Angiotensin- II Receptor Blockers (ARBs) for the treatment of hypertension and heart failure

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The MMP recommends CANDESARTAN as the preferred ARB for the treatment of hypertension and heart failure in adults.

- ❑ This recommendation is based on a number of factors including cost, prescribing frequency, patient factors, contraindications and cautions.
- ❑ A full evaluation report is available at www.hse.ie/yourmedicines

Therapeutic Indications for Candesartan[3]

- Treatment of essential hypertension.
- When angiotensin-converting enzyme (ACE) inhibitors are not tolerated, the treatment of patients with heart failure and impaired left ventricular systolic function (left ventricular ejection fraction ≤ 40%) or as add-on therapy to ACE inhibitors in patients with symptomatic heart failure, despite optimal therapy, when mineralocorticoid receptor antagonists are not tolerated.

Candesartan dosing information[3]

Indication	Initial Dose	Titration	Note
Hypertension	8 mg once daily	Increase to 16 mg once daily and to a maximum of 32 mg once daily according to BP response.	Most of the antihypertensive effect is attained within 4 weeks
Heart Failure	4 mg once daily	Double the dose at intervals of 2 weeks up to target dose of 32 mg once daily.	

Initiating and monitoring of ARBs[1,2]

Check the following 1-2 weeks prior to starting treatment, 1-2 weeks after each dose increase and regularly throughout treatment:

1. Check **serum electrolytes** - sodium and potassium.
2. **Measure renal function** (serum creatinine and estimated glomerular filtration rate [eGFR]).
3. Check **blood pressure** (BP) 4 weeks after each dose titration.
4. For people who are at higher risk of hyperkalaemia or deteriorating renal function, consider checking renal function and serum electrolytes sooner (within 1 week).

Once the target or maximum tolerated dose of an ARB is reached, treatment should be monitored monthly for three months and then at least every six months, and at any time the person becomes acutely unwell.

Contraindications with ARBs[1,2]

- **Hypersensitivity** to the active substance or any of the excipients.
- **Pregnancy**: Use of ARBs is not recommended during the first trimester of pregnancy. Contraindicated during second and third trimesters of pregnancy.
- **Concomitant use of an ARB with aliskiren-containing products** in patients with diabetes mellitus or renal impairments (eGFR < 60 ml/min/1.73 m^2).
- **Severe hepatic impairment, cholestasis or biliary obstructive disorders.**

Cautions with ARBs[1,2]

- **Dual blockade of the Renin-angiotensin-aldosterone system (RAAS):** Concomitant use of ACE inhibitors, ARBs or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function.
- **Hyperkalaemia**: Concomitant use of ARBs with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium etc. may increase the risk of hyperkalaemia.
- **Renal impairment**: Caution is recommended for use in patients with creatinine clearance < 30 ml/min or in patients undergoing dialysis.
- **Renal artery stenosis:** ARBs may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney.
- **Ethnic differences**: ARBs are less effective in lowering BP in people of black African/ African-Caribbean family origin due to higher prevalence of low-renin status.
- **Aortic or mitral valve stenosis:** Patients suffering from haemodynamically relevant aortic or mitral valve stenosis, or obstructive cardiomyopathy.
- **Hypotension and electrolyte/fluid imbalance**: Symptomatic hypotension, especially after the first dose and after an increase in dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting.

Adverse effects with ARBs[2]

Renal impairment	Hyperkalaemia
Angioedema	Dizziness

Abbreviations: ACE: angiotensin-converting enzyme; ARBs: angiotensin-II receptor blocker; BP: blood pressure; eGFR : estimated glomerular filtration rate; RAAS: renin-angiotensin-aldosterone system; SmPC: Summary of product characteristics.

References: 1. British National Formulary (BNF). 2021. Pharmaceutical Press. [Online]. 2. National Institute for Health and Care Excellence - Clarity's Diagnosis and Treatment Guidance: Angiotensin-II receptor blockers (2022). 3. Summary of Product Characteristics (SmPCs) Atacand 4 mg, 8 mg, 16 mg.

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