

## Medication Alert

# Medicines Safety in Renal Impairment

Alert

200

For the attention of:  
For action by:  
For information to:

# Draft

### Purpose of this alert

- To emphasise the importance of appropriate drug dose adjustment in patients with renal impairment
- To identify key drugs requiring caution in renal impairment
- To emphasise the need for recognition of renal impairment, prior to prescribing for at-risk patients

### Background to this Safe Use of Medicines Alert

- Managing drug treatment safely in renal impairment requires a clear understanding of the pit-falls in monitoring renal function and a sound knowledge of the principles of renal drug elimination. See over for further information

### Recommended Action

1. **Estimated GFR (eGFR) should be reviewed for every patient prior to prescription of any drug which is excreted >75% unchanged by the kidneys. Maintenance dosing should then be carefully reviewed if the estimated GFR is <60ml/min**
2. **eGFR should be used in patients with renal impairment to improve drug treatment in the following cases:**
  - Hydration prior to IV contrast media
  - Treatment with non-steroidal inflammatory drugs (NSAIDs)
  - Treatment with ACE inhibitors
  - Dosing with other drugs or drugs with active metabolites with >75% excretion unchanged in urine
3. **Commonly used drugs to consider in patients with e GFR <60ml/min**

Tramadol

Low Molecular Weight Heparin

Allopurinol

Atenolol

Aciclovir

Lithium

Glibenclamide

Fluconazole

Methotrexate

Bezafibrate

Simvastatin

Gentamicin

Vancomycin

Digoxin

Metformin

Sotalol

Norfloxacin

Cephalosporins (except ceftriaxone/cefaperazone)

Augmentin

Amoxicillin

NSAIDs (including COX 2 inhibitors)

ACE-inhibitors

## Estimating renal function:

1. The plasma creatinine is most useful in the clinical setting of *changing* renal function, but it is a poor predictor of GFR.
  - Some drugs interfere with the chromogenic method of creatinine measurement eg. cephalosporins; others interfere with tubular secretion of creatinine eg. cimetidine and trimethoprim or impair creatinine degradation in the gut eg. broad spectrum antibiotics
  - Muscle wasting is common in the elderly, chronically ill and hospitalised patients, leading to lower levels of plasma creatinine for the same GFR and overestimation of GFR, compared to healthy individuals
2. Creatinine Clearance can be derived from plasma creatinine, age and *lean body weight* from the Cockcroft and Gault formula (Nephron; 1976 16: 31-41); or as the estimated GFR (eGFR) from the Modification of Diet in Renal Diseases (MDRD) equation (Ann Intern Med; 1999, 130: 461-470). The eGFR is now routinely provided with a serum creatinine result by most laboratories in NZ
  - Either method will give a similar estimated GFR in most people, but significant differences may occur if the eGFR is >60 ml/min, in oedematous states, extremes of body weight (<40kg or >100kg), children under 18 years of age, pregnancy, and if plasma creatinine is <0.06 mmol/L
  - Both methods may be used for drug dose adjustment in renal impairment, with the above provisos, although the MDRD equation has not been fully validated

**Highlighted points for specific drugs**

**Low molecular weight heparin-accumulates in renal impairment. If e-GFR<30ml/min the daily dose should be halved. For enoxaparin 1mg/kg once daily or 0.66mg/kg twice daily**

**Morphine—accumulation of morphine and its active metabolites occurs rapidly in renal impairment**

**Allopurinol—the toxic metabolite oxypurinol accumulates in renal impairment and the usual daily dose of 300mg must be reduced to 100mg if e-GFR <60ml/min (Hande K et al. Am J Med 1984, 76: 47-56)**

**Metformin– the risk of lactic acidosis is greatly increased in renal impairment (Aust Adverse Reactions Bulletin 2001, 20:2-3)**

**NSAIDs– can significantly worsen renal function, particularly in unstable renal impairment, as can some cephalosporins, when adequate hydration is critical**

**Simvastatin-the risk of myositis and rhabdomyolysis is dose dependent and is significantly increased in renal impairment**

**Sotalol– accumulates in renal impairment with increased risk of torsade de pointes. The risk of arrhythmia may increase approximately 10 fold when prescribed in high doses (>160mg daily) in the presence of renal impairment (Basta M et al. Aust NZ J Med 1996, 26:167-70)**

**ACE-inhibitors and Atenolol– are frequently prescribed in excessive doses in the treatment of hypertension, leading to hypotension, symptomatic bradycardia, heart block and worsening renal function, particularly in the presence of renal impairment**

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These recommendations are based on a review of the currently available information in order to assist practitioners. The recommendations are general guidelines only and are not intended to be a substitute for individual clinical decision making in specific cases

**If you require any further information or wish to provide feedback on this alert, please go to [www.safeuseofmedicines.co.nz](http://www.safeuseofmedicines.co.nz)**

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