SYMPTOM CONTROL IN THE LAST DAYS OF LIFE

Guidelines for Healthcare Professionals Bradford, Airedale, Wharfedale & Craven

Signs and symptoms that suggest someone may be entering the last days of life:
(NB for patients with an underlying progressive condition the background of a gradual deterioration over weeks/months is important)

- Sleepiness, difficulty waking, generalised weakness (conscious level may be reduced or patient may become unconscious)
- Difficulty swallowing (including medication), reduced interest in eating and drinking
- Loss of control of bladder and bowel function
- Restless movements (as though in pain)
- Changes in breathing pattern
- Noisy breathing
- Cold feet, hands, legs and arms
- Confusion and disorientation

It is important to identify any *potentially reversible causes* for the patient's deterioration (the decision about how appropriate it will be to investigate and/or treat these should be discussed with the patient/family and the MDT)

Potentially reversible causes to consider includes:

- Dehydration
- Infection
- Opioid toxicity
- Steroid withdrawal
- Adverse effect of other drugs
- Acute kidney Injury (AKI)
- Delirium
- Hypercalcaemia
- Constipation
- Hypo or hyperglycaemia

Fundamental to the practice of palliative care is an emphasis on individualised care for the patient. If symptoms fail to respond to usual measures, or if you are concerned that the recommendations given here may not be appropriate to the clinical situation, please contact your local Specialist Palliative Care Team (SPCT).

SPCT advice can be sought from:

Working hours (Mon-Fri 8am-5pm):

- BTHFT Inpatients: Hospital Palliative Care Team 01274 364035 or #6479 / #6435 / #6571
- ANHSFT Inpatients: Hospital Palliative Care Team 01535 292184 or bleep 3148 / 3242
- Bradford Community (inc Community Hospitals /Care Homes): Community Palliative Care Team 01274 323511
- Airedale, Craven and Wharfedale Community (inc care homes): Community Palliative Care Team 01535 642308

Out of Hours:

Contact On-call Consultant in Palliative Medicine via Marie Curie Hospice (01274 337000) or Manorlands Hospice (01535 642308)
On Call CNS (7 day Airedale, Wharfedale and Craven ONLY) 01535 292184 or bleep 3148

Key Prescribing Points

This guidance is about managing symptoms in the last days of life when it is clear that the patient is dying. The following should be considered when prescribing for dying patients:

1. ANTICIPATORY OR 'AHEAD OF TIME' PRN MEDICATION

All patients should have 'as required' (PRN) medication for symptom control prescribed, which includes: medication for the relief of pain, nausea/vomiting, restlessness, shortness of breath and respiratory tract secretions before they occur, unless there are contraindications. This means that symptoms can be controlled without delay even if they arise overnight.

Where a dose range has been prescribed, start with the lowest dose and assess benefit. If patients require more than 2 doses in 6 hours, staff should seek medical advice.

Examples of appropriate medication for anticipatory 'as required' prescribing:

- Opioid analgesic subcutaneous (SC), hourly as required; dose depends on the patient, clinical problem and previous opioid use.
  - 1/6th of 24 hour dose of any regular opioid.
  - If not on a regular opioid, prescribe morphine sulphate SC 2.5mg to 5mg hourly.
- Anxiolytic sedative: midazolam SC 2.5mg to 5mg, hourly.
- Anti-secretory medication: hyoscine butylbromide (Buscopan) SC 20mg, hourly.
- Anti-emetic: haloperidol 1.5mg SC, 12 hourly.

2. ONCE THE ORAL ROUTE IS LOST. Think About:

Is the medicine still needed?

- Consider if medication is still needed for comorbidities (see page 6)
- Non-opioid analgesia e.g. paracetamol, antidepressants, anti-epileptics can usually be stopped when oral route is lost: continuing opioids is usually sufficient.
- Anticonvulsants for seizures should be continued via an alternative route (see page 6).

Is there an alternative route?

- Most opiates will have an alternative SC route

Is a syringe pump required to administer necessary medications subcutaneously?

- A syringe pump is used not only to replace existing medication (e.g. regular MST Continus) but is titrated where necessary to take account of additional (PRN) medication

3. PROBLEMS TO CONSIDER

- Managing uncontrolled symptoms – see page 3 onwards
- Managing acute and distressing terminal events – see page 6

4. REVIEW AND ASSESS BENEFIT OF ANY INTERVENTIONS

PAIN

Opioid analgesics must NOT be used to sedate dying patients
Sudden increase in pain: exclude urinary retention, constipation or other reversible cause.

• Paracetamol or Non-Steroidal Anti-Inflammatory Drugs (NSAID) (as liquid/dispersible). NSAID benefits may outweigh risks in a dying patient; can help bone, joint, pressure sore, inflammatory pain. If unable to manage via oral route and still requires NSAID, seek specialist palliative care advice

If not on any regular opioid, prescribe PRN morphine SC 2.5mg – 5mg as per anticipatory guidance

If unable to manage oral medication, or requiring more than 2 doses PRN over 24 hours, convert the total 24 hour oral morphine to a 24 hour, SC infusion: Divide the TOTAL daily dose of oral morphine by 2.
e.g. oral morphine 30mg = SC morphine 15mg /24hrs
If already on oral oxycodone use SC oxycodone. Divide TOTAL daily dose of oral oxycodone by 2
e.g. oral oxycodone 15mg = SC oxycodone 7.5mg /24hrs

Breakthrough (PRN) analgesia should be prescribed hourly as required:

• 1/6th of total 24 hour dose of any regular opioid, both orally and subcutaneous equivalent dose

Total daily dose of oral morphine	Equivalent total daily dose of sc morphine	PRN oral morphine dose	PRN sc morphine dose
60mg	30mg	10mg	5mg

If patient is already using FENTANYL or BUPRENORPHINE transdermal patches, these should be continued in dying patients. If they have been requiring additional PRN opioid on a regular basis, with benefit, this can be added to a syringe pump. Ensure that both patch and pump dose are taken into account when calculating appropriate breakthrough dose.

For patients with **stage 4-5 chronic kidney disease**, **severe liver failure** or **elderly**:

- Use opioids cautiously.
- Smaller doses will be required
- Length of action will be increased (e.g. by 12 hours or more)
- Continuous infusions are seldom required
- Opioids other than morphine may be better tolerated. Seek specialist advice

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

AGITATION / DELIRIUM

Sudden increases in agitation; exclude urinary retention, constipation or other reversible cause
Consider a nicotine replacement patch in heavy smokers who may have withdrawal symptoms.

NB: If requiring more than 2 doses of PRN medication in 24 hours, consider starting a 24 hour SC infusion via syringe pump.

Anxiety / distress	midazolam SC 2.5mg to 5mg, PRN hourly	
Confusion / delirium	haloperidol SC 0.5mg to 1.5mg, once or twice daily PRN *(caution in elderly, give reduced dose)*	
Prolonged terminal delirium/ distress with no reversible causes	1st line midazolam SC 10mg to 30mg *(depending on previous 24hr requirements)* **and/or** Haloperidol 3mg to 5mg over 24 hours in a syringe pump + midazolam SC 5mg PRN hourly, as required	2nd line **Seek Specialist Palliative Care Advice**

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

NAUSEA and /or VOMITING (last days of life)

	SC INJECTION	24HR SYRINGE PUMP	PRN
If already controlled with an oral antiemetic		Use the same drug in a SC infusion (e.g. metoclopramide, cyclizine, haloperidol). NB: domperidone should be switched to metoclopramide parenteral	SC Levomepromazine 2.5mg to 6.25mg 6 hourly (max 25mg/24hr)
New nausea & vomiting 1st line	haloperidol SC 1.5mg up to 12 hourly, or 1.5mg to 3mg once daily *(caution in elderly)*	If requiring regular dose: commence Haloperidol 1.5mg to 3mg SC in syringe pump (max 5mg/24hr)	SC Levomepromazine 2.5mg to 6.25mg 6 hourly (max 25mg/24hr)
2nd line	Levomepromazine SC 2.5mg to 6.25mg once daily.	Stop haloperidol (or other antiemetic) and prescribe Levomepromazine 6.25mg to 12.5mg SC in syringe pump	SC Levomepromazine 2.5mg to 6.25mg 6 hourly (max 12.5mg PRN /24hr) **Seek SPCT advice**

- Avoid cyclizine in severe heart failure
- Avoid haloperidol and metoclopramide in Parkinson's Disease
- Persistent vomiting due to bowel obstruction: an NG tube, if tolerated, may be better than medication, but this would require inpatient admission.

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

MOUTH CARE IN THE LAST DAYS OF LIFE

Dry mouth and thirst are common symptoms in people who are dying. Good mouth care can help prevent thirst and maintain comfort.

Patients should continue to be offered oral fluids. They may be able to manage sips even in the last days of life. Where patients can no longer manage oral fluids, staff must provide regular mouth care.

Treatment

Mouth care should be offered hourly, especially for patients who are unable to take oral fluids. Where possible family/carers can perform mouth care, giving them greater involvement.

Clean mouth using water and a sponge stick (depending on local policy) or a soft toothbrush.
Pineapple juice can be used to cleanse.

Avoid lemon and glycerin swabs as they can increase dryness.

Oxygen therapy may aggravate dry mouth. Consider whether this is still required, or whether it could be administered via nasal cannulae rather than a face mask. Consider humidification if on > 4L/28% via face mask.

	LIPS DRY /CRACKED	DRY MOUTH	SORE MOUTH
1st Line	Petroleum jelly (NB if patient on oxygen use water based lubricant e.g. aquagel)	Biotene Oralbalance gel	Gelclair apply directly, undiluted.
2nd Line		Glandosane spray	Seek specialist palliative care advice.

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

BREATHLESSNESS

A table or handheld fan should be tried, and a more upright position can help.
Explanation / reassurance and promoting a calm environment is important
Consider relaxation techniques (if appropriate)

Oxygen may relieve distress even if the patient is not hypoxic. Try 2-4 l/min via nasal cannula unless contraindicated.

If there are signs of Pulmonary Oedema, consider need for diuretics (e.g. Furosemide 40mg SC / IV) or seek advice from SPCT

Intermittent Breathlessness and /or distress	Midazolam SC 2.5mg to 5mg hourly, PRN as required **or** Lorazepam sublingual 500mcg to 1mg, 4-6 hourly, PRN as required. Opioid (hourly as required) • if on regular opioid → use the appropriate breakthrough dose for pain or breathlessness (1/6th of the total 24 hour dose) • if no opioid → try morphine PO 2.5mg to 5mg PRN or morphine SC 2.5mg (see opioid conversion guidance page 3)
Persistent distressing breathlessness	If on regular oral opioid or benzodiazepine, convert to a 24hour SC syringe pump (seek SPCT advice if unsure) If has required 2 or more doses in previous 24 hours, consider prescribing syringe pump over 24 hours e.g. Midazolam SC 5mg to 20mg (dependent on individual need) + morphine SC 5mg to 10mg (if no previous opioid use)

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

RESPIRATORY TRACT SECRETIONS

Terminal secretions can be controlled in about 60% of cases; fluid overload, recent aspiration and respiratory infection increase the incidence. Reduce the risk by avoiding fluid overload; **if symptoms develop** review any artificial hydration / nutrition (IV/SC fluids, feeding). Any changes to artificial hydration /feeding should be carefully discussed with family, explaining clearly the rationale for treatment withdrawal.

Explain cause of problem to family /carers and any changes to management

- Changing the patient's position may help.
- Oropharyngeal suction is rarely beneficial

	PRN	**24 hr Syringe Pump**
1st line:	Hyoscine butylbromide (Buscopan) SC 20mg, PRN hourly as required (max. dose 120mg/24 hrs).	If PRN beneficial, consider Hyoscine Bultylbromide 60mg via syringe pump (max dose 120mg /24 hrs)
2nd line	Glycopyrronium bromide SC 200micrograms, PRN hourly as required (max. dose 1.2mg/24 hrs)	Seek specialist palliative care advice

If symptoms are still troublesome consider if there are signs of pulmonary oedema and need for diuretics e.g. Furosemide 20 - 40mg SC / IV. (Note: max 20mg/2ml as SC injection)

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

ACUTE & DISTRESSING TERMINAL EVENTS

Dying patients occasionally develop acute distress; this can be due to:

- Bleeding: catastrophic haemorrhage from the GI or respiratory tract, or an external tumour
- ACUTE pain: bleeding into a solid tumour, a fracture, or a ruptured organ.
- ACUTE respiratory distress, tracheal obstruction

Management

- Where it is possible to anticipate this could be an issue, agree an anticipatory care plan with the patient, if possible, family carers and key professionals
- For severe acute pain or respiratory distress give stat dose of breakthrough opiate sc. Please note that higher doses may be required. If symptoms do not respond, double the previous PRN dose and seek specialist palliative care advice promptly.
- For catastrophic haemorrhage prescribe sedation e.g. Midazolam 5mg to 10mg IM stat dose in advance if the patient is at risk; warn the family.

If symptoms persist and you are unsure what to do or are concerned about side effects: seek specialist palliative care advice

WHAT CAN BE STOPPED? MANAGING COMORBIDITIES IN LAST DAYS OF LIFE

DIABETES AND INSULIN

When a patient is dying imminently and focus of care is solely symptomatic decisions should be made regarding diabetes management given that oral intake is likely to be minimal. Discuss changing approach to diabetes management with patient and/or family, if not already explored. **Seek advice from Diabetic Specialists if unsure**

Type 1 diabetes	• Insulin should be continued in these patients • Simplify insulin regime – ideally once daily long-acting insulin e.g. Lantus or Humulin I at a reduced equivalent dose. • Check capillary blood glucose (CBG) once a day prior to giving insulin • Aim to run CBG 8-15mmols. (Priority is to prevent hypoglycaemia) 1. If below 8mmols/l reduce insulin by 10-20% 2. If above 20mmols/l increase insulin by 10-20% to reduce risk of symptoms or ketoacidosis
Type 2 diabetes	• Aim to stop capillary blood glucose monitoring and stop/reduce diabetic medication • If unresolved symptoms that may be attributable to hyperglycaemia consider urinalysis, if glucose 2+ check CBG and seek advice from SPCT or Diabetic Specialists

EPILEPSY AND ANTI-SEIZURE MEDICATION

At the end of life, once the patient can no longer take oral medication required to prevent seizures, their seizures should be prevented with subcutaneous midazolam:

- Prescribe **midazolam** 20mg to 30mg over 24 hours via SC syringe pump (the diluent is water) *and* **midazolam** 5mg to 10mg PRN SC
- An alternative for patients on oral Levetiracetam is to convert to a SC infusion i.e. 1:1 ratio, seek advice from SPCT
- If the SC route is not readily available for PRN use (e.g. the patient is in their own home), alternatives include:
  - **diazepam rectal (PR) enema** (0.5mg/Kg up to a maximum dose of 30mg PRN)
  - **buccal midazolam†** (BuccolamTM) 10mg PRN sublingually
- Increase the syringe pump dose if PRN doses are needed and effective
- If seizures persist despite midazolam 60mg/24hrs via SC syringe pump, seek advice from SPCT

CORTICOSTEROIDS	
Steroids *not contributing to symptom relief*	Stop at the end of life when the oral route is no longer available. If the dying process is already established, Addisonian withdrawal effects are not usually relevant.
Steroids *contributing to symptom relief* (i.e. symptoms likely to recur if stopped such as severe headaches or vomiting after cerebral bleed)	Convert to a subcutaneous (SC) bolus of dexamethasone each morning. Seek SPCT advice if unsure
CARDIOVASCULAR CONDITIONS	
Angina	Medication can usually be discontinued without substituting an alternative once the patient is unable to take orally. The minimal exertion at the end of life minimises the risk of angina occurring. If angina symptoms are suspected, or there is particular concern, consider symptomatic management with opioids and seek advice from SPCT
Hypertension	Antihypertensives should be discontinued in the last days of life and can often be stopped before then. Statins can be stopped if the prognosis is less than 1 year
Heart Failure	***Mild-moderate***: medication usually discontinued without substituting an alternative once the patient is unable to take orally because of the minimal fluid intake at this stage. ***Severe*** (e.g. the patient is dying from end-stage heart failure), then consider: • Subcutaneous furosemide. Usually given as a SC bolus OD or BD or via SC 24 hours syringe pump: Seek advice from SPCT • Opioids (See Breathlessness section page 6)
NEUROLOGICAL CONDITIONS	
Parkinsons Disease	Consider giving medication via an alternative route e.g. topical patch. Seek specialist palliative care advice.

Unlicensed Use of Licensed Medicines ("Off label" use)
Use of drugs in these guidelines and their routes of administration are outside their product licences ''Off Label'' The unlicensed use of medicines is necessary when clinical need cannot be met by the licensed medicines available. The recommendations in this guide do include unlicensed use of licensed medicines. These recommendations are based on current accepted palliative care practice in the UK. In practice, approximately 25% of prescribed medicines for palliative care patients are used in an unlicensed way (e.g. given by subcutaneous injection when licensed for IM or IV use, or for the treatment of nausea and vomiting when only licensed as an antipsychotic). Further information regarding unlicensed use of individual palliative care medicines can be found in the current version of the Palliative Care Formulary www.palliativedrugs.com