DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

SACUBITRIL/VALSARTAN (ENTRESTO®)

For the treatment of symptomatic chronic heart failure with reduced ejection fraction

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant/specialist nurse and the patient's GP that the patient's condition is stable or predictable. Specialist is responsible for initiation, titration and stabilisation of treatment before transferring prescribing responsibility.
- Patients will only be referred to the GP once the GP has agreed in each individual case.
- When transferred, the patient will be given a supply of sacubitril/valsartan sufficient for 4 weeks maintenance therapy

2. AREAS OF RESPONSIBILITY

GP responsibilities	Consultant/specialist nurse responsibilities
1. Prescribe sacubitril/valsartan at the dose determined by the consultant/specialist nurse **2. Ensure that the patient's repeat prescription for ACE inhibitors or ARBs is stopped** **3.** Refer to secondary care physician if the patient's condition deteriorates. **4.** Perform monitoring tests as outlined in section VI. **5.** Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arise. **6.** Report any adverse effects to the referring specialist and the MHRA	**1.** To confirm the patient has no contra-indications to treatment and consider the relevance of any cautions. **2.** To discuss the benefits and possible side-effects of treatment with the patient. As part of this process the patient will be provided with a patient information leaflet about the therapy and specific information about stopping ACEi / ARB therapy. **3.** To initiate sacubitril/valsartan (**stop ACE inhibitors or ARBs**) for the licensed indication in accordance with the manufacturer's Summary of Product Characteristics (SPC) and local heart failure guidelines, and provide at least 4 weeks' supply. **4.** Perform monitoring tests as outlined in section VI. **5.** To discuss the possibility of sharing prescribing and monitoring of sacubitril/valsartan with the patient's GP; to provide a copy of this shared care agreement for their consideration and not to transfer prescribing responsibility until the GP has formally agreed to share care in this way. **6.** To advise on the clinical relevance of concomitant medication after initiation of sacubitril/valsartan, as well as potential drug interactions **7.** To ensure that arrangements are in place for GPs to obtain advice and support where needed. **8.** To communicate promptly with the GP the results of any monitoring undertaken in secondary care and any changes to treatment made by the specialist.

Patient responsibilities

1. Report to the consultant/specialist nurse or GP if he/she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with sacubitril/valsartan.
3. Present rapidly to the GP or secondary care specialist should their condition significantly worsen.
4. Report any other adverse effects to the specialist or GP whilst taking sacubitril/valsartan.
5. Agree to attend for blood tests and monitoring when required

3. COMMUNICATION AND SUPPORT

i. Hospital contact:	ii. Out of hours contact and procedures:
Royal Derby Hospital Foundation Trust Consultant/specialist nurse via switchboard: 01332340131 **Chesterfield Royal Hospital Foundation Trust** Consultant/specialist nurse via switchboard: 01246 77271 **South Derbyshire Heart Failure Team (DCHS)** Tel: 01332 564879	Pharmacy, RDH, ask for on-call pharmacist via switchboard: 01332 340131 Cardiology, RDH, ask for on-call Cardiology Consultant via switchboard: 01332 340131 Contact the CRH on-call Medic for the relevant specialty via switchboard: 01246 277271

4. CLINICAL INFORMATION

i. Prescribed indications	Sacubitril/valsartan (Entresto®) is indicated as per NICE TA388 for the treatment of symptomatic chronic heart failure with reduced ejection fraction in people: • With New York Heart Association (NHYA) 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 (ARB)
ii. Therapeutic summary	Sacubitril/valsartan is an angiotensin receptor neprilysin inhibitor, including both a neprilysin inhibitor (sacubitril) and the angiotensin II receptor blocker (ARB) (valsartan).
iii. Dose & Route of administration	**Sacubitril/valsartan (Entresto) must not be administered until 36 hours after discontinuing ACE inhibitor or ARB therapy** In patients currently taking an ACE inhibitor or ARB: • The recommended starting dose is one tablet of 49mg/51mg (100mg) twice daily, increasing after 2-4 weeks to the target dose of one tablet of 97mg/103mg (200mg) twice daily, as tolerated by the patient Note: The valsartan within sacubitril valsartan is more bioavailable than that in other formulations; 26mg, 51mg and 103mg of valsartan in sacubitril valsartan is equivalent to 40mg, 80mg and 160mg in other formulations, respectively.
iv. Duration of treatment	Indefinite
v. Adverse effects	**Very common** Hyperkalaemia, hypotension, renal impairment **Common** Anaemia, hypokalaemia, hypoglycaemia, dizziness, headache, syncope, vertigo, orthostatic hypotension, cough, diarrhoea, nausea, gastritis, renal failure (renal failure, acute renal failure), fatigue, asthenia **Uncommon** Hypersensitivity, dizziness postural, pruritis, rash, angioedema For a full list of all potential adverse event please refer to the SPC https://www.medicines.org.uk/emc/product/7751/smpc
vi. Monitoring Requirements	**Consultant/heart failure team** **Baseline monitoring:** • Blood pressure • U& E including serum potassium • LFT • FBC **After dose increase (between 2-4 weeks)** • Blood pressure • U&E including serum potassium **GP monitoring** **Every 6 months**: Blood pressure, U&E **Yearly**: LFT, FBC

Side Effects	Actions to be taken
Hypotension	Review medication and consider adjusting any other medicines that are contributing to low blood pressure Local advice -if patient asymptomatic and SBP consistently below 90 or if patient is symptomatic seek specialist advice. Specialist may consider reducing dose or stopping therapy.
Hyperkalaemia	An increase in potassium <5.5mmol/l is acceptable. If potassium rises to ≥5.5 mmol/l sacubitril/valsartan should be stopped and specialist advice sought.
Renal Impairment	Monitor renal function closely if eGFR trending downwards. Check for other causes e.g. dehydration, infection etc. Repeat U&Es when patient stable and if still reduced renal function contact the HF team for advice. An increase in creatinine up to 50% above baseline or 266micromol/l, whichever is smaller is acceptable. If creatinine increases by >100% or to above 310 micromol/l sacubitril/valsartan should be stopped and specialist advice sought.
Hepatic impairment	Severe hepatic impairment, biliary cirrhosis or cholestasis (Child-Pugh C classification) discontinue sacubitril/valsartan. Moderate liver impairment; consider dose reduction (Child-Pugh B classification) and contact HF team for advice.
Angioedema	Discontinue sacubitril/valsartan if angioedema occurs. Patient should be given appropriate therapy and monitored for airway compromise. Refer to secondary care.

vii. Clinically relevant drug interactions

- **ACEi:** avoid concurrent use. Allow 36 hours when switching between ACEi and sacubitril/valsartan due to risk of angioedema
- **ARB:** sacubitril/valsartan contains valsartan, and therefore should not be co-administered with another ARB containing product
- **Aliskiren:** the combination use of sacubitril/valsartan with alikiren-containing products is contra-indicated in patients with diabetes mellitus or in patients with renal impairment. The combination of sacubitril/valsartan with aliskiren is potentially associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (inc. acute renal failure)
- **Statins:** sacubitril/valsartan increased the plasma concentration of atorvastatin and its metabolites. Use with caution when co-administering sacubitril/valsartan with statins
- **PDE5 inhibitors including sildenafil:** the addition of a single dose of sildenafil in patients with hypertension can result in a significant reduction in blood pressure. Caution should be exercised when sildenafil or another PDE5 inhibitor is initiated in patients treated with sacubitril/valsartan
- **Potassium sparing diuretics, mineralocorticoid antagonists, potassium supplements, salt substitutes containing potassium or other agents:** may lead to increases in serum potassium, and to increase in creatinine. Monitoring of serum potassium is recommended if sacubitril/valsartan is co-administered with these agents
- **NSAIDs including COX-2 inhibitors:** concomitant use may lead to an increased risk of worsening renal function. Avoid combination – if concomitant use is necessary monitoring of renal function is recommended when initiating or modifying treatment
- **Lithium:** increases in serum lithium concentration and toxicity have been reported during concomitant administration of lithium with ACEi or angiotensin II receptor antagonists. Therefore, the concomitant use of litium

	with sacubitril/valsaratan is not recommended. If this combination is unavoidable, careful monitoring of lithium levels is recommended. • **Nitrates:** Heart rate may be reduced when sacubitril/valsartan is co-administered with nitrates. In general no dosage adjustment is required • **OATP and MRP2 transporters:** co-administration of sacubitril/valsartan with inhibitors of OATP1B1, OATP1B3, OAT3 (e.g. rifampicin, ciclosporin), OAT1 (e.g. tenofovir, cidofovir) or MRP2 (e.g. ritonavir) may increase the systemic exposure of sacubitril or valsartan. Appropriate care should be exercised when initiating or ending concomitant treatment with such medicinal products • **Metformin:** co-administration of sacubitril/valsartan with metformin can lead to a reduction in the plasma concentration of metformin. Therefore, when initiating therapy blood sugars should be monitored and the dose of metformin adjusted accordingly • **Trimethoprim**: Both trimethoprim and sacubitril/valsartan can increase the risk of hyperkalaemia (hyperkalaemia is particularly notable when given with spironolactone or eplerenone).
viii. Contraindications	• Hypersensitivity to the active substances or to any of the excipients • **Concomitant use with ACE inhibitors or ARBs.** Sacubitril/valsartan (Entresto) must not be administered until 36 hours after discontinuing ACE inhibitor or ARB therapy • Known history of angioedema related to previous ACE inhibitor or ARB therapy • Hereditary or idiopathic angioedema • Concomitant use with alikiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60ml/min/1.73m^2) • Severe hepatic impairment, biliary cirrhosis and cholestasis • Second and third trimester of pregnancy
ix. Supply of ancillary equipment	Not applicable
x. Supply, storage and reconstitution	Not applicable
xi. Prepared by **In consultation with**	University Hospitals of Derby & Burton Dominic Moore, Lead Pharmacist Commissioning Pardeep Dhillon, Chief Pharmacy Technician – Interface Dr R McIntosh, Consultant Cardiologist Dr N Ahmed, Consultant Cardiologist Chesterfield Royal Hospital Dr J Cooke, Consultant Cardiologist Martin Shepherd, Head of Medicines Management Derbyshire Community Health Services Martin Melville, Heart Failure Specialist Nurse (North) Mandie Santon, Heart Failure Specialist Nurse (South) Derbyshire Medicines Management Guideline Group

This does not replace the SPC, which should be read in conjunction with it.
Date Prepared: February 2019 **Review Date:** January 2022

Sample Transfer Letter

{Insert Hospital Logo here}

Hospital No: «HOSPITAL_NUMBER»
NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL
«GP_TITLE» «GP_INITIALS» «GP_SURNAME»
«GP_ADDRESS_1»
«GP_ADDRESS_2»
«GP_ADDRESS_3»
«GP_ADDRESS_4»
«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»
«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»
«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. I have initiated the following medication ***{Insert drug name}*** and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date ***{Insert medicine name}*** started	Date for GP to start prescribing ***{Insert medicine name}*** from
The baseline test results are (if applicable): **See overleaf for initiation criteria.**		

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been	*Yes / No*

explained and agreed	
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care)

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed**.** For this reason I am unable to take clinical responsibility for prescribing this medication at this time,	

	therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

Yours sincerely

{GP name}
{Surgery}

Please send a copy of this response to:

1. The specialist/consultant requesting shared care
2. **AN ANONYMISED COPY OF THIS FORM ONLY** to the Medicines Management and Clinical Policies and Decisions Team, 1st Floor East Point, Cardinal Square, 10 Nottingham Road, Derby, DE1 3QT or E-MAIL: ddccg.medicinesmanagement@nhs.net

(Sending a copy of this form to the Medicines Management and Clinical Policies and Decisions Team will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG prescribing group of the reasons shared care is not being undertaken allowing for changes to be made in future updates to improve patient care).