# Guidelines for Medicines Optimisation in Patients with Acute Kidney Injury in Secondary Care


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# Guidelines for Medicines Optimisation in Patients with Acute Kidney injury in Secondary Care

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Thanks to the UK Renal Pharmacy Group, who developed the original AKI pharmacists' toolkit and allowed us to tailor this specifically for the Think Kidneys programme.

This document is being issued as a draft after some small scale piloting. We would welcome comments which would help improve future versions. Please e-mail any comments to Julie Slevin at julie.slevin@renalregistry.nhs.uk

## 1. Introduction

Acute kidney injury (AKI) is the sudden loss of kidney function over a period of hours or days. Since the kidneys are one of the major excretory pathways for the removal of drugs from the body, this sudden loss of kidney function can have major implications for a patient's prescribed medication regime.

The term 'nephrotoxic' should be used with caution. Few medications truly have direct toxic effects on the kidneys, but several have the potential to impair renal function if used under certain circumstances, such as where the patient has a degree of chronic kidney disease in conjunction with hypovolaemia and acute illness. Under these circumstances, continued use of these medications may further exacerbate an episode of AKI.

The Think Kidneys Programme has taken the decision to avoid the use of the term nephrotoxic.

Many medications are cleared via the kidneys, so have the potential to accumulate during an episode of AKI. The result of this may be a further deterioration in kidney function, or there may be other adverse effects such as bone marrow or CNS toxicity. Hence it is necessary to review the use of these medications and amend the doses appropriate to the level of the patient's renal function.

When a patient is either admitted with AKI, or develops AKI during an admission episode, a thorough review of medication is required in order to:

- Eliminate the potential cause/risk/contributory factor for AKI
- Avoid inappropriate combinations of medications in the context of AKI
- Reduce adverse events
- Ensure that doses of prescribed medication are appropriate for the patient's level of renal function
- Ensure that all medicines prescribed are clinically appropriate

Points to note and questions to ask in the medicines management of these patients include:

- Which medications should be suspended?
- Which medications should not be suspended?
- Which medications may be used with caution?
- Are there any alternative therapeutic options?

If a medication must be used, in order to minimise harm:

- Amend doses appropriate to the patient's level of renal function
- Monitor blood levels of drugs wherever possible
- Keep course of treatment as short as possible
- Discuss treatment with pharmacist/microbiologist

Ensure appropriate information and advice is given on discharge:

- From the ICU to the ward
- From the ward to the GP (and care home if required)
- From the ward to the patient and their family/carers

## 2. Acute kidney injury – Medication Optimisation Pro forma

In order to optimise the prescribing of medications to a patient with AKI, the following points should be considered:

1. Is the patient receiving medication which may impair renal function?

   - Contrast media
   - ACE Inhibitor
   - NSAIDs
   - Diuretics
   - Angiotensin receptor blocker

   Consider withholding these agents during an episode of AKI.

2. Medication

   - Is the patient taking any other medications which could exacerbate AKI? Consider withholding them.
   - Is the patient prescribed any medications where the dose needs to be amended in renal impairment?
   - Amend medication doses appropriate to the patient's degree of renal impairment.
   - In house guidelines for drug use in AKI are recommended for example for. antibiotics, analgesia, contrast media, chemotherapy.

3. Educate the patient before discharge about which medications to restart and when, which medicines to avoid etc.

4. Ensure comprehensive information on which medications to restart and when is communicated to the GP or next care setting.

Other useful reference sources to facilitate dose adjustment in AKI include:

| Group of medicines | Suggested guidelines |
|---|---|
| Anti-retrovirals /HAART | National Institute of Health HIV/AIDS Treatment Guidelines |
| Chemotherapy | North London Cancer Network Guidelines |
| Mental Health | The Maudsley Prescribing Guidelines |
| General medications | The Renal Drug Database |
| General medications | Manufacturers' Summary of Product Characteristics |

## 3. High risk medicines and actions

The following list of medications is not exhaustive. Remember to consider ALL medications including any 'usual' long term medications. Remember to check medication history thoroughly and ask about 'over the counter' preparations, herbal remedies/teas and alternative therapies. Check recreational use of drugs (cocaine, ketamine etc) as these have been implicated in rhabdomyolysis.

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| **Analgesics** | | | |
| NSAIDs / COX II inhibitors | Acute interstitial nephritis. Altered haemodynamics within the kidney leading to underperfusion and reduced glomerular filtration | Avoid | Avoid taking whilst at risk of hypovolaemia |
| Opioid analgesics | Accumulation of active metabolites (especially morphine, pethidine and codeine) – increased incidence of CNS side effects & respiratory depression | Avoid XL / SR preparations.<br><br>Reduce dose and use short acting preparations wherever possible | May accumulate in acute kidney injury. Seek advice if at risk of dehydration<br><br>If needed, use opiates with minimal renal excretion e.g. fentanyl, oxycodone, hydromorphone |
| Tramadol | Accumulation leading to increased sedation, mental confusion and respiratory depression | Reduce dose<br><br>Avoid XL preparations | May accumulate in acute kidney injury |
| Benzodiazepines | Accumulation of drug & active metabolites leading to increased sedation & mental confusion | Reduce dose | |
| **Antibiotics / Antifungals / Antivirals** | | | |
| Aciclovir | Crystal nephropathy<br><br>Accumulates in reduced renal function leading to mental confusion, seizures<br><br>Avoid rapid infusions. Infuse IV over one hour | Reduce dose | Encourage patient to drink plenty<br><br>Beware if patient is at risk of dehydration |
| Aminoglycosides | Tubular cell toxicity, ototoxicity | Avoid if possible. If use is unavoidable, reduce dose &/or increase dosing interval<br><br>Monitor drug levels and renal function 2 – 3 times per week | |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Amphotericin IV – Fungizone® | Tubular cell toxicity, Hypokalaemia<br><br>Avoid rapid infusion | Avoid<br><br>Consider Ambisome® preparation | |
| Co-trimoxazole | Crystal nephropathy<br><br>Hyperkalaemia | Reduce dose<br><br>Seek medical advice if patient is fluid restricted and requiring IV infusion preparation | Encourage patient to drink plenty<br><br>Beware if patient is at risk of dehydration |
| Fluconazole | Accumulation leading to acute mental confusion, coma, seizures | Reduce dose<br><br>Check for drug interactions that may be contributing to AKI | Interactions, e.g. withholding statins as risk of rhabdomyolysis |
| Ganciclovir IV | Crystal nephropathy<br><br>Accumulates in reduced renal function leading to neutropenia, anaemia and thrombocytopenia<br><br>Avoid rapid infusions | Reduce dose | Monitor renal function and full blood count |
| Penicillins | Acute interstitial nephritis<br><br>Glomerulonephritis<br><br>Accumulation leading CNS side effects including seizures | Reduce dose | |
| Teicoplanin | Accumulation leading to CNS excitation, seizures, & blood dyscrasias | Reduce dose<br><br>Monitor levels | |
| Tetracycline | Acute interstitial nephritis<br><br>Accumulation leading to renal dysfunction, benign cranial hypertension, jaundice, hepatitis | Avoid | |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Trimethoprim | Increased risk of hyperkalaemia<br><br>Acute interstitial nephritis (rare)<br><br>Interferes with tubular secretion of creatinine leading to a rise in serum creatinine (without affecting actual GFR), which can make the diagnosis of AKI more difficult<br><br>Accumulation leading to hyperkalaemia (particularly with high doses), nausea and vomiting | Avoid or reduce dose | Studies have shown that elderly patients prescribed trimethoprim have a 12 x greater risk of developing life-threatening hyperkalaemia if already taking spironolactone, a 7-fold increased risk of life-threatening hyperkalaemia, and a 1.5 x increased risk of sudden death if already taking an ACEI or ARB. |
| Valganciclovir | Accumulates in reduced renal function leading to neutropenia, anaemia and thrombocytopenia | Reduce dose | Monitor renal function and full blood count |
| Vancomycin | Acute interstitial nephritis<br><br>Accumulation leading to renal toxicity, ototoxicity | Reduce dose / increase dose interval<br><br>Monitor levels | |
| **Antiepileptics (including drugs used for neuropathic pain)** | | | |
| Gabapentin | Accumulation in kidney impairment – increase in CNS side effects | Reduce dose | Monitor for excessive sleepiness or confusion |
| Phenytoin | Acute interstitial nephritis<br><br>Risk of phenytoin toxicity if patient has low serum albumen levels | Monitor levels<br><br>Correct phenytoin levels for uraemia and low serum albumen. | |
| Pregabalin | Accumulation leading to increase in CNS side effects | Reduce dose | Monitor for excessive sleepiness or confusion |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Levetiracetam | Accumulation leading to increase in CNS side effects | Reduce dose | |
| Antihypertensives<br><br>(including Ca-channel blockers, α-blockers, β-blockers etc) | Hypotension<br><br>May exacerbate renal hypoperfusion<br><br>Longer acting, renally cleared drugs may accumulate in renal impairment | Consider withholding / reduce dose depending on clinical signs | Some patients who continue taking β-blockers during an episode of AKI have developed complete heart block and required temporary pacing |
| ACEI / ARBs / Aliskiren | Altered haemodynamics<br><br>Hyperkalaemia | These drugs can impair the kidneys' ability to maintain GFR when perfusion is compromised<br><br>In some situations, e.g. heart failure with a decent blood pressure; continuing them might actually be helpful<br><br>Seek nephrologist advice if undergoing contrast procedure or at risk of AKI.<br><br>NICE guidelines recommend that ACEI/ARBs be withheld pre-contrast exposure | Avoid taking whilst at risk of hypovolaemia<br><br>Monitor BP<br><br>If patient is hypertensive, consider alternative antihypertensive agents, eg, calcium channel blockers, alfa-blockers, beta-blockers if appropriate |
| Contrast Media | Direct tubular toxic effect<br><br>Incidence of CIN higher with high- & iso-osmolar contrast media, and lower with low-osmolar, non-ionic contrast media | Seek nephrologist advice if undergoing contrast procedure or at risk of AKI | Ensure patient is well hydrated pre-exposure to contrast, PROVIDED the patient is able to tolerate IV fluids<br><br>This is NOT recommended for patients with congestive heart failure pre-coronary angiogram<br><br>IV sodium chloride or sodium bicarbonate are most effective |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Thiazide & Loop Diuretics | Hypoperfusion of the kidneys<br><br>Loop diuretics (furosemide & bumetanide) preferred as thiazides less effective if GFR very low<br><br>However thiazides can potentiate the effects of loop diuretics<br><br>Use of loop diuretics depends on volume state<br><br>Higher doses may be needed to achieve a diuresis in patients with fluid overload. Over-diuresis causing fluid depletion can cause or exacerbate AKI | Monitor and adjust dose as necessary | Dose reduction may be required<br><br>Seek medical advice if at risk of hypovolaemia |
| Diuretics – potassium sparing | Hyperkalaemia<br><br>Hypoperfusion | Avoid | Dose reduction may be required<br><br>Beware if patient at risk of hypovolaemia |
| Hypoglycaemic agents | Accumulation leading to hypoglycaemia | Avoid MR / longer acting agents<br><br>Reduce dose<br><br>Monitor blood glucose levels | |
| Metformin | Lactic acidosis<br><br>Accumulation leading to hypoglycaemia | Avoid if GFR < 30 ml/min<br><br>Seek nephrologist advice if undergoing contrast procedure or at risk of AKI | Avoid taking whilst at risk of hypovolaemia or sepsis |
| **Immunosuppressants (DMARDs, chemotherapy)** | | | |
| Calcineurin inhibitors e.g. ciclosporin, tacrolimus | Increased risk of nephrotoxicity, neurotoxicity and hyperkalaemia | Seek advice of transplant centre regarding monitoring levels and dose adjustment | Seek medical advice / advice from transplant team if at risk of hypovolaemia |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Methotrexate | Crystal nephropathy<br><br>Accumulation increases side effects e.g. excessive bone marrow suppression, mucositis, acute hepatic toxicity, acute interstitial pneumonitis | Avoid<br><br>Monitor levels and consider folinic acid rescue<br><br>Correct fluid balance | May accumulate in reduced renal function<br><br>Avoid if patient is at risk of hypovolaemia |
| **Others** | | | |
| Allopurinol | Acute interstitial nephritis<br><br>Allopurinol and its metabolites accumulate in renal impairment leading to agranulocytosis, aplastic anaemia, thrombocytopenia | Reduce dose | |
| 5 – aminosalicylates | Tubular and glomerular damage | Avoid | |
| Anticholinergic side effect of drugs: Antihistamines, Anti-psychotics, Anti spasmodics | Urinary retention<br><br>Consider as possible cause of drug induced kidney injury | Reduce dose<br><br>Avoid XL preparations | Monitor patient for difficulty in passing urine |
| Ayurvedic medicines | Cases of renal impairment have been reported<br><br>Some ayurvedic medicines also contain heavy metals | Avoid<br><br>Check drug history thoroughly<br><br>Patients may not consider herbal preparations/teas as medicines | Seek medical advice if considering alternative medicines for effects on disease, side effects and possible interactions |
| Bisphosphonates IV | Can cause impaired renal function – especially when given in high doses and short duration infusions | Reduce dose and infuse at correct rate | Advantages of correction of severe hypercalcaemia may outweigh risks<br><br>Seek specialist advice |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Colchicine | Diarrhoea / vomiting causing hypovolaemia<br><br>Exacerbating hypoperfusion if also taking a NSAID | Low doses e.g. 500mcg bd or tds are effective | Short course of 2 -3 days treatment should be followed<br><br>Seek medical advice if diarrhoea and vomiting develops<br><br>Do not use NSAIDs for gout; if Colchicine causes unacceptable adverse effects, consider a short course of corticosteroids |
| Digoxin | Accumulation leading to bradycardia, visual disturbances, mental confusion<br><br>Aggravates hyperkalaemia | Reduce dose<br><br>Monitor drug level | May accumulate in acute kidney injury |
| Herbal preparations | Chinese herbal medicines with aristocholic acid implicated in interstitial nephritis<br><br>Cat's Claw has anti-inflammatory properties and has been implicated in causing AKI and hypotension with antihypertensives<br><br>The toxic effects of herbal remedies to the kidneys may be exacerbated when used with concomitant medicines which can affect kidney function | Some herbal medicines also interact with prescribed medicines e.g. St. John's Wort potentiates the effects of ciclosporin & tacrolimus.<br><br>Avoid<br><br>Check drug history thoroughly<br><br>Patients may not consider herbal preparations/teas as medicines | Seek medical advice if considering alternative medicines for effects on disease, side effects and possible interactions |
| Lipid-lowering agents e.g. fibrates, statins | Rhabdomyolysis | Avoid | Stop if patient develops unexplained/persistent muscle pain |

| Drug | Problem | Action in presence of AKI | Education Points |
|---|---|---|---|
| Lithium | Accumulation leading to nausea, diarrhoea, blurred vision, light headedness, fine resting tremor, muscular weakness and drowsiness, increasing confusion, blackouts, fasciculation and increased deep tendon reflexes, myoclonic twitches and jerks, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor<br><br>Chronic interstitial nephropathy<br><br>Kidney impairment exacerbated in hypovolaemia and in combination with ACE inhibitors / ARB / NSAIDs | Avoid where possible<br><br>Monitor levels<br><br>Seek advice for alternative | Encourage patient to drink plenty<br><br>Seek medical advice if at risk of dehydration<br><br>Be aware that patients on long-term lithium nearly always have a degree of diabetes insipidus and are therefore at serious risk of developing hypernatraemia due to true dehydration when unwell without ready access to adequate water intake<br><br>Be prepared to use high volumes of iv 5% dextrose and monitor serum sodium concentration regularly |
| Nitrates / Nicorandil | Hypotension<br><br>May exacerbate hypoperfusion | Consider withholding / reduce dose depending on clinical signs | Avoid taking whilst at risk of hypovolaemia<br><br>Seek medical advice if at risk |
| **Anticoagulants** | | | |
| Low molecular weight heparins | Risk of accumulation in AKI leading to increased risk of bleeding | Monitor anti-Xa levels and consider reducing dose or switching to an alternative agent as per local guidelines | |
| Warfarin | INR may be raised due to acute rise in urea and warfarin displacement from binding sites | Monitor INR and consider reducing dose or withholding depending on indication for use | Beware if unexplained bruising or bleeding occurs |

## 4. Conclusion

These guidelines are not exhaustive and are only intended to act as an aide memoire to the medicines optimisation of patients with AKI. For further advice, please contact a renal pharmacist or nephrologist.

## Checklist for medicines optimisation in patients with acute kidney injury (AKI) in secondary care

1. **Is the patient on any of the following medications?**

   ACEI ☐

   ARB ☐

   Diuretics ☐

   NSAIDs ☐

   Metformin ☐

   Aminoglycosides ☐

Consider withholding them – discuss with the medical team

2. **Is the patient taking any other medications which could exacerbate AKI?** ☐

Consider withholding them

3. **Is the patient prescribed any medications where the dose needs to be amended in renal impairment?** ☐

Amend doses appropriate to level of renal function

4. **Monitor U&Es & re-assess renal function daily** ☐

5. **Monitor blood levels of relevant drugs e.g. Aminoglycosides** ☐

6. **Ensure the patient is counselled before discharge in regards to which medications to restart and when, and which medications to avoid** ☐

7. **Ensure comprehensive information on which medications to restart and when is communicated via the discharge summary to the GP and/or next care setting** ☐