





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

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.

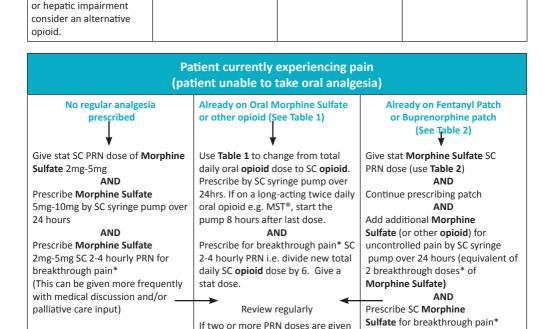
Details of Palliative Care Network Pharmacies and Palliative Care Supply Service pharmacies (i.e. those with extended opening hours who are contracted to stock the regional palliative care medicines list) can be found at Palliative Care (hscni.net) https://hscbusiness.hscni.net/services/2481.htm

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 Already on regular "weak" **Already on Oral Morphine** Already on Fentanyl or or PRN analgesia. opioid (max dose) e.g. Co-Sulfate or other opioid Buprenorphine patch codamol 30/500, Tramadol (see Table 1) i (See Table 2) Anticipatory prescribing Stop current oral Use conversion Table 1 to Continue prescribing patch analgesia. change from total daily Prescribe Morphine AND oral Morphine Sulfate to AND Sulfate 2mg - 5mg SC SC Morphine Sulfate or Use conversion Table 2-4hourly PRN Prescribe Morphine **other opioid.** Prescribe 2 and prescribe SC AND Sulfate 10mg-15mg by SC by SC syringe pump over Morphine Sulfate for Review after 24 hours. syringe pump over 24hrs. 24 hours. breakthrough pain* 2-4 If patient has required 2 hourly. or more doses consider AND AND prescribing up to this total Prescribe Morphine Prescribe breakthrough of Morphine Sulfate dose Sulfate 2mg SC 2-4hourly analgesia* i.e. divide total by SC syringe pump over PRN for breakthrough Morphine Sulfate or other 24 hours. pain* opioid dose by 6 and give 2-4 hourly PRN In moderate/severe renal



in 24 hours increase syringe pump

dose by 30% to 50% to control pain. Increase SC PRN dose accordingly.

(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

Table 2. Transdermal Patch Conversions

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PO (Oral) to SC (Subcutaneous)	Fentanyl Patch eg. Mezolar®, Durogesic® Replace patch every 3 DAYS		
Oral Morphine to SC Morphine - Divide by 2 Eg. 30mg Oral Morphine = 15mg SC Morphine	Fentanyl Patch (micrograms/hr)	Oral Morphine Dose	
Oral Morphine to SC Diamorphine - Divide by 3 Eq. 30mg Oral Morphine = 10mg SC Diamorphine	12	30-59	
,	25	60-89	
ral Oxycodone to SC Oxycodone - Divide by 2 g. 10mg Oral Oxycodone = 5mg SC Oxycodone	37	90-119	
	50	120-149	
ral Morphine to SC Alfentanil - Divide by 30 g. 30mg Oral Morphine = 1mg SC Alfentanil	62	150-179	
fentanil may be used in patients with severe renal	75	180-239	
pairment; seek specialist advice when necessary	100	240-299	
C (Subcutaneous) to SC	125	300-359	
Morphine to SC Diamorphine – Divide by 1.5	150	360-419	
15mg SC Morphine = 10mg SC Diamorphine	175	420-479	
C Morphine to SC Oxycodone – Divide by 2 g. 20mg SC Morphine = 10mg SC Oxycodone	200	480-539	
ote this may differ from other available conversions	Buprenorphine Patch eg. Butec [®] , BuTrans [®] Replace patch every 7 DAYS		
PO (Oral) to PO	Patch Strength	Oral Morphine Dose over	
ral Morphine to Oral Oxycodone - Divide by 2 g. 30mg Oral Morphine = 15mg Oral Oxycodone	(micrograms per	hr) 24 hours (mg) ~10 - 12	
Oral Codeine / Dihydrocodeine / Tramadol to Oral Morphine - Divide by 10	10	~20 - 24	
g. 240mg Oral Codeine = 24mg Oral Morphine	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. $30 \div 2 = 15$ mg 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 $1/6^{th}$ of the dose e.g. $30 \div 6 = 5$ mg 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 $24h = 15 \div 6 = 2.5mg$. 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.

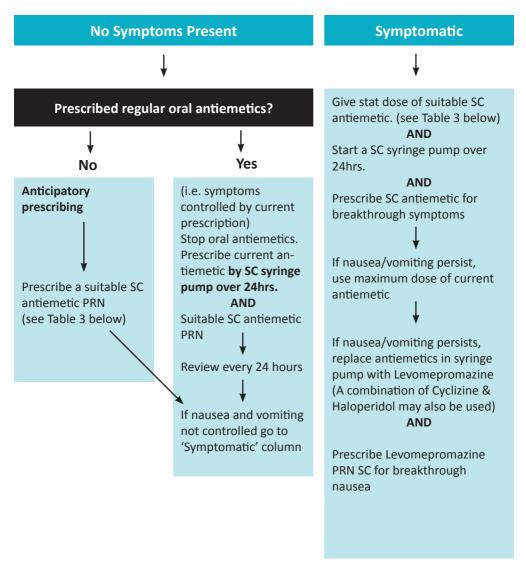


Table 3. Choice of Antiemetic

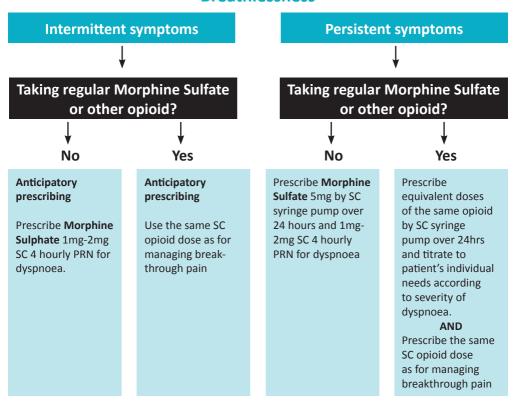
Lower doses are indicated in severe renal or hepatic impairment

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



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.

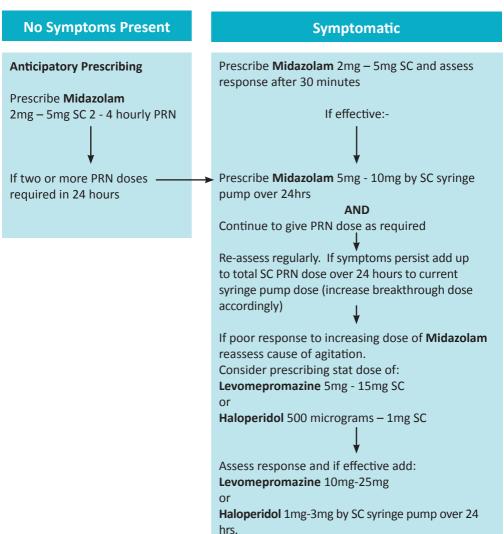
If patient is breathless AND anxious, consider: Midazolam 2mg SC PRN and/or Midazolam 5mg-10n

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.



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.

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

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

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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	

