Northern Lincolnshire
Area Prescribing Committee

GUIDELINES FOR THE PRESCRIBING OF SACUBITRIL/VALSARTAN

Approving body:	Northern Lincolnshire Area Prescribing Committee
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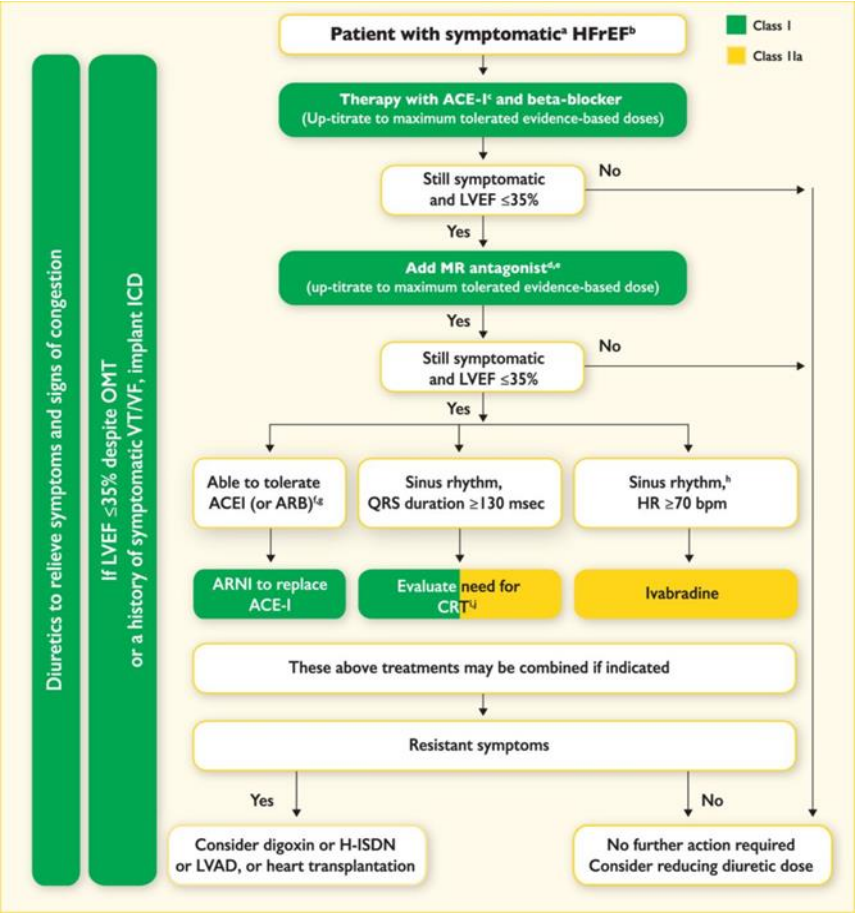
1.0 Clinical Guideline Summary



From: 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

Eur Heart J. 2016;37(27):2129-2200.

2.0 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.

2.1 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 m^2), 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.

2.2 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

2.3 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. rifampicin, ciclosporin, tenofovir, cidofovir) or efflux transporters (e.g. ritonavir) – may increase valsartan levels

2.4 Adverse effects

The most commonly reported adverse reactions are hypotension, hyperkalaemia and renal impairment. Angioedema has been reported (≥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).

2.5 Information to patients

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 valasartan.

Patients will be given a patient information leaflet which highlights the need to stop ACE inhibitor/ARB and will be given a copy of the clinic letter. Free website www.action-hf.co.uk

3.0 Area

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 Northern Lincolnshire and Goole NHS Foundation trust, 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 a heart failure specialist. Once stabilised on treatment the responsibility for continued prescription of sacubitril valsartan would pass to the patient's GP.

REFERRAL AND INITIATION	
Specialist Responsibilities	
1	To assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP.
2	The specialist will: • initiate and stabilise treatment; • obtain consent from the patient's GP to continue prescribing once treatment has been stabilised (usually after a minimum of 4 weeks); • The patient will be under the Heart failure inactive list, if there is no improvement in their LV function or discrepancies in their blood chemistry please refer to heart failure team.
3	To provide the GP with appropriate prescribing information and any additional information requested.
4	To be available for advice if the patient's condition changes.
5	To ensure that procedures are in place for the rapid re-referral of the patient by the GP.
6	To ensure the patient has given informed consent to their treatment.
7	To liaise with the GP on any suggested changes in prescribed therapy.
General Practitioner Responsibilities	
1	Initially refer the patient for specialist advice where not already under the care of a heart failure team
2	Where appropriate to continue to prescribe sacubitril valsartan once the treatment has been stabilised, usually at least 4 weeks after treatment has been initiated
3	Measure and record blood pressure and heart failure symptoms such as ankle swelling, referring to the specialist team where necessary (suggested threshold for referral SBP ≤95mmHg)
4	Monitor the patient and their therapy at six monthly intervals. Monitor renal function and electrolytes at least 6 monthly and more often during periods of illness, referring to the specialist team where necessary. Consider referral where any significant decrease in renal function is noted. See Cautions or refer to SPC for dosing in renal impairment.
5	Deal with general health issues of the patient
6	Monitor concordance with therapy and raise concerns with the specialist team as appropriate

4.0 Prescribing and monitoring responsibilities

Heart failure specialist should review baseline blood pressure and Blood Chemistry Profile (for renal function, hepatic function and potassium levels), initiate treatment (1 month supply) and write to patient's GP. All patients will be discussed at MDT before initiation.

Heart failure specialist will 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.

After dose optimisation and patient being stable GP will undertake 6 month review to include BP and BCP. However, there is scope for GP's who have agreed to any enhanced services to take on the role of optimisation and monitoring.

Specialist team can be contacted for further advice:

Scunthorpe 03033 302895

Grimsby 03033 303823

Community Cardiology service: The NEL Community Cardiologist Service can be contacted by: 01472 266950 or CPG.CommunityCardiologyService@nhs.net

4.1 Key points for GP's

- The patient should have been provided with a patient information leaflet.
- Is the patient on a stable dose? Heart failure specialist should monitor and TITRATE dose, only when patient is on a stable dose should they be transferred to GP prescribing
- The patients GP should be informed in writing:
  - About initiation of the drug
  - Any special considerations they need to be aware of for that patient
- GP to check BP and BCP at 6 months
- GP to complete medicines reconciliation on GP clinical system to ensure that previous ACE I or ARB are **removed** from medication list (**ACE inhibitors, ARB's and Aliskiren must not be given concomitantly with Sacubitril/Valsartan)**

IMPORTANT for ACE inhibitors ONLY: a mimimum 48hour washout period is required when changing patients from an ACE inhibitor to Sacubitril/Valsartan or if changing back from Sacubitril/Valsartan to an ACE inhibitor.

5.0 GP monitoring

The GP is required to undertake 6 monthly BCP and BP check.

6.0 Practical advice

- Swallow whole with a glass of water. Tablets can be taken with or without food.
- Follow sick day rules as for ACE and ARB.
- Increased risk of hypotension if patients >65 years or with eGFR <60ml/min
- Avoid NSAID
- Beware of low salt substitutes which can have high potassium content.

7.0 References

1. NICE Technology Apprasial Guidance (2016) Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction (TA388). https://www.nice.org.uk/guidance

2. McMurray J, Packer M, Desiai A, et al (2014) Angiotension-Neprolysin inhibition Enalipril in heart failure. The New England Journal of Medicine 371:993-10044

8.0 Definitions

Severe heart failure ejection fraction less than 35% New York Heart Association (NYHA 11-1V)

9.0 Consultation

Heart Failure teams

Heart Failure lead

Cardiology Business and governance committee

Medicines and Therapeutic Committee

Area Prescribing Committee

10.0 Dissemination

Approved at Cardiology business and governance committee
Approved at Northern Lincolnshire and Goole Medicines and Therapeutics' committee
Approved at Local medical committee
Approved at Area Prescribing Committee

11.0 Implementation

Training has been provided for relevant specialists undertaking the prescribing of this drug. CPD/Education training for GP's will be made available.

12.0 Document History

New document.

13.0 Acknowledgements

Guideline developed using guidance and permission from the Hull and East Riding Prescribing Committee and Dorset Medical Advisory Group.

14.0 Equality Act (2010)

Northern Lincolnshire and Goole NHS Foundation Trust is committed to promoting a pro-active and inclusive approach to equality which supports and encourages an inclusive culture which values diversity.

The Trust is committed to building a workforce which is valued and whose diversity reflects the community it serves, allowing the Trust to deliver the best possible healthcare service to the community. In doing so, the Trust will enable all staff to achieve their full potential in an environment characterised by dignity and mutual respect.

The Trust aims to design and provide services, implement policies and make decisions that meet the diverse needs of our patients and their carers the general population we serve and our workforce, ensuring that none are placed at a disadvantage.

We therefore strive to ensure that in both employment and service provision no individual is discriminated against or treated less favourably by reason of age, disability, gender, pregnancy or maternity, marital status or civil partnership, race, religion or belief, sexual orientation or transgender (Equality Act 2010).

Appendix 1

The following checklist must be completed and sent to the GP when sacubitril valsartan therapy is initiated. Following titration to the maximum tolerated dose that is maintained for a minimum of one month, care may be transferred to the GP. At this point, a transfer of care document should be completed and sent to the GP.

Important information for GPs: This is notification that **sacubitril valsartan** has been started for your patient **Please ensure that any ACE-I or ARBs are discontinued on repeat prescription.**	
Patient Details	**GP Details**
Surname:	Name:
Forename:	Address:
Address:	
	Tel:
Postcode:	Fax:
NHS No:	NHS.net email:
DOB: Sex: Male / Female	
Date of treatment initiation:	
ACE-I/ARB being stopped:	

Eligibility Criteria (Refer to the SPC for full details of licensed indications) **NICE/ local consensus criteria for sacubitril valsartan** *Note: all four criteria must be met to be within license for use* (Tick yes or no as appropriate)	**Yes**	**No**
1. Left ventricular ejection fraction ≤ 35%		
2. New York Heart Association (NYHA) class II to IV		
3. Taking a stable dose angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor-blockers (ARBs)		
4. No contraindications to treatment (refer to prescribing guideline for full details)		
Patient Information (Tick yes or no as appropriate)	**Yes**	**No**
1. Patient is aware of the indication of sacubitril valsartan therapy		
2. Patient is aware of the benefits and risks sacubitril valsartan therapy		
3. Patient has consented to therapy		

Baseline assessment of renal function		
	Date of test	**Result**
Baseline serum creatinine		
Estimated GFR		

Details of sacubitril valsartan dosing initiation schedule (Tick as appropriate)	**TICK**
Standard dose: **One tablet of 49mg/51mg twice daily** doubled every 2-4 weeks to the target dose of one tablet of 97mg/103mg twice daily	
Reduced dose: **One tablet of 24mg/26mg twice daily** with slow dose titration. • SBP ≥100 to 110 mmHg • Estimated GFR 30-60ml/min/1.73m^2 • Hepatic impairment (Child-Pugh B) or AST/ALT greater than twice the upper limit of the normal range	

AUTHORISATION (practitioner undertaking assessment)	
Signature:	**Print name:**
Position:	**Organisation:**
Contact number:	**Date:**

Appendix 2

Transfer of Prescribing Responsibility

In the event that there are any concerns regarding the acceptance of the prescribing responsibility for this medication please contact the initiating prescriber or heart failure team.

To be completed by the initiating organisation / clinician

Patient Detail

Name:..... …. **DOB**: ...../...../.....

Hospital Number: …… **Address:……..**

NHS Number: …….. **…….....**

GP Practice Details:	**Consultant Details:**
Name: …… Address: …… Tel no: …… Fax no: …… NHS.net e-mail: ……	Consultant Name:..... Organisation Name:..... Clinic Name:…… Address: …… Tel no: ……..…… Fax no:: …… NHS.net email:: ……

Dear Dr…….

This patient has been initiated on sacubitril valsartan in accordance with Northern Lincolnshire APC guidelines / formulary for treatment of chronic heart failure with reduced ejection fraction.

Details of treatment plan

	Date initiated	**Dose on transfer**	**Date of next review**
Sacubitril Valsartan (ENTRESTO®)			

This patient is on maximum tolerated dose and I am writing to transfer the prescribing responsibility for this patient's on-going treatment from ….. /…../……

This transfer of care document should be reviewed in conjunction with the screening checklist and notification sent previously by the initiating clinician. If this has not been received contact the consultant named above for details

All patients receiving sacubitril valsartan therapy should be reviewed at least six monthly throughout their treatment. Please refer to the prescribing document for more details.

Monitoring

Test		**Result**	**Date of test**	**Please repeat test in:**
Serum Creatinine				6 months
Estimated GFR				
Potassium				6 months
Blood pressure				6 months
Liver Function Tests	ALT			6 months
	ALP			

Other relevant information: ……
……

- I confirm that I have prescribed in accordance with the local heart failure guidelines
- I confirm that the patient has been made aware of the benefits and risks of sacubitril valsartan and that they Know how to seek medical help
- I confirm the patient has consented to treatment

Signed:…… Name of Clinician:…… Date: …….