

Prescribing Angiotensin Receptor Blockers (ARBs) for patients with heart failure due to left ventricular systolic dysfunction

The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

ARBs (sartans) have a more limited evidence base than ACE inhibitors (ACEI) and have not shown superiority over ACEI in any large robust clinical trial. There are currently no compelling indications for the use of ARBs routinely first line in heart failure. ARBs should only be considered second line in patients intolerant to ACEI.

Indication

Candesartan is the ARB of choice for use in heart failure and impaired left ventricular systolic function (ejection fraction $\leq 40\%$), and should be considered for the following patients:

- **Patients intolerant of ACE inhibitors or**
- **Symptomatic CHF patients already on maximum tolerated dose of ACE inhibitor and beta-blocker, unless also taking an aldosterone antagonist (under specialist advice)**

Contra-indications	Cautions
<ul style="list-style-type: none"> - History of hypersensitivity to ARB or any excipients. - Pregnancy and breastfeeding. - Severe hepatic impairment and/or cholestasis; biliary cirrhosis. - Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. - Patient on both an ACEI and aldosterone antagonist. - Baseline potassium > 5.5 mmol/L. 	<ul style="list-style-type: none"> - Symptomatic or severe asymptomatic hypotension (systolic blood pressure (BP) < 90mmHg). - Moderate to severe renal impairment i.e. serum creatinine $> 150\mu\text{mol/L}$ or eGFR $< 50\text{ml/min}$. See individual SPCs for dose adjustment requirements - Patients with volume depletion such as those on high dose diuretics may lead to symptomatic hypotension therefore volume should be restored prior to administration. - Bilateral renal artery stenosis, or renal artery stenosis in a single functioning kidney - Patients on haemodialysis. - Kidney transplant recipients - Hepatic impairment. - Haemodynamically relevant aortic or mitral valve stenosis. - Hypertrophic cardiomyopathy. - Primary aldosteronism. - Patients taking potassium supplements or other drugs that may increase potassium. - Baseline potassium > 5 to 5.5mmol/l

Seek specialist advice prior to initiation:

- **Concomitant therapy with an ACEI.**
- Suspected or confirmed aortic or mitral valve disease.
- Primary aldosteronism.
- Hypertrophic cardiomyopathy.
- Hyponatraemia (serum sodium $< 135\text{mmol/L}$).
- Symptomatic or severe asymptomatic hypotension (systolic BP $< 90\text{mmHg}$).
- Significant renal dysfunction / renovascular disease e.g. creatinine $> 150\mu\text{mol/L}$ or eGFR $< 50\text{ml/min}$ or hyperkalaemia (serum K $> 5.0\text{mmol/L}$).
- Renovascular disease (diagnosed as well as undiagnosed and clinically silent disease) e.g PVD or severe generalised atherosclerosis.
- Kidney transplant recipients.

Initiation and monitoring

- Check baseline blood chemistry (e.g. serum creatinine, urea, potassium, sodium and eGFR) and blood pressure (BP).
- Discontinue potassium supplements/potassium sparing diuretics (with the exception of aldosterone antagonists and review need for concomitant nephrotoxic drugs e.g. NSAIDs).
- Consider reducing diuretic dose.
- Start with the lowest recommended dose of ARB and titrate as suggested below. Aim for the target dose, failing that, the maximum tolerated dose. **Some ARB is better than no ARB.**

Dose titration

- BP and blood chemistry (e.g. serum creatinine, urea, potassium, sodium and eGFR) should be checked within **two weeks** of initiation or each change of dose.
- Recheck at 1, 3, and 6 months after achieving maintenance dose, then 6 monthly thereafter. More frequent monitoring may be required especially if patients are on combined loop and thiazide diuretic therapy, or are taking aldosterone antagonists Reduce dose/stop according to “worsening renal function” and “symptomatic hypotension” in “problem solving” below.
- ARB dose can be doubled at no less than **2 weekly** intervals if appropriate. Smaller increments may be more clinically suitable for certain patients.

ARB	Starting Dose (mg)	Target Dose (mg)
Candesartan	4mg once daily	32mg daily
Losartan	12.5mg daily	150mg daily
Valsartan	40mg twice daily	160mg twice daily Max 80mg daily in mild to moderate hepatic impairment without cholestasis

- Valsartan is licensed for the treatment of symptomatic heart failure when ACE inhibitors cannot be used, or as add-on therapy to ACE inhibitors when beta-blockers cannot be used – it is a black triangle drug for these indications and therefore under intensive monitoring the Medicines and Healthcare products Regulatory Agency.
- Losartan is a black triangle drug for chronic heart failure; it is under intensive monitoring from the Medicines and Healthcare products Regulatory Agency.

Patients taking combination of ACEI and ARB (following specialist advice)

- The risk of adverse events, especially renal impairment and hyperkalaemia, may increase when ARBs are used in combination with an ACE inhibitor. Patients with such treatment should be monitored regularly and carefully.
- Further checks of blood chemistry should be made every 4 weeks for 3 months and then 3 monthly for one year and then at least 6 monthly, but more frequently if clinically indicated.

Problem solving

- Angioedema:** Rare but life threatening. Discontinue therapy and seek immediate advice from accident and emergency.
- Worsening renal function:** An increase in urea, creatinine and K^+ is to be expected after initiation/titration of ARB. If the increase is small and asymptomatic, no action is necessary. Please see the table below for recommended actions.

Recommendations for monitoring ARB therapy in patients with normal renal function*

Blood Chemistry	Action
Creatinine ↑ up to 50% above baseline or to 265µmol/L (whichever is smaller). OR K+ ↑ to ≤5.5 mmol/L .	No action required. Repeat blood chemistry (urea, creatinine and potassium) within 2-4 weeks.
Creatinine ↑ > 50% but < 100% above baseline or between 265µmol/L and 310µmol/L (whichever is smaller). OR K+ ↑ to ≥ 5.5 - ≤5.9 mmol/L .	Review required- consider: a. Stopping concomitant nephrotoxic drugs e.g. NSAID's, non essential vasodilators (e.g. calcium antagonists, nitrates) and if no signs of fluid retention, reduce the dose of diuretic. b. Review causes of high potassium. Stop other agents that cause hyperkalaemia e.g. potassium sparing diuretics. c. If despite adjusting medication the creatinine and K^+ remain higher than above the dose of ACEI should be halved and the blood chemistry re-checked in 5-7 days. If the response to this is not satisfactory, seek specialist advice. Continue to monitor serum K^+ and serum creatinine / eGFR until stable.
Creatinine ↑ by >100% (from baseline) or to above 310µmol/L . OR K+ ≥ 6mmol/L .	Discontinue ARB and discuss with cardiologist It is very rarely necessary to stop an ARB and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.

*[Additional recommendations for monitoring ARB therapy in patients with chronic kidney disease \(CKD\) Stage 3 and above.](#)

- Asymptomatic hypotension:** Does not usually warrant a change in therapy.

d. Symptomatic hypotension:

- Consider dehydration and address as appropriate.
- Review diuretic dose with a view to decreasing dose if patient free of symptoms suggestive of fluid retention.
- If dizziness and light-headedness and/or confusion occur in the setting of low blood pressure, consider stopping nitrates, calcium channel blockers and other vasodilators.
- Monitor closely and allow longer intervals between dose titrations. Consider reduction of ARB to the previous tolerated dose.
- Seek specialist advice if measures do not resolve symptomatic hypotension.

Patient information

- ARB treatment will improve day to day symptoms, prevent heart failure worsening, reduce risk of hospital admission and prolong life
- It may take a few weeks for symptoms to significantly improve after starting therapy
- Hypotension and dizziness are the most common side effects
- Avoid over the counter anti-inflammatory drugs (NSAIDs), such as ibuprofen, soluble tablets and salt substitutes high in potassium

References

- [Chronic Heart Failure: NICE clinical Guideline CG108. Issued Aug 2010](#)
- [ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012.](#)
- Summary of product characteristics for Amias. Available online at www.medicines.org.uk
- British National Formulary March 2012

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