Guidance for the Management of Symptoms in Adults in the Last Days of Life

This guidance provides recommendations to healthcare professionals on managing commonly experienced symptoms at the end of life.

Updated Jan 2018 Peter Armstrong & Dr Kiran Kaur on behalf of the Regional Palliative Medicine Group (RPMG)
The focus of this guidance is on administration by subcutaneous (SC) injection and SC syringe pump over 24 hours, recognising that the dying person may be unable to take or tolerate oral medicines. It includes the management of the following five symptoms:

**Pain**

**Breathlessness**

**Nausea and vomiting**

**Anxiety, delirium and agitation**

**Noisy respiratory secretions**

When it is recognised that a person may be entering the last days of life:

- Review their current medicines.
- Stop any prescribed medicines not providing symptomatic benefit or that may cause harm.
- Discuss and agree any medication changes with the dying person and those important to them (as appropriate).

Anticipatory prescribing by the subcutaneous route to cover the five symptoms above ensures a supply of medicines are available to relieve symptoms as soon as they occur.

- These recommendations are a GUIDE, and should be used as such. They may differ from other recommendations but have been chosen to reflect expert opinion, best evidence and safety.
- Users are advised to monitor patients carefully for side effects and response to treatment. Responsibility for the use of these recommendations lies with the healthcare professional(s) managing each patient.
- When prescribing, **always start with the lowest dose** in the range specified in this guide.
- Seek specialist advice in moderate to severe renal or hepatic impairment or those with complex needs.
- Consider the non-pharmacological management of symptoms at the end of life.

Further information is available from your Specialist Palliative Care Team, the Palliative Adult Network Guidelines (PANG) Book 2016 and at www.book.pallcare.info
Opioid Conversions Tables

• Refer also to HSC Guidance “Northern Ireland guidelines on converting doses of opioid analgesics for adult use 2018”.

Table 1. Opioid Conversions

| PO (Oral) to PO |  |
|----------------|  |
| Oral Morphine to Oral Oxycodone - Divide by 2 | Eg. 30mg Oral Morphine = 15mg Oral Oxycodone |
| Oral Codeine / Dihydrocodeine / Tramadol to Oral Morphine - Divide by 10 | Eg. 240mg Oral Codeine = 24mg Oral Morphine |

| PO (Oral) to SC (Subcutaneous) |  |
|-------------------------------|  |
| Oral Morphine to SC Morphine - Divide by 2 | Eg. 30mg Oral Morphine = 15mg SC Morphine |
| Oral Morphine to SC Diamorphine - Divide by 3 | Eg. 30mg Oral Morphine = 10mg SC Diamorphine |
| Oral Oxycodone to SC Oxycodone - Divide by 2 | Eg. 10mg Oral Oxycodone = 5mg SC Oxycodone |
| Oral Morphine to SC Alfentanil - Divide by 30 | Eg. 30mg Oral Morphine = 1mg SC Alfentanil |

Alfentanil may be used in patients with severe renal impairment; seek specialist advice when necessary

| SC (Subcutaneous) to SC |  |
|------------------------|  |
| SC Morphine to SC Diamorphine – Divide by 1.5 | Eg. 15mg SC Morphine = 10mg SC Diamorphine |
| SC Morphine to SC Oxycodone – Divide by 2 | Eg. 20mg SC Morphine = 10mg SC Oxycodone |

Note this may differ from other available conversions

Table 2. Transdermal Patch Conversions

| Fentanyl Patch eg. Mezolar®, Durogesic® Replace patch every 3 DAYS |  |
|---------------------------------------------------------------|  |
| Fentanyl Patch (micrograms/hr) | Oral Morphine Dose over 24 hours (mg) |
| 12 | 30-59 |
| 25 | 60-89 |
| 37 | 90-119 |
| 50 | 120-149 |
| 62 | 150-179 |
| 75 | 180-239 |
| 100 | 240-299 |
| 125 | 300-359 |
| 150 | 360-419 |
| 175 | 420-479 |
| 200 | 480-539 |

Buprenorphine Patch eg. Butec®, BuTrans® Replace patch every 7 DAYS

<table>
<thead>
<tr>
<th>Patch Strength (micrograms per hr)</th>
<th>Oral Morphine Dose over 24 hours (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>~10 - 12</td>
</tr>
<tr>
<td>10</td>
<td>~20 - 24</td>
</tr>
<tr>
<td>20</td>
<td>~40 - 48</td>
</tr>
</tbody>
</table>
**Pain**

Patient does not have pain or pain controlled by current prescription (patient unable to take oral analgesia)

<table>
<thead>
<tr>
<th>No analgesia prescribed or PRN analgesia.</th>
<th>Already on regular “weak” opioid (max dose) e.g. Co-codamol 30/500, Tramadol</th>
<th>Already on Oral Morphine Sulfate or other opioid (see Table 1)</th>
<th>Already on Fentanyl or Buprenorphine patch (See Table 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticipatory prescribing</strong></td>
<td><strong>Stop current oral analgesia.</strong> <strong>AND</strong> <strong>Prescribe Morphine Sulfate</strong> 10mg-15mg by SC syringe pump over 24 hours. <strong>AND</strong> <strong>Prescribe Morphine Sulfate</strong> 2mg SC 2-4hourly PRN for breakthrough pain*</td>
<td><strong>Use conversion Table 1 to change from total daily oral Morphine Sulfate to SC Morphine Sulfate or other opioid.</strong> <strong>Prescribe by SC syringe pump over 24 hours.</strong> <strong>AND</strong> <em><em>Prescribe breakthrough analgesia</em> i.e. divide total Morphine Sulfate or other opioid dose by 6 and give 2-4 hourly PRN</em>*</td>
<td><strong>Continue prescribing patch</strong> <strong>AND</strong> <em><em>Use conversion Table 2 and prescribe SC Morphine Sulfate for breakthrough pain</em> 2-4 hourly.</em>*</td>
</tr>
</tbody>
</table>

- **Morphine Sulfate** is the first line choice of strong opioid in non-specialist settings.

<table>
<thead>
<tr>
<th><strong>Recommended strengths and pack size to prescribe</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine Sulfate 10mg/ml injection</td>
</tr>
<tr>
<td>Morphine Sulfate 30mg/ml injection</td>
</tr>
</tbody>
</table>

* Breakthrough analgesia is usually worked out as 1/6th of the total 24 hour opioid dose, but can also be given as 1/10th of the total 24 hour opioid dose. Refer to BNF “Prescribing in Palliative Care” section.
# Pain

**Patient currently experiencing pain**
*(patient unable to take oral analgesia)*

<table>
<thead>
<tr>
<th>No regular analgesia prescribed</th>
<th>Already on Oral Morphine Sulfate or other opioid (See Table 1)</th>
<th>Already on Fentanyl Patch or Buprenorphine patch (See Table 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give stat SC PRN dose of <strong>Morphine Sulfate</strong> 2mg–5mg <strong>AND</strong></td>
<td>Use <strong>Table 1</strong> to change from total daily oral opioid dose to SC opioid. Prescribe by SC syringe pump over 24hrs. If on a long-acting twice daily oral opioid e.g. MST®, start the pump 8 hours after last dose. <strong>AND</strong></td>
<td>Give stat <strong>Morphine Sulfate</strong> SC PRN dose (use <strong>Table 2</strong>) <strong>AND</strong></td>
</tr>
<tr>
<td>Prescribe <strong>Morphine Sulfate</strong> 5mg – 10mg by SC syringe pump over 24 hours <strong>AND</strong></td>
<td>Prescribe for breakthrough pain* SC 2-4 hourly PRN i.e. divide new total daily SC opioid dose by 6. Give a stat dose. <strong>AND</strong></td>
<td>Continue prescribing patch <strong>AND</strong></td>
</tr>
<tr>
<td>Prescribe <strong>Morphine Sulfate</strong> 2mg – 5mg SC 2-4 hourly PRN for breakthrough pain* <strong>AND</strong></td>
<td>Review regularly</td>
<td>Add additional <strong>Morphine Sulfate</strong> (or other opioid) for uncontrolled pain by SC syringe pump over 24 hours (equivalent of 2 breakthrough doses* of <strong>Morphine Sulfate</strong>) <strong>AND</strong></td>
</tr>
<tr>
<td><em>(This can be given more frequently with medical discussion and/or palliative care input)</em></td>
<td>If two or more PRN doses are given in 24 hours increase syringe pump dose by 30% to 50% to control pain. Increase SC PRN dose accordingly.</td>
<td>Prescribe SC <strong>Morphine Sulfate</strong> for breakthrough pain* (1/6th of total 24 hour opioid dose) and give 2-4hourly PRN</td>
</tr>
</tbody>
</table>

* Breakthrough analgesia is usually worked out as 1/6th of the total 24 hour opioid dose, but can also be given as 1/10th of the total 24 hour opioid dose. Refer to BNF “Prescribing in Palliative Care” section.
Nausea and Vomiting

No Symptoms Present

Prescribed regular oral antiemetics?

No

Anticipatory prescribing

Prescribe Cyclizine SC PRN (see Table 3)

(i.e. symptoms controlled by current prescription)

Stop oral antiemetics. Prescribe current antiemetic by SC syringe pump over 24hrs.

AND

Suitable SC antiemetic PRN

Review every 24 hours

If nausea and vomiting not controlled go to ‘Symptomatic’ column

Yes

Symptomatic

Give stat dose of suitable SC antiemetic. (see Table 3)

AND

Start a SC syringe pump over 24hrs.

AND

Prescribe SC antiemetic for breakthrough symptoms

If nausea/vomiting persist, use maximum dose of current antiemetic

If nausea/vomiting persists, replace antiemetic drugs in syringe pump with Levomepromazine

(A combination of Cyclizine & Haloperidol may also be used)

AND

Prescribe Levomepromazine PRN SC for breakthrough nausea

No Symptoms Present

Symptomatic

Prescribed regular oral antiemetics?

No

Anticipatory prescribing

Prescribe Cyclizine SC PRN (see Table 3)

(i.e. symptoms controlled by current prescription)

Stop oral antiemetics. Prescribe current antiemetic by SC syringe pump over 24hrs.

AND

Suitable SC antiemetic PRN

Review every 24 hours

If nausea and vomiting not controlled go to ‘Symptomatic’ column

Yes

Symptomatic

Give stat dose of suitable SC antiemetic. (see Table 3)

AND

Start a SC syringe pump over 24hrs.

AND

Prescribe SC antiemetic for breakthrough symptoms

If nausea/vomiting persist, use maximum dose of current antiemetic

If nausea/vomiting persists, replace antiemetic drugs in syringe pump with Levomepromazine

(A combination of Cyclizine & Haloperidol may also be used)

AND

Prescribe Levomepromazine PRN SC for breakthrough nausea

No Symptoms Present

Symptomatic

Prescribed regular oral antiemetics?

No

Anticipatory prescribing

Prescribe Cyclizine SC PRN (see Table 3)

(i.e. symptoms controlled by current prescription)

Stop oral antiemetics. Prescribe current antiemetic by SC syringe pump over 24hrs.

AND

Suitable SC antiemetic PRN

Review every 24 hours

If nausea and vomiting not controlled go to ‘Symptomatic’ column

Yes

Symptomatic

Give stat dose of suitable SC antiemetic. (see Table 3)

AND

Start a SC syringe pump over 24hrs.

AND

Prescribe SC antiemetic for breakthrough symptoms

If nausea/vomiting persist, use maximum dose of current antiemetic

If nausea/vomiting persists, replace antiemetic drugs in syringe pump with Levomepromazine

(A combination of Cyclizine & Haloperidol may also be used)

AND

Prescribe Levomepromazine PRN SC for breakthrough nausea

If symptoms persist contact your Specialist Palliative Care Team
Table 3. Choice of Antiemetic

Lower doses are indicated in severe renal or hepatic impairment

<table>
<thead>
<tr>
<th>1st line</th>
<th>Drug</th>
<th>Indications for Use</th>
<th>SC stat PRN dose</th>
<th>SC 24 hour dose</th>
<th>Strength and Pack size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclizine</td>
<td>Non-specific nausea &amp; vomiting Mechanical bowel obstruction. Raised intracranial pressure</td>
<td>50mg every 8 hours PRN</td>
<td>100mg – 150mg</td>
<td>50mg injection Pack of 5</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Chemical/ Metabolic causes.</td>
<td>500 micrograms - 1mg every 6 - 8 hours PRN</td>
<td>1.5mg *</td>
<td>5mg/ml injection Pack of 10</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Partial mechanical bowel obstruction Gastric stasis (Prokinetic antiemetic - discontinue if colic develops).</td>
<td>10mg every 6 - 8 hours PRN (max TDS)</td>
<td>30mg *</td>
<td>10mg/2ml injection Pack of 10</td>
<td></td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Broad spectrum antiemetic Sedation at high doses</td>
<td>5mg every 4 - 6 hours PRN</td>
<td>5mg - 25mg</td>
<td>25mg/ml injection Pack of 10</td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>Intractable vomiting due to chemical, abdominal and cerebral causes when above approaches fail</td>
<td>4mg - 8mg every 6 - 8 hours PRN</td>
<td>8mg - 24mg</td>
<td>4mg or 8mg injection Pack of 5</td>
<td></td>
</tr>
</tbody>
</table>

*Higher doses may be used in specialist practice.*
Breathlessness

Intermittent symptoms

Taking regular Morphine Sulfate or other opioid?

No

Anticipatory prescribing

Prescribe Morphine Sulfate 1mg-2mg SC 4 hourly PRN for dyspnoea.

Yes

Anticipatory prescribing

Use the same SC opioid dose as for managing breakthrough pain.

Persistent symptoms

Taking regular Morphine Sulfate or other opioid?

No

Prescribe equivalent doses of the same opioid by SC syringe pump over 24hrs and titrate to patient’s individual needs according to severity of dyspnoea.

AND

Prescribe the same SC opioid dose as for managing breakthrough pain.

Yes

Prescribe Morphine Sulfate 5mg by SC syringe pump over 24 hours and 1mg-2mg SC 4 hourly PRN for dyspnoea.

For patients on other opioids use Table 1 for opioid conversions and use guidance as above.

For patients who are conscious and can tolerate oral medicines consider oral opioid in a dose equivalent to the SC doses recommended above.

Oxygen is only indicated for patients who are hypoxic.

If patient is breathless AND anxious, consider:

Midazolam 2mg SC PRN and/or Midazolam 5mg-10mg via SC syringe pump over 24 hours. If tolerating oral medicines consider Lorazepam tablets 500 micrograms sublingually 4-6 hourly PRN.

Recommended strengths and pack size to prescribe

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Strength/Package</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine Sulfate</td>
<td>10mg/ml Pack of 10</td>
</tr>
<tr>
<td>Midazolam</td>
<td>10mg/2ml Pack of 10. Preferred strength to use in palliative care to provide low volume SC injections</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1mg tablets Pack of 28. Annotate ‘Genus brand’ as this preparation dissolves more easily sublingually than other brands</td>
</tr>
</tbody>
</table>

If symptoms persist contact your Specialist Palliative Care Team
Anxiety, Delirium and Agitation

Assess the patient first to exclude potentially reversible and treatable causes such as pain, drug withdrawal including nicotine, urinary retention or severe constipation.

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**No Symptoms Present**

**Anticipatory Prescribing**

- Prescribe **Midazolam** 2mg – 5mg SC 2 - 4 hourly PRN
- If two or more PRN doses required in 24 hours

**Symptomatic**

- Prescribe **Midazolam** 2mg – 5mg SC and assess response after 30 minutes
  - If effective:-
    - Prescribe **Midazolam** 5mg - 10mg by SC syringe pump over 24hrs.
    - **AND**
      - Continue to give PRN dose as required
      - Re-assess regularly. If symptoms persist add total SC PRN dose over 24 hours to current syringe pump dose (increase breakthrough dose accordingly)
      - If poor response to increasing dose of Midazolam reassess cause of agitation.
      - Consider prescribing stat dose of:
        - **Levomepromazine** 5mg - 15mg SC
        - **Haloperidol** 500 micrograms – 1mg SC
      - Assess response and if effective add:
        - **Levomepromazine** 10mg-25mg
        - **Haloperidol** 1mg-3mg by SC syringe pump over 24 hrs.

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**Recommended strengths and pack size to prescribe**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Pack Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam 10mg/2ml injection</td>
<td>Pack of 10. Preferred strength to use in palliative care to provide low volume SC injections</td>
</tr>
<tr>
<td>Levomepromazine 25mg/ml injection</td>
<td>Pack of 10</td>
</tr>
<tr>
<td>Haloperidol 5mg/ml injection</td>
<td>Pack of 10</td>
</tr>
</tbody>
</table>

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If symptoms persist contact your Specialist Palliative Care Team
Noisy Respiratory Secretions

Review the use of intravenous or subcutaneous fluids and decrease or discontinue if appropriate.

**No Symptoms Present**

**Anticipatory Prescribing**

Prescribe **Glycopyrronium** 200 micrograms SC 4-6 hourly PRN

If two or more PRN doses are required in 24 hours

**Symptomatic**

Give stat dose of **Glycopyrronium** 200 micrograms SC

**AND**

Prescribe **Glycopyrronium** 600 micrograms by SC syringe pump over 24hrs.

**AND**

Prescribe **Glycopyrronium** 200 micrograms SC 4-6 hourly PRN for breakthrough symptoms

If symptoms persist, increase total 24 hour dose to 1.2mg.

Review after 24 hours. If symptoms persist consider changing to:

**Hyoscine Butylbromide** 120mg by SC syringe pump over 24hrs.

or

**Hyoscine Hydrobromide** 2.4mg* by SC syringe pump over 24hrs.

*Hyoscine Hydrobromide may cause sedation and paradoxical agitation

**Recommended strengths and pack size to prescribe**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pack Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopyrronium Bromide 200 micrograms/ml injection</td>
<td>Pack of 10</td>
</tr>
<tr>
<td>Hyoscine Butylbromide 20mg/ml injection</td>
<td>Pack of 10</td>
</tr>
<tr>
<td>Hyoscine Hydrobromide 400 micrograms/ml injection</td>
<td>Pack of 10</td>
</tr>
</tbody>
</table>

If symptoms persist contact your Specialist Palliative Care Team