.5mg 5 - 25mg	broad spectrum antiemetic terminal restlessness	sedating at higher doses
Metoclopramide	30 – 60mg	antiemetic	irritation at site extrapyramidal effects non-sedating avoid in obstruction
Midazolam	5 – 80mg	terminal restlessness anticonvulsant anxiolytic	
Glycopyrronium	600 – 1200micrograms	antimuscarinic for noisy secretions	Start asap for noisy secretions
Hyoscine hydrobromide	800 – 2400micrograms	noisy secretions	can cause agitation and confusion
Hyoscine butylbromide (buscopan)	40 – 120mg	intestinal obstruction noisy secretions	non-sedative
Diamorphine	no ceiling doses	analgesic	
Morphine	480mg maximum quantity in a 20ml syringe. 630mg in a 30ml syringe. Higher doses will require 2 syringe drivers or seek specialist advice.	analgesic	
Oxycodone	160mg maximum quantity in a 20ml syringe. 210mg in a 30ml syringe. Higher dose will require 2 syringe drivers or seek specialist advice.	analgesic	do not mix with cyclizine

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## SPECIFIC SYMPTOMS - (also refer to respective chapters)

### PAIN

If a continuous subcutaneous infusion (CSCI) of analgesia is appropriate, use the information in Chapter 3 Pain and Guidance on opioid conversion on page 22 to calculate the dose for the syringe driver and the breakthrough doses.

If the patient is opioid naive use as required doses of analgesia subcutaneously for the first 24 hours. If three or more doses of analgesia are required in 24 hours, consider starting a syringe driver based on the doses required in the previous 24 hours.

If the patient is in pain when a syringe driver is being set up, the first "breakthrough" dose can be given at the same time the syringe driver is started to cover the time it will take for the infusion to reach steady state.

In impaired renal function toxicity may occur. Consider giving a reduced dose if using morphine, diamorphine or oxycodone or switching opioids to one more appropriate in renal failure - seek Specialist Palliative Care advice before prescribing.

#### Switching between other analgesic presentations and a syringe driver

**IMPORTANT** : This covers timing only. Check appropriate sections for dose conversions.

- **Changing from twice daily MR morphine (e.g. MST) to the syringe driver.**  
The syringe driver can be started when the next MST dose is due.  
However, individual subcutaneous doses may be needed for pain control.
- **Changing from once daily MR morphine (e.g. MXL) to the syringe driver.**  
MXL lasts for 24 hours, so diamorphine will not be needed in the syringe driver until the patient cannot swallow the next MXL dose when due.
- If the MXL dose has been taken but the syringe driver is needed for other symptoms, omit the diamorphine from the first syringe. When the next MXL dose is due, change the syringe and include the diamorphine with the other drugs.
- **Changing from a syringe driver to once daily MR morphine (e.g. MXL).**  
Ideally, start MXL at least four hours before the syringe driver is discontinued. If the driver is taken down earlier, monitor the patient's need for breakthrough analgesia.
- **Changing from a Fentanyl patch to a syringe driver.**  
See information in Chapter 3 Pain, page 17.

### OTHER ANALGESICS

Ketorolac (non-steroidal anti-inflammatory drug); Clonazepam, Ketamine and Methadone (for neuropathic pain) should only be used under Specialist Palliative Care advice or in a Specialist Palliative Care unit.

**NAUSEA AND VOMITING** - see Chapter 6.

**FOR USE OF SYRINGE DRIVERS IN THE TERMINAL PHASE** - see Chapter 23.

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## 23. THE TERMINAL STAGE

**The terminal stage is when death is imminent, within hours or days.**

**Common terminal symptoms include:**

- Noisy breathing
- Pain (may be several simultaneously)
- Restlessness and agitation
- Urinary incontinence/retention
- Breathlessness
- Dry/sore mouth
- Sweating
- Nausea and vomiting
- Jerking, twitching, plucking
- Confusion
- Extreme fatigue

During this stage, symptom control alone forms only part of the care necessary for dying people and their carers. Advance planning for medications is critical, because medicines are the mainstay of therapy. Frequent symptom review is essential; if the situation is unstable, at least every 4 hours. There is no evidence that the appropriate use of opioids for symptom control in this setting shortens life.

**Remember the potentially reversible causes of distress:**

- Constipation
- Urine retention
- Infection
- Hypercalcaemia
- Gastric dilatation
- Fear

**The three important steps in medication planning are:**

1. Rationalising regular medication
2. Anticipating the drug administration route
3. Ensuring availability of parenteral medicines

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## RATIONALISING REGULAR MEDICATION

Only medicines which will control or prevent distressing symptoms should be prescribed regularly at this time. It will require considerable skill, tact and sensitivity when explaining this to relatives.

Many medications previously regarded as essential need to be reviewed and some may need to be discontinued.

Prescribe medication for new symptoms, which may arise. Write a treatment plan for any breakthrough of symptoms.

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## ROUTE OF ADMINISTRATION

Oral administration, even liquids, may become more difficult to administer. Consider alternative routes e.g. subcutaneous, iv, rectal.

If subcutaneous infusion is a likely option, discuss this with carers. If this is overlooked, families may blame the syringe driver for rapid deterioration. Explain that using the syringe driver is just switching to an alternative route of administration when a patient cannot swallow and is not a way of escalating the dose.

Not all dying patients need a syringe driver. If a patient is deteriorating rapidly and is within one or two hours of death, intermittent injections may be sufficient.

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## AVAILABILITY OF PARENTERAL MEDICINES

It is necessary to anticipate the possible use of a small number of drugs which are commonly used in the terminal phase. Drugs commonly used in this setting include Diamorphine, Morphine, Oxynorm, Cyclizine, Haloperidol, Levomepromazine, Midazolam, Hyoscine hydrobromide and Hyoscine butylbromide (Buscopan) and Glycopyrronium.. Specific details are given in the relevant symptom section and/or syringe driver section of this booklet.

In the home, make sure these are prescribed and obtained in good time, to avoid difficulties out-of-hours or at weekends. In case of unforeseen symptoms, find out what arrangements are in place locally before you need to use them.

The medication must be prescribed on an appropriate administration sheet so that the district nurses or ward staff can administer these drugs appropriately. With adequate training and discussion amongst team members, it is usually possible for doctors to write appropriate dose ranges for particular drugs to allow for changing circumstances.

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## IMPORTANT POINTS TO CONSIDER AT THE END OF LIFE

### STEROIDS

Continue with steroids if they are considered essential for symptom control. Otherwise reduce and discontinue. Steroids should be given in a separate syringe driver or as a single daily s/c dose. (The oral dose of Dexamethasone is the same as by injection).

### ANITCONVULSANTS

If no longer able to take oral anticonvulsants consider Midazolam 10mg via syringe driver over 24 hours (increasing if necessary to a maximum of 60mg). Make available prn benzodiazepines for ictal activity (e.g. Midazolam 5mg s/c) or Diazemuls 5-10mg prn.

### BOWEL OBSTRUCTION

Total cessation of nausea/vomiting may be impossible in complete obstruction. Consider Hyoscine butylbromide (Buscopan) 60-120mg in 24 hours via syringe driver to maximise antispasmodic and antisecretory actions. Make available Hyoscine butylbromide 20mg s/c 6 hourly prn stat doses.

If you require further advice regarding any of the above or if symptoms persist contact the Palliative Care Service for advice

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## GUIDANCE ON USE OF FENTANYL PATCHES AT THE END OF LIFE

The options listed below provide general guidance only.

The patient should always have a pain assessment.

If in doubt regarding pain management then seek advice from Specialist Palliative Care.

It is usual practice to leave the Fentanyl patch in place.

To calculate the breakthrough dose of Diamorphine/Morphine s/c prn for a Fentanyl patch see the opioid conversion table or the manufacturers guidance.

If the patient develops unstable pain Diamorphine/Morphine s/c stats may be used in addition to the patch.

If more than two breakthrough doses of s/c Diamorphine/Morphine are required in 24 hours Diamorphine/Morphine can be put in the driver. The total number of breakthrough doses of s/c Diamorphine/Morphine needed in a 24 hours period is placed in a syringe driver and run alongside the Fentanyl patch.

If the syringe driver containing Diamorphine/Morphine is started continue to make available prn Diamorphine/Morphine.

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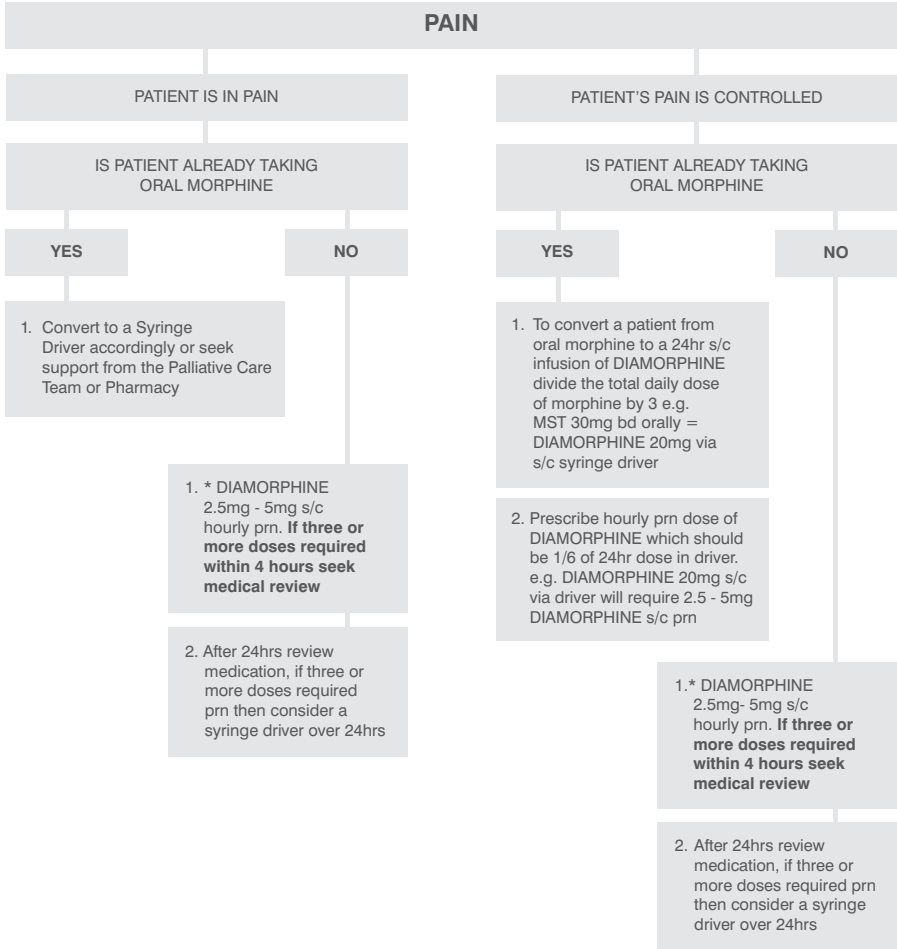
## TERMINAL RESTLESSNESS AND AGITATION

This involves restlessness, anguish, agitated delirium, myoclonic jerks, confusion, crying out or moaning, in the last hours or days of life. Urgent management is essential for the sake of the patient and carers. A calm environment is important.

Restlessness and agitation can be mistaken for pain, leading to inappropriately escalating doses of strong opioids. This may lead to further agitation and confusion in the dying person. Opioid-induced myoclonic jerks may be mistaken for "jumping with pain". Consider dose reduction or an alternative opioid. Explanation to the relatives is very important. Other drug causes of restlessness include Hyoscine, drugs with antimuscarinic properties and corticosteroids, even if previously tolerated; nicotine withdrawal (consider nicotine patch); alcohol withdrawal.

Exclude potentially reversible causes of distress such as pain, urine retention, constipation, gastric stasis, fear.

## PAIN CONTROL AT THE END OF LIFE

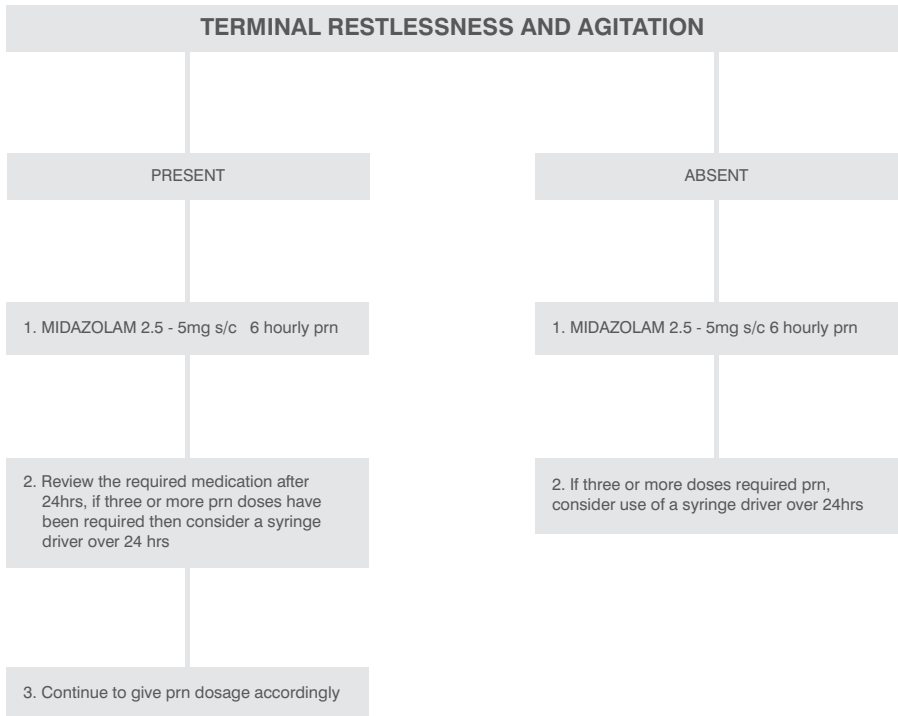


### Supportive information

- \* Morphine 5 – 10mg s/c hourly prn may be utilized as an alternative.
- To convert other strong opioids (e.g. Oxycodone or Fentanyl) to subcutaneous route contact Palliative Care Team/ Pharmacy for further advice & support on conversion ratios. Also see Palliative Care Guidance on opioid dose conversion and Fentanyl prescribing notes, pages 20 and 63.
- If symptoms persist contact the Palliative Care Team.
- Anticipatory prescribing in this manner will ensure that in the last hours/days of life there is no delay responding to a symptom if it occurs.
- **If patient has impaired renal function consider reducing doses or alternative opioid.**



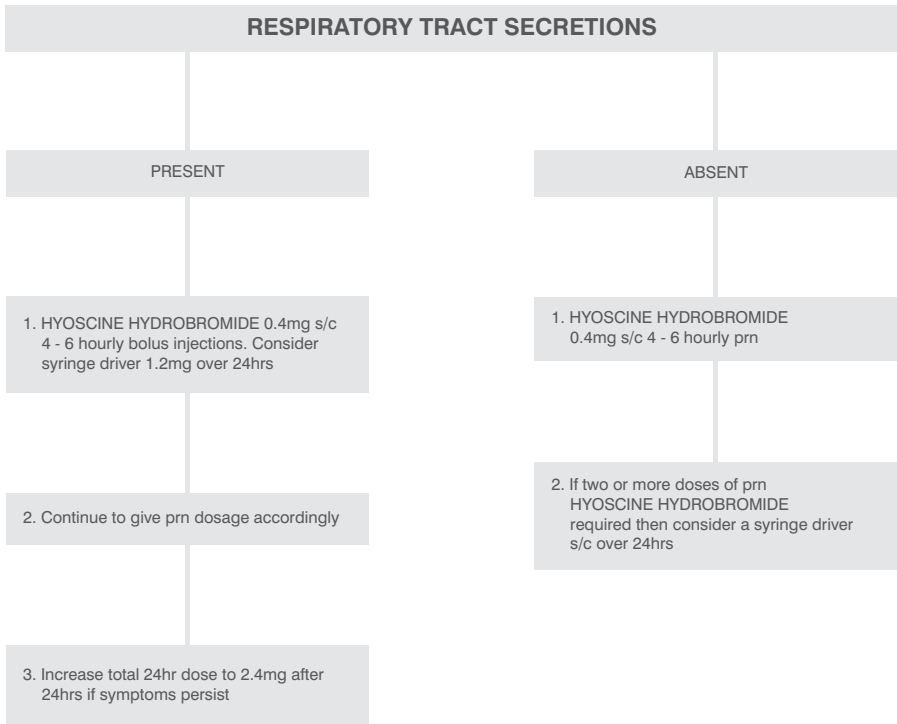
## TERMINAL RESTLESSNESS AND AGITATION



### Supportive information:

- Exclude reversible causes e.g. urinary retention, constipation, pain.
- If symptoms persist contact the Palliative Care Team
- Anticipatory prescribing in this manner will ensure that in the last hours / days of life there is no delay responding to a symptom if it occurs.

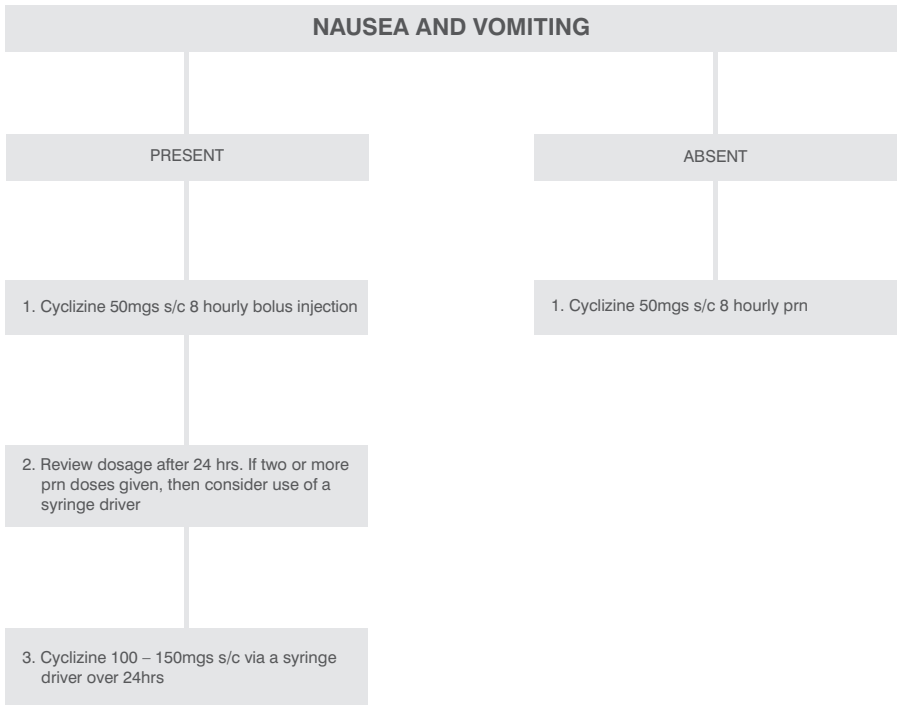
## RESPIRATORY TRACT SECRETIONS AT THE END OF LIFE



### Supportive information:

- Consider turning patient.
- If symptoms persist contact the Palliative Care Team
- Anticipatory prescribing in this manner will ensure that in the last hours / days of life there is no delay responding to a symptom if it occurs.
- NB Glycopyrronium is the preferred antisecretory in some units (notably teams in Lancaster and Blackpool). A stat dose prn of 200micrograms 4-6 hrly with a syringe driver dose of 600-1000 micrograms is recommended.

## NAUSEA AND VOMITING AT THE END OF LIFE



### Supportive information:

- N.B Always use water for injection when making up Cyclizine.
- If symptoms persist contact the palliative Care Team.
- Cyclizine is not recommended in patients with heart failure.
- Alternative antiemetics according to local policy & procedure may be prescribed

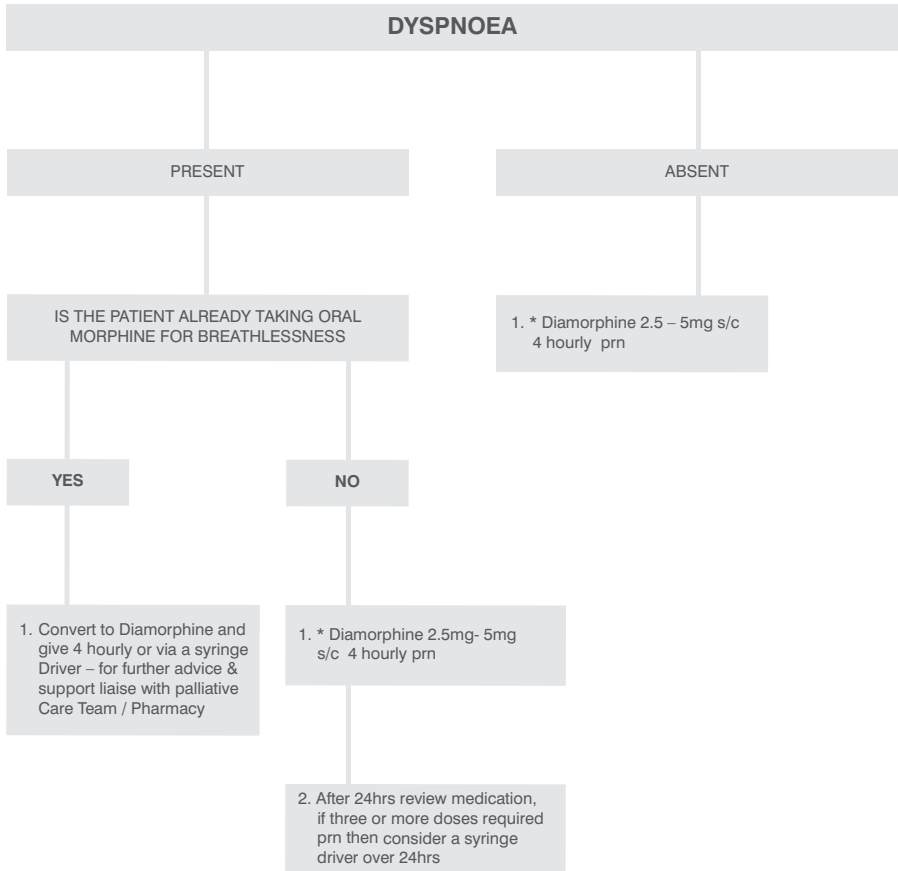
**e.g.**

**Haloperidol s/c 2.5mg - 5mg 8 hourly prn (up to 5mg via a Syringe Driver over 24hrs)**

**Levomopromazine s/c 2.5mg - 5mgs 8 hourly prn (up to 12.5mg via Syringe Driver over 24hrs)**

- Anticipatory prescribing in this manner will ensure that in the last hours /days of life there is no delay responding to a symptom if it occurs.

## DYSPNOEA AT THE END OF LIFE



### Supportive information:

- \* Morphine 5 – 10mg s/c 4 hourly prn may be utilized as an alternative.
- If the patient is breathless and anxious consider Midazolam 2.5mg s/c 4 hourly prn. This can also be added to the syringe driver.
- If symptoms persist contact the Palliative Care Team.
- Anticipatory prescribing in this manner will ensure that in the last hours / days of life there is no delay responding to a symptom if it occurs.
- These guidelines are produced according to local policy & procedure and you may want to alter them for local use and reference accordingly.

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## 24. REFERENCES AND RESOURCES

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### GENERAL

British National Formulary: Guidance on prescribing: Prescribing in Palliative Care.

Changing Gear – Guidelines for managing the last days of life in Adults 1997.

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### WEB SITES

BACUP. [www.cancerbacup.org.uk](http://www.cancerbacup.org.uk)

Palliativedrugs.com, Dr Robert Twycross, Dr Andrew Wilcock.  
[www.palliativedrugs.com](http://www.palliativedrugs.com)

Palliative Medicine Matters, Dr Ian Back. [www.pallcare.info](http://www.pallcare.info)

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## INFORMATION SOURCES AND SPECIALIST ADVICE

Specialist Palliative Care advice may be sought from a number of hospital Palliative Care Teams, hospices and community Clinical Nurse Specialists in Palliative Care, throughout the region. For children seek a specialist opinion.

### For details:

Barrow In Furness Macmillan Service	01229 615625
East Lancashire Hospitals NHS Trust	01254 732316
East Lancashire Hospice, Blackburn	01254 342810
Furness General Hospital	01229 491362
Hospice of St Mary of Furness	01229 583072
Lancashire Teaching Hospitals NHS Foundation Trust	
Preston site	01772 522055
Chorley site	01257 245356
Macmillan service, Kendal	01539 738650
Pendleside Hospice, Burnley and Pendle	01282 440100
Rosendale Hospice, Rosendale	01706 240084
Royal Lancaster Infirmary	01524 583703
St Catherine's Hospice, Preston	01772 629171
St. John's Hospice, Lancaster	01524 382538
Trinity Hospice & Palliative Care Services, Blackpool	01253 359379

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## NOTES



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