Information for primary care – Sacubitril/valsartan (Entresto).

RAG Status – Green +

Background/Summary information

Sacubitril/valsartan (Entresto) is the first of a new class of medicines called dual acting angiotensin-II receptor and neprilysin inhibitors (ARNI) used in the treatment of chronic heart failure.

Treatment with sacubitril/valsartan **must** be started by a heart failure specialist with access to a multidisciplinary heart failure team.

Related NICE guidance

NICE (TA388) https://www.nice.org.uk/guidance/ta388

See manufacturer's SPC for full prescribing information
https://www.medicines.org.uk/emc/medicine/31244

Licensed indication

Sacubitril/valsartan is recommended as an option for adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction 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 inhibitors (ACEi) or angiotensin II receptor-blockers (ARBs)

Dosage and administration

Dose: Sacubitril/valsartan 97mg/103mg twice daily
It is usually started at a lower dose 49mg/51mg twice daily and then up-titrated in one or two steps in a similar way to ACEI or ARBs.
A lower dose of 24/26mg is available for patients who are unable to tolerate higher doses, or for a more cautious initiation.

Key points for safe use:

- **It is essential that ACE inhibitors are discontinued 48hours before initiation of sacubitril/valsartan due to an increased risk of angioedema when the two are used together**
- Angiotensin receptor blockers and Angiotensin Converting Enzyme inhibitors **must not** be taken with sacubitril/valsartan.
- The manufacturer states that sacubitril/valsartan must be stored in its original package therefore use in compliance aids (dosette boxes or MCAs) cannot be recommended.

GP and specialist responsibilities

- The heart failure specialist team are responsible for washout of ACEI, initiation of treatment and will ensure that the patient understands the changes to their medicines i.e. that they must not restart ACEI or ARBs that have been discontinued by the specialist team.
- The heart failure specialist team are responsible for the monitoring of the drug through the titration phase and response to treatment.
- The heart failure specialist team will be responsible for titration in all cases. However, there may be rare instances when GPs are asked to issue a prescription during the titration phase (for example if blood results are not returned in a timely fashion).
- The CHS heart failure specialist team have advised that there should be no additional clinical risk to patients above that of the current situation – as a result of delayed correspondence – the

required heart failure medication is not up-titrated as intended.

- The GP will provide prescriptions for the patient in line with the dose advised by the heart failure specialist team once a maximum tolerated dose is established.
- The heart failure specialist team are happy to provide general advice regarding sacubitril/valsartan, and can be contacted via the hospital switch board (0191 5656256). Patient specific queries should be dealt with via the initiating prescriber.

Contraindications

Sacubitril/valsartan is contraindicated in patients with a known history of angioedema.
An increased risk of angioedema has been observed in patients taking both sacubitril/valsartan and ACEIs. For this reason, a 48 hour washout period must exist between discontinuing ACEIs and initiating sacubitril/valsartan and cannot be co-administered.
Sacubitril/valsartan also cannot be co-administered with ARBs due to its valsartan content.
Sacubitril/valsartan is contraindicated in the second and third trimester of pregnancy (it is not recommended in the first trimester of pregnancy).

Cautions

If angioedema occurs whilst taking sacubitril/valsartan, immediately discontinue use and start appropriate therapy and monitoring until complete and sustained resolution of signs and symptoms. **It must not be re-administered to patients who have developed angioedema whilst taking sacubitril/valsartan.**

Side effects

The most commonly observed side effects of sacubitril/valsartan are hyperkalaemia, renal impairment and hypotension.

Drug interactions

Sacubitril/valsartan has multiple drug interactions. This list includes ACE inhibitors, Aliskiren, ARBs. See SPC.

Monitoring

- Once the patient is on a stable dose review every 6 months for measurement of blood pressure, renal function and electrolytes.
- Review every 3 months if also treated with spironolactone or eplerenone.
- This should usually by in primary care, unless otherwise advised by the initiating specialist.
- If patients experience a change in renal function, or for any other issues, GPs should refer back to the heart failure service.
- Other monitoring arrangements may be necessary for patients on other medicines – see SPC.

Sacubitril/valsartan has black triangle status (▼). Report all suspected adverse drug reactions via the Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

Cost £91.56 for 28 days