

Shared Care Guideline For for Entresto® in the management of Chronic Heart Failure

This shared care guideline (SCG) has been written to enable the continuation of care by primary care clinicians of patients initiated on Sacubitril valsartan (Entresto) by the secondary care cardiology team at Barnsley Hospital or the Heart failure team within Barnsley Integrated Services Care Group where this is appropriate and, in the patients', best interests. Primary care will only be requested to take over prescribing of sacubitril valsartan (Entresto) within its licensed indication unless specifically detailed otherwise below.

Introduction

Indication/Licensing information

Sacubitril valsartan (Entresto®) is indicated in adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction.

NICE recommends Sacubitril valsartan (Entresto®) 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 of 35% or less and
- who are already taking a stable 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 (NICE TA 388). Dose titration and monitoring should be performed by the most appropriate team member as defined in NICE guideline NG106 Chronic heart failure in adults: diagnosis and management.

Pharmacology

Sacubitril: Neprilysin inhibitor; neprilysin is responsible for degradation of atrial and brain natriuretic peptide; the cardiovascular and renal effects of sacubitril's active metabolite (LBQ657) in heart failure are attributed to the increased levels of peptides that are degraded by neprilysin (eg, natriuretic peptide); administration results in increased natriuresis, increased urine cGMP, and decreased plasma MR-proANP and NT-proBNP.

Valsartan: Angiotensin II receptor type I inhibitor; decreases blood pressure and blocks vasoconstrictor and aldosterone-secreting effects of angiotensin II

Dosage and administration

Sacubitril valsartan is administered orally. The recommended starting dose is one 49/51 mg tablet, twice daily. 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.

A reduced starting dose of one tablet of 24mg/26mg TWICE daily with a slow dose titration (doubling every 3 to 4 weeks) should be considered for patients with:

- Systolic blood pressure between 100 to 110mmHg

- Moderate renal impairment (eGFR 30 to 60ml/min/1.73m²). Note for patients with severe renal impairment (eGFR less than 30ml/min/1.73m²), sacubitril valsartan should be used with caution due to very limited experience and greater risk of hypotension.
- Moderate liver impairment (Child-Pugh B classification or with AST/ALT greater than twice the upper limit of normal range) – use with caution due to limited clinical experience.
- Patients who have previously been taking low dose* of ACEi/ARB.

* Enalapril 10mg (or less), Lisinopril 10mg (or less), Ramipril 5mg (or less), Valsartan 160mg (or less), Losartan 50mg (or less) and Olmesartan 10mg (or less).

Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP ≥100 to 110 mmHg.

Entresto should not be co-administered with an ACE inhibitor 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.

Renal impairment

- No dose adjustment is required in patients with mild (Estimated Glomerular Filtration Rate [eGFR] 60-90 ml/min/1.73 m²) renal impairment.
- A starting dose of 24 mg/26 mg twice daily should be considered in patients with moderate renal impairment (eGFR 30-60 ml/min/1.73 m²).
- As there is very limited clinical experience in patients with severe renal impairment (eGFR <30 ml/min/1.73 m²) Entresto should be used with caution and a starting dose of 24 mg/26 mg twice daily is recommended.
- There is no experience in patients with end-stage renal disease and use of Entresto is not recommended.

Hepatic impairment

- No dose adjustment is required when administering Entresto to patients with mild hepatic impairment (Child-Pugh A classification).
- There is limited clinical experience in patients with moderate hepatic impairment (Child-Pugh B classification) or with AST/ALT values more than twice the upper limit of the normal range. Entresto should be used with caution in these patients and the recommended starting dose is 24 mg/26 mg twice daily.
- Entresto is contraindicated in patients with severe hepatic impairment, biliary cirrhosis or cholestasis (Child-Pugh C classification)

Available as: Sacubutril 24mg Valsartan 26mg film coated tablets
Sacubutril 49mg Valsartan 51mg film coated tablets
Sacubutril 97mg Valsartan 103mg film coated tablets

Responsibilities of the specialist clinician initiating treatment

Summary

- To assess the suitability of the patient for treatment.
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable.
- To perform baseline tests and if appropriate routine tests until the patient is stable.
- To prescribe for the first 12 weeks of treatment (early shared care referral (i.e. less than 12 weeks) can be made to primary care where secondary care has titrated the patient up to the maximum dose and where the patient's condition is stable).
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (See Shared care request form in Appendix A).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To advise the GP when the patient will next be reviewed by the specialist.
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).
- To provide the GP with contact details in case of queries.
- To provide patient / carer with contact details for support and help if required; both in and out of hours.

Baseline Tests

Prior to initiation and before and after each dose titration the following should be monitored:

- Blood pressure
- Renal function
- Electrolytes including serum potassium
- Liver function and full blood count (initiation only)

Routine Tests:

Once the patient is stabilised on sacubitril valsartan therapy ongoing monitoring by the GP should include:

- Blood pressure, renal function and electrolyte monitoring every 6 months
- Liver function and full blood count monitoring every year

Disease Monitoring:

Once stable, review in clinic every 6 months.

Responsibilities of the primary care clinician

Acceptance of Responsibility by the Primary Care Clinician

It is optional for the primary care clinician to participate in taking on responsibility for shared care for the patient. Primary care clinicians will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible (early shared care referral (i.e. less than 12 weeks) can be made to primary care where secondary care has titrated the patient up to the maximum dose and where the patient's condition is stable).
- To prescribe and adjust the dose as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring as agreed with secondary care in the monitoring section below.
- To inform the specialist if the patient discontinues treatment for any reason.
- To seek the advice of the specialist if any concerns with the patient's therapy. For example:
 - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
 - Advice in respect of concordance.
 - Special situations, (e.g. Pregnancy).
- Discontinue the drug as directed by the specialist if required.
- To conduct an annual medication review or more frequently if required.
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow Card scheme).

Responsibilities of Patients or Carers

Summary

- To be fully involved in, and in agreement with, the decision to move to shared care.
- To attend hospital and primary care clinic appointments and to bring monitoring information e.g. booklet (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking Sacubitril valsartan (Entresto®).
- To read the product information given to them.
- To take Sacubitril valsartan (Entresto®) as prescribed.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Clinical Particulars

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (<https://www.medicinescomplete.com/#/>) and the SPC (<https://www.medicines.org.uk/emc/>) remain authoritative.

BNF therapeutic class	Sacubitril with Valsartan belongs to the Angiotensin II receptor antagonists, and Neprilysin inhibitors drug class (ARNI)
Contraindications	• Hypersensitivity to the active substance / excipients • Concomitant use with ACEi. Sacubitril valsartan must not be administered until 36 hours after discontinuing ACEi therapy. • Concomitant use with another ARB (as the combination drug contains valsartan) • Concomitant use with aliskiren containing products in patients with

	diabetes mellitus. Also avoid concomitant use with aliskiren containing products in patients with renal impairment (eGFR less than 60ml/min/1.73m²) • Known history of angioedema related to previous ACEi or ARB therapy • Hereditary or idiopathic angioedema • Systolic blood pressure (SBP) less than 100mmHg • End stage renal disease • Bilateral renal artery stenosis • Serum potassium greater than 5.4mmol/L • Severe hepatic impairment, biliary cirrhosis and cholestasis (Child-Pugh C) • Pregnancy and breast feeding
Cautions	• Serum potassium levels greater than 5mmol/L • Renal artery stenosis • Renal impairment. Patients with eGFR less than 30ml/min/1.73m² are at greater risk of hypotension • Moderate hepatic impairment (Child-Pugh B) or with alanine transaminase (ALT) / aspartate aminotransferase (AST) values more than twice the upper limit of normal • Dehydration due to risk of worsening renal function • NYHA class IV – patients will not routinely be started on treatment
Adverse Drug Reactions	Hypotension (Very common) - Review medication and consider adjusting any other medicines that are contributing to low blood pressure or review the dose of sacubitril valsartan which may need to be reduced. Consider discontinuing therapy if SBP is consistently below 100mmHg despite above measures. Hyperkalaemia (Very common) - Consider dose reduction where the potassium level is 5mmol/L or greater. Discontinue sacubitril valsartan if potassium level is 5.4mmol/L or greater and contact Cardiology team for advice. Renal Impairment (Very common) - Monitor renal function closely if eGFR trending downwards. Consider dose reduction if moderate renal impairment (eGFR 30 to 60 ml/min/1.73m²). In severe renal impairment (eGFR less than 30ml/min/1.73m²) contact Cardiology team for advice. Angioedema (Uncommon) - Discontinue sacubitril valsartan if angioedema occurs. Patient should be given appropriate therapy and monitored for airway compromise.
Monitoring	• When initiating therapy or during dose titration with Entresto, blood pressure should be monitored routinely. If hypotension occurs, temporary down-titration or discontinuation of Entresto is recommended • Monitoring of serum potassium is recommended, especially in patients who have risk factors such as renal impairment, diabetes mellitus or hypoaldosteronism or who are on a high potassium diet or on mineralocorticoid antagonists • Monitoring of serum potassium is recommended if Entresto is co-administered with potassium-sparing diuretics (triamterene, amiloride), mineralocorticoid antagonists (e.g. spironolactone, eplerenone), potassium supplements, salt substitutes containing potassium or other agents.

	• Caution is required in patients with renal artery stenosis and monitoring of renal function is recommended. • monitoring of renal function is recommended when initiating or modifying treatment in patients on Entresto who are taking NSAIDs concomitantly
Interactions	ACEi - Avoid concurrent use and allow a washout period of at least 36 hours when switching between ACEi and sacubitril valsartan due to risk of angioedema. ARB - Avoid prescribing any additional ARBs as sacubitril already contains the ARB valsartan. Aliskiren - Avoid concurrent use due to increased frequency of adverse effects such as hypotension, hyperkalaemia and renal impairment. Potassium sparing diuretics, mineralocorticoid antagonists, potassium supplements, salt substitutes or any agent that increases potassium - Monitoring of serum potassium is recommended due to risk of hyperkalaemia. Statins - Sacubitril valsartan increases the plasma concentration of atorvastatin and its metabolites. Caution should be exercised when co-administering statins. Phosphodiesterase type 5 (PDE5) inhibitors e.g. sildenafil, tadalafil, vardenafil - Concomitant use can result in a significant reduction in blood pressure after a single dose. Caution should be exercised if a PDE5 inhibitor is initiated. Nitrates - Co-administration may reduce heart rate, in general no dosage adjustment is required. NSAIDs - including cyclooxygenase-2 (COX-2) inhibitors - Concomitant use of sacubitril valsartan and an NSAID can worsen renal function – generally avoid combination. If concomitant use is necessary close monitoring of renal function is required. Lithium - ACEi and ARBs are known to cause reversible increases in lithium levels and toxicity, therefore the concomitant use of sacubitril and valsartan is not recommended, if unavoidable close monitoring of lithium levels is necessary. Metformin - Sacubitril valsartan can reduce the plasma concentration of metformin, monitor blood sugars and adjust metformin dose if necessary. Metabolic interactions - Caution should be exercised with the co-administration of sacubitril valsartan with inhibitors of OATP1B1, OATP1B3, OAT3 (e.g. rifampicin, ciclosporin), OAT1 (tenofovir, cidofovir) or MRP2 (e.g. ritonavir) as these may increase levels of the sacubitril active metabolite or of valsartan.

Communication and contact details

Specialist to primary care clinician

The specialist will inform the primary care clinician when they have initiated drug X. When the patient is near completing the satisfactory initiation period, the specialist will write to the primary care clinician to request they take over prescribing and where possible give an indication as to the expected length of treatment. The specialist will also send a shared care request form to support the primary care clinician in undertaking shared care. (Appendix A)

Primary Care Clinician to specialist

If the primary care clinician has concerns over the prescribing of sacubitril valsartan, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Dr David Robson, Consultant Cardiologist	01226 432169	d.robson1@nhs.net
Dr Abdul Negahban, Consultant Cardiologist	01226 432572	a.negahban@nhs.net
Dr Deoraj Zamvar, Consultant Cardiologist	01226 432169	deoraj.zamvar@nhs.net
Dr Naeem Tahir, Consultant Cardiologist	01226 432169	naeem.tahir@nhs.net
Henry Frankland, Lead Pharmacist (Cardiology & Respiratory)	01226 431931	henry.frankland@nhs.net
Daniel Kaye, Cardiology Nurse Specialist	01226 434981	danielkaye@nhs.net
Nicola Wilkinson, Cardiology Nurse Specialist	01226 434981	n.wilkinson@nhs.net
Mark Balchin, Cardiology Nurse Specialist	01226 434981	markbalchin1@nhs.net
Nicola Woodhouse, Heart Failure Nurse Specialist	07795453291	nicola.woodhouse@swyt.nhs.uk
Christopher Adams, NMP, Heart Failure Service	07901 680736	Christopher.adams@swyt.nhs.uk

References

- British National Formulary. Available at: www.medicinescomplete.com/mc/bnf/current/
- Summary of Product Characteristics for Entresto. Available at: <https://www.medicines.org.uk/emc/product/7751>
- NICE TA388. Available at: <https://www.nice.org.uk/guidance/ta388>
- NICE NG106. Available at <https://www.nice.org.uk/guidance/ng106>

<https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf>

Development Process

This guidance has been produced following an AMBER classification status of Entresto® by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 8th October 2025.

Appendix A – Shared Care request form (Amber) for Entresto ®

- Specialist to complete when requesting primary care clinician to enter a shared care arrangement.
- Primary care clinician to return signed copy of form. [Insert details of how to return the form e.g. to a safe haven e-mail address, postal address if the form should be returned by post]
- Both parties should retain a signed copy of the form in the patient's record.

From (Specialist): _____ **To (Primary care clinician):** _____

As per the agreed Barnsley shared care guideline for [insert drug name or clinical area], this patient is now suitable for prescribing to move to primary care.

The patient fulfils the criteria for shared care and I am therefore requesting your agreement to participate in shared care. I have carried out baseline tests and initial monitoring as detailed in the shared care guideline.

Patient details

Name: _____	NHS Number: _____
Address: _____	DOB: _____
Diagnosed condition: _____	

Amber Drug details

Drug name: _____	Dose and frequency: _____
Date of initiation: _____	Length of treatment: _____
The patient has been provided with sufficient medication to last until: _____	
The patient will be reviewed by the consultant on: _____	
The patient should be reviewed by the primary care clinician by: _____	

Monitoring

The following monitoring should be undertaken by the primary care clinician. Refer to the monitoring section of the shared care guideline.		
Parameter	Date next test due	Frequency

Communication

Consultant	
Telephone number: _____	Fax number: _____
Email address: _____	
Specialist Nurse	
Telephone number: _____	Fax number: _____
Email address: _____	

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____	
Specialist (Doctor/Nurse) signature: _____	Date: _____
I,, can confirm I :	
☐ accept the request to participate in shared care for the patient named above and will complete the monitoring as set out in the shared care guideline for this medicine/condition.	
☐ reject the request to participate in shared care for the patient named above. The reason for this being	
Signature of primary care clinician: _____	Date: _____

To save resources you have been sent appendix A of the shared care document. The full document (.....date approved) can be accessed on the Barnsley BEST website at the following link:

<http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/>

Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk