North of Tyne Guidelines for Management of Heart Failure
Revised May 2016
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Introduction

This guidance is intended to inform the diagnosis and management of patients with chronic and acute heart failure. It has been developed jointly between primary and secondary care and identifies and interprets the recommendations from the NICE Heart Failure guideline\(^1\) published in August 2010 for local implementation and updates earlier local guidelines. The guidance also recognises that new evidence has been published since the NICE guideline was completed and incorporates recommendations about this and also acknowledges the recommendations in the ESC heart failure guidelines\(^2\). A further update in 2016 has also incorporated the most recent recommendations from NICE for device therapy\(^3\), and includes recommendations for treatment with sacubitril valsartan.

**Underpinning principles**

- The guideline is only intended for patients who are suspected of having heart failure or who have an established diagnosis of heart failure.
- Clinical assessment is fundamental in diagnosing and managing patients and should be performed by a clinician competent to do so.
- Consideration should be given to ensure that diagnostic testing is performed to high quality standards.
- The guideline is intended to guide clinical management, but every patient should be assessed and managed individually, taking into consideration the evidence which underpins the different therapeutic interventions.
- In making recommendations for drug treatment it is assumed that clinicians will exclude contra-indications, referring to the BNF and local formulary as necessary, when managing individual patients.
- This local guideline is not a rewrite of NICE guidance, but is a summary of the main points with additional information for local implementation. The NICE guidelines should be referred to as appropriate.

**Using the guideline**

This guideline is intended to be used by clinicians in Newcastle, North Tyneside and Northumberland who are responsible for diagnosing patients presenting with suspected heart failure or who have an established diagnosis of heart failure. The flow charts (which can be laminated) summarise the diagnostic and management pathways for patients with heart failure and left ventricular systolic dysfunction and heart failure with preserved left ventricular ejection fraction, as well as a flow chart summarising assessment and management of acute heart failure, with additional notes thereafter.

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\(^1\) NICE CG 108 Management of chronic heart failure in adults in primary and secondary care

\(^2\) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. EHJ (2012) 33;1787–1847

\(^3\) https://www.nice.org.uk/guidance/ta314
The BNF and the North of Tyne Formulary should be referred to as appropriate. Information about drug costs (sourced May 2016) is included in the appendix, to help inform prescribing decisions.
Diagnosis of heart failure: recommended for use in patients without an established diagnosis of heart failure or left ventricular dysfunction

Suspected heart failure?

- Yes: Assess and investigate for alternative diagnoses as appropriate
- No: Take a detailed clinical history, perform a clinical examination and arrange an ECG

If heart failure still suspected, consider starting appropriate treatment (usually diuretics), and arrange further diagnostic testing

Has the patient had a previous MI (history or definite past MI on the ECG) and/or does the ECG show LBBB?

- Yes: Take blood for FBC, U&E, eGFR, LFT, TFT, HbA1c, lipids if indicated (see FATS) within 24 working hours
- No: Take blood for NT-proBNP, FBC, U&E, eGFR, LFT, TFT, HbA1c, lipids if indicated (see FATS) within 24 working hours.

Specialist assessment and Doppler echocardiography

Within 2 weeks

Clinical assessment and echo consistent with heart failure?

- Yes: Assess precipitating factors, type of cardiac dysfunction, severity and aetiology
- No: Consider measuring NT-proBNP if levels unknown

NT-proBNP high (age dependent values)*

Within 6 weeks

NT-proBNP normal (age dependent values)*

Raised levels (age dependent values)

Consider other diagnoses

Heart failure due to other cardiac abnormality

Heart failure due to left ventricular systolic dysfunction

Heart failure with preserved ejection fraction

Heart failure unlikely, consider other diagnoses

* NT-proBNP age dependent thresholds

<table>
<thead>
<tr>
<th>Raised levels</th>
<th>Age &lt; 60 years</th>
<th>Age 60-74 years</th>
<th>Age ≥ 75 years</th>
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</thead>
<tbody>
<tr>
<td>High levels</td>
<td>≥ 50 ng/L</td>
<td>≥ 100 ng/L</td>
<td>≥ 250 ng/L</td>
</tr>
</tbody>
</table>

Hildebrandt et al. EHJ 2010;31:1881-1889
Personal communication. Paul Collinson
Management of patients with chronic heart failure

Patient with heart failure due to LVSD

Review blood results and identify any contra-indications to medications

Assess fluid status and ensure appropriate diuretic treatment

Patient with heart failure and preserved LV ejection fraction

Assess fluid status and ensure appropriate diuretic treatment

Manage co-morbid conditions such as diabetes, hypertension and IHD

Symptoms / signs of fluid overload found

ACE inhibitor initially

Add ACE inhibitor or licensed beta blocker, dependent on current treatment

Assess response to first line treatment.
If still symptomatic (NYHA II-IV) despite optimising diuretics, ACEI and beta blocker treatment, in particular if LVEF ≤ 35%, review renal function and add a mineralocorticoid antagonist (MRA) if no contra-indications
Consider obtaining specialist advice

Second line treatment
ARB in combination with an ACE inhibitor
Hydralazine in combination with nitrates particularly if patients of African or Caribbean origin
Consider ivabradine if sinus rhythm (refer to criteria)

Assess response to treatment and consider NYHA grade
- Consider specialist referral if not already obtained
- Consider the addition of digoxin

No symptoms / signs of fluid overload found

ACE inhibitor or beta blocker licensed for heart failure

Consider hydralazine in combination with nitrates if ACEI/ARBs not tolerated, following advice from specialist care

If LVEF < 35%, consider eligibility for device therapy (see text)

Sacubitril / valsartan may be substituted for an ACEI inhibitor / ARB managed within specialist care.
ACE inhibitors and ARBs are contra-indicated in patients treated with sacubitril / valsartan

Review
All patients require at least a 6 monthly review, some require more frequent follow up (days to weeks), including:
- Clinical assessment of functional capacity, fluid status, cardiac rhythm (pulse palpation minimum), nutritional status and cognitive function
- Drug review - ? Optimised, ? Adverse effects ? Need for changes
- Measure minimum of renal function and electrolytes. Digoxin level (8-12 hours after the last dose) only if toxicity or non-adherence is suspected.
- Patient information and education – self management, what to do if condition deteriorates, other informational care
- Review social care needs

4 See appendix for recommended target doses of ACE inhibitors and beta blockers, and comparative drug costs
Management of patients with acute heart failure in hospital (refer to local trust guidelines as appropriate)

Suspected acute heart failure?

- Yes
  - Assess and investigate for alternative diagnoses as appropriate

- No
  - Clinical assessment – history, examination, ECG, chest x ray, blood tests, other ancillary investigations as appropriate,
    - Consider reversible causes requiring specific early treatment eg arrhythmia, myocardial infarction. Treat as appropriate
    - Initiate first line treatment for acute heart failure
      - Instigate appropriate monitoring – type and frequency
      - Assess response within 30 minutes

Is second line treatment required?

- Yes
  - Initiate second line treatment
    - Assess response within 30 minutes
      - Should inotropes and or non invasive ventilation be considered (response to initial treatment, ABG)?

- No
  - Review and modify regular treatment, arrange any further investigation required, manage reversible causes
  - Continue acute management, review and modify regular treatment, review goals of therapy. Arrange any further investigation required, manage reversible causes

Other treatments

- Continue beta blockers if possible, but reduce / stop if heart failure is refractory or hypotension a problem
- Continue ACE inhibitors / ARBs unless hypotension and or renal function are a problem.
- Review any drugs which might exacerbate heart failure

First line treatment for acute heart failure

- Sit patient up
- Oxygen (see local oxygen guidelines)
- IV furosemide 40-120 mg (lower dose if diuretic naïve)

Second line treatment for acute heart failure

- GTN IV infusion, increased as tolerated by BP (managed in at least level 2 care bed)
- Consider repeating first line treatments
- Ensure managed in the most appropriate setting

Other treatments

- Continue beta blockers if possible, but reduce / stop if heart failure is refractory or hypotension a problem
- Continue ACE inhibitors / ARBs unless hypotension and or renal function are a problem.
- Review any drugs which might exacerbate heart failure

Assess response within 30 minutes

- Should inotropes and or non invasive ventilation be considered (response to initial treatment, ABG)?

- Yes
  - Initiate appropriate treatment, continue / repeat other treatments
    - Assess response within 30 minutes
      - Should more intensive interventional treatment be considered?

- No
  - Continue acute management, review and modify regular treatment, review goals of therapy. Arrange any further investigation required, manage reversible causes
  - Arrange further interventional treatment as appropriate
Diagnosis of chronic heart failure

The diagnostic pathway is summarised in the first flow chart above and is recommended for use in patients without an established diagnosis of heart failure or left ventricular dysfunction. The summary in the quick reference version of the NICE chronic heart failure guideline has been refined to incorporate more explicit recommendations for performing an ECG, and to consider treating patients pending the outcome of specialist assessment and further investigation. The local guideline development group also felt it was appropriate to include recommended timescales within which initial blood tests should be performed. A fasting sample is not required.

Measurement of natriuretic peptides is recommended in patients with no past history of MI to determine if further diagnostic testing is indicated or if heart failure can be ruled out, and it was agreed to use NT-proBNP locally. There is good evidence that levels are influenced by a number of factors, including a powerful influence by age, and in younger patients in particular the thresholds recommended in the NICE guideline were considered to be too conservative. From published evidence and personal communication by Dr Neely with Dr Paul Collinson, thresholds for inclusion in the local guideline were agreed, and are included in the flow chart. These thresholds have already been adopted in London and initial information from Dr Collinson is that there has been no major increase in the demand for echocardiograms.

Management of patients with chronic heart failure

This guideline only includes recommendations for management of patients with left ventricular systolic dysfunction and patients with heart failure with preserved ejection fraction. Patients with other causes of chronic heart failure, including for example valvular heart disease and management of atrial arrhythmias are not included. Management is summarised in the second flow chart above.

Drug treatment in patients with chronic heart failure and left ventricular systolic dysfunction

The key components to consider in all patients include:

First line treatment

- Diuretics as required to control congestion
- ACE inhibitors and beta blockers in all patients in the absence of contra-indications.

In patients who still have evidence of congestion, ACE inhibitors, such as lisinopril or ramipril, should be started before beta blockers, and beta blockers started once the congestion is controlled. In those without congestion, either ACE inhibitors or beta blockers can be started first. Beta blockers should be started in low dose and up-titrated slowly. In all cases, ACE inhibitors and beta blockers should be up-titrated to target doses if possible. Beta blockers licensed for heart failure should be used (and if necessary other beta blockers should be switched to a licensed preparation). Recommended target doses of commonly prescribed ACE inhibitors and beta blockers are included in the appendix.

The NICE heart failure guideline emphasises that beta blockers should be considered for all patients including in older patients, and those with peripheral arterial disease, erectile dysfunction, diabetes, interstitial lung disease and COPD without reversibility.
ARBs should only be used in place of ACE inhibitors if patients have been shown to be intolerant of an ACE inhibitor. 

Renal function and electrolytes should be measured during titration of ACE inhibitors and ARBs, and periodically when stable.

The local guideline for initial management of hyperkalaemia should be referred to if hyperkalaemia is found in primary care.

If patients are intolerant of both ACE inhibitors and ARBs, hydralazine in combination with nitrates should be considered following advice from specialist care.

The NICE chronic heart failure guideline recommends that mineralocorticoid receptor antagonist (MRAs) are confined to second line treatment in patients with more severe heart failure, and generally to be used with advice from specialist care. However, more recent evidence has shown that eplerenone is also effective in patients with milder symptoms of heart failure if they have other high risk features, including age at least 55 years, and left ventricular ejection fraction no more than 30%, (or if >30% to 35% if the QRS duration is > 130 msecs on ECG). In addition patients had been admitted to hospital for a cardiovascular indication within the last 6 months or the natriuretic peptides were high on other treatment.

It is not recommended for local implementation that natriuretic peptides are measured to determine if patients with mild heart failure should be treated with an aldosterone antagonist, but an MRA (spironolactone or eplerenone) should be considered in all patients with left ventricular systolic dysfunction, in particular if left ventricular ejection fraction is ≤ 35%, providing there are no contraindications (this is also consistent with ESC recommendations). If patients are treated with spironolactone and develop oestrogenic side effects, patients should be considered for a switch to eplerenone.

Renal function and electrolytes (particularly potassium) must be measured at baseline and a week after starting a MRA, after 4 weeks, 3 months and periodically thereafter and as a minimum every 6 months. More frequent measurements may be required in patients with chronic kidney disease and or concerns about developing hyperkalaemia. A recent MHRA alert emphasised the importance of monitoring these patients.

**Second line treatment**
These drugs will generally be used with advice from specialist care.

- Sacubitril valsartan may be substituted for an ACE inhibitor or ARB (and cannot be given in combination with either of those), in line with NICE guidance. This should only be initiated from specialist care, with robust arrangements for safe initiation and monitoring. Further information is included in appendix 1.

- Angiotensin II receptor antagonists in combination with an ACE inhibitor
An ARB might be considered in addition to an ACE inhibitor. Careful monitoring of renal function and electrolytes is necessary.

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7 https://www.nice.org.uk/guidance/ta388
• Hydralazine in combination with a nitrate, in addition to an ACE inhibitor
  Might be considered as an option particularly in patients of African or Caribbean origin.

• Ivabradine\(^8\)
  Is now licensed and has been evaluated by NICE as a single technology appraisal\(^6\) which states:

  1.1 Ivabradine is recommended as an option for treating chronic heart failure for people:
      • with New York Heart Association (NYHA) class II to IV stable chronic heart
        failure with systolic dysfunction and
      • who are in sinus rhythm with a heart rate of 75 beats per minute (bpm) or
        more and
      • who are given ivabradine in combination with standard therapy including
        beta-blocker therapy, angiotensin-converting enzyme (ACE) inhibitors and
        aldosterone antagonists, or when beta-blocker therapy is contraindicated or
        not tolerated and with a left ventricular ejection fraction of 35% or less

  1.2 Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimised
      standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists.

  1.3 Ivabradine should be initiated by a heart failure specialist with access to a
      multidisciplinary heart failure team. Dose titration and monitoring should be carried out by
      a heart failure specialist, or in primary care by either a GP with a special interest in heart
      failure or a heart failure specialist nurse.

  When the use of ivabradine in chronic heart failure North of Tyne was considered before it
  was licensed, there was a consensus North of Tyne that patients being considered for
  ivabradine should have been seen and assessed as suitable for treatment by a
  cardiologist, with primary care being able to continue the long term prescribing. GPs could
  also titrate ivabradine if they were happy to do so, and there was a clear management
  plan.

  Beta blockers remain first line and ivabradine is not a substitute when beta blockers are
  not contra-indicated, are tolerated and achieve the required therapeutic response.

**Recommended doses:**

  Initial dose ivabradine 5 mg bd
  After 2 weeks
  If heart rate > 60 beats per minute, increase to 7.5 mg bd
  If heart rate 50 to 60 beats per minute, continue 5 mg bd
  If heart rate < 50 beats per minute and or symptoms and signs of
  bradycardia reduce dose to 2.5 mg bd.

  If necessary to manage bradycardia, the dose of ivabradine should be reduced, not the
  dose of beta blocker.

• Digoxin
  May be considered in patients with on-going symptoms of moderate to severe heart failure
  despite all other optimal management, particularly those with recent admission(s) to

\(^8\) NICE single technology appraisal. Ivabradine for treating chronic heart failure.
hospital with worsening heart failure. Lower doses, compared to those for arrhythmia management, are often sufficient.

**Drug treatment in patients with chronic heart failure and preserved ejection fraction**
- Diuretics as required to control to congestion
- Other drugs should be used as appropriate to manage co-morbid conditions.

**Other drugs**
Other agents should be considered as appropriate for co-morbid conditions, taking into account any contra-indications.

In all patients who develop heart failure a review of existing drug treatment is recommended. NSAIDs should be avoided if possible, and alternative hypoglycaemic agents substituted for glitazones for example.

**Device therapy (implantable defibrillators and cardiac resynchronisation therapy)**

The NICE TAG\(^9\) clearly sets out recommendations for considering device therapy in patients with left ventricular systolic dysfunction. Patients with an initial left ventricular ejection fraction ≤ 35% should have a reassessment of left ventricular function once established taking optimal medical therapy for 3 months. If left ventricular ejection fraction remains ≤ 35% the table below from the NICE TAG summarises the indications for device therapy.

<table>
<thead>
<tr>
<th>QRS interval</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120 milliseconds</td>
<td>ICD if there is a high risk of sudden cardiac death</td>
<td>ICD and CRT not clinically indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120–149 milliseconds without LBBB</td>
<td>ICD</td>
<td>ICD</td>
<td>ICD</td>
<td>CRT-P</td>
</tr>
<tr>
<td>120–149 milliseconds with LBBB</td>
<td>ICD</td>
<td>CRT-D</td>
<td>CRT-P or CRT-D</td>
<td>CRT-P</td>
</tr>
<tr>
<td>≥150 milliseconds with or without LBBB</td>
<td>CRT-D</td>
<td>CRT-D</td>
<td>CRT-P or CRT-D</td>
<td>CRT-P</td>
</tr>
</tbody>
</table>

LBBB, left bundle branch block; NYHA, New York Heart Association

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\(^9\) [https://www.nice.org.uk/guidance/ta314](https://www.nice.org.uk/guidance/ta314)
Management of patients with resistant heart failure, including right heart failure with congestion

These recommendations are for patients being managed in hospital or if as an out-patient, in liaison with a specialist clinician.

- Remember salt and fluid restriction, and bed rest
- DVT prophylaxis
- Increase diuretic dose (furosemide can be increased up to 500 mg od or more, particularly in CKD)
- Consider switching furosemide to bumetanide: experience is that in some patients this leads to a better diuresis
- Consider IV diuretic: intermittent bolus or infusion
- Consider the combination of a loop diuretic with a thiazide eg furosemide 120 mg od / bendroflumethiazide 1.25 – 2.5 mg od initially. Watch U&E
- High dose bendroflumethiazide or intermittent metolazone, in combination with a loop diuretic may be needed.

Lifestyle advice

- Smoking cessation
- Alcohol; within safe limits unless patients have an alcohol related cardiomyopathy when complete abstinence should be recommended.
- Physical activity
- Diet, including avoiding excess salt and fluid intake
- Make recommendations to address over weight and obesity
- Vaccination

Patient education and information

Patients should have information about their condition, including information to allow them to participate in planning their care and in the on-going management of their condition as appropriate.

Other advice should be tailored to the individual, for example with respect to occupational and leisure activities, driving requiring category 2 licence (refer to DVLA website), travel and sexual activity.

Appropriate and accurate information should be provided about prognosis when it is timely to do so.

Review and monitoring

There should be secure arrangements for clinical review and monitoring. All patients require at least a 6 monthly review, some require more frequent follow up (days to weeks), including;

- Clinical assessment of functional capacity, fluid status, cardiac rhythm (pulse palpation minimum), nutritional status and cognitive function.
- Assess patients as appropriate, for symptoms of anxiety and depression
- Drug review - ? optimised, ? adverse effects ? need for changes
- Is there an indication for device therapy
- Measure minimum of renal function and electrolytes. Digoxin level (8-12 hours after the last dose) only if toxicity is suspected
- Patient information and education – self management, what to do if condition deteriorates, other informational care
- Review social care needs

**Cardiac rehabilitation**
Stable patients should be offered a supervised exercise based programme designed for patients with heart failure as local resources allow. The programme should include psychological and educational components.

**Integration between primary and secondary care, and with social care**
Individual patient management plans and service provision should be integrated between primary, community and secondary care with effective communication between them, and with the patient. Social care needs should also be considered and addressed.

**Other interventions**

- Transplantation and left ventricular assist devices

- There is no good evidence for revascularisation in patients with coronary artery disease for the management of heart failure, and NICE guidelines do not recommend it is done routinely. Studies about this are ongoing.

**End of life care**
This should be discussed when it is appropriate to do so, tailored to the wishes of individual patients. Deactivation of ICDs should be done in line with other local guidelines for this (http://www.necvn.nhs.uk/content.aspx?id=1972&terms=ICD+deactivation).
Management of acute heart failure

Initial management is summarised in the third flow chart, and any local Trust guidelines, including for the local diagnostic pathway for suspected heart failure, should also be referred to. All patients should be treated as an emergency and following initial investigation and treatment should be reassessed within a timescale appropriate for the individual, this might be within a few minutes, but as a minimum within 30 minutes. Ongoing monitoring and identification and management of any reversible causes are important, and patients’ longer term regular treatment and management plan should always be reviewed. NICE recommend specialist advice about management is obtained for all patients admitted because of heart failure.

If possible treatment with beta blockers should be continued, but may need to be reduced or stopped if heart failure is refractory and or hypotension is a problem. In many patients ACE inhibitors/ARBs can be continued, but may need to be stopped if renal function and or hypotension is a particular problem.

Discharge should be:

- When stable
- With a management plan and with arrangements for follow up in the community with the GP and a heart failure nurse.

The provision of heart failure nurse follow up and monitoring will be determined by available capacity, but ideally should be available to all patients. Community heart failure nursing should integrate with primary and secondary care.
Appendices
Appendix 1

Criteria and operational arrangements for the local implementation of sacubitril valsartan in Newcastle, North Tyneside, and Northumberland

Patients should meet the following criteria

- The NICE TAG\textsuperscript{10} states that “Sacubitril valsartan is recommended 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)”.
- Patients should be optimally treated with ACE inhibitor or ARB, beta blockers and spironolactone as tolerated, and recent left ventricular ejection on treatment ≤ 35%
- Recent (within the last 4 weeks) serum potassium ≤ 5.4 mmol/l
- Recent (within the last 4 weeks) e GFR ≥ 30 ml/min/1.73m\textsuperscript{2}
- Systolic blood pressure ≥ 100 mmHg
- Seen by a consultant cardiologist for a discussion about the advantages of treatment, and also about possible side effects and the uncertainty about potential long term adverse effects
- Access to a specialist heart failure nurse, with capacity to manage and monitor the patient during initiation and stabilisation of treatment

Process for initiation and monitoring treatment

Request to initiate and monitor the sacubitril valsartan to be sent by letter by the cardiologist to the specialist heart failure nurse team in the appropriate locality, with a copy to the GP.

The specialist heart failure nurse team will:

Ensure they have sufficient capacity to initiate and monitor treatment
Discuss and ensure secure arrangements for the patient to stop the ACE inhibitor / ARB for 48 hours before starting sacubitril valsartan.

\textsuperscript{10} https://www.nice.org.uk/guidance/ta388
Ensure baseline renal function and potassium have been measured and are within the acceptable limits and systolic blood pressure is ≥ 100 mmHg

Arrange initiation of treatment with sacubitril valsartan after the ACE inhibitor / ARB has been stopped for a minimum of 48 hours.

Recommended starting dose one tablet of 49 mg/51 mg twice daily, reduced to 24 mg/26 mg twice daily, if systolic blood pressure 100 – 110 mmHg and or in moderate renal impairment, ie eGFR 30-60 ml/min/1.73 m². A lower starting dose may also be considered if there are concerns about tolerability eg lower tolerated dose of ACE inhibitor / ARB before being switched

Ensure patients have the “Entresto alert card”, that they know to carry this with them and show it to any health professional who may be considering them for any additional treatment.

Ensure that patients have appropriate information and education about sacubitril valsartan and in particular that they must not all also take an ACE inhibitor and or ARB.

Ensure that patients have a telephone number to contact the specialist heart failure nurse team and that there are secure arrangements for follow up and monitoring

Review the patient, check blood pressure and check renal function and serum electrolytes after 1 to 2 weeks (or earlier if clinically indicated).

If repeat renal function and serum potassium on initial treatment are within acceptable limits, and systolic blood pressure ≥ 100 mmHg, uptitrate sacubitril valsartan as tolerated, doubling the dose with a target dose of one tablet of 97 mg/103 mg twice daily, as tolerated.

Continue to review and monitor the patient, including checking blood pressure and renal function and electrolytes, until clinically and biochemically stable, on a stable dose of sacubitril valsartan for at least 3 months, before discharging for ongoing management in primary care (unless the patient remains for an extended period of monitoring with the specialist heart failure nurse team).

Ensure that all changes in medication are communicated to the GP and that the GP is informed when the patient is discharged from regular management by the specialist heart failure nurse team.

Patients will be reviewed 6 monthly in primary care, including with repeat measurement of renal function and electrolytes, (3 monthly if also treated with spironolactone or eplerenone), or more frequently if there are concerns about change in renal function and or electrolytes.
Troubleshooting / other points

If patients experience problems such as systolic blood pressure ≤95 mmHg, symptomatic hypotension, hyperkalaemia, renal dysfunction, management should be individualised, and may include adjustment of other drugs dependent on fluid status, and if necessary temporary down-titration or discontinuation of sacubitril valsartan.

The specialist heart failure nurse / GP should obtain additional advice from the consultant cardiologist if necessary.

If a consultant cardiologist chooses to initiate and prescribe sacubitril valsartan themselves, the consultant will ensure there are arrangements for safely initiating this after a wash out period for the ACEI/ARB and for follow up and monitoring.

The SPC states that “Entresto” be stored in the original package in order to protect from moisture. Further clarification has been asked for from the company regarding a compliance aid being used with “Entresto” who have responded that they cannot recommend the storage of a product other than as detailed in its Summary of Product Characteristics, and that there is no information on the storage of “Entresto” tablets in compliance aids. At the present time, the use of a compliance aid therefore cannot be endorsed, pending further information11.

Natriuretic peptide levels are affected by sacubitril / valsartan. The SPC states “BNP is not a suitable biomarker of heart failure in patients treated with Entresto because BNP is a neprilysin substrate. NT-proBNP is not a neprilysin substrate and is therefore a more suitable biomarker.”

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11 Added June 2016: The manufacturer has further responded, stating that the Summary of Product Characteristics (SmPC) provides the following information regarding storage:

**From Section 6.4 Special precautions for storage**

*This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.*

Any storage of the product other than as stated in the SmPC would be off licence and is therefore not recommended by Novartis. Furthermore, no studies on storing Entresto in dosette boxes have been conducted.

With this in mind, please be informed that stability studies have been conducted on Entresto in so called ‘open dish’ conditions, where tablets were exposed to an ambient temperature (25°C) and 60% relative humidity without any packaging. Please note all tablets were found to be stable for at least 3 months under those conditions.

Please note, Novartis recommends that the product should only be stored in compliance with its SmPC. If any storage medium other than the original licensed packaging is used, this is under the responsibility of the concerned healthcare professional.
Appendix 2

Examples of recommended target doses of commonly prescribed ACE inhibitors, beta blockers and ARBs

Lisinopril 30-40 mg od
Ramipril 5 mg bd or 10 mg od
Perindopril 8 mg od
Bisoprolol 10 mg od
Carvedilol 25 mg bd (in the absence of severe heart failure, 50 mg bd if weight > 85kg)
Candesartan 32 mg od
Losartan 150 mg od

Costs of heart failure drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength</th>
<th>Form</th>
<th>Pack size</th>
<th>Drug Tariff Price (May 2016)</th>
</tr>
</thead>
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<td>Ivabradine</td>
<td>5mg</td>
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<td>56</td>
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<td></td>
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Appendix 3

Membership of the group (2016)
Dr Kristian Bailey, Consultant Cardiologist, Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Rachel Cooper, GP, Newcastle Gateshead CCG
Vivienne Crisp, BHF Heart failure specialist nurse, Newcastle upon Tyne Hospitals NHS Foundation Trust
John Eastland, Heart failure specialist nurse, Northumbria Healthcare NHS Foundation Trust
Matthew Lowery, Formulary Pharmacist, Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Guy MacGowan, Consultant Cardiologist, Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Steve Kirk, GP, Newcastle Gateshead CCG
Dr Dave Morris, Consultant Cardiologist, Northumbria Healthcare NHS Foundation Trust
Dr Frances Naylor, GP, Northumberland CCG
Dr Dermot Neely, Consultant in Clinical Biochemistry, Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Mark Redpath, Consultant in Clinical Biochemistry, Northumbria Healthcare NHS Foundation Trust
Judith Robson, Community heart failure nurse, Northumbria Healthcare NHS Foundation Trust
Dr Craig Runnett, Consultant Cardiologist, Northumbria Healthcare NHS Foundation Trust
Dr Mike Scott, GP, Newburn, Newcastle
Dr David Shovlin, GP, West Northumberland
Dr Jane Skinner, Consultant Community Cardiologist, Newcastle upon Tyne Hospitals NHS Foundation Trust
Dr Caroline Sprake, GP, North Tyneside CCG
Sarah Tulip, Medicines Management, Newcastle and Gateshead CCG
Susan Turner, Medicines Management, Northumberland CCG

Date of guideline
May 2011, mini revision (ivabradine section) February 2013, updated May 2016

Review date
May 2019