Sacubitril Valsartan▼ for Heart Failure

Bath and North East Somerset, Swindon and Wiltshire Clinical Commissioning Group

Sacubitril Valsartan (Entresto®▼) – Amber, specialist initiated including dose titration to a stable dose

Criteria for use

- NICE TA388 recommends sacubitril valsartan 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 (LVEF) of 35% or less **AND**
  - who are already taking a stable and optimised dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor-blockers (ARBs)

Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team. ALWAYS PRESCRIBE GENERICALLY

Local Pathways for access (BaNES/Swindon/Wiltshire)

- NICE recommend this drug is best suited to be initiated and titrated in a community heart failure clinic, where they can select the most suitable patients and monitor them closely for side-effects and titrate the dose accordingly
- Once stable, the patient can then be sent out to the GP for them to continue to prescribe
- Wiltshire does not currently have such a service but the Sarum primary care heart failure pilot has been extended to Sept 2020
- At the current time, any suitable patients outside of south Wiltshire will have to be referred to secondary care cardiology clinics for initiation and titration.
- For patients in BaNES, Virgin services do have a heart failure specialist nurse who are prescribers and have access to a MDT.
- For patients in Swindon, patients should be referred to the community heart failure service
- **GPs should not initiate this drug themselves (unless they have a specialist interest in heart failure)**

Important Drug Information

Sacubitril/valsartan must not be used concurrently with ACE inhibitors due to the risk of life threatening angioedema. It should also not be used with ARBs due to its angiotensin II receptor blocking activity

- Sacubitril/valsartan is a fixed dose combination preparation containing a first-in-class: Angiotensin Receptor Antagonist Neprilysin inhibitor (ARNi). It is a complex of valsartan and sacubitril

Dose Information (PRESCRIBE GENERICALLY)

- For full drug information please refer to the Summary of Product Characteristics https://www.medicines.org.uk/emc/medicine/31244
- STOP the ACE-I that the patient was on for at least 36 hours before starting sacubitril/valsartan. (In practice, a more pragmatic 2 days washout will be used, but the SPC stipulates at least 36 hours). A washout period is not needed if switching from a ARB to Sacubitril/valsartan
- The usual recommended starting dose is one tablet of 49 mg/51 mg BD with or without food
- The dose should be doubled every 2-4 weeks to the target dose of one tablet of 97 mg/103 mg BD as tolerated by the patient
- U&Es should be checked prior to initiation and before each dose tiration
- Patients should have been titrated up to maximum tolderated doses of ACE-Is or ARBS before trying Sacubitril/Valsartan
- If systolic blood pressure between 100-110mmHg or moderate renal impairment (eGFR 30-60 ml/min/1.73m2) consider starting with lowest dose (24/26mg)
- For patient information see: https://www.medicines.org.uk/emc/

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Further information on use in renal and hepatic impairment, adverse effects and drug interactions

- **Drug interactions of note (not exhaustive) : (see SPC for full details)**
  - Statins, PDE5 inhibitors, Rifampicin, ciclosporin and anti-virals, Metformin, Lithium, NSAIDS, Cox-2 inhibitors
- **Contraindications (not exhaustive):**
  - Do not use with Aliskiren in patients with diabetes mellitus or renal impairment (eGFR <60 ml/min/1.73 m^2)
  - Patients with a known history of angioedema related to previous ACE-I or ARB therapy
  - SBP is less than 100mmHg
- Renal and Hepatic impairment - no dose adjustment required in mild renal impairment or mild hepatic impairment.
- Caution is recommended when using sacubitril/ valsartan in severe renal impairment or end stage renal disease or moderate hepatic impairment; use a starting dose of 24mg/26mg BD
- Overall the adverse effect profile including the incidence of hypotension and associated adverse effects, particularly the propensity for sacubitril/valsartan to precipitate renal impairment (due to decreased renal perfusion) is unclear from the available trial data
- Side effects listed as very common (≥ 1/10) in the SPC are hyperkalaemia, hypotension and renal impairment
- Careful upward titration may be needed to ensure patient tolerability and safety which in turn may lead to a decrease in overall efficacy and mortality. A lower strength is licensed to facilitate a lower initial dose and upward titration.
- Sacubitril/Valsartan is a black triangle drug, please monitor for and report any side effects via the yellow card reporting system: www.mhra.gov.uk/yellowcard
- **Once Sacubitril/Valsartan has been started, please ensure that the previous ACE-I or ARB the patient was on is REMOVED from their repeat medication list, ensure there is no electronic "live" prescriptions on the prescribing system and inform community pharmacist.**

Tolerability

- If patients experience tolerability issues such as those listed below, dose adjustment of concomitant medications, temporary down-titration or discontinuation of sacubitril/valsartan may be required. This should be dealt with by the specialist team.
- Systolic blood pressure ≤95mmHg
- Symptomatic hypotension
- Hyperkalaemia (If above 5.4mmol/l consider discontinuation)
- Renal dysfunction
- Symptomatic hypotension and decreased renal function is more likely to occur if the patient has been volume depleted, e.g. by diuretic therapy, concomitant NSAID use, dietary salt restriction, diarrhoea or vomiting.
- If a patient has tolerability problems after previously tolerating it then seek further advice on management.

Cost information (Feb 2020)

- Sacubitril 24mg/valsartan 26mg 28 tabs: £45.78 Dose:1 bd
- Sacubitril 49mg/valsartan 51mg 56 tabs: £91.56 Dose: 1 bd
- Sacubitril 97mg/valsartan 103mg 56 tabs: £91.56 Dose: 1 bd
- Due to the flat pricing structure, it is important that prescribers ensure dose optimisation to minimise cost (e.g. 1 x 49/51mg NOT 2 x 26/24mg)
- The cost of treating one patient with sacubitril/valsartan for one year = £1,098

Other information

- The NNT to prevent one primary event and one death was 21 and 32 respectively (from Paradigm HF trial)
- There is limited data beyond 27 months. The long term efficacy and safety profile of sacubitril/valsartan has not been defined. There is also limited data in patients aged less than 18 years and patients over 75 years of age
- There is limited comparative data with alternative treatments for heart failure
- Improvement in quality of life measures have not been adequately assessed to date
- There is limited clinical experience with use of sacubitril/valsartan in NYHA class IV patients, use with caution.

Contact details of local services

- RUH: Dr Jacob Easaw (Consultant cardiologist) secretary: 01225 825442
- SFT: Helen Moule, secretary to Dr Tom Jackson (Consultant Cardiologist) 01722 336262 extension 4223
- GWH: 01793 604273
- Salisbury community heart failure service (pilot): community.salisburyhfteam@nhs.net
- BaNES CCG for advice: vcl.bathneshfs@nhs.net
- GWH community heart failure service: Rachel Hurt and Martin Larner: 01793 605921 or GWH.HeartFunctionTeam@nhs.net