Clinical fact sheet: pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF)[1]

**HFrEF refers to patients with symptoms ± signs of heart failure associated with a left ventricular ejection fraction less than 50%*

Heart Foundation

- **Approximately 480,000 Australians have heart failure (HF)[2].**
- **Only 50 percent of patients diagnosed with chronic heart failure will be alive 5 years later[3, 4].**

The basics of pharmacological management of chronic HFrEF:

✓ **Commence initial treatment and uptitrate to maximum tolerated dose**

✓ **Repeat echocardiogram in 3-6 months and alter therapy**

1. Commence initial treatment and uptitrate to maximum tolerated dose (see figure 1)

The combination of an angiotensin converting enzyme (ACE) inhibitor, beta-blocker and mineralocorticoid receptor antagonist (MRA) can decrease mortality over 1–3 years by 50–60%[5].

- **Double doses** of heart failure medications, one at a time, every two weeks or as tolerated until the maximum tolerated dose is reached
- Do not uptitrate one drug at the exclusion of **starting other drugs** which reduce mortality
  - E.g. in patients who are clinically euvolaemic, beta-blockers may be commenced before achieving target doses of ACE inhibitors.
- Most patients with HFrEF will also require either intermittent or long-term diuretic therapy. The goal of diuretic therapy is for symptom relief and to manage congestion, without causing over-diuresis.
  - **Diuretic therapy** should not be prioritized over initiation and titration of treatments that have been shown to decrease mortality and hospitalisation (including ACE inhibitors, angiotensin receptor blockers (ARBs), beta blockers, MRAs and angiotensin receptor neprilysin inhibitors (ARNIs)).
- **Monitoring** should occur following initiation and each dose escalation and should generally include clinical review, blood pressure (BP), renal function, serum potassium, heart rate.

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2. Repeat echocardiogram in 3-6 months and alter therapy

- Unless a reversible cause has been corrected, neurohormonal antagonists (ACE inhibitors or ARBs or ARNIs, beta blockers and MRAs) should be continued at target doses in patients with heart failure associated with a recovered or restored ejection fraction, to decrease the risk of recurrence.

ISSUE	TROUBLESHOOTING
Hypotension *(If asymptomatic: continue therapy)*	• Assess volume status. Review the need for other drugs not shown to improve outcomes in HF that lower blood pressure (e.g., diuretics, calcium channel blockers and nitrates) ▪ If the above strategies are unsuccessful, ACEI/ARB, ARNI, MRA, or beta blocker may need to be decreased (or ceased) and specialist advice sought.
Reduced renal function **(eGFR decrease by more than 30%)** **Or hyperkalaemia** **(serum [K] >5.5 mmol/L)** *If small change in renal function (e.g. eGFR decreases by ≤30%): continue therapy*	• Assess volume status. Review the need for other drugs not shown to improve outcomes in HF that impact renal function or serum potassium (e.g. nonsteroidal anti-inflammatory drugs (NSAIDs), diuretics and potassium supplements) ▪ If the above strategies are unsuccessful, ACEI/ARB, ARNI or MRA may need to be decreased (or ceased) and specialist advice sought. • **Serum [K] increase > 6.0 mmol/L**: cease MRA, seek specialist advice
Symptomatic bradycardia (<50 bpm)	• Document rhythm with ECG. Review the need for other drugs not shown to improve outcomes in heart failure that lower heart rate (e.g. digoxin, amiodarone). ▪ If the above strategies are unsuccessful, the beta-blocker dose may need to be decreased and specialist advice sought
Increasing congestion	• Increase diuretic. Consider a reduction in beta-blocker dose. Temporary withdrawal of the beta-blocker may occasionally be required, especially if recently commenced
Angioedema	• Cease ACEI or ARNI and seek specialist advice
Cough	• Consider whether this is due to pulmonary congestion or lung disease. A dry non-productive cough may be due to ACEI. If dry cough is interfering with the patient's quality of life, change ACEI to ARB.

DRUG	STARTING DOSE[6]	TARGET DOSE[6]	STARTING DOSE[6]	TARGET DOSE [6]
ACEI or ARB *ARBs are usually reserved for patients with HFrEF who do not tolerate an ACEI (dry cough)*	Captopril 6.25mg TDS Enalapril 2.5mg D Fosinopril 5mg D Lisinopril 2.5mg D Perindopril arginine 2.5mg D Perindopril erbumine 2mg D Quinapril 5mg D Ramipril 2.5mg BD Trandalopril 0.5mg D	75mg BD 20mg D 40mg D 50mg D 10mg D 8mg D 20mg D 5mg BD 4mg D	Candesartan 4mg D Eprosartan 400mg D Irbesartan 75mg D Losartan 25mg D Olmesartan10mg D Telmisartan 40mg D Valsartan 40mg BD	32mg D 600mg D 300mg D 100mg D 40mg D 80mg D 160mg BD
Beta blocker ***Ensure that the patient is clinically stable and euvolaemic before commencing beta-blockers.***	Bisoprolol 1.25mg D Carvedilol 3.125mg BD Metoprolol succinate MR 23.75mg D Nebivolol 1.25mg D	10mg D 50mg BD 190mg D 10mg D		
MRA *Avoid or use cautiously in patients with stage 4 or 5 CKD or serum [K] > 5 mmol/L.*	Eplerenone 25mg D Spironolactone 25mg D	50mg D 50mg D		
Sacubutril/valsartan (ARNI) *Ensure that ACEIs are stopped at least 36 hours before commencing an ARNI*	Sacubutril/valsartan 49/51mg BD	97/103mg BD		

D: daily; BD: twice daily; TDS: three times a day; MR: modified release

References

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4. Taylor CJ, et al. Fam Pract. 2017;34(2):161-8.
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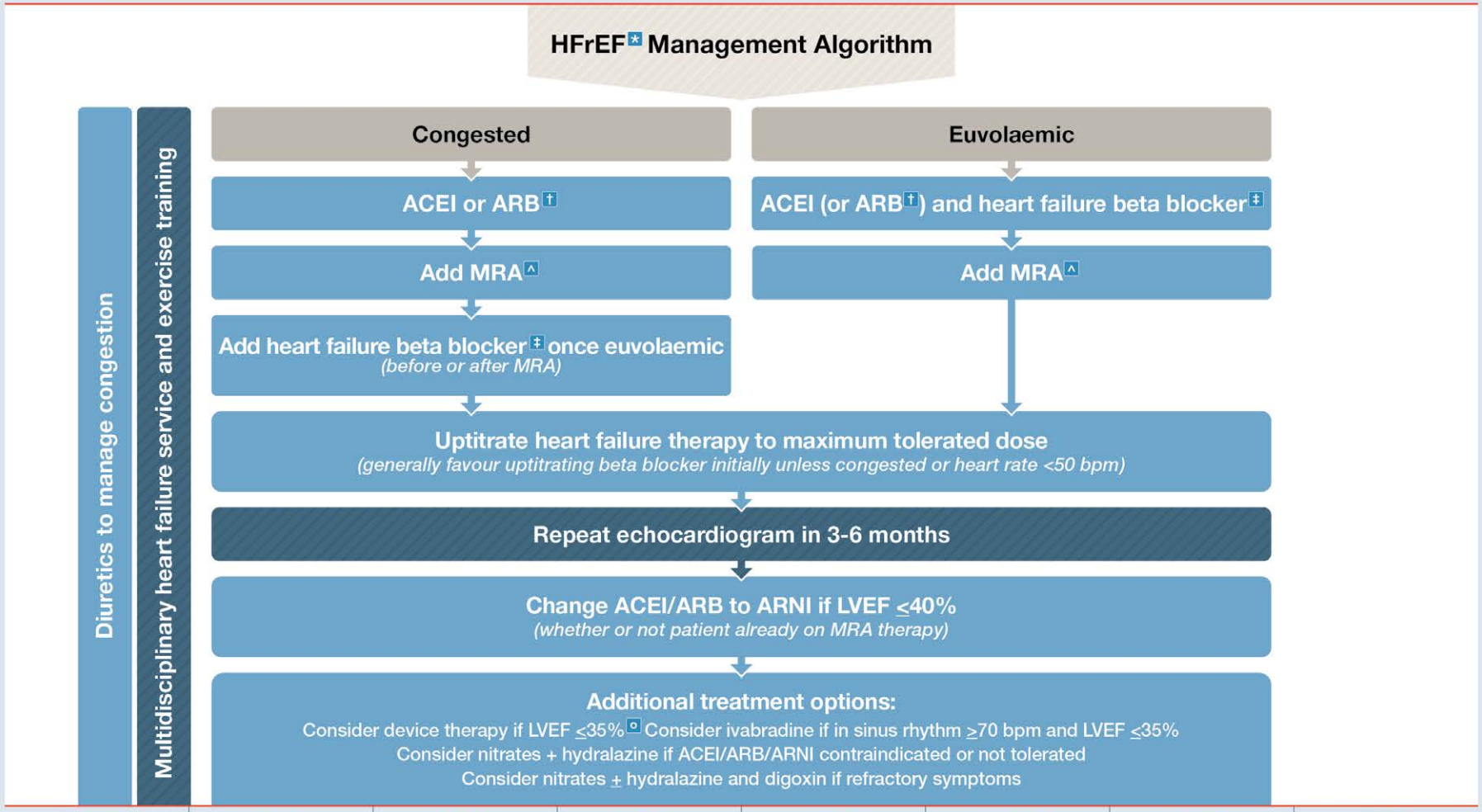
Figure 1: Management of patients with heart failure with reduced ejection fraction



HFrEF	ACEI	ARB	MRA	ARNI	LVEF	ICD	CRT
heart failure with reduced ejection fraction	angiotensin converting enzyme inhibitor	angiotensin receptor blocker	mineralocorticoid receptor antagonist	angiotensin receptor neprilysininhibitor	left ventricular ejectionfraction	implantable cardioverter defibrillator	cardiac resynchronisation therapy

* HFrEF refers to patients with symptoms and/or signs of heart failure associated with an LVEF less than 50% (unless otherwise specified)
† ARB should only be used if ACEI is contraindicated or not tolerated
‡ carvedilol, bisoprolol, metoprolol succinate, nebivolol
^ Commencing MRA usually avoided if serum K >5 mmol/L or CrCl <30 mL/minute
o ICD and/ or CRT

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