

# Symptom control in patients with chronic kidney disease/ renal impairment

## Introduction

- This guideline covers modifications to standard symptom control that are recommended in patients with chronic kidney disease or acute renal impairment.
- Renal impairment is common in patients with diabetes, cardiovascular disease or cancer (from disease or treatment eg. chemotherapy, obstructive uropathy, myeloma).
- Symptom control is complicated by delayed drug clearance, dialysis effects and renal toxicity associated with commonly used medication (eg. NSAIDs).
- 50% of dialysis patients have pain. Depression and other symptoms are common.

## Assessment

Chronic kidney disease (CKD)		
<b>CKD stage 1</b>	Normal renal function	
<b>CKD stage 2</b>	Mild impairment (eGFR 60-89 ml/min)	Asymptomatic
<b>CKD stage 3a</b>	Moderate impairment (eGFR 45-59 ml/min)	Asymptomatic
<b>CKD stage 3b</b>	Moderate impairment (eGFR 30-44 ml/min)	Anaemia, fatigue, muscle cramps
<b>CKD stage 4</b>	Severe impairment (eGFR 15-29 ml/min)	In addition: anorexia, nausea, insomnia, neuropathy, gout
<b>CKD stage 5</b>	End stage renal disease (eGFR < 15 ml/min)	In addition: itch, headache, cognitive impairment; death

- Pain is common and associated with many of the complications of advanced CKD.
- Look for multiple types of pain and/or other symptoms due to:
  - renal disease (polycystic kidneys, liver cysts, amyloid).
  - co-morbidity (diabetes, vascular disease, angina).
  - dialysis (abdominal pain in peritoneal dialysis, headache, fistula problems).
  - other pathology (cancer, osteoarthritis).
- Pain in patients with chronic kidney disease:
  - Musculoskeletal pain.
    - Muscle spasm, cramps, restless leg syndrome.
    - Osteoporosis.
    - Renal osteodystrophy.
    - Osteomyelitis, disc infection.
    - Carpal tunnel syndrome.
  - Neuropathic pain – renal or diabetic peripheral neuropathy.
  - Ischaemic pain – peripheral vascular disease, vasculitis.
  - Calciphylaxis – complex pain caused by tissue ischaemia due to calcification of small vessels/ subcutaneous tissue.
- Identify chronic pain (needs regular analgesia) and any intermittent/ episodic pain as this often needs managed separately with short acting analgesics/ non-drug measures. (see: Pain management, Pain assessment)
- Some drugs will be cleared by dialysis; an extra dose during or after dialysis may be needed.
- Patients are often on multiple drugs with a high risk of interactions/side effects.

## Management

- Much of the advice in the palliative care guidelines is applicable to patients with renal disease. See table for renal prescribing advice.
- There is another renal palliative care guideline: Last days of life (renal).
- Choice and dose of opioids depends on the degree of renal impairment.
- Mild renal impairment; use lower starting doses of renally excreted opioids (codeine, dihydrocodeine, morphine, diamorphine, oxycodone) and slower titration.
- Stages 3-5 chronic kidney disease; use a modified WHO analgesic ladder (see page 2).

## Pain management in renal disease

### STEP 1: Mild Pain

**Paracetamol +/- adjuvant analgesic**  
1g, qds

Assess pain fully before treatment.  
Ask the patient regularly about their pain.  
Record a pain score.  
(See: Pain management, Pain assessment)

### STEP 2: Mild to moderate pain

**Paracetamol + low dose opioid +/- adjuvant analgesic**

- Low dose oxycodone or tramadol can be used; if GFR > 30ml/min – reduce dose and frequency, monitor closely for side effects (drowsiness, hallucinations, confusion).

### STEP 3: Moderate to severe pain

**Paracetamol + selected opioid +/- adjuvant analgesic**

- Fentanyl patch – opioid of choice for stable pain; well tolerated, not renally excreted or removed by dialysis. Can accumulate with longer term use; monitor and adjust dose. Treat breakthrough pain with an oral opioid as in Step 2.
- Alfentanil injection– used as a SC injection, sublingually, or as a subcutaneous infusion. (see: Fentanyl patches, Alfentanil)
- Methadone – titration complex so only use on specialist advice.

### Adjuvant analgesics (for prescribing advice see table below)

**Antidepressant or anticonvulsant:** for nerve pain

Start at a low dose; titrate slowly. No clear difference in efficacy.

- amitriptyline (side effects: confusion, hypotension, dry mouth)
- gabapentin (side effects: sedation, tremor); adjust dose for renal function
- sodium valproate
- carbamazepine
- clonazepam

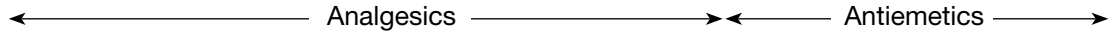
**Ketamine:** complex neuropathic pain including calciphylaxis  
(see: Ketamine on website; use is unlicensed)

### Seek advice:

- ◆ Severe pain.
- ◆ Pain not responding to treatment.
- ◆ Dose of opioid has increased rapidly but patient is still in pain.
- ◆ Episodes of acute severe pain.
- ◆ Pain worse on movement.

### Symptom control in renal disease (see prescribing advice tables)

- Depression – common and underdiagnosed. (see: Depression)
  - SSRI antidepressant (eg sertraline) is often used.
- Dialysis associated symptoms (hypotension, nausea, cramps, fatigue) – review dialysis prescription.
- Hiccups – (see: Hiccup)
  - Treat any other underlying cause eg gastro-oesophageal reflux.
  - Prokinetic antiemetic (metoclopramide or domperidone).
  - Baclofen – adjust dose for renal function.
- Itch – common and distressing. (see: Itch)
  - Good skin care with regular use of emollients +/- antihistamine.
  - Ondansetron has been used for intractable uraemic itch; 4-8mg twice daily.
- Nausea/ vomiting – assess likely cause (see: Nausea/ vomiting).
  - Gastric stasis is common – treat with metoclopramide (short term) or domperidone
  - Levomepromazine is a useful broad spectrum antiemetic; use low doses and monitor for hypotension.
  - Cyclizine worsens dry mouth in patients on fluid restriction.
- Restless leg syndrome – affects 20-40% of uraemic patients.
  - Clonazepam orally starting at 0.5mg nocte.
  - Gabapentin 100-300mg nocte (adjust dose for renal function).
- Other common symptoms include anorexia, constipation and fatigue – see relevant palliative care guidelines.



### Prescribing advice for palliative care patients with chronic kidney disease/renal impairment – Part 1

For further information see: other Palliative Care Guidelines & Last days of life (renal) guideline

Drug	Renal Impairment			Dialysis Clearance		Comments
	Mild: GFR 60-89 ml/min	Moderate: GFR 30-59 ml/min	Severe: GFR 15-29ml/min	HD	PD	
Paracetamol (oral)	Normal starting dose	6 hourly dosing	6-8 hourly dosing	Cleared	No	Safe non-opioid
NSAIDs	50-75% normal dose CAUTION	AVOID	AVOID	No	No	Nephrotoxic, ↑ risk of GI bleed (platelet dysfunction). Only used when patient is dying.
Codeine/ dihydrocodeine	Normal starting dose (monitor closely)	AVOID or use small dose and titrate slowly	AVOID codeine; dihydrocodeine: v small dose, slowly titrated	Unknown	Unknown	Metabolites accumulate. Reports of severe toxicity in CKD stage 4/5.
Tramadol	Normal starting dose	50 -100mg, oral, 12 hourly (Max 200 mg / 24 hrs)	CAUTION	Yes	Unknown	Use 50mg orally, 12 hourly for dialysis patients. Risk of confusion/ delirium. Drug interactions. Check BNF.
Nefopam (NHS Lothian only)	Restricted use; if eGFR < 45ml/min	30mg, oral, 6-8 hourly	30mg, oral, 8 hourly	Unlikely	Unknown	Can accumulate if on dialysis. Full dose ≈ fentanyl 12 microgram patch.
Morphine/ diamorphine	75% normal dose	50% normal dose, 6 hourly	AVOID or use very small doses – seek advice	Yes Occasionally – post dialysis dosing.	No	CNS depot clears slowly in HD. Metabolites accumulate in PD. Single dose post HD can be used. Monitor closely.
Oxycodone (see: guideline)	Normal starting dose	50-75% normal dose, reduce dose frequency to 8 hourly	AVOID or use very low dose & monitor closely.	Unknown	Unknown	↑ half life, and ↓ excretion of metabolites. Avoid modified release preparation.
Fentanyl (see: guideline)	Normal starting dose	75% normal dose	50% normal dose	No	No	Can accumulate after longer term use; monitor and adjust dose.
Alfentanil (see: guideline)	Normal starting dose	Normal starting dose	Normal or reduced starting dose	No	No	Short acting.
Methadone	Normal starting dose	Normal starting dose	50% normal dose	No	No	Seek specialist advice re dose and titration.
Metoclopramide	Oral starting dose (10mg, 8 hourly)	75% dose, 8 hourly	50% dose, 8 hourly	Yes	No	Reduced clearance; more risk of extrapyramidal side effects.
Domperidone	Oral starting dose (10mg, 6-8 hourly)	Normal starting dose	Normal starting dose	Unknown	Unknown	Dry mouth. More CNS side effects.
Cyclizine	Oral starting dose (25mg, 8 hourly)	Normal starting dose	Normal starting dose	Unknown	Unknown	Hypotension, tachyarrhythmias reported.
Haloperidol	Oral starting dose (1mg, nocte)	Normal starting dose	50% normal dose	No	No	Lowers seizure threshold, ↑risk cardiac arrhythmias, may accumulate.
Levomopromazine	Oral starting dose (3mg, nocte)	Start low & titrate	Start low & titrate	Unknown	Unknown	Sedation at higher doses. Causes hypotension. Lowers seizure threshold.
Ondansetron/ Granisetron	Normal starting dose	Normal starting dose	Normal starting dose	No	Unknown	May help itch, constipating.

### Prescribing advice for palliative care patients with chronic kidney disease/ renal impairment – Part 2

For further information see: other Palliative Care Guidelines & Last days of life (renal) guideline

Drug	Renal Impairment			Dialysis Clearance		Comments
	Mild: GFR 60-89ml/min	Moderate: GFR 30-59 ml/min	Severe: GFR 15-29 ml/min	HD	PD	
Diazepam	Normal starting dose	Start lower	Start lower & titrate	No	No	Used for insomnia, anxiety and muscle spasm/ myoclonus.
Lorazepam	0.5mg, oral, 6 hourly or nocte	Start lower	Start lower & titrate	No	Unlikely	Start lower and titrate dose for all benzodiazepines. Metabolites excreted renally and protein binding is reduced.
Midazolam SC	2.5mg,oral, 1-2 hourly	Start lower	Start lower & titrate	No	Unlikely	
Temazepam	Normal starting dose	Max dose 20mg, oral	Max dose 10mg, oral	No	Unknown	
Clonazepam	0.5mg, oral, nocte	Start low dose & titrate	Lower dose & titrate	No	Unknown	
Gabapentin	300mg, oral, 12 hourly	300mg, oral, nocte	300mg oral, alternate days.	Yes: 300mg post HD	Probable	Parent drug accumulates. Withdraw gradually, over a week.
Sodium valproate	Oral starting dose 100-200mg, 12 hourly	Normal starting dose	Normal starting dose	No	Unknown	Well tolerated, avoid if liver disease. Titrate slowly .
Carbamazepine	Oral starting dose 100-200mg, 12 hourly	Normal starting dose	Normal starting dose	No	No	Drug interactions. Check BNF.
Amitriptyline	Oral starting dose 10mg, nocte	Normal starting dose	Normal starting dose	No	No	Drug interactions, side effects, and contraindications can limit use. Titrate slowly.
Citalopram	Normal starting dose	Normal starting dose	Use with caution	No	No	Check BNF for drug interactions (eg. with tramadol). Start at lowest dose and titrate carefully in CKD stages 4/5.
Sertraline	Normal starting dose	Normal starting dose	Normal starting dose			
Mirtazapine	Normal starting dose	Normal starting dose	Start at low dose and monitor closely.			
Baclofen	5mg, oral, 8 hourly	5mg, oral, 12 hourly	5mg, oral, daily		Unknown	Withdraw gradually.
Ketamine oral or SC (see guideline on website; use is unlicensed)	Oral starting dose 5-10mg, 6 hourly	Normal starting dose	May be tolerated in standard doses but start at low dose and monitor closely.	No	Unknown	Little information available. Less than 2-3% of ketamine is excreted unchanged. Can accumulate. Seek specialist advice.
Ranitidine	Normal starting dose	Normal starting dose	50-100% dose	Yes	Unknown	Accumulates.
Fluconazole	Normal starting dose	Normal starting dose	50% dose	Yes	Yes	Drug interactions. Check BNF.
Hyoscine butylbromide (Buscopan) SC	20mg SC, oral, 1-2 hourly	Normal starting dose	Normal starting dose	Unknown	Unknown	Use for respiratory secretions, bowel colic, bladder spasms.

← Benzodiazepines → ← Adjuvants → ← Anti-depressants → ← Other →

**SIGN 103 recommends that creatinine clearance estimated by the Cockcroft-Gault formula be used for drug dosing as published recommendations are based on this prediction equation for GFR. The tables are a guide to dose adjustments. Each patient should be assessed and monitored individually.**

## Measuring renal function

- Prediction equations are more accurate than serum creatinine or 24-hour urine creatinine clearance.
- The equations are affected by age, sex and weight so are less reliable in older people and those with cachexia, obesity or oedema.
- eGFR is reported in routine laboratory results but is less accurate at values of > 60ml/ min.
- Cockcroft-Gault formula is recommended in drug manufacturer's information.

$$\text{GFR (ml/min)} = \frac{(140 - \text{Age}) \times \text{IBW (kg)} \times 1.23 \text{ (if male)} \times 1.04 \text{ (if female)}}{\text{serum creatinine (micromoles/l)}}$$

Ideal Body Weight (IBW) is recommended for the calculation particularly if the patient is oedematous or obese.

= male 50 + 2.3kg per inch over 5 feet

= female 45.5 + 2.3kg per inch over 5 feet

## Key references

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