

Safe Prescribing for Patients with Reduced Kidney Function

Therapeutic Brief

Key Points

- **Check your patient's kidney function prior to prescribing medicines if you suspect reduced kidney function (e.g. older patients, First Nations Australians, and those with hypertension, cardiovascular disease or diabetes).**

 - **Use eGFR, medicines information resources and medicines reviews to guide appropriate selection and dosing of medicines.**

 - **Be aware of commonly used medicines that may require dose adjustment in patients with reduced kidney function.**
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Reduced kidney function is a problem commonly encountered in general practice.¹ Around 1.7 million adult Australians are living with chronic kidney disease (CKD).² Yet less than 10% of people are aware they have the condition.¹

Older people, First Nations Australians, and those with a history of hypertension, cardiovascular disease (CVD) or diabetes are at increased risk of developing CKD.¹ These populations are commonly prescribed medicines that can result in problems when used in the context of reduced kidney function,⁴ increasing risk of serious adverse drug reactions² which are associated with poor outcomes^{3,4} including reduced quality of life, hospital admissions and death.^{2,4} >



By stopping and thinking 'kidney function' each time you prescribe medicine for someone you suspect of having reduced kidney function, you can identify patients with CKD and ensure their medicines are safe and effective for them.⁵ ●

Does the patient have reduced kidney function?

Reduced kidney function can be acute (lasting less than 3 months) or chronic (lasting more than 3 months).¹² Both conditions are interconnected, sharing risk factors, outcomes and prognostic factors.⁶ CKD increases a person's risk of experiencing AKI, while AKI increases risk of developing incident CKD further progression of existing CKD.²

CKD is defined as:¹

- An estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² that is present for ≥ 3 months with or without evidence of kidney damage.

Or

- Kidney damage, with or without decreased GFR that is present for ≥ 3 months.

Patients with a risk factor for CKD (Table 1) should be offered a Kidney Health Check every one to two years.^{1,13} This includes:

- eGFR
- Urine albumin/creatinine ratio (uACR)
- Blood pressure monitoring



Table 1: Reasons to suspect reduced kidney function

Patient demographics and history	Contextual factors
<ul style="list-style-type: none">• Diagnosed with CKD or other kidney abnormality• Risk factors for developing CKD¹<ul style="list-style-type: none">◦ aged 60 years and older◦ First Nations Australians aged 18 years or over◦ BMI > 30 kg/m²◦ current or former smokers or vapers◦ family history of kidney failure◦ medical history of:<ul style="list-style-type: none">▸ diabetes▸ hypertension▸ established CVD▸ AKI	<ul style="list-style-type: none">• Recent acute illness, e.g.,⁷<ul style="list-style-type: none">◦ dehydration◦ urinary tract infection◦ myocardial infarction◦ pneumonia• Recent discharge from hospital⁸• Experiencing symptoms suggestive of an adverse effect from a medicine⁸• Extreme hot weather (potential for dehydration)

What actions to take, and when?

Check the patient's kidney function before prescribing medicines if you suspect reduced kidney function

Prescribing a medicine for the management of hypertension, CVD, or diabetes can serve as a useful trigger to consider the patient's kidney function and ensure their medicines are safe and effective.⁸ Stopping to think about kidney function when prescribing medicines for people who are older age, or First Nations Australians can also help to ensure CKD is not overlooked, reducing medicine-related risk.

If the patient's health has been stable, a recent estimate of kidney function (within the past three months) can be used to guide medication dosing. If there has been a change in context (see Table 1) a current estimate of kidney function is recommended. In situations where kidney function is not stable, consult a nephrologist for advice. >



Kidney function can be estimated using creatinine-based equations:⁷

- **eGFR** - routinely provided with laboratory reports that include serum creatinine (calculated using the CKD-EPI formula)
- **Creatinine clearance (CrCl)** - can be calculated using the [Cockcroft-Gault equation](#) (a CrCl calculator is included in most GP practice software).

Both methods provide estimates of kidney function that can be used to guide dosing of medicines in most cases.⁹

Situations where estimates can be less accurate include:

- underweight (BMI < 18.5kg/m²)¹⁰
- obesity (BMI > 30kg/m²)¹⁰
- low or high muscle mass^{1,10,11}
- very low or high intake of dietary protein^{1,10}
- rapidly changing or unstable kidney function^{1,10,11}
- taking a medicine that elevates serum creatinine (e.g. trimethoprim)^{1,11}



Cockcroft-Gault equation



In patients who are low or high bodyweight, calculate a [de-indexed eGFR](#) to provide a more reliable estimate, or seek further advice from your pharmacist, local medicines information service or nephrologist.

$$\text{De-indexed eGFR (mL/min)} = \frac{\text{eGFR (mL/min/1.7m}^2\text{)} \times \text{BSA (m}^2\text{)}}{1.73}$$



De-indexed eGFR: How to adjust drug doses in chronic kidney disease



Body surface area calculator

Code the CKD diagnosis in the practice software

If your patient has a diagnosis of CKD, make sure this is coded in the practice software.¹ Doing so will provide you with electronic decision support to ensure safe prescribing and can assist with audit activities. >



Use medicines information and decision support to inform prescribing

If reduced kidney function is detected, it may be necessary to reduce the dose, extend the dosing interval, or avoid a particular medicine.⁹ The action required will depend on the patient's level of kidney function, the properties of the medicine, and the clinical context.⁹



If eGFR is $<60\text{ml}/\text{min}/1.73\text{m}^2$, consult a medicines information resource to ensure safe and effective prescribing.⁹

Most practice software has inbuilt decision support to guide safe prescribing when CKD is coded as a diagnosis. In other cases, consult a medicines information resource such as:

- The Australian Medicines Handbook (AMH)
- Therapeutic Guidelines (see antimicrobial dosage modification in renal impairment)

If in doubt, or if your practice does not have access to these resources, contact your local pharmacist or Medicines Information Service for advice.



Did you know? Australian pharmacies are required by Law to have the latest editions of the AMH and Therapeutic Guidelines available.

Undertake ongoing monitoring and review of prescribed medicines

After starting a medicine, monitor your patient for clinical and adverse effects, measure drug concentrations when relevant (e.g. lithium, digoxin), and adjust the dose if necessary.¹² >



A reversible drop in eGFR is expected after the introduction of ACE inhibitors, ARBs and SGLT2 inhibitors:

- **ACE inhibitors and ARBs:** check eGFR within 2 weeks of initiation. If reduction of eGFR is more than 25% from baseline value, cease the medication and consider referral to nephrologist.^{1, 12}
- **SGLT2 inhibitors:** a drop in eGFR (by 3-5mL/minute/1.73m²)¹² is expected to peak at 4 weeks following initiation, after which eGFR rebounds.¹ Specific testing of eGFR for this purpose is not necessary.¹

The optimal frequency of kidney function testing for the ongoing monitoring of medicines more generally is unclear. Consider testing kidney function routinely every three to six months and more frequently if there are clinical concerns.



Safety of medicines can change over time.⁸ Kidney function progressively declines with age, with rate of decline accelerating around the age of 65 years. A person aged 80 years old has about half the kidney function they had when aged 20.³ Doses of some medicines may need to be re-adjusted as the patient ages.³

Refer for a Medicines Review

Refer patients with reduced kidney function for a Home Medicines Review (HMR) or a Residential Medication Management Review (RMMR) to reduce adverse medicine-related effects.¹³

An HMR or an RMMR is an effective way to:

- review all medicines used by the patient, including those purchased over the counter
- identify medicines that can accumulate and cause adverse effects as a result of slower elimination in reduced kidney function
- identify medicines that can worsen kidney function or cause acute kidney injury
- identify medicines that are less effective in reduced kidney function



- highlight for review, or calculate appropriate dosing of medicines based on the patient's kidney function
- identify medicines that may need to be stopped.

Advise the pharmacist why the review is being requested and include kidney function test results and medical history in the referral. The MBS item numbers for an HMR and an RMMR are 900 and 903, respectively.¹⁴



The Medicines Advice Initiative Australia (MAIA) patient information brochure 'Medicines review in chronic kidney disease (CKD)' helps explain how CKD impacts medicines taken for chronic conditions and the medicine review process.



[Consumer Brochure](#)

Educate and empower your patients

If your patient is diagnosed with CKD, take the time to explain this to them.

- Provide patients with their eGFR results and current medication lists to communicate to other care providers (e.g., My Health Record, print outs)
- Guide your patients toward credible sources of consumer information:
 - The MAIA patient information brochure 'Medicines review in chronic kidney disease'.
 - [Kidney Health Australia](#) has an array of consumer resources.
- Talk to your patients with CKD about the risk of AKI and ask them to seek advice from a health practitioner immediately if they experience acute illness or dehydration or consider a [Sick Day Action Plan](#). >



[Kidney Health Australia](#)



[Sick Day Action Plan](#)



Temporarily withhold medicines in people with CKD when sick and dehydrated

Consensus based guidelines recommend certain medicines should be temporarily withheld in patients with CKD who are experiencing acute illness and dehydration, and recommenced once their condition is stable.^{7,16}

These medicines are represented by the mnemonic SADMANS:

- **S**ulfonylureas
- **A**CE-inhibitors
- **D**iuretics
- **M**etformin
- **A**RBs
- **N**SAIDs
- **S**GLT2 inhibitors

Some patients may be suitable for a [Sick Day Action Plan](#) to enact during acute illness or dehydration. This can be developed under a GP Management Plan.¹⁶



[Sick Day Action Plan](#)

What medicines should be front of mind?

Medicines that cause adverse effects

Medicines excreted by the kidneys can accumulate in people with reduced kidney function. Examples include **metformin**, **pregabalin**, **venlafaxine** and **apixaban**. These medicines may require a dose reduction or extended dosage interval to reduce the risk of adverse effects.¹⁵

In patients with severe loss of kidney function, some medicines such as **dabigatran** and **epplerenone** should be avoided or a safer alternative chosen.¹² >



Medicines that contribute to kidney injury

Nephrotoxic medicines (e.g., **aminoglycosides**, **lithium**) require precaution when used in people with reduced kidney function and may need to be avoided when loss of function is severe.

NSAIDs including **COX-2 inhibitors** have direct action on the kidney and increase risk of AKI⁷ so should be avoided in people with reduced kidney function.¹² Risk of AKI increases when NSAIDs are used in combination with medicines that affect fluid and electrolyte balance such as **diuretics**, **ACE inhibitors**, and **ARBs**.¹

Medicines that become less effective

Some medicines become less effective in people with reduced kidney function.

Loop diuretics (e.g. furosemide) typically require a dose increase to maintain effectiveness.¹² **Thiazide diuretics** (e.g. hydrochlorothiazide) become less effective as diuretics but may retain their anti-hypertensive effects in reduced kidney function.¹²

SGLT2 inhibitors (dapagliflozin, empagliflozin) are used to slow the progression of CKD, but their glucose-lowering effect is decreased in people with reduced kidney function.¹² They should not be started in people with severe reduction of kidney function but may be continued with ongoing monitoring depending on the individual patient's needs.¹² >



Figure 1: When prescribing a medicine, stop and think ‘kidney function’

Is there reason to suspect reduced kidney function?	
<ul style="list-style-type: none"> • Age 60 years and older • First Nations Australian aged over 18 years • BMI > 30kg/m² • Smoker or vaper (current or former) • Family history of kidney failure 	Medical history of <ul style="list-style-type: none"> • Diabetes • Hypertension • Established CVD • Acute kidney injury • CKD or other kidney abnormality

Does the medicine require caution in reduced kidney function? (Commonly prescribed examples - not an exhaustive list)		
Diabetes medicines	CVD system medicines	Other medicines
<ul style="list-style-type: none"> • Metformin • SGLT2 inhibitors (empagliflozin, dapagliflozin) • DPP-4 inhibitors (alogliptin, saxagliptin, sitagliptin, vildagliptin) • Glibenclamide 	<ul style="list-style-type: none"> • ACE inhibitors • ARBs/Sartans • Thiazide diuretics • Loop diuretics • MRA/aldosterone antagonists • Rosuvastatin, pravastatin • Apixaban, rivaroxaban, dabigatran • Digoxin 	<ul style="list-style-type: none"> • SNRI antidepressants • NSAIDs and COX-2 inhibitors • Pregabalin, gabapentin • Nirmatrelvir/ritonavir • Codeine, tramadol, morphine • Lithium

Has anything changed recently?

- Recent acute illness
 - Dehydration (e.g. acute gastroenteritis)
 - Urinary tract infection
 - Myocardial infarction
 - Pneumonia
- Recently discharged from hospital
- Experiencing symptoms suggesting an adverse effect from a medicine
- Extreme hot weather (potential for dehydration)

Yes	No
Obtain a current eGFR or CrCl to guide selection and dosing of medicines	Use a recent eGFR or CrCl to guide selection and dosing of medicine
+	+
Consider the need to temporarily withhold medicines (SADMANS) and monitor	Monitor at regular intervals, more frequently if initiating a medicine or clinical concerns arise

Abbreviations: SGLT2 sodium-glucose co-transporter 2, DPP-4 dipeptyl peptidase 4, CVD cardiovascular disease, ACE angiotensin converting enzyme, ARB angiotensin receptor blocker, MRA mineralocorticoid receptor antagonist, SNRI serotonin and noradrenaline reuptake inhibitors, NSAIDs non steroidal anti-inflammatory drugs, COX-2 cyclo-oxygenase 2, BMI body mass index, eGFR estimated glomerular filtration rate, CrCl creating clearance, SADMANS sulfonylureas, ACE inhibitors, Diuretics, Metformin, ARBs, NSAIDs, SGLT2 inhibitors



Abbreviations

ACE	Angiotensin converting enzyme
AKI	Acute kidney injury
ARB	Angiotensin receptor blocker
BMI	Body mass index
BSA	Body surface area
CKD	Chronic kidney disease
CKD-EPI	Chronic kidney disease epidemiology collaboration equation
COX-2	Cyclo-oxygenase 2
CrCl	Creatinine clearance
eGFR	Estimated glomerular filtration rate
GFR	Glomerular filtration rate
GP	General Practitioner
HMR	Home medicines review
MAIA	Medicines Advice Initiative Australia
NSAIDS	Non-steroidal anti-inflammatory drugs
RMMR	Residential medication management review
SGLT2	Sodium-glucose co-transportase 2

Take home messages

- If you have reason to suspect your patient has reduced kidney function, check before you prescribe the medicine. Prescribing to people of older age, First Nations Australians, and those with a history of CVD, hypertension or diabetes can serve as a useful trigger to stop and think 'kidney function'.
 - Use eGFR to guide selection and dosing of medicines. If the patient is stable, use a recent eGFR. If there are context-related risks, make sure the eGFR is current.
 - If the patient is known to have CKD, code the diagnosis in the practice software to enable inbuilt decision support when prescribing.
 - Consult medicines information resources to guide selection and dosing. Contact your pharmacist or medicines information service if you need advice.
 - Utilise the Medicines Review programs available. They can assist you to identify medicines that are impacted by reduced kidney function and advise on any ongoing monitoring that is required.
 - Educate and empower your patients with CKD to be active members of their healthcare team.
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For a list of useful links and reference list, please visit our website [MedicinesAdvice.net.au](https://www.MedicinesAdvice.net.au)

Medicines Advice Initiative Australia (MAIA)

PROVIDED BY

University of South Australia,
Quality Use of Medicines and Pharmacy
Research Centre

IN ASSOCIATION WITH

Australian Medicines Handbook (AMH)

Drug and Therapeutics Information
Service (DATIS)

Discipline of General Practice,
The University of Adelaide

National Aboriginal Community Controlled
Health Organisation (NACCHO)

Pharmaceutical Society of Australia (PSA)

Council of Australian Therapeutic
Advisory Groups (CATAG)

MAIA is funded by the Australian
Government through the Quality Use
of Diagnostics, Therapeutics and
Pathology Program.



Australian Government
Department of Veterans' Affairs

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Supporting quality use
of medicines.