Guidance for Clinicians:
Medical management for RENAL patients dying from COVID-19 related illness

This document covers the medical management of dyspnoea, respiratory secretions and delirium at the end of life, as well as symptoms specific to those with pre-existing renal failure.

- *Psychological and spiritual distress may be significant (for patients, whānau and staff); consideration should be made to minimize this and provide appropriate support.*
- *When converting opioids oral to subcutaneous – halve the dose (morphine 10mg orally = morphine 5mg SC)*
- ***eGFR <30mL/min we recommend use of fentanyl (if available) instead of morphine or oxycodone.***
- *In an end of life (EOL) context, the complex pharmacology of methadone may make this a less favorable choice unless the patient is already established on it.*
- *SC = subcutaneous, CSCI = continuous subcutaneous infusion via syringe driver, OME = oral morphine equivalent*
- *When converting opioids oral to subcutaneous – halve the dose (morphine 10mg orally = morphine 5mg SC)*
- *In the absence of syringe driver availability resort to regular SC opioid dosing (morphine and oxycodone only); NB: patients in renal failure will require much less frequent dosing, in the order of Q12H, no more than Q6H.*
- *All medications discussed in this document are compatible with each other and can be mixed in various combinations in the same syringe for CSCI, with the exception of frusemide which must be in a separate syringe.*
- *Vital sign monitoring is unnecessary, care should be guided by symptom needs and patient comfort*
- *In the absence of Niki-T34 syringe drivers – see use of Alternate infusion devices for EOL medication administration guideline*

Management of dyspnoea:

- Optimise positioning as guided by patient comfort – likely prone (at least 16 hours per day).
- Air movement, such as achieved using a fan, can reduce the sensation of breathlessness
- Supplementary oxygen (via any device) should be titrated to dyspnoea not saturations
- Remove oxygen delivery device if it is causing agitation/patient not tolerating
- The sensation of dyspnoea, in patients NOT requiring opioids for pain, normally responds to an OME of <30mg per 24 hours. If substantially more opioid is required, *palliative medicine consult is recommended.*

Opioid naïve patients:

	PRN Oral dosing	*PRN Injectable (SC) dosing*
Fentanyl	25 - 50 microg buccally Q1H	25 - 50 microg Q1H
Oxycodone elixir	1 - 10 mg Q4H	2.5 - 5 mg Q4H

Patients already on background opioids:

- Continue background opioid
- If patient has a fentanyl patch continue this
- Use approximately 1/6th of their total daily opioid dose PRN Q4H as a starting dose and titrate to effect.

Benzodiazepine dosing:
Useful in addition to opioids if significant anxiety/panic associated with dyspnoea.

- lorazepam 0.5 mg PO TDS PRN
- clonazepam tablets 0.25 - 0.5 mg BD PRN
- clonazepam drops (buccal 1 drop = 100 micrograms) 2-3 drops buccally Q8H PRN
- midazolam 2.5 – 5 mg SC Q1H PRN for anxiety associated with dyspnoea; start at lowest dose and titrate to effect.

Diuretics:

- Diuretics may still have a role if dyspnoea is due to fluid overload and pulmonary oedema, provided the patient has some urinary output. A trial of diuretic is reasonable, continued only if good diuresis results.
- Frusemide can be given SC either as a bolus or via CSCI if no IV access possible
- Due to volume limitations the maximum bolus dose per SC line is 40mg (4mL) and per CSCI is 300mg. If higher daily doses are required this can be achieved by:
    - CSCI 300 mg over 12 hours (giving a total of 600 mg in 24 hours)
    - CSCI 300 mg over 8 hours (giving a total of 900 mg over 24 hours)

CSCI dosing:
CSCI will take approximately 4 hours to reach peak effect, if symptoms remain uncontrolled after 8 hours consider dose titration or contact Palliative Specialist on call for advice.

Generic CSCI starting doses for management of dyspnoea for opioid and benzodiazepine naive:

- fentanyl 100 microg + midazolam 10 mg over 24 hours

NB: If already on PRNs - use previous 24-hour PRN use of opioid and benzodiazepine as a guide for CSCI prescribing. *For example:*

- *If patient has used 300microg of SC fentanyl and 15 mg of midazolam in PRN's over previous 24 hours to control dyspnoea prescribe 2/3 of this as a CSCI – ie. CSCI fentanyl 200microg, midazolam 10mg over 24 hours.*

Ensure SC opioid and benzodiazepine PRNS are prescribed (as above) in addition to CSCI

NB: for patients already on long acting opioids (and benzodiazepines) the CSCI starting dose and PRN doses will need to be calculated based on their current baseline.

Management of acute respiratory distress or severe dyspnoea at the end of life:

Crisis medications should be available for all patients at risk of respiratory crisis at end of life; aiming to rapidly sedate patient in the context of extreme respiratory distress

If escalating opioid and benzodiazepine doses are required to control respiratory distress, consider adding levomepromazine (Nozinan).

- levomepromazine can be effective in reducing respiratory distress without causing respiratory depression.
    - levomepromazine 6.25 - 12.5 mg SC Q2H PRN, titrate to effect
    - levomepromazine CSCI starting dose 12.5 mg over 24 hours, increase in 12.5 mg increments to effect.

Generic SC crisis medications for opioid and benzodiazepine naïve patients:

- fentanyl 100 micrograms Q10min PRN
- midazolam 10 mg Q10mins PRN
- If inadequate sedation with above, consider:
    - Levomepromazine 25-50mg SC stat
    - Phenobarbitone 200mg SC stat *(MUST be discussed with Palliative Specialist on-call)*

SC Crisis medication for patients on background opioids:

- Multiply their usual PRN opioid dose by 3 and give stat. For example, if patients' regular PRN is fentanyl 25microg SC, chart 75microg SC as their crisis dose.

Management of excessive respiratory tract secretions:

- Avoid IV fluids;
    - These are futile at EOL and can contribute significantly to the volume of respiratory secretions
    - There is no evidence that parenteral fluids (SC or IV) improve a patient's sense of thirst
    - Thirst is mitigated by oral fluids and, if unable to swallow, good mouth care.
- Optimise positioning (as tolerated) to allow drainage of secretions
- Avoid suctioning - there is limited role for suctioning, only consider if visible secretions in the mouth are distressing the patient

Anti-secretory medications to reduce respiratory secretions include:

- hyoscine butylbromide (Buscopan) 20 mg SC Q4H AND/OR start CSCI 60 mg over 24 hours (maximum 120 mg total per 24 hours)
- glycopyrronium bromide (Glycopyrrolate) 200 - 400 micrograms SC Q4H/PRN AND/OR start CSCI 800-1600 micrograms over 24 hours (maximum 1600 micrograms total per 24 hours)
- octreotide 100 - 200 micrograms Q8H SC regularly OR CSCI 200 - 600 micrograms over 24 hours

Management of delirium/agitation/restlessness:

- Exclude urinary retention, faecal impaction or uncontrolled pain
- Pharmacological options: antipsychotic medication is recommended first line, not benzodiazepines

Antipsychotic dosing:

- haloperidol 0.5 - 1 mg SC Q4H PRN (max 5 mg in 24 hours – if needing more than this to control agitation switch to levomepromazine)
- levomepromazine (more sedating than haloperidol) 6.25 mg SC Q4H PRN is a reasonable starting dose, a range of 6.25 – 12.5 mg may be used (doses of 25-50mg/24 hours are typically sedating)
- If agitation is severe a higher bolus dose of levomepromazine such as 25 - 50 mg may be required and/or commencement of a CSCI

Management of nausea related to uraemia:

- haloperidol 0.5 mg SC Q4H/PRN OR CSCI 1 - 3 mg over 24 hours (max 5mg total over 24 hours); if haloperidol ineffective in controlling nausea switch to levomepromazine
- levomepromazine (Nozinan) 3.125 - 6.25mg Q4H/PRN OR CSCI starting dose 6.25mg over 24 hours up to 25mg over 24 hours (doses greater than 25mg are unlikely to provide additional antiemesis and will cause sedation).

Management of uraemic itch:

- Topical - Aqueous cream 1% menthol
- If able to swallow; consider:
    - gabapentin 100 mg or pregabalin 25mg nocte (do not increase dose)
    - mirtazapine 15mg nocte
    - paroxetine 10mg mane

Management of bleeding:

- Platelet dysfunction associated with uraemia increases bleeding risk in renal patients; usually limited to mucosal bleeding.
- Avoid anticoagulation
- If risk of catastrophic bleed please follow our **Management of Catastrophic Bleeding** guideline available on the Waikato DHB Palliative Care Service intranet site: https://intranet.sharepoint.waikato.health.govt.nz/site/pol/published/Catastrophic%20Bleeding,%20management%20of%20(Palliative%20Care).pdf#search=oncology%20palliative%20care

For management of other symptoms such as pain please refer to our guidelines:

Waikato DHB Palliative Care Service intranet site:
https://intranet.sharepoint.waikato.health.govt.nz/Pages/Regional%20Cancer%20Centre/Palliative-Care-services-and-resources.aspx

Hospice Waikato website:
Health professionals: https://www.hospicewaikato.org.nz/education
Clinical guidelines and drug protocols:
https://www.hospicewaikato.org.nz/clinicalguidelinesdrugprotocols

For further Specialist Palliative Care advice contact the SMO oncall via switchboard