renal failure, both acute and chronic, is caused by loss of function of nephrons. In chronic kidney disease (CKD) this process is usually gradual with permanent loss of kidney function over time. Although renal medicine is a speciality in its own right, most clinical pharmacists will regularly encounter patients with compromised renal function. It is therefore essential to have a basic understanding of creatinine concentrations. Most standard references still use Cockcroft and Gault when offering advice on drug dosing. Use of the MDRD equation in this case can lead to potentially dangerous dosing errors.

Impact of CKD on medication
As renal function declines, medicines eliminated by the kidneys show reduced clearance and a prolonged plasma half-life.

Monitoring renal function
Creatinine is almost exclusively eliminated by the kidneys and has proved to be a useful surrogate for estimating renal function. However, serum creatinine concentrations can be influenced by factors such as age, gender, race, weight and even diet. The “Cockcroft and Gault” and “Modification of diet in renal disease” (MDRD) equations are used to determine glomerular filtration rate (GFR) — see Box 1 (p180). Because they use different parameters they can produce different results. It is therefore essential to understand when to use each equation.

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How to approach prescriptions for patients with renal impairment


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Impact of CKD on medication
As renal function declines, medicines eliminated by the kidneys show reduced clearance and a prolonged plasma half-life.
Medicines metabolised to inactive compounds or excreted by non-renal routes are not affected; thus normal doses can be used.

It is also necessary to consider the therapeutic index of medicines used for renally impaired patients. Medicines that are renally excreted but have a wide therapeutic index are unlikely to be problematic in clinical practice. Medicines that are cleared renally and have a narrow therapeutic index (eg, aminoglycosides and vancomycin) have little safety margin and require careful dose adjustment.

Medicines for CKD When reviewing a prescription, the medicines prescribed can sometimes offer clues to the patient’s renal status. Commonly prescribed medicines for patients with CKD are listed in Box 3.

Renal replacement therapy Ultimately, when the kidneys fail it is necessary to replace their critical functions with artificial methods. Types of renal replacement therapy (RRT) include haemodialysis, peritoneal dialysis, and haemodiafiltration. Depending on their properties, medicines may be removed from the bloodstream by RRT. Drug molecules that are not bound to plasma proteins, or that have a low molecular weight, high water solubility or low volume of distribution, tend to be cleared more rapidly by RRT. Depending on how well a medicine is dialysed and the type of RRT, additional doses or even administration post-RRT can be required to avoid subtherapeutic levels. Specialist reference texts should be consulted when offering dosing advice for patients receiving RRT.

Some patients with established renal failure (CKD stage 4–5) have sufficient residual renal function to support life. They can therefore survive with little external renal support. However, it is extremely important to avoid nephrotoxic medicines for such patients.

Transplantation challenges Transplant recipients pose different challenges for the clinical pharmacist. They have nearly normal renal function, although this can vary significantly within and between such patients. It is therefore advisable to establish their current renal function. Furthermore, nephrotoxic drugs should be avoided or used only under specialist care.

Immunosuppressants prescribed to prevent rejection have narrow therapeutic windows and numerous drug interactions. This must be borne in mind when clinically checking prescriptions for renal transplant patients.

Information sources Although most clinical pharmacists head straight for ‘The Renal Drug Handbook’, it is wise to start by checking the most readily available resources. A 2005 review of four common reference sources highlighted a

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### Box 1: Equations for estimating glomerular filtration rate

Cockcroft and Gault equation

\[
\text{Creatinine clearance, } \text{CrCl (ml/min)} = F \times \frac{(140 - \text{age (years)}) \times \text{weight (kg)}}{\text{Serum creatinine (μmol/L)}}
\]

F = 1.23 in males and 1.04 in females

Modification of diet in renal disease (MDRD) equation

\[
eGFR (\text{ml/min/1.73m}^2) = 175 \times \left(\frac{\text{SrCr (μmol/L)}}{88.4}\right)^{-1.154} \times \text{age (years)}^{-0.203}
\]

x 0.742 if female

x 1.21 if African or African Caribbean

Normal GFR is roughly 100ml/min/1.73m²

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### Box 2: Classifying CKD

<table>
<thead>
<tr>
<th>STAGE DESCRIPTION</th>
<th>eGFR (ml/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Normal or increased eGFR (&gt;90ml/min/1.73m²) and other evidence of renal damage</td>
<td></td>
</tr>
<tr>
<td>2 Mildly decreased eGFR (60–89ml/min/1.73m²) and other evidence of renal damage</td>
<td></td>
</tr>
<tr>
<td>3 Moderately decreased eGFR (30–59ml/min/1.73m²)</td>
<td></td>
</tr>
<tr>
<td>4 Severely decreased eGFR (15–29ml/min/1.73m²)</td>
<td></td>
</tr>
<tr>
<td>5 Patient on dialysis or established renal failure (eGFR&lt;15ml/min/1.73m²) — formerly “end-stage renal failure”</td>
<td></td>
</tr>
</tbody>
</table>

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### Box 3: CKD medicines

The medicines most commonly prescribed for patients with renal disease include:

- **Antihypertensives** — eg, angiotensin-converting enzyme inhibitors, calcium channel blockers, alpha-blockers, beta-blockers. Often more than three such medicines are needed
- **Phosphate binders** — eg, calcium carbonate, sevelamer, lanthanum, calcium acetate
- **Treatment for anaemia** — eg, epoetin, intravenous iron, oral iron
- **Vitamins and supplements** — eg, alfalcacidol, colecaltiferol, folic acid
- **Medicines used to control common symptoms** — eg, diuretics, quinine, corticosteroids, antiemetics

Most patients with renal disease have comorbidities (eg, diabetes, cardiovascular disease) requiring an array of medicines.

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### Recommended reading


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### Risk factors for CKD

The following are among the risk factors for developing chronic kidney disease:

- Diabetes
- Hypertension
- Vascular disease
- Genetic predisposition
- Old age
- Male gender
- Raised cholesterol
- Taking nephrotoxic drugs
variation in definition of CKD as well as the advice offered. Box 4 illustrates advantages and disadvantages of common reference sources.

**Clinically checking prescriptions**

A prescription for a patient with CKD might seem daunting at first glance; however, the eight steps listed in the Box (above right) can be useful when clinically checking the prescription. We appreciate it is not always possible to undertake a complete and thorough clinical evaluation of all the medicines taken by a patient with renal dysfunction. However, by using a structured approach pharmacists can ensure the safety of a prescription and prevent major errors in prescribing. With experience pharmacists can learn where to focus their attention.

**References**


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**Box 4: Advantages and disadvantages of common reference sources**

<table>
<thead>
<tr>
<th>RESOURCE</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘British National Formulary’ (<a href="http://www.bnf.org">www.bnf.org</a>)</td>
<td>Readily available; simple to use; refers to manufacturers’ advice</td>
<td>Limited specialist advice; limited information on RRT; only updated six-monthly</td>
<td>Good starting point to direct enquiry</td>
</tr>
<tr>
<td>Summaries of product characteristics (<a href="http://www.emc.medicines.org.uk">www.emc.medicines.org.uk</a>)</td>
<td>Detailed information; easy to access electronically; up to date; can offer dosing in the different stages of renal impairment and also RRT</td>
<td>Only information within the licence is provided; not all monographs offer advice in renal impairment</td>
<td>Should be referred to in most cases because the information pertains to the UK licence</td>
</tr>
<tr>
<td>Drugdex (Micromedex) (<a href="http://www.micromedex.com/drugdex">www.micromedex.com/drugdex</a>)</td>
<td>Offers advice on medicines outside the UK licence; can provide detailed information</td>
<td>US-based information; not all monographs provide useful information</td>
<td>Useful when UK monographs offer little information</td>
</tr>
<tr>
<td>‘The Renal Drug Handbook’, Third Edition’ (electronic version also available)</td>
<td>Specialist information including RRT; offers advice on administration, drug interactions and common practice; easy to use</td>
<td>Not always readily accessible; not updated frequently; information offered can be outside product licence</td>
<td>Thorough and extensive; should be used after checking the SPC</td>
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<tr>
<td>Internet search engines (eg, Google)</td>
<td>Easy to perform; may find obscure references</td>
<td>Unreliable source; variable/unknown validity of references found; may not reflect UK practice; excessive volume of information to review; search terms used may not be valid</td>
<td>Only use if all of the above fail to provide information/advice</td>
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