



MHRA

Drug Safety Update

October 2019



Prescribing medicines in renal impairment:

Using the appropriate estimate of renal function to avoid the risk of adverse drug reactions

For most patients and most medicines, estimated Glomerular Filtration Rate (eGFR) is an appropriate measure of renal function for determining dosage adjustments in renal impairment. However, in some circumstances, the Cockcroft-Gault formula should be used to calculate creatinine clearance (CrCl). GFR can overestimate renal function compared with CrCl in some patient groups or clinical situations. This overestimation can result in patients receiving higher than recommended doses of their medicine in relation to their renal function.

When to use estimated creatinine clearance

Existing guidance from the BNF advises prescribers to use calculated CrCl rather than eGFR when initiating or adjusting dose in people taking nephrotoxic drugs, elderly patients, and patients at extremes of muscle mass. CrCl should also be considered for dosage adjustment of medicines that are substantially renally excreted and have a narrow therapeutic index.

In particular, CrCl should always be used to guide dose adjustment for direct-acting oral anticoagulants (DOACs; apixaban, Dabigatran, etexilate, edoxaban ▼, and rivaroxaban ▼). Use of eGFR for dosing of DOACs is known to increase risk of bleeding events as a consequence of overestimating renal function.

Other medicines that are largely renally excreted and have a narrow therapeutic index include digoxin and sotalol.

Calculation of creatinine clearance

It is normal to calculate CrCl based on the Cockcroft-Gault formula rather than measuring it via 24-hour urine collection. Applications such as <https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation> provide the ability to use adjusted body weight, ideal body weight, or actual bodyweight as appropriate when calculating the Cockcroft-Gault CrCl value.

Harm related to incorrect renal impairment calculations

A recent cross-sectional study of data from 80 general practices in the UK1 reviewed the application of prescribing recommendations in older people with reduced kidney function. Prescribing of drugs outside recommendations for use in patients with reduced kidney function was widespread for the 8 drugs analysed. The prescribed dose was too high for kidney function in up to 40% of people aged 65 years and older, and up to 80% of people aged 85 years and older. Use of eGFR overestimated kidney function for up to 28% of those aged 65 years and older, and up to 58% of those aged 85 years and older.

Advice for healthcare professionals

Creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault formula to determine dosage adjustments for:

- direct-acting oral anticoagulants (DOACs)
- patients taking nephrotoxic drugs (examples include vancomycin and amphotericin B)
- elderly patients (aged 75 years and older)
- patients at extremes of muscle mass (BMI <18 kg/m² or >40 kg/m²)
- patients taking medicines that are largely renally excreted and have a narrow therapeutic index, such as digoxin and sotalol

When dose adjustment based on CrCl is important and no advice is provided in the relevant BNF monograph, consult the Summary of Product Characteristics healthcare professionals