

Sacubitril Valsartan (Entresto®) Prescribing Advice and Guidance

Therapeutic indication

Sacubitril Valsartan (Entresto®) is licensed for the treatment of symptomatic chronic heart failure in adults with reduced ejection fraction.

Selection criteria

Patients should fit all of the following criteria:

- Symptomatic chronic heart failure, with
- New York Heart Association (NYHA) class II to IV symptoms, and
- a left ventricular ejection fraction of 35% or less on echocardiogram or equivalent function on alternative imaging not older than 12 months, and
- On optimal medical therapy for HF including angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor-blockers (ARB) (mandatory), beta-blocker and aldosterone antagonist (spironolactone or eplerenone) for at least 3 months.
- Raised natriuretic peptides: BNP > 150pg/ml (NT-proBNP>600pg/ml) or if hospitalisation for heart failure within the last 12 months, BNP>100pg/ml (NTproBNP>400pg/ml).
- Systolic blood pressure (SBP) ≥100 mmHg
- eGFR ≥30 ml/min/1.73 m²
- Serum potassium <5.4 mmol/l

Contra-indications

- Known history of angioedema related to previous ACEI or ARB therapy
- Hereditary or idiopathic angioedema
- Pregnancy
- Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg
- eGFR <30 ml/min/1.73 m²
- Severe hepatic impairment, biliary cirrhosis and cholestasis
- Sacubitril valsartan should not be co-administered with an ACEI or an ARB
- Concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m²)
- Hypersensitivity to the active substances or to any of the excipients

Initiation and up-titration

- Initiation of sacubitril valsartan is to be undertaken under the supervision of a consultant with an established expertise in managing patients with heart failure and access to a multidisciplinary team.
- Sacubitril valsartan should not be co-administered with an ACEI or an ARB. Due to the potential risk of angioedema when used concomitantly with an ACE inhibitor, it must not be started for at least 36 hours after discontinuing ACE inhibitor therapy. For those taking an ARB, discontinue ARB and start sacubitril valsartan at next scheduled dose of ARB.
- Initiation and titration to stable maintenance dose will be undertaken by the heart failure specialist. It is estimated this may take up to 3 months.
- Starting dose and titration in those on established ACEI or ARB (after ceasing ACEI or ARB):
 - Initiate 49mg/51mg sacubitril valsartan twice daily for 2-4 weeks then
 - Increase to 97mg/103mg sacubitril valsartan twice daily thereafter
- Starting dose in those patients taking low ACEI or ARB dose:

- Initiate 24mg/26mg sacubitril valsartan twice daily for 3-4 weeks then
- The dose should be doubled every 3-4 weeks to the target of 200 mg (97mg/103mg) twice daily, as tolerated by the patient
- A starting dose of 24mg/26mg sacubitril valsartan should be considered in patients with moderate renal impairment (eGFR 30-60 ml/min/1.73 m²).
- A starting dose of 24 mg/26 mg sacubitril valsartan twice daily should be considered for patients with SBP ≥100 to 110 mmHg.
- Monitoring of renal function and blood pressure to be undertaken after each dose titration.

Down-titration or discontinuation

Adjustment of concomitant medicinal products, temporary down-titration or discontinuation of sacubitril valsartan is recommended:

- If SBP <95 mmHg at follow up
- If symptomatic hypotension
- If eGFR decreases >35% at follow up
- If serum potassium >5.4 mmol/L at follow up

Maintenance and transfer to primary care

- Following titration to optimum tolerated dose, maintenance will be continued in primary care.
- Please ensure that previous ACEI or ARB treatment is removed from the repeat prescription template and not continued.
- Ongoing monitoring of urea and electrolytes every 6 months for signs of renal impairment or hyperkalaemia.
- Blood pressure should be monitored routinely.

Further prescribing information

- Please refer to the Summary of Product Characteristics (SPC) for further information regarding side effects, drug interactions and special warnings:
<http://www.medicines.org.uk/emc/medicine/31244>
- Sacubitril Valsartan (Entresto®) has been approved by NICE (TA388):
<https://www.nice.org.uk/guidance/ta388/resources/sacubitril-valsartan-for-treating-symptomatic-chronic-heart-failure-with-reduced-ejection-fraction-82602856425157>

Patient support and information

- A patient information leaflet will be offered to patients to support treatment initiation of sacubitril valsartan therapy. Additionally, it will detail instructions to avoid concomitant ACEI or ARB and confirm advice for patients during sick days.
- Novartis has developed a wallet sized card for patients to carry that can be shown to health care professionals to alert them to the interactions of sacubitril valsartan and ACEI. The heart failure specialist team will have access to this resource to provide to patients.

Primary care support

- GP to refer back to the specialist, who has initiated sacubitril valsartan if there are concerns about contra-indications, cautions, monitoring results or prescribing responsibilities.
- Consultant contact details for advice and support:
 - Dr Barbagallo email address: Rossella.Barbagallo@btuh.nhs.uk
 - Dr Barbagallo's secretary's tel no (Jane Holliday): 01268 494332

References

- Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care. NICE clinical guideline 108 (2010).
- Ivabradine for treating chronic heart failure. NICE technology appraisal guidance no. 267 (2012).
- Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure. NICE technology appraisal guidance no. 314 (2014)
- Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction. NICE technology appraisal guidance no. 388 (2016). www.nice.org.uk/guidance/ta388
- NICE Chronic Heart Failure Guidelines: www.nice.org.uk/guidance/cg108/evidence
- Ponikowski P, Voors AA, Anker SD et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, available at doi: 10.1093/eurheartj/ehw128
- McMurray JJV, Packer M, Desai AS et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Eng J Med 2014; 371:993-1005.
- Summary of Product Characteristics, <http://www.medicines.org.uk/emc/medicine/31244>
- North East and North Central London Position Statement: Sacubitril valsartan for HFrEF Date released: June 2016
- Sacubitril Valsartan (Entresto®) Prescribing Pathway – Princess Alexandra Hospital, Harlow. Date released: July 2016