All Wales Guidance to Support Care in the Last Days of Life: Symptom Control Guidance

Commonly used PRN medicines and doses for end-of-life care

<table>
<thead>
<tr>
<th>Indication</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Morphine</td>
<td>*</td>
<td>2-4 hrly</td>
<td>SC</td>
</tr>
<tr>
<td>Diamorphine</td>
<td>*</td>
<td>2-4 hrly</td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td>Nausea / Vomiting</td>
<td>Cyclizine</td>
<td>50mg</td>
<td>4hrly (max 150mg/24hr)</td>
<td>SC</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>1.25 - 1.5 mg</td>
<td>4hrly</td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>6.25 mg</td>
<td>4 hrly</td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td>Anxiety / Distress</td>
<td>Midazolam</td>
<td>2.5 or 5mg</td>
<td>2hrly</td>
<td>SC</td>
</tr>
<tr>
<td>Respiratory Secretions</td>
<td>Hyoscine hydrobromide</td>
<td>400 micrograms</td>
<td>4hrly (max 2.4mg / 24hr)</td>
<td>SC</td>
</tr>
<tr>
<td>Glycopyrronium</td>
<td>200 micrograms</td>
<td>4hrly (Max 1.2mg / 24hr)</td>
<td>SC</td>
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</table>

* Opioid prescriptions should be tailored according to the patient’s circumstances:
  For a patient on regular opioid analgesics: calculate one sixth of the 24-hour dose for PRN use. Some patients will be able to continue with oral morphine liquid.

If the oral route is no longer possible, use subcutaneous (SC) opioid analgesics. Morphine or diamorphine can be used. Note that although similar starting doses are suggested, the two medicines are not interchangeable as they have different potency. (See conversion chart below). The choice of medicine may depend on prescriber preference or availability from the local pharmacy.  
**Check whether a prescription is also needed for ‘Water for injection’ for SC medications.**

If a patient is opioid-naïve: 
**Prescribe starting dose of morphine or diamorphine 2.5mg or 5mg SC PRN 2-4 hrly.** Assess effect over next 24 hours. Consider starting a syringe driver once opioid needs known. You do not need to start a syringe driver with morphine or diamorphine unless your patient has previously taken regular opioids.

To change from regular oral to SC medication
SC morphine is half the amount of oral morphine. SC diamorphine is one third the amount of oral morphine.
- First, calculate the total dose of oral morphine (regular and PRN doses) used in previous 24 hr.
- Then, convert to SC equivalent / 24 hours (eg 30mg oral morphine = 15mg SC morphine or 10mg diamorphine in 24 hours).
- Prescribe this 24 hour SC dose to start a syringe driver (CSCI)

To calculate appropriate PRN dose: Divide the 24 hr syringe driver dose by 6.
eg: 15mg SC morphine in syringe driver over 24 hrs ÷ 6 = 2.5mg SC PRN morphine. You may need to ‘round’ up or down the PRN dose (eg 10mg SC diamorphine /24 hr ÷ 6 = 1.67, so prescribe 2.5mg SC PRN). Always use caution when switching from one opioid to another. It can be helpful to check dose conversions with colleagues.
For patients on regular Oxycodone, use the same principles to calculate the total daily dose of oral oxycodone, then convert to the appropriate SC dose equivalent to start a syringe driver. Calculate the PRN dose in exactly the same way as for morphine or diamorphine: Use half to two thirds the amount of oral oxycodone for SC oxycodone. If you do not have access to oxycodone injection, use diamorphine instead. Contact your palliative care team for advice if needed.

**Approximate opioid equivalent doses over 24hr**

![Diagram showing opioid equivalence]

CSCI = continuous subcutaneous infusion over 24 hours

**Fentanyl / Buprenorphine patches and Syringe Drivers**

Fentanyl or buprenorphine transdermal patches can continue to be used in the last few days of life.

*If patient’s pain is under control:*
Continue current medication i.e. fentanyl or buprenorphine patch, refreshing the patch at the prescribed frequency as previously. Prescribe diamorphine SC PRN for breakthrough pain.

*If patient requires additional pain control:*
Do not alter the dose of the patch, as there will be a delay before the changes are clinically apparent. Instead, continue the same strength patch and start a syringe driver with diamorphine.

NB. **Always leave the patch in situ when commencing a syringe driver.**
- Continue patch at its current dose, and add diamorphine CSCI via syringe driver.
- Calculate syringe driver dose based on the previous 24 hr PRN requirements:
  - e.g. 2 doses of oral morphine 30mg given in the last 24 hr = 60mg oral morphine / 24 hr
  - = 20mg diamorphine / 24 hr CSCI via syringe driver.

**Calculating breakthrough doses for patients with Fentanyl patches and syringe drivers:**
- The PRN SC diamorphine dose should be 1/6th of the total daily (24 hr) opioid used.
- Note the approximate daily oral morphine equivalence of patch and convert this to diamorphine.
- Add calculated diamorphine patch equivalence to diamorphine used in syringe driver for total daily opioid dose.
- Divide the total daily opioid dose by 6 for appropriate diamorphine SC PRN breakthrough dose.

*If in any doubt, contact the local Specialist Palliative Care Team for advice*
**Symptom Control Guidance**

### Approximate opioid equivalence – Morphine/Diamorphine and Fentanyl patches

<table>
<thead>
<tr>
<th>Oral morphine / SC diamorphine (24-hour daily dose)</th>
<th>Fentanyl patch (change every 72 hr)</th>
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<tbody>
<tr>
<td>Oral morphine 30 mg</td>
<td>Diamorphine SC 10mg</td>
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<tr>
<td>Oral morphine 60 mg</td>
<td>Diamorphine SC 20mg</td>
</tr>
<tr>
<td>Oral morphine 120 mg</td>
<td>Diamorphine SC 40mg</td>
</tr>
<tr>
<td>Oral morphine 180 mg</td>
<td>Diamorphine SC 60mg</td>
</tr>
<tr>
<td>Oral morphine 240 mg</td>
<td>Diamorphine SC 80mg</td>
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Further details available in BNF and LHB Formulary.

### Nausea and Vomiting

- **Prescribe PRN medication:** cyclizine 50mg SC bolus 4hrly to maximum 150mg/24hrs or haloperidol 1.25 or 1.5mg SC PRN 4 hrly to maximum 5mg / 24 hrs or levomepromazine 6.25mg SC PRN 4 hrly to maximum 25 mg / 24 hrs.

  If patient has congestive heart failure, use haloperidol or levomepromazine, rather than cyclizine.

- **If nauseous or vomiting:**
  - Prescribe syringe driver over 24hr with cyclizine 150mg, or haloperidol up to 5mg.
  - If problem persists:
    - Combine haloperidol up to 5mg with cyclizine 150mg via syringe driver over 24h or Replace above drugs with levomepromazine 12.5mg via syringe driver over 24 hr.
    - Contact Specialist Palliative Care Team
  - If bowel obstruction present: contact Specialist Palliative Care Team for advice.

### Restlessness, Agitation, Anxiety

- **Prescribe PRN midazolam 2.5 or 5mg SC 2 hrly**

  If patient is restless:
  - Add 10mg midazolam to syringe driver over 24 hr
  - Give midazolam up to 5mg SC 2 hourly PRN

  The dosage in the syringe driver can be increased if needed in 50% increments to a maximum of 30mg in 24 hours. If patient remains restless, review for reversible causes, contact Palliative Care Team.

### Noisy Breathing due to Respiratory Tract Secretions

- **Prescribe hyoscine hydrobromide 400 micrograms SC 4-hourly or glycopyrronium 200 micrograms SC PRN 4 hourly.**

  If symptoms present:
  - Give hyoscine hydrobromide 400 micrograms SC bolus
  - Add hyoscine hydrobromide 1.2mg SC to syringe driver over 24h.

  Alternative: Use glycopyrronium 200 micrograms SC bolus and glycopyrronium 600 micrograms SC to syringe driver/24hr.

  If symptoms persist:
  - Increase hyoscine to 2.4mg (in 24h) or glycopyrronium to 1.2mg (in 24 hours).
  - Contact Specialist Palliative Care Team for advice.
Renal Impairment / Renal Failure and End of Life Care

Many of the medicines used for symptom control in end of life care are eliminated by the kidney to a greater or lesser degree. Morphine and diamorphine (or their active metabolites) accumulate in even modest degrees of renal impairment; great care is needed to avoid toxicity.

**Renal Impairment:**
- Oxycodone is often used as an alternative to morphine/diamorphine in mild to moderate renal impairment.
- NSAIDs can worsen renal impairment.
- Most other drugs (used for symptom control in end of life care) can be used in renal impairment as long as the patient is regularly reviewed; consider starting with smaller doses and/or longer intervals between doses (e.g. 50% normal recommended dose).

**Renal Failure:**
Prescribing for end of life care in patients with end stage renal failure is complex and advice should usually be sought from the renal/palliative care specialists.
- Consider Oxycodone 1-2mg SC PRN 4 hrly for pain.
- Seek advice if starting syringe driver and/or pain remains a problem.

- If treatment needs to be started for excess respiratory secretions or ‘rattle’, glycopyrronium 200 micrograms stat SC is recommended.
  
  If glycopyrronium is not available, consider hyoscine hydrobromide 200-400 micrograms SC.

- For midazolam, haloperidol and levomepromazine, administer half of the usual dose subcutaneously stat.

- Repeat doses on a PRN basis, to allow for negligible elimination of the drug.

For more information:
- contact your local specialist palliative care team for advice:

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<th>In hours contact details:</th>
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<table>
<thead>
<tr>
<th>Out of Hours Specialist Palliative Medicine Telephone Advice Line:</th>
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<tbody>
<tr>
<td>North Wales: 01978 316800</td>
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<tr>
<td>South East Wales: 02920 426000</td>
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<tr>
<td>South West Wales: 01792 703412</td>
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<tr>
<td>Shropdoc (for Powys): 08444 068888</td>
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