RPMG

Palliative Care in partnership

NIPCPG
NI Palliative Care Pharmacy Group

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

This guidance relates to the prescribing of medicines to manage symptoms for patients in the last days of life. Not every patient will require symptom management but individual need can be difficult to anticipate and therefore proactive prescribing (anticipatory prescribing) reduces the delay in administration of medicines to relieve symptoms when needed. There are five key symptoms that can affect patients in the last days of life:

- **Pain**
- **Breathlessness**
- **Nausea and vomiting**
- **Anxiety, delirium and agitation**
- **Noisy respiratory secretions**

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The guidance recognises the dying person may be unable to tolerate oral medicines. Therefore, administration is via the subcutaneous (SC) route (SC injection and SC syringe pump over 24 hours).

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

- Consider any potentially reversible causes for the patient's symptoms e.g. hypoglycaemia, infection, medication side effects, hypercalcaemia.
- Ensure the patient or their family are aware time is short.
- Review current medicines and stop any not providing symptomatic benefit.
- Discuss and agree any medication changes with the dying person (where appropriate) and those important to them.
- Inform the dying person (where appropriate) and those important to them that some of the medications have the potential to increase drowsiness.

Users are advised to:

- **Review patients regularly** for side effects and response to treatment.
- When prescribing **always start with the lowest dose** in the range specified in this guide.
- Seek specialist advice in moderate or severe **renal and/ or hepatic impairment** or those with complex needs.
- Consider the non-pharmacological management of symptoms at the end of life e.g. repositioning to manage pain.
- Higher doses of the agents included in this guideline may be advised by the Specialist Palliative Care Team.
- The 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, safety and local practice in NI. Responsibility for the use of these recommendations lies with the health care professional(s) managing each patient.

Careful assessment for the underlying cause of symptoms is required and patient's should always be managed in the context of their individualised end of life care plan.

Details of Palliative Care Network Pharmacies and Palliative Care Supply Service pharmacies (i.e. those with extended opening hours who are contracted to stock the regional palliative care medicines list) can be found at **Palliative Care (hscni.net) https://hscbusiness.hscni.net/services/2481.htm**

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

Pain

Morphine Sulfate is the 1st line choice of strong opioid in non-specialist settings. Renal failure is an exception - see choice of 1st opioid with renal impairment section below.

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

No analgesia prescribed or PRN analgesia.

Anticipatory prescribing

Prescribe **Morphine Sulfate** 2mg – 5mg SC 2-4hourly PRN

AND

Review after 24 hours. If patient has required 2 or more doses consider prescribing up to this total of **Morphine Sulfate** dose by SC syringe pump over 24 hours.

In moderate/severe renal or hepatic impairment consider an alternative opioid.

Already on regular "weak" opioid (max dose) e.g. Co-codamol 30/500, Tramadol

Stop current oral analgesia.

AND

Prescribe **Morphine Sulfate** 10mg-15mg by SC syringe pump over 24hrs.

AND

Prescribe **Morphine Sulfate** 2mg SC 2-4hourly PRN for breakthrough pain*

Already on Oral Morphine Sulfate or other opioid (see Table 1)

Use conversion **Table 1** to change from total daily oral **Morphine Sulfate** to SC **Morphine Sulfate** or **other opioid.** Prescribe by SC syringe pump over 24 hours.

AND

Prescribe breakthrough analgesia* **i.e.** divide total **Morphine Sulfate** or **other opioid** dose by 6 and give 2-4 hourly PRN

Already on Fentanyl or Buprenorphine patch (See Table 2)

Continue prescribing patch

AND

Use conversion **Table 2** and prescribe SC **Morphine Sulfate** for breakthrough pain* 2-4 hourly.

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

No regular analgesia prescribed

Give stat SC PRN dose of **Morphine Sulfate** 2mg-5mg

AND

Prescribe **Morphine Sulfate** 5mg-10mg by SC syringe pump over 24 hours

AND

Prescribe **Morphine Sulfate** 2mg-5mg SC 2-4 hourly PRN for breakthrough pain*
(This can be given more frequently with medical discussion and/or palliative care input)

Already on Oral Morphine Sulfate or other opioid (See Table 1)

Use **Table 1** 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.

AND

Prescribe for breakthrough pain* SC 2-4 hourly PRN i.e. divide new total daily SC **opioid** dose by 6. Give a stat dose.

Review regularly

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.

Already on Fentanyl Patch or Buprenorphine patch (See Table 2)

Give stat **Morphine Sulfate** SC PRN dose (use **Table 2**)

AND

Continue prescribing patch

AND

Add additional **Morphine Sulfate** (or other **opioid**) for uncontrolled pain by SC syringe pump over 24 hours (equivalent of 2 breakthrough doses* of **Morphine Sulfate)**

AND

Prescribe SC **Morphine Sulfate** for breakthrough pain* (1/6th of **total** 24 hour opioid dose) and give 2-4hourly PRN

Opioid Conversions Tables

- Refer also to HSC Guidance "Northern Ireland guidelines on converting doses of opioid analgesics for adult use".
- Morphine Sulfate is the first line choice of strong opioid in non-specialist settings. Renal failure is an exception- see choice of 1st opioid with renal impairment section below.

Recommended strengths and pack size to prescribe	
Morphine Sulfate 10mg/ml injection	Pack of 10
Morphine Sulfate 30mg/ml injection	Pack of 10

* 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.

Table 1. Opioid Conversions

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
E.g. 20mg SC Morphine = 10mg SC Oxycodone
Note this may differ from other available 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

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

Patch Strength (micrograms per hr)	Oral Morphine Dose over 24 hours (mg)
5	~10 - 12
10	~20 - 24
20	~40 - 48

Example Opioid Calculations

Changing from Oral Morphine to SC Morphine via syringe pump.

1. Work out total oral dose Morphine in 24 hours
   e.g. MST 15mg BD = 30mg morphine total/ 24 hrs
2. Convert from oral to SC route
   e.g. 30 ÷ 2 = 15mg Morphine SC syringe pump over 24hours

And

Calculating the oral breakthrough/ PRN dose (immediate release preparation)

1. Work out total oral dose Morphine in 24 hours
   e.g MST 15mg BD = 30mg total/24hours
2. Divide by 6 to get 1/6th of the dose
   e.g. 30 ÷ 6 = 5mg Morphine Sulfate Oral Solution (Oramorph®) PRN 2 to 4 hourly

And

Calculating the SC breakthrough/ PRN dose

Divide total SC morphine dose in 24h by 6
e.g. Morphine 15mg via syringe pump over 24h = 15 ÷6 = 2.5mg. Prescribe 2mg Morphine Sulfate injection SC PRN 2 to 4 hourly. For safety and clarity, prescribe in whole **milligrams**. Use of decimal places should be avoided.

Note: 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.

Choice of first opioid with renal impairment

- Opioids may accumulate in renal impairment and thus Morphine Sulphate should not be initiated with an eGFR< 60ml/min.
- Prescribing in renal failure at the end of life has many nuances including the rate of renal function decline, degree of opioid tolerance, level of pain, imminence of dying and level of opioid toxicity.
- Blood tests to determine renal function probably would not be appropriate for patients in the last hours/days of life.
- If the patient is in last hours/ very short days of life and tolerating their current opioid, it may be appropriate for them to remain on this regardless of renal function. However, ensure close monitoring for signs of toxicity and have a low threshold for seeking specialist palliative care advice.
- Alfentanil is drug of choice for syringe pumps when eGFR is 20ml/min or less although specialists may recommend earlier, especially where a rapid decline in renal function is anticipated.
- If using Alfentanil the PRN opioid of choice is SC Oxycodone.
- Oxycodone can be used in renal failure/ renal disease at end of life but there is greater potential for opioid toxicity than with Alfentanil and so caution is advised when using Oxycodone and increased dosing intervals may be appropriate. Different care settings may impact on ease of availability of medicines.
- **For patients with rapidly changing or complex problems please discuss with the specialist palliative care team.**

Nausea and Vomiting

Consider potentially reversible causes such as constipation, hypercalcaemia, infection and raised intracranial pressure. Choice of antiemetic should be influenced by likely underlying causes.

No Symptoms Present

Prescribed regular oral antiemetics?

No

Anticipatory prescribing

Prescribe a suitable SC antiemetic PRN
(see Table 3 below)

Yes

(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

Symptomatic

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

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 antiemetics in syringe pump with Levomepromazine (A combination of Cyclizine & Haloperidol may also be used)

AND

Prescribe Levomepromazine PRN SC for breakthrough nausea

Table 3. Choice of Antiemetic

Lower doses are indicated in severe renal or hepatic impairment

Drug	Indications for Use	Cautions to consider (see BNF for full list)	SC stat PRN dose	SC 24 hour dose	Strength and Pack size
Haloperidol†	Chemical/ metabolic causes.	Extrapyramidal side effects (EPSE), Parkinson's Disease (PD), Lewy body disease (LBD). Seizures.	500 micro-grams - 1mg every 6 - 8 hours PRN	1.5mg *	5mg/ml injection Pack of 10
Metoclopra-mide	Gastric stasis. Prokinetic antiemetic - discontinue if colic develops.	Complete bowel obstruction, EPSE, PD, LBD, Epilepsy.	10mg every 6 - 8 hours PRN (max TDS)	30mg *	10mg/2ml injection Pack of 10
Cyclizine	Non-specific nausea & vomiting Mechanical bowel obstruction. Raised intracranial pressure	Severe heart failure, potent antimuscarinic. Must use water as diluent.	50mg every 8 hours PRN	100mg – 150mg	50mg/ml injection Pack of 5
Levomeproma-zine†	Broad spectrum antiemetic. Sedation can oc-cur at high doses.	At high risk of seizures, EPSE, PD, LBD.	2.5mg - 5mg every 4 - 6 hours PRN	5mg - 25mg	25mg/ml injection Pack of 10
Ondansetron†	Intractable vomiting due to chemical, abdominal and cerebral causes. Narrow spectrum antiemetic so probably should add to levomepromazine rather than replace.		4mg - 8mg every 6 - 8 hours PRN	8mg – 24mg	4mg/2mls or 8mg/4mls injection Pack of 5

* Higher doses may be used in specialist practice.

† Levomepromazine, haloperidol and ondansetron can prolong QT interval but **benefit likely outweighs risk in the last days of life.**

Breathlessness

Intermittent symptoms

Taking regular Morphine Sulfate or other opioid?

No

Anticipatory prescribing

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

Yes

Anticipatory prescribing

Use the same SC opioid dose as for managing break-through pain

Persistent symptoms

Taking regular Morphine Sulfate or other opioid?

No

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

Yes

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

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	
Morphine Sulfate 10mg/ml injection	Pack of 10
Midazolam 10mg/2ml injection	Pack of 10. Preferred strength to use in palliative care to provide low volume SC injections
Lorazepam 1mg tablets	Pack of 28. Annotate 'Genus brand' as this preparation dissolves more easily sublingually than other brands

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.

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 up to total SC PRN dose over 24 hours to current syringe pump dose (increase breakthrough dose accordingly)

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If poor response to increasing dose of **Midazolam** reassess cause of agitation.
Consider prescribing stat dose of:
Levomepromazine 5mg - 15mg SC
or
Haloperidol 500 micrograms – 1mg SC

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Assess response and if effective add:
Levomepromazine 10mg-25mg
or
Haloperidol 1mg-3mg by SC syringe pump over 24 hrs.

Recommended strengths and pack size to prescribe	
Midazolam 10mg/2ml injection	Pack of 10. Preferred strength to use in palliative care to provide low volume SC injections
Levomepromazine 25mg/ml injection	Pack of 10
Haloperidol 5mg/ml injection	Pack of 10

Noisy Respiratory Secretions

- Repositioning can be beneficial. Early use of anti-secretory agents should be considered and can prevent accumulation of new secretions, although has limited effect in clearing those already accumulated.
- Reassure family and carers that although respiratory secretions sound uncomfortable, if the patient is deeply asleep or unconscious, they are most likely not distressed by them. They are present because the patient is not coughing or clearing their throat as they normally would.
- Good mouth care is essential in reducing the sensation of thirst. Use of intravenous or subcutaneous fluids should be reviewed as part of the patient's individualised care plan.

No Symptoms Present

Anticipatory Prescribing

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

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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 4-6hourly PRN for breakthrough symptoms

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

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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	
Glycopyrronium Bromide 200 micrograms/ml injection	Pack of 10
Hyoscine Butylbromide 20mg/ml injection	Pack of 10
Hyoscine Hydrobromide 400 micrograms/ml injection	Pack of 10