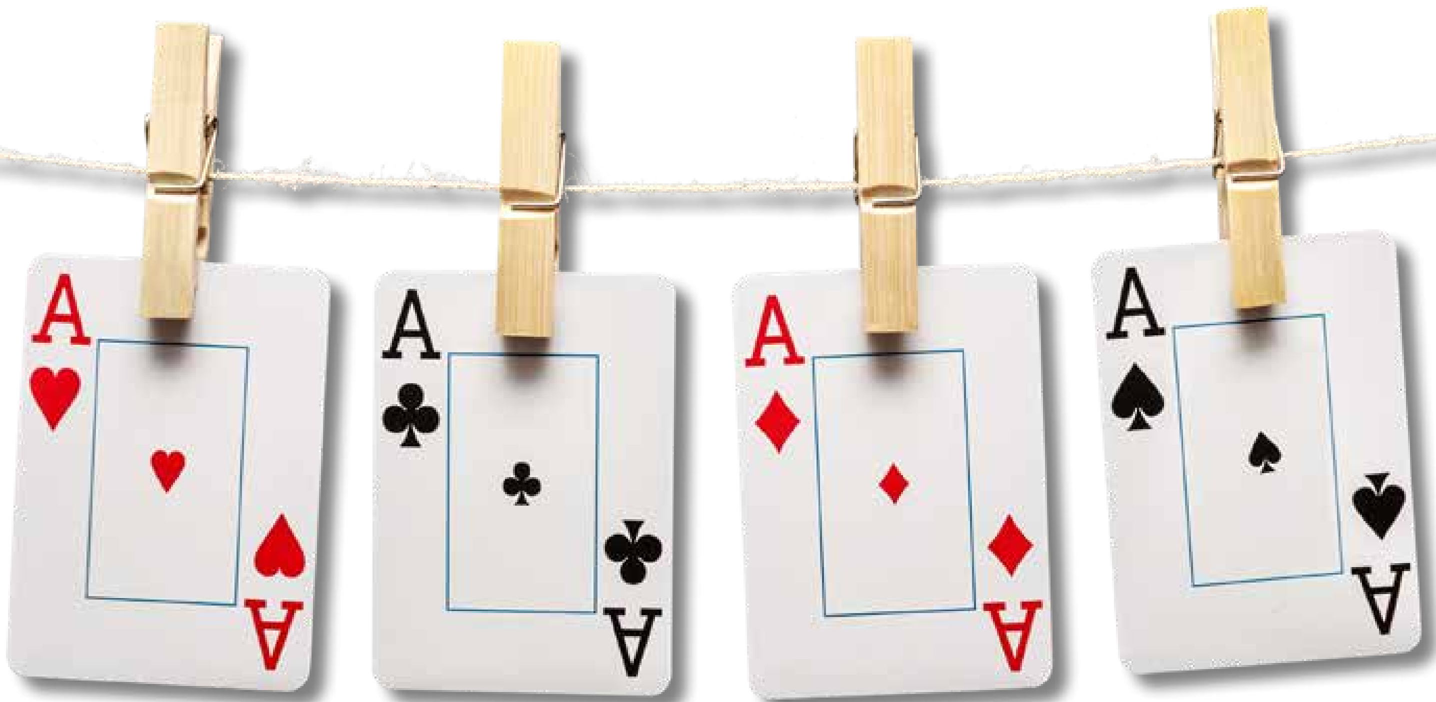
He Ako Hiringa
Learning Always



Changing ACEs
The new line up

Notable changes to the availability of angiotensin-converting enzyme (ACE) inhibitor preparations have recently occurred. Cilazapril, and quinapril with hydrochlorothiazide (Accuretic) are being delisted; and ramipril and a high dose perindopril tablet are new on the scene. This booklet summarises changes to ACE inhibitor (ACEI) availability and provides guidance for switching between medicines

Uncertainty around continued, uninterrupted supply of cilazapril has led to the decision to delist it from the Pharmaceutical Schedule. Pharmac has been encouraging prescribers to move away from the use of cilazapril, to minimise the impact on patients and on prescriber workflows when it becomes unavailable in 2023.

Recent changes to supply of ACE inhibitors in New Zealand include:

- cilazapril with hydrochlorothiazide (Inhibace Plus) – delisted March 2020
- cilazapril – funding restricted to existing patients May 2021
- quinapril with hydrochlorothiazide (Accuretic) – supply withdrawn October 2022.

To help with these changes, new ACE inhibitor options have been listed on the Pharmaceutical Schedule including ramipril capsules and a higher dose perindopril tablet.

These medicines add to the existing group of funded agents that affect the renin-angiotensin system:

- ACE inhibitors – enalapril, lisinopril, quinapril
- angiotensin receptor blockers (ARBs) – candesartan, losartan, losartan with hydrochlorothiazide, and sacubitril with valsartan (for heart failure on special authority).

Guide for choosing between an ACE inhibitor and an ARB[1]

Conditions where either an ACE inhibitor or an ARB are appropriate first-line:

- Hypertension, including people with type 2 diabetes.
- Chronic kidney disease.
- Diabetic nephropathy (unapproved indication for ARB).

Conditions where an ACE inhibitor is appropriate first-line:

- Heart failure (however, sacubitril + valsartan can be considered first-line for heart failure).
- Following a myocardial infarction.

Switching between agents

With Accuretic and cilazapril both set for delisting in 2023, patients on these therapies need to be changed to alternative medicine(s) with some urgency. The tables and examples below provide some guidance.

An ACE inhibitor or ARB may be discontinued one day and an equivalent dose of a different ACE inhibitor or ARB started the following day.[2] This is also true for thiazide diuretics.

Table 1: Approximate dose equivalence guide for ACE inhibitors and ARBs (adapted from[1–3])

Cilazapril	Quinapril	Enalapril	Lisinopril	Perindopril	Ramipril	Candesartan	Losartan
0.5mg	5mg	2.5mg	5mg	2mg	1.25mg	4mg	25mg
2.5mg	10mg	5–10mg	10mg	2–4mg	2.5mg	8mg	50mg
5mg	20–40mg*	20mg*	20–40mg	8mg	5–10mg*	16mg	50–100mg

** Divided doses for heart failure*

Table 2: Approximate dose equivalence guide for thiazide and thiazide-like diuretics (adapted from[4])

Hydrochlorothiazide	Bendroflumethiazide	Chlortalidone	Indapamide
12.5mg	2.5mg	12.5mg	2.5mg

Note that clinical trials show variations in approximate equivalent dosages for thiazide diuretics. Lower doses may be necessary in elderly people – refer to the NZ Formulary

Changing from an ACEI to another ACEI/ARB

An approximate dose equivalence guide is provided in Table 1; note that approximate equivalent doses of ACE inhibitors and ARBs vary across clinical trials. Some people will require dose adjustment, for example, patients with renal impairment. As patient responses may vary, follow-up is recommended one to four weeks after changing ACE inhibitor or ARB therapy.

Changing from Accuretic to alternative antihypertensive medicine(s)

Moving patients off Accuretic requires an extra step to accommodate the thiazide diuretic part of the product. A straight switch from Accuretic to another brand of quinapril and hydrochlorothiazide is not possible as no other combined tablet is available in New Zealand. Although the single agent quinapril tablet remains available, hydrochlorothiazide is not available here as a single agent to use alongside it. Therefore, alternative fully funded options to Accuretic include:

A. Losartan + hydrochlorothiazide (ARB and thiazide diuretic combined tablet).
B. Quinapril (single agent) or another ACEI/ARB, with a separate thiazide or thiazide-like diuretic such as bendroflumethiazide.
C. Alternative antihypertensive medicine(s).

A. Changing from Accuretic to losartan + hydrochlorothiazide

This may be the easiest option for patients as it enables continuation of treatment with a single tablet. In this combination product the dose of hydrochlorothiazide is the same as in the Accuretic formulations, but only one strength of losartan is currently available (ie, losartan 50mg + hydrochlorothiazide 12.5mg). Refer to Table 1 for dose equivalence of losartan to quinapril.

Example: For a patient taking once daily Accuretic (quinapril 10mg or 20mg + hydrochlorothiazide 12.5mg) change to once daily losartan + hydrochlorothiazide (50mg + 12.5mg). Monitor BP after two to four weeks; the dose may need to be increased if BP is elevated beyond baseline after four weeks.

B. Changing from Accuretic to quinapril (single agent) or another ACEI/ARB, with a separate thiazide or thiazide-like diuretic

This gives the option of continuing to use quinapril but will require adding a thiazide or thiazide-like diuretic as a separate tablet. Alternatively, another ACE inhibitor or ARB may be used instead of quinapril, with a thiazide or thiazide-like diuretic added as a separate tablet. These options increase the pill burden and may be problematic for patients who are already experiencing polypharmacy. The steps for this change are:

- prescribe the same dose of quinapril that the patient had on Accuretic; or prescribe an equivalent dose of another ACEI or ARB (see Table 1), and
- prescribe an equivalent dose of a thiazide or thiazide-like diuretic to the hydrochlorothiazide dose the patient had on Accuretic (see Table 2).

Example: For a patient taking Accuretic (quinapril 20mg + hydrochlorothiazide 12.5mg), change to quinapril 20mg tablets and indapamide 2.5mg tablets. Another option would be ramipril 5mg capsules and bendroflumethiazide 2.5mg tablets.

C. Changing to a single antihypertensive or adding an alternative antihypertensive medicine

While most patient's transition off Accuretic will be covered by the first two options, there may be some who would benefit from, or prefer to:

- Use an alternative medicine – calcium channel blockers may also be considered first-line for hypertension[5] and can be used as a single agent or added to quinapril (or an alternative ACE inhibitor).[6]
- Change to quinapril alone – may be an option for older adults or those with very well-controlled hypertension.

See akohiringa.co.nz for a range of other free clinical resources for primary care.

View your own cilazapril data

The He Ako Hiringa EPiC Cilazapril dashboard allows you to see how many of your patients, your practice's patients, and national patients still need moving off cilazapril. View the dashboard at epic.akohiringa.co.nz

This information is not intended to replace clinical judgement; refer to Medsafe data sheets and NZ Formulary for full prescribing details.

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