# Guidelines for the Management of Common Symptoms in the Last Few Days of Life

**Objectives:**
- To help make the last days of life comfortable and dignified
- To give guidance on the effective and safe use of drugs
- To increase confidence and satisfaction in providing palliative care

## General Guidelines

Anticipate that the oral route will not be possible, if not immediately, then in the near future. This will ensure that there is no delay in responding to a symptom. Medication should be prescribed via the subcutaneous (SC) route.

Use water for injection (WFI) as a diluent.

Consider how symptoms can be improved without using drugs:
- **Are there any underlying causes that need to be managed?**
  *For example, urinary retention can cause agitation.*
- **Are drugs the best treatment?**
  *For example, would changing the patient’s position help noisy respiratory secretions?*

If problems persist or if you are unsure what to do contact the Specialist Palliative Care Team or LOROS advice line: 0116 231 8415

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## The Use of Medicines in Syringe Drivers

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
<th>SC Starting dose /24 hours</th>
<th>Ampoule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Pain</td>
<td>1/2 total daily dose of oral morphine or 10mg-20mg if not already taking opioids</td>
<td>10mg/1ml, 15mg/1ml, 20mg/1ml, 30mg/1ml, 60mg/2ml</td>
</tr>
<tr>
<td></td>
<td>Dyspnoea</td>
<td>5-10mg if not already taking opioids</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Pain</td>
<td>1/2 total daily dose of oral oxycodone</td>
<td>10mg/1ml, 50mg/1ml</td>
</tr>
</tbody>
</table>

| **Anti-emetic** | Levomepromazine | 2.5mg-5mg (up to 25mg) | 25mg/1ml |
|                 | Cyclizine        | 100mg-150mg             | 50mg/1ml |
|                 | Ondansetron      | 4mg (up to 16mg)        | 4mg/2ml, 8mg/4ml |

| **Metoclopramide** | Impaired gastric emptying | 30mg | 10mg/2ml |

| **Sedative** | Midazolam | Terminal restlessness, Myoclonic jerking, Anticonvulsant | 5mg-10mg (up to 60mg) | 10mg/2ml |
|              | Levomepromazine | Terminal agitation and delirium | 12.5mg-25mg (up to 50mg) | 25mg/1ml |

| **Anticholinergic** | Glycopyrronium | Terminal bronchial secretions | 600-1200 microgram | 200 microgram/1ml, 600 microgram/3ml |
|                    | Hyoscine Hydrobromide (also anti-emetic) | 600-2400 microgram | 600 microgram/1ml |
|                    | Hyoscine butylbromide | Severe colic, Intestinal obstruction | 60mg-180mg | 20mg/1ml |

**Essential points in using opioids for pain management**
- Morphine is the opioid of choice for injection
- To convert from oral morphine to subcutaneous morphine, divide the total 24 hr morphine dose by 2 to obtain the total 24hr morphine dose.
- Ensure adequate breakthrough (PRN) analgesia is prescribed = 1/6th daily dose morphine
- Increase dose if required by 30% increments

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*For further information please consult:*

- *A Guide to Prescribing for Patients with Advanced Malignancy, 2016*
- *Consultants in Palliative Medicine, University Hospitals of Leicester NHS Trust & The Leicestershire and Rutland Hospice*

*Version 4 September 2016*
**PAIN**

Is the patient in pain?

Is the patient prescribed regular oral morphine?

<table>
<thead>
<tr>
<th>Yes</th>
<th>Convert to continuous morphine SC infusion via syringe driver</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Increase the infusion dose as needed to control pain by 30%</td>
</tr>
</tbody>
</table>

Prescribe PRN morphine SC for breakthrough pain

= 1/6th 24hr dose morphine

NB: Increase the PRN dose inline with the SC infusion dose

Total daily dose oral morphine (mg) = mg morphine/24hr

\[ \text{Total daily dose oral morphine (mg)} = \frac{\text{mg morphine}}{24\text{hr}} \]

If on oral oxycodone and SC morphine not appropriate conversion to SC oxycodone/24hr is 1/2 total daily oral oxycodone dose

If Morphine unavailable use diamorphine 1/3 oral morphine dose

Consult a palliative care specialist if:

1. Pain persists
2. Conversion is needed from other opioids

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**Compatibility chart for two drugs in Water for Injections (WF1) over 24 hours for Palliative Care**

Multiple factors affect drug stability and compatibility. This table is intended as a practical guide and conflicting reports do exist. Regular monitoring for precipitation, site problems and efficacy is essential, even if coded green. For further information seek specialist advice/refer to www.palliativedrugs.com

<table>
<thead>
<tr>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopyrronium</td>
<td>N/D</td>
<td>G (green) Reported compatible in WFI at doses detailed in these guidelines (data may be observed, physical or chemical or widely used but without supporting data). NB Crystallisation may occur with increasing concentrations</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>G</td>
<td>A (amber) Use with caution (compatibility may depend on drug concentrations or the order of mixing - seek advice)</td>
</tr>
<tr>
<td>Hyoscine Butylbromide</td>
<td>A</td>
<td>N/A No Data</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>N/A</td>
<td>G N/D (specialists use occasionally) N/A N/A</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>N/A</td>
<td>G N/D (specialists use occasionally) N/A N/A</td>
</tr>
<tr>
<td>Midazolam</td>
<td>A</td>
<td>G (s) N/D <strong>Widely used in specialist units</strong></td>
</tr>
<tr>
<td>Morphine Sulphate</td>
<td>G</td>
<td>G *G (at lower concentrations) N/D <strong>Widely used in specialist units</strong></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>A</td>
<td>G N/D <strong>Widely used in specialist units</strong></td>
</tr>
<tr>
<td>Cyclizine Use WFI only</td>
<td>Glycopyrronium</td>
<td>Haloperidol</td>
</tr>
</tbody>
</table>

Diamorphine: 2 drug combinations hold true if diamorphine is substituted for morphine sulphate with the following provisios: maximum concentrations must not exceed Diamorphine 20mg/ml + Cyclizine 20mg/ml, nor Diamorphine 50mg + Haloperidol 4mg/ml.

*May be incompatible at concentrations above 20mg/ml morphine + 2mg/ml Haloperidol .

**May be incompatible at concentrations above 10mg/ml + Midazolam 5mg/ml.

SEEK SPECIALIST ADVICE FOR COMBINING MORE UNUSUAL DRUGS OR MORE THAN TWO DRUG COMBINATIONS

Also see: www.palliativedrugs.com
Respiratory Tract Secretions

- Noisy respiratory tract secretions can be a normal part of dying
- Consider whether they are troublesome or need treating at all
- Changing the positioning of the patient is the first step of management
- If the patient is unconscious reassure relatives and friends that the patient is unaware and not suffering
- This can be a difficult symptom to resolve and drugs may not be effective.

Prescribe in anticipation of the symptom being troublesome:
- Glycopyrronium 200 microgram by SC injection PRN up to 2 hrly

If Secretions Troublesome:
- Give glycopyrronium 200 microgram SC and PRN, up to 2 hrly
- If two or more doses of glycopyrronium have been given and are effective, consider a SC infusion of glycopyrronium 800 microgram/24 hr
- Review after 24 hrs
If symptoms persist, increase to a maximum of 1.2 mg/24 hr glycopyrronium

Alternative: Hyoscine hydrobromide (may cause sedation and confusion) 400 micrograms SC stat and PRN; maximum 2400 microgram/24 hr

Absence of troublesome secretions

Consider:
- Patient positioning
- Stopping I.V. or subcutaneous fluids or PEG feed
- In a small number of patients, suction may be helpful

Restlessness and Agitation

A human presence often helps to calm agitated patients

Prescribe in anticipation of the symptom developing:
- Midazolam 2.5 mg-5 mg by SC injection PRN

Where anguish and anxiety are predominant:
- Give midazolam 2.5 mg-5 mg stat and PRN SC (this may need to be repeated after 30 minutes)
- If two or more doses have been given in 24 hours, with effect, consider starting a SC infusion of 5 mg-10 mg/24 hr midazolam
- The SC infusion dose may need to be increased gradually to midazolam 30 mg/24 hr

Where delirium and psychotic features are predominant (e.g. hallucinations, confusion):
- Give levomepromazine 6.25 mg-12.5 mg stat and PRN by SC injection up to a maximum total daily dose of 50 mg.
- If two or more doses have been given in 24 hours, with effect, consider starting a SC infusion of 12.5 mg-25 mg/24 hr levomepromazine
- The SC infusion dose may need to be increased gradually to levomepromazine 50 mg/24 hr

Occasionally a combination of Midazolam and levomepromazine is required. Seek specialist advice if patient is not settled with midazolam 30 mg and levomepromazine 50 mg
Nausea and Vomiting

- Is patient already on an effective antiemetic?
  - Yes
    - Prescribe this if possible
      - As SC infusion/24hr
      - As PRN dosing
  - No
    - Is nausea or vomiting present?
      - Yes
        - Give levomepromazine 2.5mg-5mg by SC injection stat and PRN
        - Review after 24 hours. If two or more PRN doses of levomepromazine have been given, and are effective, consider levomepromazine 12.5mg/24hr SC infusion
        - This can be increased if required to 25mg/24hr SC infusion
        - Alternative antiemetic: Cyclizine 50mg SC PRN up TDS or 150mg/24hr SC infusion: Ondansetron 4mg SC PRN up to 16mg/24hr.
      - No
        - Prescribe in anticipation of the symptom developing:
          - Levomepromazine 2.5mg by SC injection PRN

BREATHLESSNESS

- Is amelioration of underlying cause appropriate?
  - Removal of pleural, ascitic and pericardial fluid
  - Treatment of chest infection
  - Treatment of heart failure
  - Treatment of pulmonary emboli

- Position patient:
  - Sit up in bed
  - Comfy, reclining armchair with foot stool

- Reduced Breathlessness
- Air flow across the face is helpful: use a fan or open a window
- Trial of oxygen if SaO2 <92%

- Calm and reassure the patient and carers by touch, talking and explaining
- Severe respiratory distress
  - For relief of anxiety consider lorazepam 0.5mg-1mg SL PRN midazolam 2.5mg SC stat and PRN midazolam 5mg-10mg/24hr SC infusion
  - For relief of breathlessness consider morphine 2.5mg SC stat and PRN morphine 5mg-10mg/24hr SC infusion

NB: Prescribe prophylactic antiemetic (e.g. levomepromazine 2.5mg-5mg/24hr) if opioid naïve patient.