



Supplementary Guidance on symptom management in the last hours days of life (in response to Covid-19 pandemic)

Adapted from an original document produced by the Fylde and Wyre Palliative care team

Scope of Policy

1. Information within this document should be used alongside the Good practice in providing symptom control at end of life described in the *Clinical Practice Summary: Guidelines on consensus to managing Palliative Care Symptoms* (NHS North West Coast Strategic Clinical Network 2017)
2. Will provide guidance on both pharmacological and non-pharmacological means of symptom control and other considerations of symptom control for particular consideration in patients with Covid-19 and expected poor prognosis/dying from Covid-19 related infection
3. Provides guidance on alternative medications for use in the event of shortages of 4 key drugs in use (Morphine sulfate, glycopyrronium, levomepromazine and midazolam).
4. Current practice relies on the use of the subcutaneous syringe driver in the event of poorly controlled symptoms not adequately managed by intermittent as required SC injections when a person is no longer able to take medications orally. A significant limiting factor in the provision of good symptom management at end of life is the supply of syringe drivers and it is anticipated that there will not be sufficient supply to meet local needs. This guideline is designed to inform the management of symptoms at end of life in the event that subcutaneous syringe drivers are not available or there are insufficient staff available to facilitate their use. **This guideline is pertinent for all patients in last days of life irrespective of diagnosis or Covid-19 status.**

These guidelines assume that the patient is receiving all appropriate supportive treatments and that correctable causes of the symptoms have been managed appropriately. Examples include:

- Antibiotic treatment for a superadded bacterial infection may improve fever, cough, breathlessness and delirium
- Optimising treatment of comorbidities (e.g. COPD, heart failure may improve cough or breathlessness)

SAFE PRESCRIBING IS KEY AND IF IN DOUBT OR CONCERN THEN PLEASE CONTACT THE ST CATHERINES HOSPICE: 01772629171 –updates regarding this will be given in due course

Core Medications and alternatives to use in syringe drivers

If a syringe driver is available but any of the four core drugs in use locally (morphine, levomepromazine, glycopyrronium and midazolam) are not available then alternatives, their uses and dosing are described in the *Clinical Practice Summary* but are summarised below. Doses available in Clinical Practice Summary

Symptom	1 st line medication as per <i>Clinical Practice Summary</i>	2 nd line alternative	3 rd line alternative
Pain	Morphine	Oxycodone	Alfentanil
Nausea and vomiting	Levomepromazine	Haloperidol	Cyclizine
Respiratory secretions	Glycopyrronium	Hyoscine Butylbromide	Hyoscine Hydrobromide
Agitation/terminal restlessness	Midazolam	Levomepromazine	Haloperidol

Renal failure eGFR <30. Consider renal function before deciding any medications to be used

Symptom	1 nd line medication	2 nd line alternative
Pain	Oxycodone	See specialist palliative care advice
Nausea and vomiting	Haloperidol	
Respiratory secretions	Glycopyrronium	
Agitation/terminal restlessness	Midazolam	

Throughout the guidance, if initial measures are ineffective, escalate decision making and seek specialist palliative care advice when needed.

BREATHLESSNESS

NON-PHARMCOLOGICAL METHODS

- Positioning (various advice depending on position: sit upright, legs uncrossed, let shoulders droop, keep head up; lean forward)
- Relaxation techniques
- Controlled breathing techniques include positioning, pursed-lip breathing, breathing exercises and coordinated breathing training
- Reduce room temperature
- Cooling the face by using a cool flannel or cloth
- Oxygen in hypoxia may be indicated. When oxygen is available, consider a trial of oxygen therapy and assess whether breathlessness improves
- **Portable fans not recommended for use in health and social care facilities** (Hospitals, hospices, care/nursing homes etc) due to potential risk of cross infection but may have role in patients own home with discussion with family and carers.

PHARMACOLOGICAL APPROACHES

"In the last days of life, for patients with distressing breathlessness at rest, the combined use of an opioid with a benzodiazepine is more effective than either alone." PCF 6

Patients with severe COVID-19 symptoms, especially severe breathlessness, who are not expected to survive their illness often deteriorate quickly over a short period of time. As a result, they may need higher starting and maintenance doses of opioids / anxiolytics than suggested previously for breathlessness and associated anxiety.

Clinical scenario	Treatment
Opioid naive (not currently taking opioids) and able to swallow	Oral treatment Morphine sulfate immediate release 2.5 mg to 5 mg every 2 hours as required (start lower in elderly persons) or morphine sulfate modified-release 5 mg twice a day, increased as necessary (maximum 30 mg daily)
Already taking regular opioids for other reasons (for example, pain relief)	Oral treatment Morphine sulfate immediate release 5 mg to 10 mg every 2 hours as required or one twelfth of the 24-hour dose for pain, whichever is greater
Unable to swallow	Parenteral treatment Morphine sulfate ¹²³ 2.5 mg to 5 mg subcutaneously every 2 hours as required, increasing the dose as necessary

¹ At the time of publication (April 2020) or updated NICE guidance: COVID-19 rapid guideline: managing symptoms (including at the end of life) in the community NICE guideline [NG163], opioids and benzodiazepines did not have a UK marketing authorisation for moderate to severe breathlessness (see the General Medical Council's guidance on prescribing unlicensed medicines for further information)

² Sedation and opioid use should not be withheld because of an inappropriate fear of causing respiratory depression.

	If needed frequently (more than twice daily), a subcutaneous infusion via a syringe driver may be considered (if available), starting with morphine sulfate 10 mg over 24 hours
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- Oxycodone (when eGFR <30) Half dose of morphine (refer to clinical practice summary for guidance on dosing)
- Midazolam 2.5-5mg SC prn 2 hourly if symptoms persist or notable agitation as a contributing factor

Non-injection alternatives if able to take

- Buccal Midazolam 2.5 – 5mg PRN four hourly⁴⁵
- Lorazepam oral tablet 500 microgram – 1mg SL Sublingual 4 hourly as required (max 4mg per 24 hours)⁶. Reduce the dose to 250-500 microgram 4 hourly as required in elderly or debilitated patients (maximum 2 mg in 24 hours). Lorazepam dissolve the tablet in a few drops of warm water, draw up into 1ml oral syringe and put between the patient's cheek and gum

³ If estimated glomerular filtration rate (eGFR) is less than 30 ml per minute, use equivalent doses of oxycodone instead of morphine sulfate – see Clinical Practice Summary or Prescribing in palliative care in the BNF for more details

⁴ 85% bioavailability as buccal (95% sc). Therefore largely equipotent and doses are the same.

⁵ Giving Midazolam (Injectable solution) by buccal route to help with Agitation/restlessness or breathlessness in last days of Life. To be used when buccal specific preparations (Buccalam & Epistatus) not available. See additional guidance.

⁶ Lorazepam dissolve the tablet in a few drops of warm water, draw up into 1ml oral syringe and put between the patient's cheek and gum. Oral tablets can be used sublingually (off-label use)

Continuous syringe driver (consider if needing more than 2 prn doses per day)

Treatment	Dosage
Opioid	Morphine sulfate 10 mg over 24 hours via a syringe driver, increasing stepwise to morphine sulfate 30 mg over 24 hours as required
Benzodiazepine if required in addition to opioid	Midazolam 10 mg over 24 hours via the syringe driver, increasing stepwise to midazolam 60 mg over 24 hours as required
Add PRN parenteral morphine or midazolam if required	Morphine sulfate 2.5 mg to 5 mg subcutaneously as required; Midazolam 2.5 mg subcutaneously as required. (See BNF for more details on dosages).

Pharmacological measures – severe breathlessness (akin to ARDS scenarios)

Patients with severe COVID-19 symptoms, especially severe breathlessness, who are not expected to survive their illness often deteriorate quickly over a short period of time. As a result, they may need higher starting and maintenance doses of opioids / anxiolytics than suggested previously for breathlessness and associated anxiety.

- morphine 5-10mg SC prn 2 hourly (oxycodone 2.5-5mg SC prn 2 hourly if low eGFR)
- midazolam 5-10mg SC prn 2-4 hourly (may need in some cases to be hourly)
- consider morphine 10-20mg and / or midazolam 10-20mg over 24 hours via syringe driver
- syringe driver dosing may need to be reviewed 8-hourly rather than every 24 hours if the patient's prn requirements are escalating rapidly without control of their symptoms
- dosing requirements may not 'fit' with established practice and may have to be determined on a case by case basis – always prescribe safely, but don't be afraid to prescribe in line with your patients' requirements
- the bottom line is that, if a patient is going to die, we need to ensure they die without distress
- syringe drivers may be in short supply or needed for non-COVID-19 patients requiring palliative care support. Where possible, use 'as required' dosing for COVID-19 patients
- IV administration may be indicated when possible and indicated in severe cases in extremis

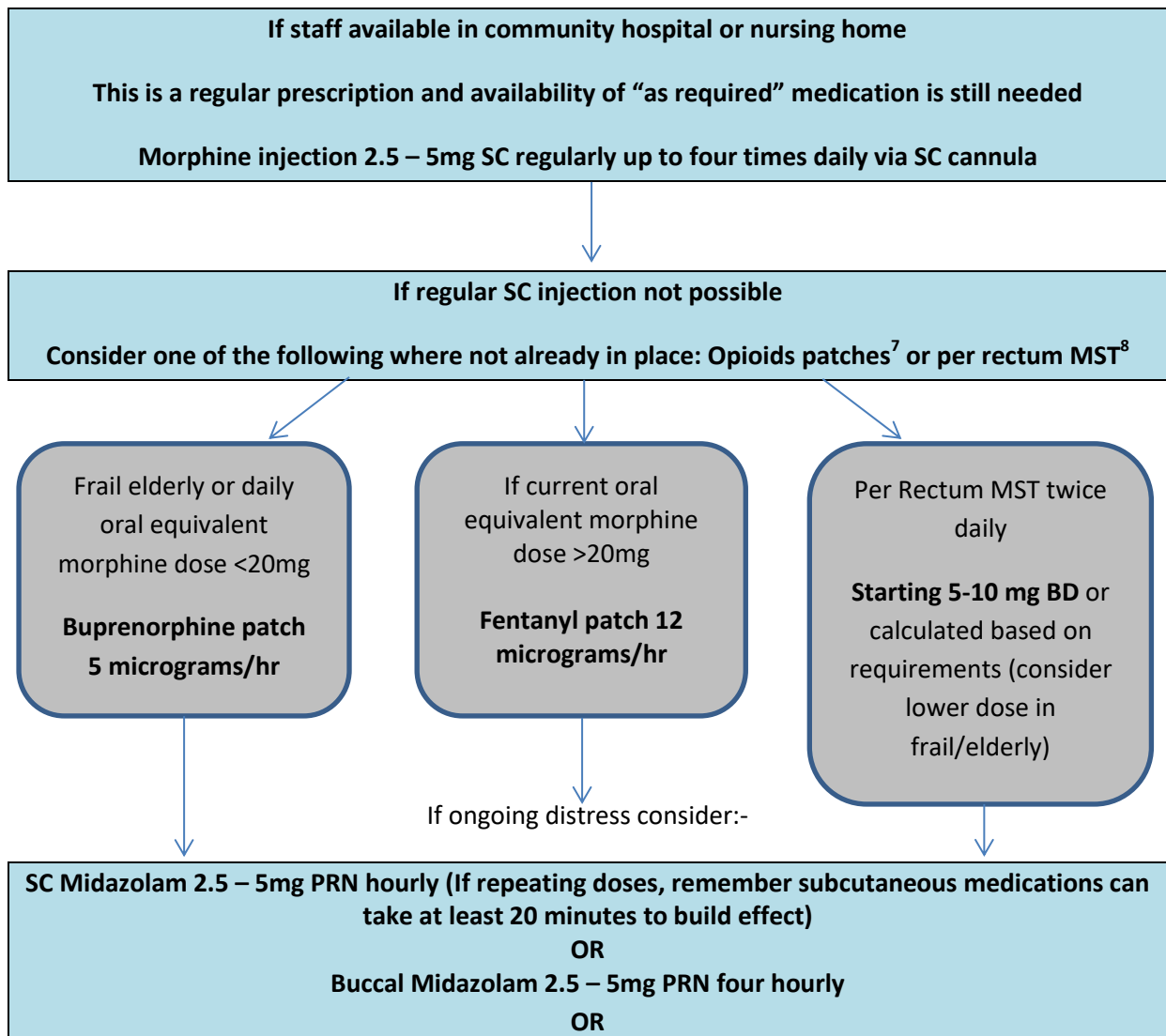
Sedation and opioid use should not be withheld because of an inappropriate fear of causing respiratory depression.

Injectable Midazolam can be given by buccal/sublingual/intranasal route but practical considerations make administration difficult (Midazolam for injection 10mg/2mls ampoules) but this may be necessary dependent on supply of the buccal preparations

Consider need to prescribe laxative and anti-emetics when prescribing opioid medications

Throughout the guidance, if initial measures are ineffective, escalate decision making and seek specialist palliative care advice when needed.

WHEN SYRINGE DRIVER NOT AVAILABLE AND NOT TOLERATING ORAL MEDICATIONS



⁷ Note patches take 8-12 hours to reach steady state therefore access to as required medications will be required during this period

⁸ Per Rectum MST (has to be MST tablet, not other preparations). Quicker onset of action than patch, equipotent to oral. Coronaviruses are known to be found in faeces, but the risk can be minimised by the normal practice using gloves when giving meds PR. Covid-19 infection is not a contraindication to PR medications. Contraindicated in those with diarrhoea

Lorazepam oral tablet 500 microgram – 1mg Sublingual 4 hourly as required (max 4mg per 24 hours) Reduce the dose to 250-500microgram 4 hourly as required in elderly or debilitated patients (maximum 2 mg in 24 hours).

Note patches take 8-12 hours to reach steady state therefore access to as required medications will be required during this period

COUGH

TO MINIMISE THE RISK OF CROSS-TRANSMISSION:

- cover the nose and mouth with a disposable tissue when sneezing, coughing, wiping & blowing the nose
- dispose of used tissues promptly into clinical waste bin used for infectious or contaminated waste
- clean hands with soap and water, alcohol hand rub or hand wipes after coughing, sneezing, using tissues, or after contact with respiratory secretions or objects contaminated by these secretions

NON-PHARMCOLOGICAL METHODS

- humidify room air where possible
- oral fluids
- warm lemon and honey drink or a spoonful of honey
- suck cough drops / hard sweets
- elevate the head when sleeping
- avoid smoking

PHARMACOLOGICAL APPROACHES

- Codeine linctus **or** codeine tablets 15-30 mg every 4 hours as required, up to 4 doses in 24 hours. If necessary, increase dose to a maximum of 30-60 mg 4 times a day (maximum 240 mg in 24 hours)
- or**
- Morphine sulfate oral solution 2.5-5 mg when required every 4 hours. Increase up to 5-10 mg every 4 hours as required. If the patient is already taking regular morphine increase the regular dose by a third

Continuous syringe driver

If severe / end of life: Morphine sulfate injection 10mg CSCI over 24 hours and 2.5-5mg SC 4 hourly prn (If opioids naïve). Appropriate syringe driver dose to be calculated if already on background opioid

NICE guidance comments on avoiding cough suppressant in chronic bronchitis and bronchiectasis. As this guidance is focussed on last hours and days of life, cough suppressant medication should be considered to manage symptoms at end of life.

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DELIRIUM

Delirium is a feature of COVID-19 and older people are at the greatest risk from COVID-19. If infected they may present with or develop a delirium. However, delirium is not exclusive to older people and may well be seen in any patient with severe infection, adult respiratory distress syndrome, and those requiring invasive ventilation on Critical Care units.

Delirium and the management of COVID-19: Delirium, especially its hyperactive motor form, will present significant additional challenges in the context of the COVID-19 crisis. Standard non-pharmacological measures to treat or prevent delirium may well be not possible in isolation environments, and these environments may themselves worsen delirium. Medications may need to be utilised earlier than would normally be expected

NON PHARMACOLOGICAL METHODS

- identify and manage the possible underlying cause or combination of causes
- ensure effective communication and reorientation (for example explaining where the person is, who they are, and what your role is) and provide reassurance for people diagnosed with delirium
- consider involving family, friends and carers to help with this (may be limited with Covid 19 infection and isolation restrictions)
- ensure that people at risk of delirium are cared for by a team of healthcare professionals who are familiar to the person at risk
- avoid moving people within and between wards or rooms unless absolutely necessary
- ensure adequate lighting

Where these interventions are ineffective or more rapid control is required to reduce the risk of harm to the patient and others, it may be necessary to move to pharmacological management earlier than would normally be considered.

PHARMACOLOGICAL APPROACHES

Treatment	Dosage
Anxiety or agitation and able to swallow: lorazepam tablets	Lorazepam 0.5 mg to 1 mg 4 hourly as required (maximum 4 mg in 24 hours) Reduce the dose to 250-500 microgram 4 hourly as required in elderly or debilitated patients (maximum 2 mg in 24 hours) Oral tablets can be used sublingually (off-label use) Buccal midazolam 2.5 -5mg 4 hourly as required
Anxiety or agitation and unable to swallow: midazolam injection	Midazolam 2.5 mg to 5 mg subcutaneously hourly as required

	<p>If needed frequently (more than twice daily), a subcutaneous infusion via a syringe driver may be considered (if available) starting with midazolam 10 mg over 24 hours</p> <p>Reduce dose to 5 mg over 24 hours if estimated glomerular filtration rate is less than 30 ml per minute</p> <p>Patients in the last hours to days of their life who are terminally agitated may require larger doses of benzodiazepines. If requiring more than 30mg in 24 hours please consider discussion with specialist palliative care</p>
<p>Delirium and able to swallow: haloperidol tablets</p>	<p>Haloperidol 0.5 mg to 1 mg at night and every 2 hours when required. Increase dose in 0.5-mg to 1-mg increments as required (maximum 10 mg daily, or 5 mg daily in elderly patients)</p> <p>The same dose of haloperidol may be administered subcutaneously as required rather than orally, or a subcutaneous infusion of 2.5 mg to 10 mg over 24 hours</p> <p>Consider a higher starting dose (1.5 mg to 3 mg) if the patient is severely distressed or causing immediate danger to others</p> <p>Consider adding a benzodiazepine such as lorazepam or midazolam if the patient remains agitated (see dosages above)</p>
<p>Delirium and unable to swallow: levomepromazine injection</p>	<p>Levomepromazine 12.5 mg to 25 mg subcutaneously as a starting dose and then hourly as required (use 6.25 mg to 12.5 mg in the elderly)</p> <p>Maintain with subcutaneous infusion of 50 mg to 200 mg over 24 hours, increased according to response (doses greater than 100 mg over 24 hours should be given under specialist supervision)</p> <p>Consider midazolam alone or in combination with levomepromazine if the patient also has anxiety (see dosages above)</p>

Throughout the guidance, if initial measures are ineffective, escalate decision making and seek specialist palliative care advice when needed.

FEVER⁹

Be aware that, on average, fever is most common 5 days after exposure to the infection

NON PHARMACOLOGICAL METHODS

- Drink fluids regularly to avoid dehydration (no more than 2 litres per day)
- Reduce room temperature
- Wear loose clothing
- Cooling the face by using a cool flannel or cloth
- **Portable fans not recommended for use** in health and social care facilities due to potential risk of cross infection but may have role in patients own home with discussion with family and carers.

Consider antipyretics if symptomatic from fever

Paracetamol 1g PO / IV / PR QDS (dose adjust for weight)

****NSAIDs contraindicated in COVID-19**** (Day, 2020) It is not advised to use NSAIDs in patients who may recover from COVID-19

Throughout the guidance, if initial measures are ineffective, escalate decision making and seek specialist palliative care advice when needed.

⁹ If persistent fever not manageable, please note that patches may be more rapidly absorbed increasing risk of toxicity – Seek guidance

Symptom management flowchart to use alongside Clinical Practice Summary
for last days of life where syringe driver not available

Pain in the last days of life when syringe driver not available

Pain in last hours/days of life, not tolerating oral medications and syringe driver not available

If staff available:

Opioid naïve or equivalent based on prn requirements:

- Morphine injection 2.5 – 5mg SC four times daily via SC cannula
- Oxycodone injection 1-2 mg (eGFR<30) SC four times daily via SC cannula

For patients already on oral opioids, calculate total subcutaneous equivalent in 24 hours and divide in to 4 equivalent doses

If regular SC injection not possible (in the community)

Calculate daily oral morphine equivalent (OME) based on current opioid use (See Clinical Practice Summary).

Oral Morphine Equivalent <20 mg
Buprenorphine transdermal patch 5 micrograms/hr

Oral Morphine Equivalent 20-40 mg
Fentanyl patch 12 micrograms/hr

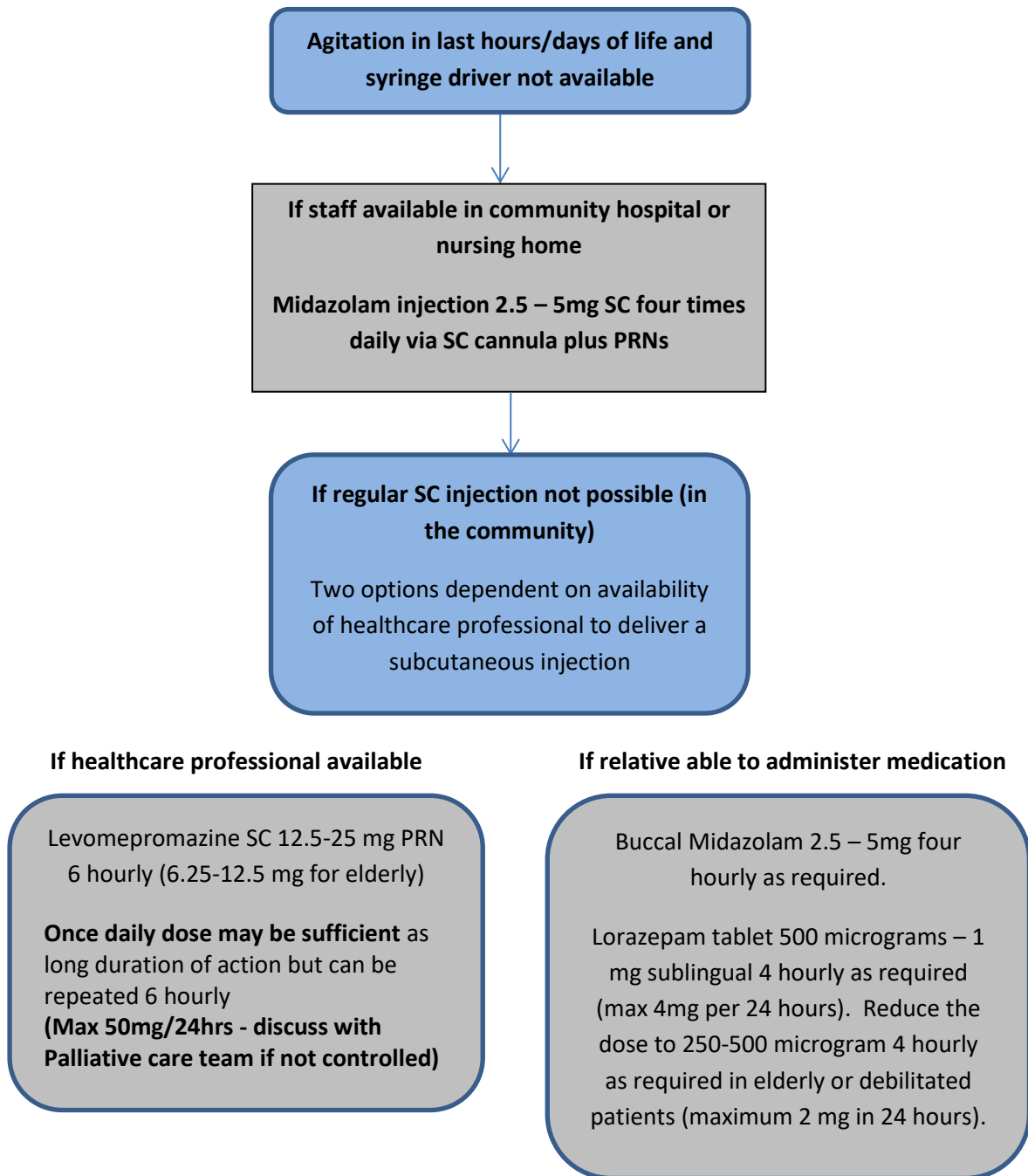
Oral Morphine Equivalent 40-60 mg
Fentanyl patch 25 micrograms/hr

Per Rectum MST twice daily

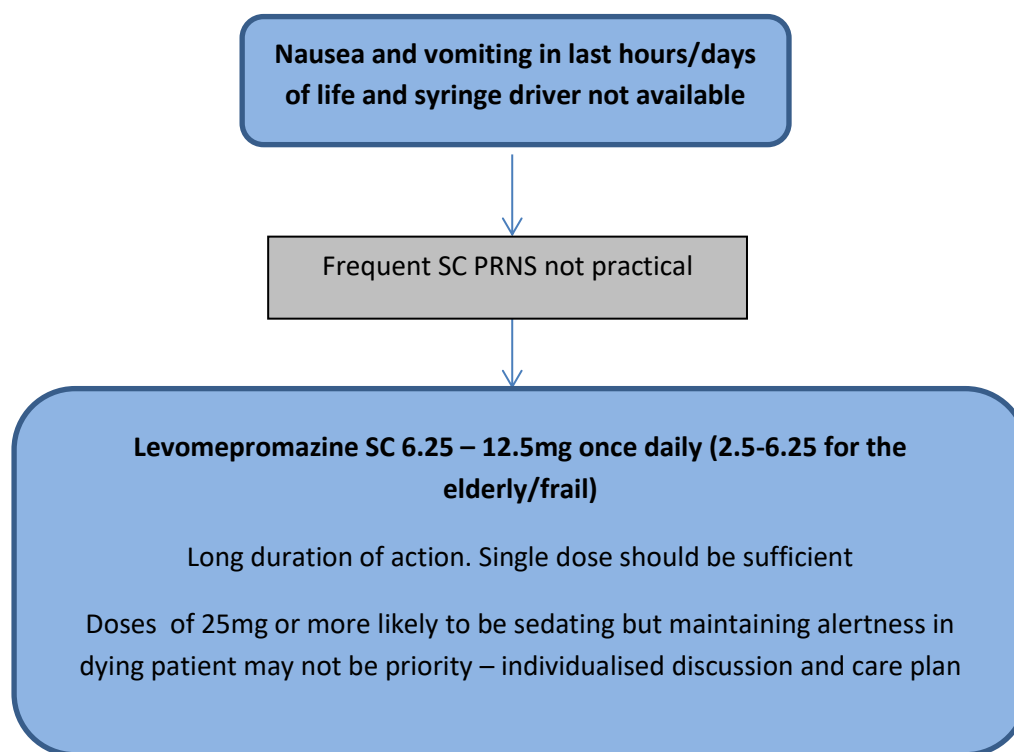
Calculate daily oral morphine equivalent and divide by 2 and administer twice daily

If background Oral Morphine Equivalent is higher than 60mg, guidance should be sought

Agitation/Terminal Restlessness in the last days of life when syringe driver not available



Nausea and Vomiting in the last days of life when syringe driver not available

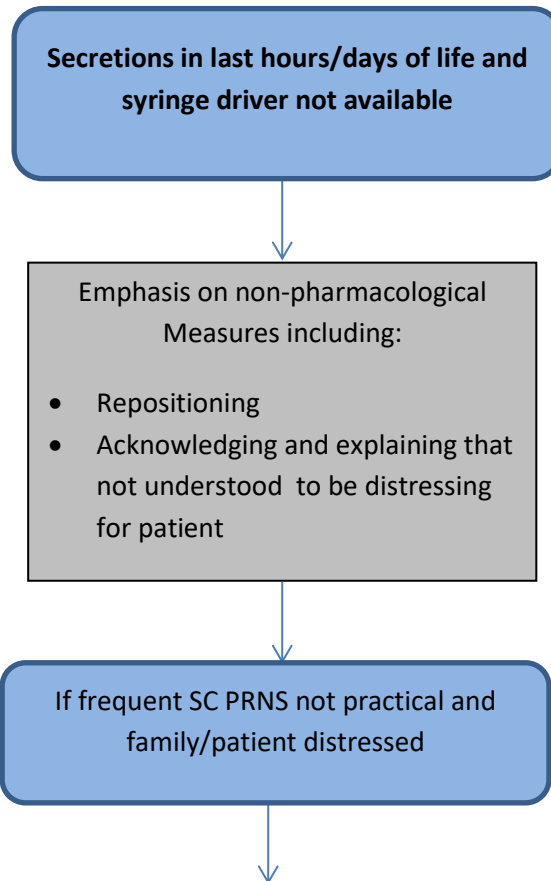


Alternative options

- Haloperidol 500 microgram - 1.5mg BD orally or subcutaneously (max 3mg per day)
- Prochlorperazine (buccal tablet)/Buccastem 3mg BD
- Cyclizine 50mg TDS subcutaneously¹⁰

¹⁰ Note can be irritant as stat injections

Respiratory Tract secretions in the last days of life when syringe driver not available



Hyoscine hydrobromide patch¹¹ (1mg per 72hr) Apply 1 patch every 72 hours

Or

Hyoscine hydrobromide tablets (Kwells) 150-300 microgram 6 hourly if required

¹¹ Note can be sedating

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