

Guidelines for the Prescribing of Sacubitril / Valsartan

1. BACKGROUND

Sacubitril valsartan is an angiotensin receptor neprilysin inhibitor, including both a neprilysin inhibitor (sacubitril) and an angiotensin II receptor blocker (ARB; valsartan). Both sacubitril and valsartan lower blood pressure.

2. INDICATION

Sacubitril valsartan is recommended as an option for treating symptomatic chronic heart failure in patients with reduced ejection fraction as specified by [NICE TA388](#)

Within Hull and East Riding, sacubitril / valsartan will be prescribed for patients with symptomatic chronic heart failure and a reduced ejection fraction, who meet the following criteria

Patients

- 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) and
- who remain symptomatic despite standard treatment with ACE inhibitors/ARBs, beta-blocker and aldosterone antagonist, where tolerated

Treatment must be initiated by heart failure team.

3. DOSE

Initial dose (as sacubitril/valsartan): 49/51 mg twice daily for 2 – 4 weeks, increased if tolerated to 97/103mg twice daily.

Reduce initial dose to 24/26mg twice daily in patients with moderate or severe renal impairment (eGFR < 60 ml/min/1.73 m²), moderate hepatic impairment (Child-Pugh B classification or with AST/ALT values more than twice the upper limit of the normal range), or patients with systolic blood pressure of 100 to 110 mmHg.

Do not start treatment until 48 hours after discontinuing ACE inhibitor therapy.

4. CONTRAINDICATIONS AND CAUTIONS

Sacubitril valsartan is contraindicated in patients with

- Known history of angioedema related to previous ACE inhibitor or ARB therapy
- Hereditary or idiopathic angioedema
- End stage renal disease
- Severe hepatic impairment, biliary cirrhosis and cholestasis
- Pregnancy and breast feeding

5. DRUG INTERACTIONS

Drug interactions where concomitant use of sacubitril valsartan is contraindicated:

- ACE inhibitors or other ARBs
- Aliskiren

Drug interactions where caution, additional monitoring or dose adjustment may be required:

- May increase statin levels – advise patient to report any new side effects
- PDE5 inhibitors – increased risk of hypotension
- Metformin – may reduce metformin levels, monitor HbA1c, blood glucose

Other interactions (as per valsartan)

- potassium sparing diuretic, aldosterone antagonists – increased risk of hyperkalaemia
- NSAIDs – increased risk of renal impairment
- Lithium – increases plasma lithium
- inhibitors of the uptake transporter (eg. rifampin, ciclosporin, tenofovir, cidofovir) or efflux transporters (e.g. ritonavir) – may increase valsartan levels

5. ADVERSE EFFECTS

The most commonly reported adverse reactions are hypotension, hyperkalaemia and renal impairment. Angioedema has been reported ($\geq 1/1,000$ to $< 1/100$)

Sacubitril Valsartan is an intensively monitored drug (black triangle drug), as such any possible adverse effects (including any considered not to be serious) relating to treatment should be reported via the yellow card scheme (www.yellowcard.gov.uk)

For further information including full details of contraindications, cautions, drug interactions and adverse effects always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

6. INFORMATION TO PATIENT

Patients should be advised of benefits and risks of treatment, including common side effects and requirement for follow up appointment for blood pressure, blood tests and dose titration.

Patients should be warned to stop taking ACE inhibitor 48 hours before starting sacubitril valsartan due to risk of angioedema. Any patient prescribed an ARB will be advised to stop taking ARB the day before starting sacubitril valsartan.

Patients will be given a patient information leaflet, which highlights need to stop ACE inhibitor / ARB and will be given copy of clinic letter.

7. PRESCRIBING AND MONITORING RESPONSIBILITIES

Heart failure specialist should review baseline blood pressure and BCP (for renal function, hepatic function and potassium levels), initiate treatment (1 month supply) and write to patient's GP.

General practitioner should review BP and BCP 2 to 4 weeks after initiation, increase dose if tolerated and re-check BP and BCP 2 weeks after any dose titration, and 6 monthly once stable.

The specialist team will review patients 6 months after initiation

Specialist team can be contacted for further advice:

Contact details

Contact consultant cardiologist as per clinic letter or Professor Clark 01482 622044

APPROVAL PROCESS

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Cardiology Department**Information about Sacubitril Valsartan (Entresto)***September 2016***Great Staff – Great Care – Great Future****INTRODUCTION**

This leaflet has been produced to give you general information about your new medicine, Sacubitril Valsartan, also known as *Entresto*. Most of your questions should be answered by this leaflet. It is not intended to replace the discussion between you and your doctor, but may act as a starting point for discussion. If after reading it you have any concerns or require further explanation, please discuss this with a member of the healthcare team caring for you.

WHAT IS SACUBITRIL VALSARTAN (ENTRESTO)

You have probably had symptoms of a condition known as heart failure, which means that your heart is not working as well as it should. You are probably already taking medicines to treat this condition but are still experiencing symptoms such as breathlessness, tiredness and ankle swelling.

Sacubitril Valsartan is a new medicine which has been shown to reduce the symptoms of heart failure. Your cardiologist (heart doctor) believes you may benefit from taking this medicine.

ARE THERE ANY RISKS?

Like all medicines, some patients experience side effects when taking Sacubitril Valsartan. The most common side effect is a fall in blood pressure, which may make you feel light headed, dizzy or faint. This side effect is likely to become less noticeable with time, but if you feel you cannot cope, then please contact the Heart Failure clinic or tell your GP.

Other side effects may include changes in levels of chemicals in your blood (e.g. potassium) and how well your kidneys work. For this reason you must have a blood test 2-4 weeks after starting your new tablets. This will usually be done at your GP surgery or the GP will advise you where it will be undertaken.

Stop taking Sacubitril Valsartan and seek immediate medical attention if you notice any swelling of the face, lips, tongue and/or throat, which may cause difficulties in breathing or swallowing. These may be signs of angioedema (an uncommon side effect which may affect up to 1 in 100 people).

For more information about cautions, warnings and side effects, please read the patient information leaflet supplied with your medicine.

HOW DO I TAKE SACUBITRIL VALSARTAN (ENTRESTO)

Your first prescription for Sacubitril Valsartan will be written by your cardiologist and should be taken to the Pharmacy Department, Castle Hill Hospital who will supply 28 days' of treatment (56 tablets)

You will usually start by taking a dose of 24 mg/26 mg or 49 mg/51 mg twice a day (one tablet in the morning and one tablet in the evening).

If you are taking medicines called ACE inhibitors (e.g. Enalapril, Lisinopril, Ramipril, Perindopril, Quinapril, Fosinopril, Trandolapril) you must STOP TAKING THESE 48 HOURS BEFORE STARTING SACUBITRIL VALSARTAN.

If you are taking medicines called Angiotensin II Receptor Antagonists or ARBs (e.g. Valsartan, Candesartan, Losartan, Irbesartan, Olmesartan, Eprosartan, Telmisartan) you MUST STOP TAKING THESE WHEN YOU START TAKING SACUBITRIL VALSARTAN.

If there are any other changes to your regular medicines, your cardiologist will tell you about these.

WHAT HAPPENS AFTERWARDS?

The Cardiology Department will write to your GP to inform them of the changes made to your medicines. You will need to make an appointment at your GP surgery for 2 weeks after starting your new tablets for a blood test. You will also need to make an appointment to see your GP 5-7 days after this blood test to discuss the results, check your blood pressure and review your medication.

If the Sacubitril Valsartan is helping, your GP will continue prescribing it. It is likely that your GP will increase the strength of the tablet, but you should still be taking ONE tablet TWICE DAILY.

Should you require further advice on the issues contained in this leaflet, please do not hesitate to contact the Cardiology Department

on tel no: (01482) 622044

This leaflet was produced by the Cardiology Department, Hull and East Yorkshire Hospitals NHS Trust and will be reviewed in October 2019 HEY 831/2016