Sacubitril valsartan for the treatment of symptomatic heart failure

Recommendation

NICE TA 388 states that sacubitril valsartan is recommended for the treatment of symptomatic heart failure if the patient meets the following criteria for use:

- Chronic stable heart failure – New York Heart Association (NYHA) class II-IV
- Left ventricular systolic dysfunction with ejection fraction <35%
- Stable on an Angiotensin-Converting Enzyme (ACE) inhibitors or Angiotensin II Receptor Blocker (ARB)

Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team. Dose titration and monitoring should be performed by the most appropriate team member as defined in NICE's guideline on chronic heart failure in adults.

It has been agreed in East Kent that before treatment with sacubitril valsartan patients should be tolerating a therapeutic dose of ACE inhibitor or ARB as specified in this document.

Approved by: East Kent Prescribing Group *(Representing Ashford CCG, Canterbury and Coastal CCG, South Kent Coast CCG and Thanet CCG)*
Date: November 2016
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Specialist Initiated Drugs Prescribing Information Sheet September 2016

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NICE recommendation

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It has been agreed in East Kent that before treatment with sacubitril valsartan patients should be tolerating a therapeutic dose of ACE inhibitor or ARB as specified below:

ACE inhibitor / ARB	**East Kent minimum dose Criteria**
Enalapril	10mg bd
Lisinopril	10mg od
Perindopril	2mg od
Ramipril	2.5mg bd or 5mg od
Losartan	50mg od
Candesartan	16mg od
Valsartan	160mg od
Irbesartan	150mg od

The target dose of sacubitril valsartan contains 103mg valsartan which is equivalent to 160mg of valsartan montherapy. Trial data from Paradigm showed superior efficacy to enalapril 10mg bd – a 3.2% reduction in mortality and 2.8 % reduction in hospitalisations.

Clinical Information

For full prescribing information see https://www.medicines.org.uk/emc/medicine/31244

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

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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.

Patients must not take other drugs acting on the angiotensin system concurrently eg. ACE inhibitors, ARBs or aliskiren. In addition patients taking ACE inhibitors must have a 48 hour washout period before they commence sacubitril valsartan because of the increased risk of angioedema. This is also required if ACE inhibitor treatment is recommenced in place of sacubitril valsartan.

Adverse Reactions

The most commonly reported adverse reactions during treatment with sacubitril valsartan are hypotension, hyperkalaemia and renal impairment. Reported adverse events are generally in line with that reported for other medicinal products acting on the renin-angiotensin-aldosterone system.

1. Cough	Not an indication to stop – unless distressing
2. Hypotension	Consider reviewing alternative causes of hypotension – diuretics / anti-hypertensives – if required, consider reducing sacubitril valsartan dose – seek advice
3. Renal dysfunction	Monitor for decline in function – **Seek advice if any decline below e GFR 60ml/min**
4. Hyperkalaemia	Consider other causes of rise in K+ - (diarrhoea / vomiting / infection) If K+ > 5.4 consider reducing / stopping sacubitril valsartan
5. Angioedema	STOP IMMEDIATELY & CALL 999

INTERACTIONS

Sacubitril valsartan should not be administered concomitantly with ACE inhibitors / ARBs or Aliskiren

Caution with:
Potassium sparing diuretics / Aldosterone Antagonists – increased potassium levels
Lithium –avoid combination but if essential monitor levels closely
NSAIDS – can reduce renal function
Statins – monitor for adverse effects – may increase statin exposure
Metformin – may reduce effectiveness of metformin – monitor effectiveness.
PDE5 inhibitors – significant hypotension

PLEASE ENSURE ALL ACE INHIBITORS/ARBs ARE REMOVED FROM THE REPEAT PRESCRIPTION

Contact details of the KCHFT Cardiac Nurse Specialist Team

Canterbury	0300 123 1412	Dover/Deal	01304 865457
Shepway	01303 858931	Thanet	0300 123 3027
Ashford	0300 7900 272		

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East Kent Prescribing Pathway for Sacubitril Valsartan

1. Recommendation to initiate sacubitril valsartan

Patients can only be initiated on this drug when they are clinically stable. They will only be recommended for initiation on this drug by a cardiologist, in liaison with the KCHFT cardiac nursing team**. All patients must be referred to the cardiac nursing team for initiation to take place.**

2. Initiation phase

- The first 4 weeks of treatment will usually be prescribed by the initiating cardiologist unless the GP prefers to prescribe. This prescription will be held by the patient's cardiac nurse until the nurse has:
  - Counselled the patient and ensured that they understand that they should no longer take their current prescription for an ACE inhibitor, ARB or aliskiren.
  - Assessed the patient's ability to concord with treatment.
  - **Ensured a 48 hour washout period for patients taking ACE inhibitors.**
  - Ensured the GP has removed any ACE inhibitors, ARBs or aliskiren from the patient's medication list and added an alert for these drugs not be prescribed to the patient's record – each nurse will agree an appropriate assurance process with individual surgeries.
  - Liaised with the patient's Community Pharmacist to ensure they do not issue or request previous ACE Inhibitor or ARB treatment.

3. Titration phase

The cardiac nurse team will:

- Monitor the patient regularly for the first 3 months of treatment, including U&Es and renal function 7- 10 days after intiation and titrating the dose up as clinically appropriate.
- Liaise with the cardiologist regarding any clinical concerns.
- Inform the GP of any clinical concerns, requirements to change the dose of sacubitril valsartan or to stop treatment.
- Provide the GP with any clinical support required.
- Report adverse reactions via yellow card system before GP takes over prescribing.

4. Ongoing Prescribing and Monitoring

- When the patient has reached a stable dose, usually after 4 weeks, the patient's GP will be requested to provide repeat prescriptions as directed by the cardiac nurse team
- After 3 months the GP will be asked to assume ongoing responsibility for monitoring – blood pressure, renal function and potassium need to be monitored at least 6 monthly.
- The GP will report adverse reactions via yellow card system.

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