Prescribing information for sacubitril valsartan (Entresto®▼) for treating symptomatic chronic heart failure with reduced ejection fraction

Licensed Indication

.
Sacubitril valsartan (Entresto®) is indicated in adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction.

NICE[1] support the use of sacubitril valsartan (Entresto®) under the following criteria:
It is recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction, only in people:

- with New York Heart Association (NYHA) class II to IV symptoms and
- with a left ventricular ejection fraction of 35% or less and
- who are already taking a stable dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor-blockers (ARBs).

Dosage and administration[2]

Sacubitril valsartan is administered orally. The recommended starting dose is one 49/51 mg tablet, twice daily (each tablet contains 48.6 mg sacubitril and 51.4 mg valsartan). The dose should be doubled at 2 to 4 weeks to the target dose of one 97/103 mg tablet (97.2 mg sacubitril and 102.8 mg valsartan) twice daily, as tolerated by the patient.

Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg. A starting dose of 24 mg/26 mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg.

ACEI or ARB should be stopped before starting sacubitril valsartan (Entresto®). Ensure 48 hour washout period if switching from ACEI (but not ARB.)

Specialist responsibilities

- Discuss the benefits and side effects of treatment with the patient.
- Initiate and stabilise treatment with sacubitril valsartan (Entresto®).
- Correct sodium and volume depletion before starting treatment and monitor BP, U&Es during initiation and dose titration.
- Ensure ACEI or ARB is stopped before starting sacubitril valsartan (Entresto®). Ensure 48 hour washout period if switching from ACEI (but not ARB.)
- Communicate to the GP re-established regimen; follow up arrangements and when to refer back.
- Communicate promptly with the GP when treatment is changed.
- Review patient annually, and give advice on stopping treatment.
- Have a mechanism in place to receive referral of a patient from the GP in the event of rare or severe side-effects.
- Ensure that clear backup arrangements exist for GPs to obtain advice and support
- Report adverse events to the MHRA (via Yellow Card) www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Primary Care responsibilities

- Prescribe the sacubitril valsartan (Entresto®) at the dose recommended, from the agreed date.
- Adjust the dose as advised by the specialist.
- Monitor serum potassium and renal function annually (more frequently if patient at risk) and report significant findings to the specialist.

- Report to and seek advice from the specialist on any aspect of patient care of concern to the GP that may affect treatment.
- Refer back to specialist if the patient's condition deteriorates.
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Report adverse events to the MHRA (via Yellow Card) www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Communication

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Hospital Pharmacy Dept:				
Other:				

Monitoring

Correct sodium and volume depletion before starting treatment and monitor BP during initiation and dose titration. Monitor serum potassium and renal function every three months. Consider dose reduction if hypotension, hyperkalaemia or renal impairment occurs

Contra-indications, Special warnings/precautions & adverse effects

Contra-indications:

ACEI or ARB should be stopped before starting sacubitril valsartan (Entresto®). Ensure 48 hour washout period if switching from ACEI (but not ARB.)

Severe hepatic impairment, biliary cirrhosis or cholestasis, end-stage renal disease, history of angioedema associated with ACE inhibitors or angiotensin II antagonists, hereditary or idiopathic angioedema, systolic BP <100mmHg, serum potassium >5.4mmol/l, pregnancy, lactation.

Special warnings/precautions:
Moderate to severe renal impairment (CrCl <60ml/min), moderate hepatic impairment. Renal artery stenosis; monitor renal function. History of angioedema, black patients. NYHA class IV heart failure.

Adverse Effects
Anaemia, hyperkalaemia, hypokalaemia, hypoglycaemia, dizziness, headache, syncope, vertigo, hypotension, cough, GI upset, renal impairment, fatigue, asthenia. Reports of angioedema (discontinue immediately).

Drug Interactions

ACE inhibitors, aliskiren, angiotensin II antagonists, NSAIDs, inhibitors or substrates of OATP1B1 or OATP1B3 (e.g., statins), inhibitors of OAT3 (e.g., rifampicin, ciclosporin), OAT1 (e.g., tenofovir, cidofovir) or MRP2 (e.g. ritonavir), PDE5 inhibitors, K^+ supplements, K^+-sparing diuretics, aldosterone antagonists, lithium.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions. Please refer to full prescribing data in the Summary of Product Characteristics or the British National Formulary.

[1] NICE TA388 April 2016
[2] Summary of Product Characteristics www.medicines.org.uk/emc/medicine/31244 Accessed 06/04/2016