NPS MEDICINEWISE

MEDICINEWISE NEWS
May 2021

Up-titrating heart failure medicines – a practical guide

Key points:

- People with HFrEF should be prescribed a combination of an ACE inhibitor (or ARB if not tolerated), a heart failure beta blocker and an MRA, up-titrated to target or maximum tolerated doses, to help improve quality of life, reduce hospitalisations and save lives.
- GPs play a vital role in starting and optimising doses of guideline medicines for patients with HFrEF.
- Up-titration guidance includes: start heart failure medicines at low doses, double the dose one medicine at a time every 2–4 weeks (except MRAs, up-titrated in 4–8 weeks) and add the next medicine before reaching target or maximum tolerated dose of the previous medicine.
- Monitor patients closely with a review 1–2 weeks after each medicine initiation and dose increase, and make variations to up-titration when required in response to adverse effects.
- Asymptomatic or mild changes in blood pressure, heart rate or renal function during up-titration do not usually require dose reduction.

Australian heart failure guidelines are clear on the goal of pharmacological management for people who have heart failure with reduced ejection fraction (HFrEF).

That goal is to prescribe a combination of:[1]

1. an angiotensin-converting enzyme (ACE) inhibitor, or if not tolerated, angiotensin receptor blocker (ARB) and
2. a heart failure beta blocker and
3. a mineralocorticoid receptor antagonist (MRA),

all at target or maximum tolerated doses.

The guidelines, developed by the National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand, also describe how to up-titrate these three medicines to reach the target or maximum tolerated doses.[1]

However GPs can find it challenging to put up-titration into practice.[2,3] This article provides a practical guide to assist GPs with the up-titration of heart failure medicines for people with HFrEF.

Evidence for a combination of heart failure medicines

The recommendation to prescribe a combination of an ACE inhibitor (or ARB if not tolerated), a heart failure beta blocker and an MRA at target or maximum tolerated doses is based on evidence that these medicines together can help improve quality of life, reduce hospitalisations and save lives for people with HFrEF.[1,4]

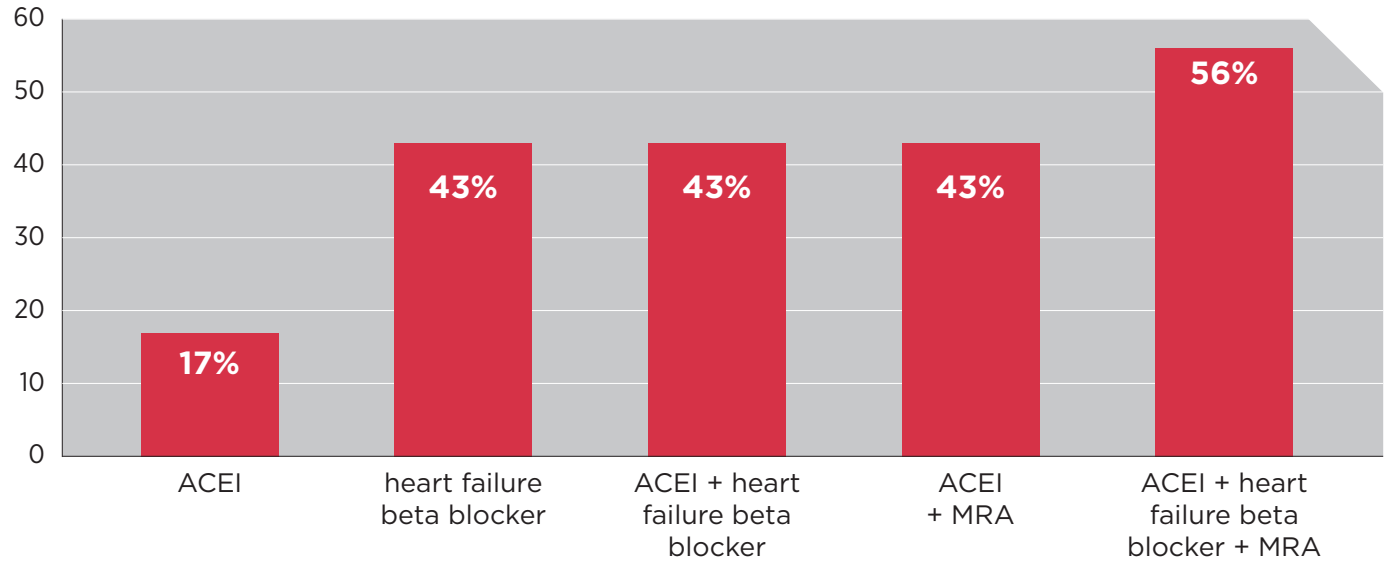
A 2017 meta-analysis found that people with HFrEF who were prescribed a combination of ACE inhibitor, heart failure beta blocker and MRA at target doses had a 56% reduction in all-cause mortality over 1–3 years, compared to placebo. This combination was much more effective than an ACE inhibitor or heart failure beta blocker alone, or a combination of two out of three medicines.[6] **See Figure 1**.

What is HFrEF?

HFrEF is defined as left ventricular ejection fraction (LVEF) < 50%, in the presence of symptoms ± signs of heart failure, where the diagnosis is confirmed with an echocardiogram.

Just under half of people with heart failure have HFrEF. The remaining have preserved ejection fraction (HFpEF). No medicines have been shown to improve survival for these patients.[1,5]

FIGURE 1: Percentage reduction in all-cause mortality over 1–3 years for people with HFrEF on selected, initial heart failure medicines versus placebo[6]



ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; MRA = mineralocorticoid receptor antagonist

Up-titration guidance

The process of up-titration recommended by Australian guidelines to reach the goal of a combination of heart failure medicines is to:[1,4]

- start each medicine at a low dose and
- gradually up-titrate them to target or maximum tolerated doses.

See Table 1 for start and target doses.

TABLE 1

Start and target doses for heart failure medicines for people with HFrEF[7]

CLASS	MEDICINE	START DOSE	TARGET DOSE
ACEI	captopril	6.25 mg TDS	75 mg BD
	enalapril	2.5 mg D	20 mg D
	fosinopril	5 mg D	40 mg D
	lisinopril	2.5 mg D	50 mg D
	perindopril arginine	2.5 mg D	10 mg D
	perindopril erbumine	2 mg D	8 mg D
	quinapril	5 mg D	20 mg D
	ramipril	2.5 mg BD	5 mg BD
	trandolapril	0.5 mg D	4 mg D
ARB	candesartan	4 mg D	32 mg D
	eprosartan	400 mg D	600 mg D
	irbesartan	75 mg D	300 mg D
	losartan	25 mg D	100 mg D
	olmesartan	10 mg D	40 mg D
	telmisartan	40 mg D	80 mg D
	valsartan	40 mg BD	160 mg BD
Heart failure beta blocker	bisoprolol	1.25 mg D	10 mg D
	carvedilol	3.125 mg BD	50 mg BD
	metoprolol succinate MR	23.75 mg D	190 mg D
	nebivolol	1.25 mg D	10 mg D
MRA	eplerenone	25 mg D	50 mg D
	spironolactone	25 mg D	50 mg D
ARNI	sacubitril/valsartan	49/51 mg BD	97/103 mg BD

HFrEF = heart failure with reduced ejection fraction; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; MRA = mineralocorticoid receptor antagonist; D: daily; BD: twice daily; TDS: three times a day; MR: modified release

* From the National Heart Foundation of Australia 2018. Clinical factsheet: pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF). Copyright 2019 by National Heart Foundation of Australia. Reprinted with permission.

However rather than a single up-titration pathway to reach this goal, there are two pathways that are differentiated by the patient's volume status when starting pharmacological management; euvolaemic or congested.[1] **See Figure 2**.

For each pathway, it is recommended to:

- double the dose of heart failure medicines, one at a time, every 2–4 weeks (except MRAs; up-titrated in 4–8 weeks), or as tolerated.[1,7,8]
- add the next medicine before reaching target or maximum tolerated dose, eg, if the patient is euvolaemic, a heart failure beta blocker may be started before achieving target or maximum tolerated dose of an ACE inhibitor.[7]
- review every 1–2 weeks after each medicine initiation and dose increase, including a clinical review and checking blood pressure, heart rate, renal function[1,7]

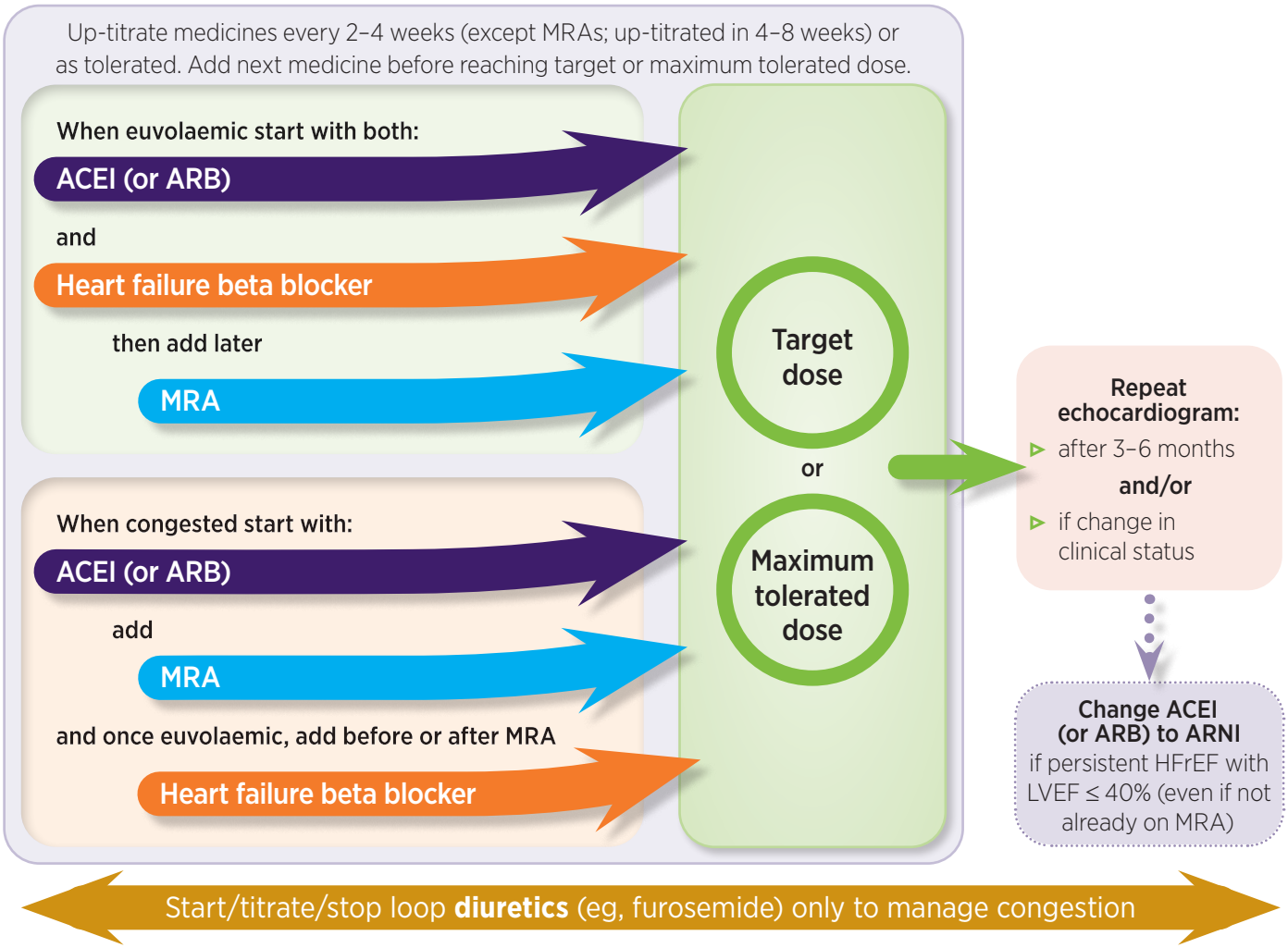
In addition, variations during up-titration may be necessary for patients who experience certain adverse effects, particularly those that are symptomatic.[1,7]

These variations include reducing dosage and pausing up-titration of a medicine with the aim of reducing or stopping the adverse effects to enable up-titration to target dose to be restarted. If adverse effects don't improve sufficiently, the patient may be considered to have reached maximum tolerated dose.[7] **See guidance on blood pressure Table 2, heart rate Table 3, renal function Table 4, volume status Table 5, and miscellaneous Table 6.**

Further down the pathways, for people with persistent HFrEF with left ventricular ejection fraction (LVEF) ≤ 40%, it's recommended to change the ACE inhibitor (or ARB) to an angiotensin receptor-neprilysin inhibitor (ARNI).[1] **See Figure 2**.

ACE inhibitors, ARBs and ARNIs may be regarded as a single group of medicines for the purposes of up-titration and adverse effects.[1]

FIGURE 2: Initial pharmacological management for people with HFrEF[1,7,8]



HFrEF = heart failure with reduced ejection fraction; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker;
ARNI = angiotensin receptor neprilysin inhibitor; MRA = mineralocorticoid receptor antagonist

* Adapted from the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Guidelines for the prevention, detection, and management of heart failure in Australia 2018. Copyright 2018 by National Heart Foundation of Australia. Reprinted with permission. https://doi.org/10.1016/j.hlc.2018.06.1042
Adapted from Tomlinson S, Atherton JJ. Heart failure - The crucial role of the GP. Medicine Today 2018; 19:19-27 with permission. https://medicinetoday.com.au/2018/march/feature-article/heart-failure-crucial-role-gp

Up-titration is straightforward for most patients

Professor Ralph Audehm, from the Department of General Practice and Primary Health Care at Melbourne University is a Melbourne GP and co-author of the National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand Heart Failure Guidelines 2018.

'GPs can be reassured that for the majority of patients with HFrEF in general practice it is straightforward to up-titrate to target doses because they are relatively well, for example, they have good blood pressure, renal function and are reasonably active.

These patients usually have no adverse effects that require a change to the up-titration of their medicines.

It's the more frail, usually older patients that can be more difficult. For them it's a matter of picking which medicine to give first for the most benefit. Then adjusting the medicines in response to any adverse effects.

You might have smaller dose increases and more time between each increase. You may also have to accept they'll reach maximum tolerated doses rather than target doses.'

Standard approach and variations that may be required

Professor Andrea Driscoll, from the School of Nursing and Midwifery at Deakin University, is a Heart Failure Nurse Practitioner at Austin Health, Melbourne and co-author of the National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand Heart Failure Guidelines 2018.

'Years ago the guidance was quite fixed about up-titrating one medication to maximum dose, then up-titrate the second one and so forth. Now it's realised the combined effect of more than one medication already started at low doses and then up-titrating all of them in turn is more beneficial and this has become the standard approach.

Most of our patients start with an ACE inhibitor, then start the heart failure beta blocker, then increase the ACE inhibitor, then increase the beta blocker. At some point before reaching their target doses, we'd start an MRA. Then we'd up-titrate all three medications in turn until we reach target doses for each one.

Variations to the above may be required to address adverse effects, particularly when they are symptomatic, in response to their medications.

For example, if the patient is feeling a little bit more dizzy than normal, I would leave the ACE inhibitor and up-titrate the beta blocker first. Or if their heart rate is a little bit too low and they're symptomatic, I would leave the beta blocker and up-titrate the ACE inhibitor.'

GPs and cardiologists working together

GPs can play a vital role with initiating and implementing up-titration of heart failure medicines. At the same time patients can benefit from a referral to a cardiologist specialising in heart failure.[9]

'A shared care approach, where a cardiologist who specialises in heart failure reviews your patient once a year, is a good thing,' says Professor Audehm.

'We wouldn't think twice about an annual review for a patient with, for example, kidney disease. Heart failure has dreadful mortality and morbidity that we can approach with the same intent,' he says.

Indeed, only 50% of people with heart failure are alive 5 years after diagnosis.[7] The all-cause readmission rate is 20% and all-cause mortality is 8% 30 days after hospitalisation with heart failure.[10]

Once the relationship with a cardiologist is established, GPs gain access to the cardiologist's guidance and management when urgently needed, says Professor Audehm.

'You can call the cardiologist if a patient is deteriorating and ask them to see the patient. You can receive advice, such as when up-titration is more difficult or challenging, and this will help build your confidence and skills.'

How a GP became confident with up-titration

Sydney GP Dr Peter Piazza took several years to feel comfortable about his patients with heart failure walking around with a systolic blood pressure of 105 mm Hg.

Dr Piazza belongs to the generation of GPs who were educated never to prescribe beta blockers for heart failure. Then in the early 2000s he learnt that this guidance had been turned on its head after participating in heart failure professional education.

The recommendation was to up-titrate heart failure beta blockers, together with ACE inhibitors (or an ARB if the ACE inhibitor isn't tolerated) and MRAs to target doses for people with HFrEF. He also learnt that low blood pressure could be tolerated by these patients.

'Initially I was nervous about the cardiologist's advice that patients could go down to a systolic blood pressure of 105. I thought that was really getting low and was concerned about patients having hypotensive syncope or a fall,' says Dr Piazza.

'I told my patients to let me know straight away if they got any symptoms and I could adjust their dosage. But I found they tended to stay asymptomatic. Then with more and more patients with that response, my confidence grew,' he says.

'I gradually realised the blood pressure number was less important than the patient's symptoms and I stopped feeling nervous.'

And it hasn't just been for low blood pressure. Dr Piazza has also become confident with his ability to manage changes in heart rate, renal function and volume status that can occur when up-titrating heart failure medicines.

How to help patients with heart failure medicines

Up-titration can also feel complex for patients who have to ensure they are correctly taking their medicines and self-managing their condition.

A patient-centred approach and keeping information and guidance as simple as possible is recommended by Professor Driscoll.

At the first visit she always includes guidance on daily weighing if the patient is congested, an action plan for when to see the GP again and when to seek emergency care and an explanation of 'the bigger picture' of their condition.

'I say to my patients that while you see the cardiologist every 3 or 6 months, you'll be seeing me much more frequently, every 2 to 4 weeks in relation to increasing the dose of your medications,' says Professor Driscoll.

'I explain that if you can increase the dose, your heart will pump better, you'll go to the hospital fewer times and survive longer. But we need to monitor the medicines, we can't just put you straight up to the top dose,' she says.

'I say this involves us asking lots of questions about any symptoms, because while there's no cure for heart failure, we can improve your symptoms with these medications.'

Patients find this approach helpful and comforting, and it helps them to achieve the best possible outcomes, says Professor Driscoll.

Blood pressure guidance

TABLE 2

Guidance for managing blood pressure adverse effects

Blood pressure (BP) – including orthostatic BP (postural drop):[11,13] Review 1–2 weeks after each medicine initiation / each medicine dose increase[1,7]

ADVERSE EFFECTS	ACTIONS[a]		
	ACEI / ARB / ARNI	HEART FAILURE BETA BLOCKER	MRA
Asymptomatic hypotension[7,11]	Continue therapy	Continue therapy	Continue therapy
Symptomatic hypotension eg dizziness, light-headedness and/or confusion[1,7,11]	**1.** Assess volume status, consider reducing or stopping diuretic if there are no signs or symptoms of congestion **2.** Review other medicines that can reduce blood pressure (eg calcium channel blockers, nitrates, diuretics) **3.** If still symptomatic: **a.** temporarily decrease dose of either ACEI/ARB, ARNI or heart failure beta blocker **b.** review patient within 1 week and if still symptomatic continue dose reduction (or cease) and seek specialist advice		Continue therapy Only consider decreasing dose if, after implementing actions for ACEI/ARB/ARNI and/ or heart failure beta blocker to address symptomatic hypotension, the patient is still symptomatic.
Severe symptomatic hypotension / cardiogenic shock eg cold and sweaty skin, dyspnoea, blue skin tone or weak and rapid pulse[1,11,12]	Immediate referral to an emergency department		

[a] Diuretic dose may be reduced at any time if euvolaemic (unless this has previously exacerbated symptoms)

Expert advice

- Hypotension is common because all of the heart failure medicines tend to lower blood pressure.
- Most patients only experience 2–3 seconds of dizziness when they stand up and, if warned (eg stop and wait for dizziness to subside before start walking), are safe and tolerate it well.
- Advice to reduce risk of falls due to dizziness may also be considered, eg, if experiencing nocturia, turn on the light when going to the toilet.
- Symptoms are more important than the actual number (mm Hg) of the systolic blood pressure.
- *'I used to get nervous below 110. I'm now quite comfortable at 100 or even just below.'*

  Professor Ralph Audehm
- *'Many of my patients are as low as 90 and some even 85. But I would stop up-titrating at 85, even if the patient was asymptomatic.'*

  Professor Andrea Driscoll
- Measures to help reduce risk of hypotension include:
  - take medicines at night
  - avoid dehydration
  - if dehydrated and taking a diuretic, reduce dosage.

Heart rate guidance

TABLE 3

Guidance for managing heart rate adverse effects

Heart rate: Review 1–2 weeks after each medicine initiation / each medicine dose increase[1,7]

ADVERSE EFFECTS	ACTIONS[a]		
	HEART FAILURE BETA BLOCKER	ACEI / ARB / ARNI	MRA
Asymptomatic bradycardia (50–60 bpm)[1,14,15]	Continue therapy	Continue therapy	Continue therapy
Symptomatic bradycardia (< 50 bpm) eg marked fatigue, dizziness light-headedness[1,11,14]	**1.** Arrange ECG to document rhythm **2.** Review need for other medicines that can lower heart rate (eg digoxin, amiodarone) **3.** If above not successful, may need to decrease dose and seek specialist advice	Continue therapy	Continue therapy

[a] Diuretic dose may be reduced at any time if euvolaemic (unless this has previously exacerbated symptoms)

Expert advice

- Symptoms are more important than the actual heart rate.
- Symptomatic bradycardia will almost only occur when the heart rate is < 50 bpm.
- Symptomatic bradycardia at 50-60 bpm is usually due to other reasons (eg hypothyroidism, arrythmias) and should be investigated before considering an adjustment to the dose of beta blocker.

Professor Andrew Sindone, Director of the Heart Failure Unit and Department of Cardiac Rehabilitation at Concord Hospital, Head of Department of Cardiology at Ryde, co-author of the National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand Heart Failure Guidelines 2018.

- *'I actively aim for patients to have a heart rate between 55 and 60. This range is based on haemodynamic optimisation. You're trying to maximise the amount of time the left ventricle has to fill up before it pumps out.'*
- *'It's not only about squeezing blood out. Everyone with heart failure reduced ejection fraction has a stiff ventricle that doesn't relax properly. As a result, the heart is not good at sucking the blood back in. So you want to maximise the amount of time it has to fill.'*

Professor Andrew Sindone

Renal function guidance

TABLE 4

Guidance for managing renal function adverse effects

Renal function: Review 1–2 weeks after each medicine initiation / each medicine dose increase[1,7]

RESULTS / ADVERSE EFFECTS	ACTIONS[a]		
	MRA	ACEI / ARB / ARNI	HEART FAILURE BETA BLOCKER
eGFR decrease ≤ 30%[7]	Continue therapy	Continue therapy	Continue therapy
eGFR decrease > 30%[1,7,11]	**1.** Assess volume status **2.** Review need for other medicines that impact on renal function (eg NSAIDs, diuretics) **3.** If above not successful:		Continue therapy
	• for MRA; decrease dose	• for ACEI/ARB/ARNI; may need to: **a.** decrease (or stop) dose **b.** seek specialist advice	
Hyperkalaemia Serum K+ (potassium) > 5.5 mmol/L[1,7]	**1.** Assess volume status **2.** Review need for other medicines that impact on serum K+ (eg potassium supplements) **3.** If above not successful:		Continue therapy
	• for MRA; decrease dose	• for ACEI/ARB/ARNI; may need to: **a.** decrease (or stop) dose **b.** seek specialist advice	
Hyperkalaemia serum K+ (potassium) > 6.0 mmol/L[1,7]	• for MRA, stop and seek specialist advice	• for ACEI/ARB/ARNI follow above steps 1, 2, 3	
Creatinine increase ≤ 30%[1]	Continue therapy	Continue therapy	Continue therapy

[a] Diuretic dose may be reduced at any time if euvolaemic (unless this has previously exacerbated symptoms)

Expert advice

- Up-titration does not have to stop because of a change to renal function.
- While MRAs can lead to hyperkalaemia and ACE inhibitors can increase serum potassium and creatinine levels, it is the degree of the change that determines if actions are recommended.
- The main challenge is when there are multiple renal function adverse effects or established renal impairment.
- *'If during up-titration of ACE inhibitor, the eGFR is low, urea and creatinine are high and the patient is not taking a diuretic, I recommend reducing the MRA before considering ACE inhibitor dose reduction.*
- *'Or for patients already with renal impairment (eg due to kidney disease) we need to decide what level of poor renal function we're prepared to tolerate and maintain low dose ACE inhibitor, or if the aim is to improve renal function when the MRA dose is already reduced, then we'd usually reduce the ACE inhibitor dose.'*

  Professor Andrea Driscoll.
- If unsure how to manage multiple changes to renal function, consider referral to a cardiologist.
- A small rise in creatinine is common after starting an ACE inhibitor; the level will usually return to baseline after around 4 weeks.

Volume status guidance

TABLE 5

Guidance for managing volume status adverse effects

Volume status: Review 1–2 weeks after each medicine initiation / each medicine dose increase[1,14]

ADVERSE EFFECTS	ACTIONS			
	DIURETIC	HEART FAILURE BETA BLOCKER	ACEI / ARB / ARNI	MRA
Congestion (fluid overload, wet) Signs and symptoms include: dyspnoea, peripheral/sacral oedema, increased jugular venous pressure, weight gain; ≥ 2 kg over 2 days[1,16,17]	If not on a diuretic; start at low dose (eg furosemide 20–40 mg daily) and adjust according to clinical response If on a diuretic; increase dose by 50%–100% with goal of reducing weight by 0.5–1 kg a day If weight continues to increase, seek specialist advice	If increasing congestion, consider: **a.** decreasing dose, or **b.** temporarily stopping if recently started	Continue therapy	Continue therapy
Dehydration (over-diuresis, dry) Signs and symptoms include: weight loss; ≥ 2 kg over 2 days, dizziness, thirst, fatigue, reduced urine output, increased urine concentration, orthostatic BP (postural drop)[1,16,17]	If on a diuretic; decrease dose (eg furosemide, reduce by 40 mg) until weight returns to baseline If weight continues to decrease, seek specialist advice	Continue therapy Closely monitor symptoms Review renal function	Continue therapy Closely monitor symptoms Review renal function	Continue therapy Closely monitor symptoms Review renal function

Expert advice

- Use of diuretics shouldn't be prioritised over the medicines that decrease mortality; ACE inhibitor/ARB/ARNI, heart failure beta blocker and MRA.
- Diuretic dose may be reduced at any time if euvolaemic (unless this has previously exacerbated symptoms).
- When using diuretics to treat congestion, be sure to use an effective dose eg if there is no response or inadequate diuresis (weight reduction) the dose should be doubled (not given BD).
- *'Diuretics are the Band-Aids of heart failure management. While they can make a patient feel better, they've never been shown to improve survival in chronic heart failure and should only have a limited role.'*

  Professor Andrew Sindone.
- *'If the patient is only mildly congested, rather than using the diuretic to reduce fluid, you may be able to increase the MRA, which also helps to increase survival and, compared to the diuretic, leads to less frequent urination for the patient.'*

  Professor Ralph Audehm.

Miscellaneous adverse effects guidance

TABLE 6 **Guidance for managing miscellaneous adverse effects**

CLINICAL INDICATOR	ADVERSE EFFECTS	ACTIONS		
		ACEI / ARB / ARNI	HEART FAILURE BETA BLOCKER	MRA
Respiratory As part of clinical review after medicine initiation and each dose up-titration	**Cough** dry, non-productive, interfering with quality of life[1]	May change ACEI to ARB	Continue therapy	Continue therapy
Allergic reactions As part of clinical review at each dose increase	**Angioedema**[1]	Manage the angioedema, stop ACEI , ARB or ARNI and seek specialist advice	Continue therapy	Continue therapy

Conclusion

A combination of an ACE inhibitor (or ARB if not tolerated), a heart failure beta blocker and an MRA up-titrated to target or maximum tolerated doses, can help improve quality of life, reduce hospitalisations and save lives for people with HFrEF.[1,4] However GPs can find it challenging to put up-titration into practice.[2,3]

Following the pathways and guidance described in this article can make it more straightforward for GPs to up-titrate heart failure medicines, particularly for the large group of patients with HFrEF who are relatively well and who usually do not experience adverse effects requiring a change to up-titration doses.

Useful resources

For health professionals

Heart Foundation

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

Medicine Today

How to optimise therapy for heart failure with reduced ejection fraction

Largely based on the *Guidelines for the Prevention, Detection, and Management of Heart Failure in Australia 2018*, this article is accessible via a subscription or once-only payment.

For your patients

NPS MedicineWise

Introducing medicines for heart failure

Heart failure: more than just your heart; an action plan for people with heart failure.

How can I take an active role in managing my heart failure?

Heart Foundation

Living well with heart failure; this booklet provides information about what heart failure is, its symptoms, self-management strategies and pharmacological management.

Heart failure; this video series provides information about what is heart failure, pharmacological management, psychological health and self-management.

References

1. Atherton JJ, Sindone A, De Pasquale CG, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Guidelines for the prevention, detection, and management of heart failure in Australia 2018. Heart Lung Circ 2018;27:1123-208. https://doi.org/10.1016/j.hlc.2018.06.1042.
2. Howlett J, Comin-Colet J, Dickstein K, et al. Clinical practices and attitudes regarding the diagnosis and management of heart failure: findings from the CORE Needs Assessment Survey. ESC Heart Fail 2018;5:172-83. https://pubmed.ncbi.nlm.nih.gov/28921886/.
3. Guirguis K. Prescribed heart failure pharmacotherapy: How closely do GPs adhere to treatment guidelines? Res Social Adm Pharm 2020;16:935-40. https://www.ncbi.nlm.nih.gov/pubmed/31690529.
4. Cardiovascular Expert Group. Therapeutic Guidelines: Heart failure. East Melbourne: Therapeutic Guidelines Ltd 2018. https://tgldcdp.tg.org.au/viewTopic?topicfile=heart-failure (accessed 29 October 2020).
5. Chan YK, Tuttle C, Ball J, et al. Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue. BMC Health Serv Res 2016;16:501. https://www.ncbi.nlm.nih.gov/pubmed/27654659.
6. Burnett H, Earley A, Voors AA, et al. Thirty years of evidence on the efficacy of drug treatments for chronic heart failure with reduced ejection fraction: a network meta-analysis. Circ Heart Fail 2017;10:e003529. https://pubmed.ncbi.nlm.nih.gov/28087688/.
7. National Heart Foundation of Australia. Pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF). Melbourne: NHF, 2019. https://www.heartfoundation.org.au/getmedia/c8889851-5843-40d1-a550-e6e9a9f7d03d/Clinical_Fact_Sheet_-_Pharmacological_Management.pdf (accessed 28 October 2020).
8. Australian Medicines Handbook. Heart failure. Adelaide: AMH Pty Ltd, 2020. https://amhonline.amh.net.au/chapters/cardiovascular-drugs/drugs-heart-failure/heart-failure (accessed 27 October 2020).
9. Audehm R, Sindone A. Rural Health Webinar Series - Heart Failure. East Melbourne: Royal Australian College of General Practitioners, 2020. https://www.racgp.org.au/racgp-digital-events-calendar/online-event-content/rural-health-webinar-series-heart-failure (accessed 26 November 2020).
10. Al-Omary MS, Davies AJ, Evans TJ, et al. Mortality and readmission following hospitalisation for heart failure in Australia: a systematic review and meta-analysis. Heart Lung Circ 2018;27:917-27. https://www.ncbi.nlm.nih.gov/pubmed/29519691.
11. Queensland Government Department of Health. Heart Failure Medication Titration Plan. Brisbane: QLD Govt DoH, 2017. https://www.health.qld.gov.au/clinical-practice/referrals/statewide-specialist-services/heart-failure-services/medication-management (accessed 16 March 2021).
12. National Heart Lung and Blood Institute. Low blood pressure. Bethesda, Maryland, USA: US Department of Health & Human Services, 2021. https://www.nhlbi.nih.gov/health-topics/low-blood-pressure (accessed 9 April 2021).
13. Chisholm P, Anpalahan M. Orthostatic hypotension: pathophysiology, assessment, treatment and the paradox of supine hypertension. Intern Med J 2017;47:370-9. https://pubmed.ncbi.nlm.nih.gov/27389479/.
14. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2013;128:e240-327. https://pubmed.ncbi.nlm.nih.gov/23741058/.
15. Sidhu S, Marine JE. Evaluating and managing bradycardia. Trends Cardiovasc Med 2020;30:265-72. https://pubmed.ncbi.nlm.nih.gov/31311698/.
16. National Heart Foundation of Australia. Fluid management algorithm. Melbourne: NHF, 2014. https://www.heartonline.org.au/media/DRL/Fluid_management_algorithm_in_heart_failure.pdf (accessed 19 March 2021).
17. Sindone AP, Driscoll A. How to optimise therapy for heart failure with reduced ejection fraction. Medicine Today 2019;20:22-7. https://medicinetoday.com.au/2019/october/supplement/how-optimise-therapy-heart-failure-reduced-ejection-fraction.

Heart Foundation

The NPS MedicineWise program on heart failure has been developed in collaboration with the National Heart Foundation of Australia.

Find this article online at https://www.nps.org.au/news/up-titrating-heart-failure-medicines

nps.org.au

Level 7/418A Elizabeth Street Surry Hills NSW 2010
PO Box 1147 Strawberry Hills NSW 2012
02 8217 8700 02 9211 7578 info@nps.org.au

Independent, not-for-profit and evidence based, NPS MedicineWise enables better decisions about medicines, medical tests and other health technologies. This program is funded by the Australian Government Department of Health.
ABN 61 082 034 393