Best Practice Message

November 2022

Cilazapril alternatives

Practice changing moments

- PHARMAC will be discontinuing cilazapril by mid-2023. Approximately 5000 patients in Hawke's Bay are prescribed cilazapril and will need to be switched to alternative therapy prior to this.
- Ramipril will be funded from the 1st of December and may be considered as an alternative to cilazapril.
- When discontinuing cilazapril, consider if ACEi therapy is most appropriate for the patient, or if another class may be more suitable.

Cilazapril Discontinuation

Cilazapril will be discontinued by mid-2023[1]. In Hawke's Bay almost half of all patients receiving Angiotensin-Converting Enzyme inhibitor (ACEi) therapy are using cilazapril. This figure is slightly higher than the national average. These patients will need to be transitioned to either an alternative ACEi or an alternative agent of a different class.

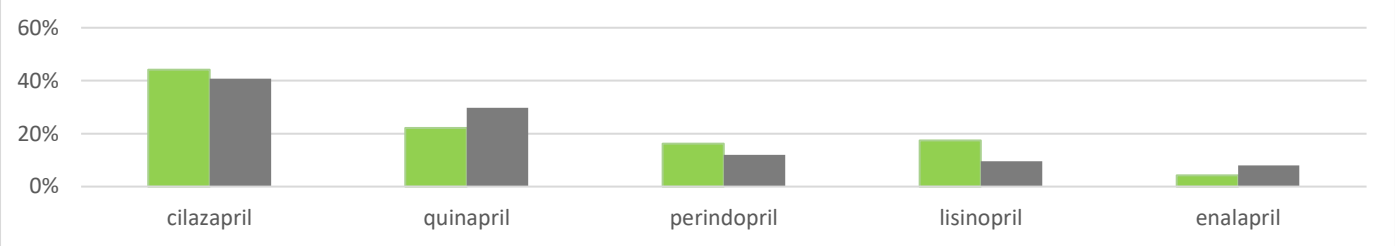

Figure 1. Comparing usage of ACE inhibitors in Hawke's Bay (green) vs National average (grey)

ACE Inhibitors and Angiotensin II Receptor Blockers

ACEi are indicated for hypertension, heart failure, diabetic nephropathy and prophylaxis of cardiovascular events[2]. There are a range of different funded ACEi. The benefits and risks, such as contraindications and interactions, associated with them are similar across the class. ACEi are generally well tolerated, with persistent cough one of the most common adverse effects.

Angiotensin II Receptor Blockers (ARBs) are considered to have similar effectiveness to ACEi when treating hypertension, chronic kidney disease and diabetic nephropathy[2]. ARBs are often a useful alternative to ACEi for patients who experience persistent cough with ACEi.

Monitoring

All ACEi and ARBs can cause a decline in renal function and elevation of potassium. It is recommended to monitor blood pressure, renal function and electrolytes 1-2 weeks after switching and after any dose adjustments. Monitor patients for angioedema, the onset may be delayed.

New Listing of Ramipril

Ramipril (Tryzan®) will be funded, from 1st December, as another ACEi option. While ramipril is new to New Zealand, it has been used internationally for decades. Ramipril has shown similar benefits to other ACEi with prevention of heart failure, myocardial infarction, stroke, and cardiovascular death[3].

Ramipril is generally well tolerated, however should the patient experience any adverse reaction, report this to CARM, as with any other medication.

Dosing

Ramipril's antihypertensive effect is relatively constant over a 24 hour period, hence it can be taken as once daily dosing[4]. Dosing starts at 1.25mg and can be increased to 20mg when used for hypertension. Strengths available are: 1.25mg, 5mg and 10mg.

Equivalent dose chart for ACE inhibitors and ARBs (doses are approximate and treatment should be patient centred).

	ACE inhibitors						ARBs	
	Cilazapril	**Perindopril**	**Lisinopril**	**Ramipril**	**Enalapril**	**Quinapril**	**Losartan**	**Candesartan**
Dose	0.5mg	2mg-4mg	5mg	1.25mg	5mg	5mg	25mg	4-8mg
	2.5mg	4mg	10mg	2.5mg-5mg	10mg	10mg	50mg	8mg-16mg
	5mg	4-8mg	20mg	5mg-10mg	20mg	20-40mg	100mg	16-32mg

Other antihypertensive agent options

The cardiovascular benefits of antihypertensive therapy are largely driven by amount of blood pressure reduction rather than the choice of agent between ACEi, ARB, thiazide-like diuretic, and calcium channel blockers. The ALLHAT trial showed no difference in cardiovascular event rates between lisinopril, chlortalidone or amlodipine[5]. Consider if patients may tolerate a different class of medication better when reviewing cilazapril alternatives.

Factors for consideration as precautions to the use of specific antihypertensive agents include:

Drug class	**Precautions for use**	
	Compelling	**Possible**

Thiazide/Thiazide-like Diuretics e.g. Indapamide, Chlortalidone	• Gout – NB dose dependent risk. Risk is highest for doses >25mg hydrochlorothiazide, chlortalidone and bendroflumethiazide >2.5mg daily	• Pregnancy
		• Dose dependant (see gout)
		  ○ Metabolic syndrome
		  ○ Glucose intolerance
		  ○ Hypercalcaemia
		  ○ Hypokalaemia

Dihydropyridine Calcium Channel Blockers		• Tachyarrhythmia • Heart Failure with reduced Ejection Fraction (HFrEF) • Pre-existing severe leg oedema
Non-Dihydropyridine Calcium Channel Blockers	• High grade sinoatrial or AV block • HFrEF • Bradycardia	• Constipation
ACE inhibitors	• Pregnancy • Previous angioneurotic oedema • Hyperkalaemia • Bilateral renal artery stenosis	• Women of childbearing potential without reliable contraception
Angiotensin II Receptor Blockers	• Pregnancy • Hyperkalaemia • Bilateral renal artery stenosis	• Women of childbearing potential without reliable contraception

Options in heart failure

For patients who are prescribed cilazapril as part of heart failure treatment, the discontinuation of the medicine could prompt a review of whether Entresto® may be an appropriate alternative. See Best Practice Entresto and the future of heart failure treatment for more details.

Tools:

- NZF Ramipril Monograph
- He Ako Hiringa Cilazapril Epic Dashboard

References:

1. Te Pātaka Whaioranga - PHARMAC. Cilazapril: No new patients from 1 May 2021 [Internet]. [cited 2022 Sep 20]. Available from: https://pharmac.govt.nz/medicine-funding-and-supply/medicine-notices/cilazapril/
2. Drugs affecting the renin-angiotensin system - New Zealand Formulary [Internet]. [cited 2022 Nov 10]. Available from: https://nzf.org.nz/nzf_1240
3. Effects of an Angiotensin-Converting–Enzyme Inhibitor, Ramipril, on Cardiovascular Events in High-Risk Patients. The New England Journal of Medicine. 2000;9.

4. Mccarron D, Group TRMS. 24-hour blood pressure profiles in hypertensive patients administered ramipril or placebo once daily: Magnitude and duration of antihypertensive effects. Clinical Cardiology. 1991;14(9):737–42.
5. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs DiureticThe Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002 Dec 18;288(23):2981–97.

Authored by: Ben Firestone **Reviewed by:** Riani Albertyn
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