Renal Impairment - Prescribing at the End of Life (including last days and hours of life) in the Community

(note there is a separate document for Secondary Care LTHT)

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This document is intended to highlight special considerations when prescribing for patients with a GFR less than 30 mL/min (usually using eGFR) or with rapidly deteriorating renal function.

Prescribing at the end-of-life guidance is presented for:

1. Palliative patients in the last weeks/months of life with renal impairment.
2. Patients in the last hours/days of life with renal impairment.

Assess the patient

Management will depend on the cause of symptoms and may be different for patients in the last days of life compared to those with a longer prognosis of weeks to months. Consider seeking specialist advice if unsure.

Common symptoms of renal failure are:

- Breathlessness (which may be related to fluid overload or acidosis)
- Myoclonic jerks (which may be related to increased drug toxicity and /or uraemia)
- Delirium
- Restless legs
- Nausea (GFR less than 10 ml/min)
- Itch (GFR less than 10 ml/min). Seek specialist advice for the management of itch

Special consideration

- Consider calculating creatinine clearance (mL/min) using the Cockroft - Gault formula in the following circumstances:
    - At extremes of muscle mass (BMI <18 kg/m2 or > 30 kg/m2)
    - Elderly patients (aged 75 years or older)
    - Patients taking nephrotoxic drugs / drugs with narrow therapeutic index if predominantly renally excreted
    - Other comorbidities or clinical concern
- Calculate using either:

  Cockcroft-Gault formula: CrCL (mL/minute) = $\frac{n \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine (micromoles/L)}}$

  where n = 1.04 (females), n= 1.23 (males)

  or online calculator at https://www.mdcalc.com/

- Consider seeking advice from a pharmacist.

General principles

- Prescribing should be individualised, balancing the risks vs. benefits and considering the patient's goals of care.
- Optimise medicines and reduce polypharmacy as much as possible. *Refer to further guidance below for medicines optimisation guidance.*

1. Symptom advice in the last weeks or months of life

Pain

Consider reversible causes and non-pharmacological management of symptoms

Paracetamol is safe to use.

NSAIDs - caution, beware aware of:

- Increased bleeding tendency.
- Increased risk of nephrotoxic effects of drugs, which may be a particular consideration for patients with mild to moderate renal impairment.
- Decision to prescribe depends on the balance of risks and benefits.

Neuropathic agents:

- **Amitriptyline -** start with 10mg once daily and titrate cautiously.
- **Gabapentin /pregabalin** - require significant dose reduction at initiation and cautious titration, see summary of product characteristics literature/ BNF.

Opioids:

- Avoid codeine and morphine. Preferred options are:

If eGFR greater than 10mL/min and not rapidly falling

- **Oral route** -
  - **Oxycodone immediate release**
    - Opioid naïve - usual starting dose 1mg to 3mg PO '**as needed,'** minimum dosage interval 2 hours is preferred. A 1-hour dosing interval could be prescribed but because of the risk of accumulation patients should be monitored for signs of opioid toxicity.
  - **Tramadol immediate release**
    - Starting dose 50 mg PO twice a day. If this is insufficient, add 50 mg **as needed** (minimum dosage interval 4 hours).

- **Transdermal (TD) route:**
  - **Buprenorphine or fentanyl TD patch**
    - Preferred opioids for background analgesia when pain is mild and or stable.
    - Usually prescribe **oxycodone 'as needed'** for breakthrough pain (1/6th to 1/10th of the total daily opioid dose). Note, fentanyl SC 'as needed' is generally felt to be too short acting for breakthrough pain.

- **Subcutaneous (SC) route**:
  - **Oxycodone SC**
    - Remember oxycodone PO to SC conversion ratio is 2:1.
    - Opioid naïve - usual starting dose 1 to 2 mg SC '**as needed'**. Dosing intervals as for oral oxycodone see above.
    - If a regular opioid is required start a continuous subcutaneous infusion (CSCI) of oxycodone. Continue with oxycodone SC 'as needed' for breakthrough pain.

If eGFR less than 10 mL/min or rapidly falling

- **Oxycodone '**as needed' can still be used.
- If a regular opioid is required start a continuous subcutaneous infusion of **alfentanil**. Continue with oxycodone SC as needed for breakthrough pain.

- If alfentanil is not available, then a continuous subcutaneous infusion of oxycodone can be used as an alternative but this can accumulate and so may require additional dose reduction and close monitoring to ensure opioid toxicity is not developing.
- Seek specialist palliative care advice regarding alfentanil conversion ratios and doses.

Request a medical review if patient remains symptomatic despite as needed medication

For in depth guidance on opioids and opioid conversions refer to further guidance below.

Delirium

- Consider reversible causes.
- Non-pharmacological management is the most important component of treatment.
- Beware of increased sensitivity to sedatives and so may need to consider increasing dosing intervals.

Nausea and vomiting

- Choice of antiemetic should be guided by the cause.
- Doses may need to be reduced and dosing intervals increased.
- **Uraemic nausea** (more likely at GFR less than10 mL/min):
    - **Haloperidol** and **levomepromazine** - start at a low dose and titrate slowly. Suggested starting doses:
        - Haloperidol 0.5 to 1 mg PO/SC daily
        - Levomepromazine
            - PO - 3 to 6.25 mg (¼ of a 25 mg tablet) daily or
            - SC - 2.5 to 6.25 mg daily
    - **5HT$_3$ antagonists** e.g., **granisetron** and **ondansetron** can also be used, caution - side effect is constipation.

Pruritis

- End stage renal failure is associated with dry skin.
- Emollients such as **Diprobase®** or **Zeroderm®** are suggested.
- Sedative antihistamines can be useful for uraemic itch (associated with GFR less than 10 mL/min)
    - **Chlorphenamine** 4 mg as needed up to 4 times a day

2. Symptom management for patients in the last days of life

The below guidance is for SC medication. If the patient is able to take oral medication, *please refer to above guidance Palliative patients in the last weeks/months of life*

Pain

Consider reversible causes and non-pharmacological management.

Pharmacological management

- Usually leave **buprenorphine** and **fentanyl** transdermal patches in place (to avoid reduction in background analgesia) and continue to change as usual.
    - Continue to use as needed analgesia. This is usually SC oxycodone.
    - If an increase in background analgesia is needed a continuous subcutaneous infusion (CSCI) of oxycodone may be added. Please seek specialist advice if unsure.
- If opioid naïve:
    - **SC oxycodone**
        - Usual starting dose - 1 to 2mg SC as needed. Minimum dosage interval 2 hours is preferred. A 1-hour dosing interval could be prescribed but because of the risk of accumulation patients should be monitored for signs of opioid toxicity.
        - Request a medical review if patient remains symptomatic despite as needed medication.
        - Consider starting a CSCI, if 2 or more as needed doses are given and effective in 24 hours.
            - If GFR 10 to 30 mL/min suggest CSCI of **oxycodone** (PO: SC is 2:1)
            - If GFR less than 10 ml/min or rapidly falling suggest:
                - Seek specialist palliative advice
                - Continuous SC infusion of oxycodone can be used but this can accumulate and so may require additional dose reduction and close monitoring
                - Alfentanil is an alternative
            - Continue 'as needed' oxycodone SC (1/6th to 1/10th of the background equivalent oxycodone 24 hour dose daily dose).

Agitation/Delirium

- Consider reversible causes.
- Non drug management is the most important strategy
- **Pharmacological Management:**
    - **Midazolam** (10mg/2mL) 2.5 mg to 5mg SC as needed (minimum dosage interval 30 minutes). It is suggested that a dose range is prescribed.

  OR

    - **Haloperidol** (5mg/mL) 500 micrograms to 1 mg SC as needed (minimum dosage interval 30 minutes to one hour). It is suggested that a dose range is prescribed. Maximum 5 mg/24 hrs.
    - For both midazolam and haloperidol review effectiveness after 30 mins.
    - Consider administering: the same dose, a higher dose or alternative medication for agitation following re-assessment. If unsure what to do seek senior review/specialist advice.
    - Consider commencing a CSCI if two or more SC doses are given with good effect on a symptom within 24 hours. Some patients require a CSCI sooner than 24 hours if they have received two or more effective doses within a few hours.

Nausea and vomiting

- If already on effective antiemetic this can be continued. If unable to take oral medication convert to SC route. The conversion from oral to SC is 1:1 for most antiemetics. Seek advice if unsure.
- For those with new or anticipated symptoms:
    - **Haloperidol** (5mg/mL), start with a low dose e.g., 500micrograms SC as needed (minimum dosage interval 30 minutes).
    - **Levomepromazine** (25mg/mL), start with 2.5mg to 6.25mg SC as needed (minimum dosage interval 1 hour).
    - For persistent symptoms both drugs have relatively long half-lives so may be given as intermittent injections (once or twice daily) or given by CSCI.

Retained respiratory secretions in the last days of life

- Non-pharmacological management such as positioning is the most important component of treatment.
- If non-pharmacological measures are not helpful then assess the effectiveness of '**as needed'** anti-secretory medication. (Note, these cause secretions to be lower in volume but thicker, so if patients are still able to cough, they may make expectorating more difficult).
- Avoid hyoscine hydrobromide because of its central sedating effects.
- **Hyoscine butylbromide** is the favoured drug treatment as it is non-sedating,
    - Hyoscine butylbromide (20mg/mL) 20mg SC **as needed** (minimum dosage interval of 1 hour).
    - Note, it is short-acting, therefore if effective consider a continuous subcutaneous infusion (typical starting dose 60mg SC over 24 hours).
    - Ensure good mouth care as dry mouth is a side effect.

Pruritis

- Treat dry skin with emollients such as **Diprobase®** or **Zeroderm®**
- **Midazolam** for sedation if causing distress and sedation acceptable.

Further guidance

- Yorkshire and the Humber End of Life Care Group: A Guide to Symptom Management in Palliative Care. Version 8 (2023).
- Symptom Management Guidance in the Last Days of Life Last Days of Life (leedsth.nhs.uk)
- The Leeds Opioid Conversion Guide for Adult Palliative Care Patients
- Specialist Community Palliative Care Team:
    - Wheatfields Hospice: 0113 2787249
    - St Gemma's Hospice 0113 2185500
    - **or** the palliative medicine consultant on call via switchboard OOH

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