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%.

- 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 euvoalaemic, 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 nepriylsin 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.

• Approximately 480,000 Australians have heart failure (HF).
• Only 50 percent of patients diagnosed with chronic heart failure will be alive 5 years later.

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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.

<table>
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<tr>
<th>ISSUE</th>
<th>TROUBLESHOOTING</th>
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| 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) | - 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 | - 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. |
| 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. |

<table>
<thead>
<tr>
<th>DRUG</th>
<th>STARTING DOSE *</th>
<th>TARGET DOSE *</th>
<th>STARTING DOSE *</th>
<th>TARGET DOSE *</th>
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<tbody>
<tr>
<td>ACEI or ARB</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ARBs are usually reserved for patients with HFrEF who do not tolerate an ACEI (dry cough)</td>
<td>Captopril 6.25mg TDS</td>
<td>75mg BD</td>
<td>Candesartan 4mg D</td>
<td>32mg D</td>
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<tr>
<td></td>
<td>Enalapril 2.5mg D</td>
<td>20mg D</td>
<td>Eprosartan 400mg D</td>
<td>600mg D</td>
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<tr>
<td></td>
<td>Fosinopril 5mg D</td>
<td>40mg D</td>
<td>Irbesartan 75mg D</td>
<td>300mg D</td>
</tr>
<tr>
<td></td>
<td>Lisinopril 2.5mg D</td>
<td>50mg D</td>
<td>Losartan 25mg D</td>
<td>100mg D</td>
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<tr>
<td></td>
<td>Perindopril arginine 2.5mg D</td>
<td>10mg D</td>
<td>Omesartan 10mg D</td>
<td>40mg D</td>
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<tr>
<td></td>
<td>Perindopril erbumine 2mg D</td>
<td>8mg D</td>
<td>Telmisartan 40mg D</td>
<td>80mg D</td>
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<tr>
<td></td>
<td>Quinapril 5mg D</td>
<td>20mg D</td>
<td>Valsartan 40mg BD</td>
<td>160mg BD</td>
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<tr>
<td></td>
<td>Ramipril 2.5mg BD</td>
<td>20mg BD</td>
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<tr>
<td></td>
<td>Trandolapril 0.5mg D</td>
<td>4mg D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Bisoprolol 1.25mg D</td>
<td>10mg D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensure that the patient is clinically stable and euvoalaemic before commencing beta-blockers.</td>
<td>Carvedilol 3.125mg BD</td>
<td>50mg D</td>
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<tr>
<td></td>
<td>Metoprolol succinate MR 23.75mg D</td>
<td>190mg D</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Nebivolol 1.25mg D</td>
<td>10mg D</td>
<td></td>
<td></td>
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<tr>
<td>MRA</td>
<td>Eplerenone 25mg D</td>
<td>50mg D</td>
<td></td>
<td></td>
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<tr>
<td>Avoid or use cautiously in patients with stage 4 or 5 CKD or serum [K] &gt; 5 mmol/L</td>
<td>Spironolactone 25mg D</td>
<td>50mg D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacubutril/valsartan (ARNI)</td>
<td>Sacubutril/valsartan 49/51mg BD</td>
<td>97/103mg BD</td>
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D: daily; BD: twice daily; TDS: three times a day; MR: modified release

References
Figure 1: Management of patients with heart failure with reduced ejection fraction

**HFrEF Management Algorithm**

**Congested**
- ACEI or ARB
- Add MRA
- Add heart failure beta blocker (before or after MRA)

**Euvolaemic**
- ACEI (or ARB) and heart failure beta blocker
- Add MRA

**Multidisciplinary heart failure service and exercise training**

**Diuretics to manage congestion**

**Primarily based on data from**

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**Additional treatment options:**
- Consider device therapy if LVEF ≤35% and LVEF ≤35%
- Consider ivabradine if in sinus rhythm ≥70 bpm and LVEF ≤35%
- Consider nitrates + hydralazine if ACEI/ARB/ARNI contraindicated or not tolerated
- Consider nitrates + hydralazine and digoxin if refractory symptoms

**HFrEF** heart failure with reduced ejection fraction

**ACEI** angiotensin converting enzyme inhibitor

**ARB** angiotensin receptor blocker

**MRA** mineralocorticoid receptor antagonist

**ARNI** angiotensin receptor neprilysin inhibitor

**LVEF** left ventricular ejection fraction

**ICD** implantable cardioverter defibrillator

**CRT** cardiac resynchronisation therapy

Adapted from Tomlinson S, Atherton JJ. Heart failure - The crucial role of the GP. MedSclasToday 2018;19:18-27 with permission.

Clinical fact sheet - pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF)

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