MANAGEMENT OF HEART FAILURE with Reduced Ejection Fraction (HFREF)

- All patients with HFREF should be considered for an ACE inhibitor and beta blocker. Introducing one drug at a time, and once the person is stable on the first drug (usually an ACE) then adding the second drug.

- Patients with heart failure with reduced ejection fraction who have ongoing symptoms of heart failure, NYHA class II to IV, LVEF ≤35%, despite optimal treatment, should be given mineralocorticoid receptor antagonists (MRA) unless contraindicated.

- No patient should receive three drugs which block the renin-angiotensin-aldosterone system as hyperkalaemia and renal dysfunction will be common. The safety and efficacy of combining an ACE inhibitor, an ARB and MRA is uncertain and the use of these three drugs together is not recommended.

- Monitoring renal function has a very important role in heart failure management.

- BNP/NTproBNP (without an MI) testing is used to screen patients before referral for ECHO in patients with suspected heart failure.

- If ECHO suggests a diagnosis of HF an ECG should be done (if not already) to help identify the underlying cause of the HF.

- Sacubitril valsartan is a treatment option to be used as per NICE TA 388. Treatment with sacubitril/valsartan is to remain with the consultant/specialist service. Patients who commence treatment will have their ACE or ARB discontinued at least 36 hours before treatment is started. (See appendix 3 for further details).

- Specialist advice should be sought for patients who deteriorate after having been stable for a number of years on optimum pharmacological treatment with an unaccountable cause.
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<th>Document update</th>
<th>Date updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacubitril/valsartan information added as per NICE TA388 p.13</td>
<td>September 2016</td>
</tr>
</tbody>
</table>

**Key**

- ACEi - angiotensin converting enzyme inhibitor
- ARB – angiotensin receptor blockers
- BNP - B-type natriuretic peptide
- CRT – cardiac resynchronisation therapy
- eGFR - estimated glomerular filtration rate
- ECG - electrocardiogram
- HFREF - heart failure with reduced ejections fraction
- HR - heart rate
- ICD – implantable cardiovascular defibrillators
- LVEF - Left ventricular ejection fraction
- MRA - mineralocorticoid receptor antagonist
- NTproBNP - N-terminal proB-type natriuretic peptide
- RAS - renin–angiotensin system
- SBP – systolic blood pressure
- U&Es - serum urea & electrolytes
Management of chronic heart failure in adults in primary and secondary care

Key recommendations

Patients with suspected chronic heart failure should receive a range of basic tests. The investigations chosen will vary depending on the presentation but should usually include BNP/NTproBNP, a full blood count, HbA1c (or fasting blood glucose), serum urea and electrolytes (U&Es), urinalysis, thyroid function, liver function tests, electrocardiogram, lipids, peak flow or spirometry and chest X-ray.

Diagnosis

- The basis for historical diagnoses of heart failure should be reviewed, and only patients whose diagnosis is confirmed should be managed in accordance with this guideline.
- Doppler 2D echocardiographic examination should be performed to exclude important valve disease, assess the systolic function of the left ventricle and detect intracardiac shunts.

Monitoring

All patients with heart failure are at risk of renal impairment and hyperkalaemia. This is a consequence of common co-morbidities (e.g. diabetes), drug treatment, or just of the heart failure itself. Monitoring renal function has a very important role in heart failure management. In some situations renal function should be measured at frequent intervals because of a change in drug treatment (e.g. initiation of spironolactone) or of an acute change in the patient's condition. When patients are clinically stable and on stable doses of medication U&E should still be checked at least twice a year in order to monitor chronic changes in renal function which might mandate modification of the patient's treatment. Heart failure treatment, especially the combination of ACEi and MRA puts the patient at risk of acute decline in renal function and hyperkalaemia. In the event of intercurrent illness, especially diarrhoea and vomiting, all patients should be counselled to contact their GP under these circumstances and to stop the ACEi and MRA (normally for 48 hours), until they have had a blood test or once they are better and taking oral fluids.

- All patients with HFREF require monitoring. This monitoring (minimum of 6 monthly for stable patients) should include:
  - a clinical assessment of functional capacity, fluid status, cardiac rhythm, and cognitive and nutritional status
  - a review of medication, including need for changes (e.g. cessation of negatively inotropic calcium channel antagonists e.g. verapamil, diltiazem) and possible side effects
  - U&Es and eGFR

- In patients that do not respond to first/second line treatment, an assessment and referral for escalation of therapy may be required either to a HF specialist nurse service or cardiology (this may include invasive strategies to improve heart failure).

Discharge

- Patients with heart failure should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised
- The primary care team, patient and carer must be made aware of the management plan.

Supporting patients and carers

1. Management of heart failure should be seen as a shared responsibility between patient and healthcare professional.

Consider referral to a specialist heart failure nurse if appropriate: (see appendix 4 for referral form)

- Chesterfield link - 01246 253061
- Derby link - 01332 258131
Diagnosing heart failure

Take a detailed history and perform a clinical examination to evaluate for possible aggravating factors and to exclude other conditions with similar presentations.

Patients with suspected chronic heart failure should receive a range of basic tests. The investigations chosen will vary depending on the presentation but should usually include BNP/NTproBNP, a full blood count, HbA1c (or fasting blood glucose), serum urea and electrolytes (U&Es), urinalysis, thyroid function, liver function tests, lipids, electrocardiogram, peak flow or spirometry and chest X-ray.

While awaiting referral and if symptoms are severe to warrant treatment (but not admission) start a loop diuretic e.g. furosemide 20mg/day to 40mg/day. Stop if possible oral NSAIDs (including OTCs) or calcium channel blockers (e.g. verapamil, diltiazem).

INVESTIGATIONS

N terminal-pro-B-type natriuretic peptide (NT-proBNP)/ B-type natriuretic peptide (BNP) greatly improves the ability to rule out heart failure before referring for ECHO. Treatment of heart failure can bring NT-proBNP into the normal range. Therefore, when questioning the diagnosis in patients on treatment, either stop their medication for three days before taking the test or leave on treatment and get an ECHO.

New York Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea or palpitations.</td>
</tr>
<tr>
<td>II</td>
<td>Slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnoea.</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms.</td>
</tr>
<tr>
<td>IV</td>
<td>Unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity.</td>
</tr>
</tbody>
</table>

Serum peptides

- High levels: BNP > 400 ng/ml
  - (116 pmol/litre) or NTproBNP > 2000 ng/ml (236 pmol/litre)
- Raised levels: BNP 100-400 ng/ml;
  - (29-116) pmol/litre or NTproBNP 400-2000 ng/ml (47-236 pmol/litre)
- Normal levels: BNP < 100 ng/ml
  - (29 pmol/litre) or NTproBNP < 400 ng/ml (47 pmol/litre)

CRHFT currently report NTproBNP.
1. Consider an ICD in line with ‘Implantable cardiovascular defibrillators for arrhythmias’ (NICE TA 394).
2. Sacubitril/Valsartan for treating chronic heart failure as per NICE TA388.
3. Consider CRT in line with ‘Cardiac resynchronisation therapy for the treatment of heart failure’ (NICE TA 314).
4. Ivabradine for treating chronic heart failure as per NICE TA 267.
5. Hydralazine in combination with nitrate (especially in people of African or Caribbean origin with moderate to severe heart failure)
6. LVAD- left ventricular assist device
Drug therapy

Treatment
1. All patients with HFREF should be considered for treatment with an ACEi.
2. Beta-blockers licensed for use in heart failure should be initiated in patients with HFREF usually but not necessarily after diuretic and ACEi therapy (even if rendered asymptomatic with diuretic and ACEi). There may though be clinical reasons for starting a beta-blocker first e.g. additional anti-anginal treatment needed.

Diuretics
- Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in patients with heart failure, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. The lowest dose required to relieve symptoms/congestion is the optimum dose.
- Furosemide dose usually given once a day (morning), but can be given twice daily (morning and lunchtime for additional diuresis (starting dose 20-40mg day to usual dose 40-240mg per day). (Bumetanide is a 2nd line option (lack of efficacy with furosemide)- starting dose 1mg/day to usual daily dose of 5mg/day)
- Check renal function and serum electrolytes 1-2 weeks after starting treatment and after each dose titration. If stable then once every 6 months.

Diuretic resistance (after specialist initiation and assessment)
- Thiazide and thiazide-like diuretics (metolazone) can be added to loop diuretics to create a synergistic and potent diuresis in patients who are failing to adequately respond to increasing doses of loop diuretics
- This combination is initiated and managed by a specialist and on-going care only handed to primary care when the clinical and renal status of the patient have been stabilised.
- This combination can be effective and avoid the need for hospitalisation, but is not without risk.

ACE inhibitors
- All patients with HFREF should be considered for treatment with an ACEi.
- ACEi therapy is usually, but not necessarily, initiated before beta-blockade is introduced.
- ACEi therapy should be initiated at the appropriate low dose (see table 1) and titrated upwards at short intervals (for example, every 2 weeks) until the maximum tolerated or target dose is achieved.
- Blood biochemistry (urea, creatinine and electrolytes) should be measured 1-2 weeks after initiation and at 1-2 weeks after each dose increment. Once the dose is stable, monitor U&Es at least every 6 months. More frequent monitoring will be dependent on the persons clinical condition, medication regimen or co-morbidities.

Renal function:
- A rise in urea, creatinine and potassium is to be expected after initiation of an ACEi.
- An increase in creatinine up to 50% above baseline or 266 micromol/l, whichever is smaller is acceptable.
- An increase in potassium <5.5mmol/l is acceptable.
- If greater rises in creatinine or potassium than those outlined above persist despite adjustment of concomitant medications (e.g. stopping of NSAIDs) other potassium supplements/retaining agents (triamterene, amiloride, spironolactone/ eplerenone) and, if there are no signs of congestion, reducing the dose of diuretic. The dose of the ACE inhibitor should be halved and blood urea, creatinine and electrolytes rechecked within one to two weeks; if there is still an unsatisfactory response specialist advice should be sought.
- If potassium rises to ≥5.5 mmol/l or creatinine increases by >100% or to above 310 micromol/l the ACE inhibitor should be stopped and specialist advice sought.
- Blood urea, creatinine and electrolytes should be monitored frequently and serially until potassium and creatinine have plateaued.
Table 1 – starting and target dose for ACEi.

<table>
<thead>
<tr>
<th>ACE inhibitor</th>
<th>Starting dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril tablets</td>
<td>2.5mg twice daily</td>
<td>10-20mg twice daily</td>
</tr>
<tr>
<td>Lisinopril tablets</td>
<td>2.5mg once daily</td>
<td>35mg once daily</td>
</tr>
<tr>
<td>Ramipril capsules</td>
<td>2.5mg once daily</td>
<td>5mg twice daily or 10mg once daily</td>
</tr>
</tbody>
</table>

**Angiotensin receptor blockers (ARB)**
- Candesartan is the ARB of choice should one be required. ARB may provide an alternative to ACE inhibitors for patients intolerant of ACEi (for example, because of cough).

Table 2 – starting and stable dose for ARB.

<table>
<thead>
<tr>
<th>ARB</th>
<th>Starting dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan tablets</td>
<td>4 or 8 mg once daily</td>
<td>32mg once daily</td>
</tr>
<tr>
<td>Losartan tablets</td>
<td>12.5- 50mg once daily</td>
<td>150mg once daily</td>
</tr>
</tbody>
</table>

Although the MHRA June 2014, advised that the combination use of medicines from two classes of the renin-angiotensin hormone system blocking agents (this includes ACEi, ARBs and aliskiren) is not recommended. There are some patients with heart failure may have a medical need for treatment with an ACEi and ARB. There is some evidence that the benefits of this combination use may outweigh the risks (hyperkalaemia, hypotension, impaired renal function) in a selected group of people with heart failure for whom other treatments are unsuitable. Candesartan is a RAS blocking agent licensed as add-on therapy to ACEi for people with symptomatic heart failure who require such a combination despite optimal therapy.

Note- The combination of ACE+ARB+MRA together is **not** recommended

- The triple combination of ACEi, beta-blocker and ARB may be considered for persistently symptomatic patients – to be initiated only by a specialist.
First-Line Management of Heart Failure due Reduced Ejection Fraction

Echocardiogram has confirmed HFREF
(mild, moderate or severe; or measured LV ejection fraction less than 50%)

General Measures in all cases:
- Discontinue aggravating drugs if possible: oral NSAID, calcium antagonists (unless absolutely essential (e.g. for angina or hypertension)
- Specific advice on fluid intake and salt in diet (<6g/day)
- Address risk factors: smoking, alcohol, obesity, hypertension, diabetes
- Follow local guidelines on primary/secondary prevention of CAD
- Advise pneumococcal vaccination and influenza vaccination
- Offer patient-held record – for therapy, weight, risk factors etc.

Initial Treatment for all patients
If signs of fluid retention (oedema, lung crackles, raised JVP, pulmonary congestion on chest X-ray) – start oral loop diuretic
- If patient in AF – refer to the AF guideline
  - Start ACEi in all patients (check baseline U&Es), unless contraindication (aortic stenosis or suspected renal artery stenosis) or specialist advice needed (see below)
  - If contraindication to ACEi Refer to Secondary Care as appropriate
- Stop potassium supplements or potassium sparing diuretics (risk of hyperkalaemia)
- Start ACEi at low dosage – warn patient about hypotensive symptoms
- Check renal biochemistry after 1-2 weeks of therapy
- If biochemistry stable, slowly titrate ACEi to target dosage or maximally tolerated dose (suggest at intervals of two weeks). Check biochemistry at each titration stage.
- Aim for target dose or maximum tolerated dose

Once on Target or Maximal tolerated dose of ACE-inhibitor
- Repeat renal biochemistry after one month. If stable, check every 6 months or more frequently if patient status changes (particularly intercurrent illness).
- Check for adverse effects – symptomatic hypotension; rise in creatinine to > 50% from baseline or >266mcmol/l whichever is the smaller; hyperkalaemia (potassium>5.5 mmol/l); intolerable cough

If truly intolerant due to cough of ACEi (except renal dysfunction or hyperkalaemia)
- Start angiotensin receptor antagonist - Candesartan 4-8 mg od : target dose 32 mg od or losartan 12.5-50mg OD:target dose 150mg OD
  (Titrate doses at intervals of two weeks).
- Check renal biochemistry according to guidelines given above for ACEi.

Seek Specialist advice before ACEi therapy in following groups:
1. Creatinine > 221 umol/l (significant renal dysfunction)
2. Potassium >5 mmol/l
3. Sodium < 130 mmol/l
4. Systolic BP < 90 mmHg
5. Diuretic Dose > 80 mg furosemide per day (or equivalent)
6. Known or suspected renal artery stenosis (e.g. severe peripheral vascular disease)
7. Pregnancy (C/I 2nd & 3rd trimester)

Once established on ACEi or Angiotensin Receptor Blocker +/- diuretic
Start titrating Beta blocker-(bisoprolol)
**Beta-blockers**

- Beta-blockers licensed for use in heart failure should be initiated in patients with symptomatic heart failure due to HFREF after diuretic and usually ACEi therapy (even if rendered asymptomatic with diuretic and ACEi).
- All patients with heart failure with reduced ejection fraction, NYHA class II-IV, should be started on beta-blocker therapy as soon as their condition is stable.
- Beta-blockade therapy for heart failure should be introduced in a ‘start low, go slow’ manner, with assessment of heart rate, blood pressure, and clinical status after each titration.
- Patients who develop heart failure due to left ventricular systolic dysfunction and who are already on treatment with a beta-blocker for a concomitant condition (for example, angina, hypertension) should continue with a beta-blocker – either their current beta-blocker or an alternative licensed for heart failure treatment. Patients who are symptom free on atenolol do not necessarily need to switch to a beta-blocker licensed for heart failure.
- Monitor heart rate, BP and clinical status (symptoms, signs, especially of congestion, body weight).
- Check blood U&Es one to two weeks after initiation and one to two weeks after final dose titration.

### Low Heart rate:

- If the heart rate is <50 beats/min with worsening symptoms and the patient is symptomatic
  - Review the need for other heart rate slowing drugs e.g. digoxin, amiodarone, diltiazem/verapamil (diltiazem, verapamil are generally contraindicated in HF)
  - Halve the dose of beta blocker or
  - If there is severe deterioration, stop beta blocker (rarely necessary) and review the need for other heart rate slowing drugs, e.g. digoxin, amiodarone, diltiazem/verapamil (diltiazem and verapamil are generally contraindicated in HF). Ivabradine is an alternative treatment option after specialist initiation as per NICE TA267.
  - Arrange an ECG to exclude heart block.
  - Seek specialist advice.

### Table 3 – starting and target dose for beta blockers

<table>
<thead>
<tr>
<th>Beta blocker</th>
<th>Starting dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25mg once daily</td>
<td>10mg once daily</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125mg twice daily</td>
<td>*25-50mg twice daily</td>
</tr>
</tbody>
</table>

*The recommended maximum dosage is 25 mg twice a day for patients with a body weight of less than 85 kg, and 50 mg twice a day for patients with a body weight above 85 kg, provided that the heart failure is not severe.

### Starting bisoprolol in heart failure

The following conditions should be satisfied before starting bisoprolol:

1. Patient should have stable chronic heart failure without acute failure during the past 6 weeks and a mainly unchanged basic therapy during the past 2 weeks.
2. Patient should usually be treated at optimal dose with an ACEi (or ARB if not tolerated).
3. Patient should not have any absolute contraindications to bisoprolol use:
   - Acute heart failure or during episodes of heart failure decompensation requiring i.v. inotropic therapy
   - Cardiogenic shock
   - AV block of second or third degree (without a pacemaker)
   - Sick sinus syndrome
   - Sinoatrial block
   - Symptomatic/severe bradycardia with less than 60 beats/min before start of therapy
   - Symptomatic/severe hypotension (SBP < 90mmHg)
   - Severe bronchial asthma or severe chronic obstructive pulmonary disease
   - Late stages of peripheral arterial occlusive disease and Raynaud’s syndrome
• Untreated phaeochromocytoma
• Metabolic acidosis

Some of the above may be relative contraindications for example NICE recommends the offering of a beta-blocker in COPD patients without reversibility – if unsure contact a cardiologist.

**The treatment with bisoprolol has to be initiated with a titration phase:**

1. 1.25mg once daily for two weeks, if well tolerated increase to
2. 2.5mg once daily for two weeks, if well tolerated increase to
3. 3.75mg once daily for two weeks, if well tolerated increase to
4. 5mg once daily for four weeks, if well tolerated increase to
5. 7.5mg once daily for four weeks, if well tolerated increase to
6. 10mg once daily for the maintenance therapy

The SPC recommends that after initiation of treatment and dose increases patients should be observed over 4 hours (BP, heart rate, signs of increasing heart failure). Locally this is not considered to be necessary and returning home to the supervision of a responsible, forewarned adult would be more than adequate.

**Notes**

1. Progression from one titration stage to the next should be as a minimum at these intervals – it doesn’t matter if it takes longer. Occurrence of adverse events may prevent all patients reaching the maximum recommended dose – some bisoprolol is better than none at all.
2. If the patient complains of worsening shortness of breath then temporarily halt the titration. Leave the bisoprolol dose unchanged but increase the diuretic dose and review in a further 2 weeks. If breathlessness has reverted to its prior level, the titration can recommence. The dose of diuretic can be reduced when appropriate.
3. An alternative strategy for shortness of breath is to temporarily reduce the bisoprolol dose and prolong the intervals between subsequent titration if the breathlessness settles.
4. No further increase in bisoprolol dose should be made, without specialist advice, if the pulse (or apex beat if in AF) drops below 50 bpm and/or the SBP is less than 90mmHg, or there is symptomatic hypotension or bradycardia above these levels.
5. Treatment with bisoprolol is not recommended to be stopped abruptly since this might lead to a transitory worsening of heart failure. Many of the patients will also have ischaemic heart disease and sudden withdrawal of beta-blockade might precipitate an angina attack or an MI. If discontinuation is necessary, the dose should be gradually decreased by dividing into halves weekly. The only indications to stop bisoprolol therapy abruptly are:
   - severe symptomatic hypotension
   - acute pulmonary oedema
   - cardiogenic shock
   - severe symptomatic brachycardia
   - 2nd or 3rd degree AV block

**Mineralocorticoid receptor antagonist (MRA)**

- Patients with HFREF (LVEF<35%) who remain symptomatic despite optimal therapy (as outlined in the algorithm) should be prescribed spironolactone at a dose of 12.5 OD or 25mg on alternate days to 25-50 mg once per day – specialist advice should be sought. Target dose is dependent on symptoms and biochemistry stability
- Patients with heart failure taking spironolactone should have blood potassium and creatinine levels monitored for signs of hyperkalaemia and/or deteriorating renal function. If hyperkalaemia is a problem then the dose of spironolactone should be halved and biochemistry rechecked. For baseline and continuous monitoring see spironolactone flowchart on page 13 for recommendations
- If a patient requires but cannot tolerate spironolactone, eplerenone (starting dose of 25mg once daily with titrated target dose of 50mg once daily usually within 4 weeks) maybe used following the advice of the specialist.

NOTE- The use of ACE+ARB+MRA together is **not** recommended
Algorithm for the use of Spironolactone (on specialist initiation only) in Heart Failure due to Reduced Ejection Fraction (HFREF)

**Confirmed HFREF** – Second-line treatment (after optimisation of ACEi and beta blocker) in patients with NYHA class II-IV HF. LVEF ≤35% should be given mineralocorticoid receptor antagonist

**Suitable for initiation of Spironolactone?**

Spironolactone Contraindicated
- Serum potassium > 5 mmol/l
- Serum creatinine > 220 umol/l (or CKD stage >3)
- Known acute liver disease

Indications for Spironolactone after
- Heart failure (NYHA II – IV)
- Already on ACEi, beta-blocker and diuretic
- No evidence of hypovolaemia

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**If spironolactone contraindicated or is withdrawn and patient is still NYHA class II – IV despite therapy with a loop diuretic, ACE-inhibitor and beta-blocker**

Refer to Secondary Care (Cardiology, Medicine, Nephrology or DME as appropriate)

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**Further Monitoring**
- Patient may become dehydrated on spironolactone – if so reduce other diuretic dosages or stop spironolactone
- If patient develops intercurrent illness that causes salt and water loss (e.g. D & V) – tell them to stop spironolactone and contact their physician
- Repeat biochemistry and monitor closely

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**Check biochemistry; stop potassium supplements and other potassium-sparing diuretics before starting spironolactone**
- Caution if low body weight (<50 kg)
- Potassium must be < 5 mmol/l
- Continue ACE-inhibitor, loop diuretics, beta-blocker and digoxin if already prescribed
- Liaise with Heart Failure Nurse Service

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**Commence spironolactone 25 mg od or on alternate days**
- Repeat U&E at 5-7 days post initiation, then at 4, 8 and 12 weeks
- Then 6 monthly thereafter*
- Repeat above also after a dose change
- Target dose 25-50 mg once daily**

*This monitoring is by local agreement with Derbyshire cardiologists/specialists

**Note:** 3 monthly or more intensively may be necessary if there are clinical reasons why the patient is at increased risk of renal impairment

**Target dose dependent on symptoms and stability of biochemistry**

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**If intolerant of spironolactone or potassium > 5.5 mmol/l or creatinine > 220 umol/l**
- Reduce dose to 25 mg alternate days if not done already
- If still clinical/biochemical problems – stop spironolactone
- If potassium > 5.9 mmol/l or creatinine to 310umol/l – stop spironolactone immediately and seek specialist advice

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*Updated: May 2016*

Review date: April 2018

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Ivabradine (as per NICE TA 267)
Ivabradine may be prescribed after consultant or specialist (with access to a multidisciplinary heart failure team) initiation following a period of 4 weeks on optimised standard therapy with ACEI, beta-blocker and aldosterone antagonist.

NICE criteria:
- with New York Heart Association (NYHA) class II to IV stable chronic heart failure with systolic dysfunction with a left ventricular ejection fraction of 35% or less 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, ACEI and aldosterone antagonists, or when beta-blocker therapy is contraindicated or not tolerated and

Note -MHRA June 2014, advice for healthcare professionals regarding posology and monitoring:
- The starting dose of ivabradine is 5 mg twice daily. The maintenance dose should not exceed 7.5 mg twice daily.
- Carefully monitor patients for bradycardia or its symptoms (e.g., dizziness, fatigue, hypotension).
- The usual recommended starting dose of ivabradine is 5 mg twice daily. After two weeks of treatment, the dose can be increased to 7.5 mg twice daily if resting heart rate is persistently above 60 bpm or decreased to 2.5 mg twice daily (one half 5 mg tablet twice daily) if resting heart rate is persistently below 50 bpm or in case of symptoms related to bradycardia such as dizziness, fatigue or hypotension. If heart rate is between 50 and 60 bpm, the dose of 5 mg twice daily should be maintained.
- Stop ivabradine treatment if the resting heart rate remains below 50 bpm or symptoms of bradycardia persist.

Sacubitril/valsartan (as per NICE TA 388) for treating symptomatic chronic HFREF
(See appendix 3 for further details)
Sacubitril/valsartan has been classified by JAPC as RED, to remain under the consultant/specialist care.

Prescribing of sacubitril/valsartan will remain the responsibility of the cardiology specialist/ heart failure nurses.
NICE criteria for initiation:
- 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 ACEi or an ARB.

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

Usual starting dose is one (49/51mg) tablet, twice daily with the dose doubled at 2 to 4 weeks to the target dose of one (97/103mg) twice daily, as tolerated by the patient.

A starting dose of 24mg/26mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg and in patients with moderate renal impairment (eGFR 30-60 ml/min/1.73 m²)

Patients on an ACE inhibitor should have the ACE inhibitor discontinued for 36 hours before initiating sacubitril/valsartan to minimise the risk of angioedema.

Tolerability issues
- SBP ≤95 mmHg or
- symptomatic hypotension
- hyperkalaemia
- renal dysfunction
Action
1. Adjustment of concomitant medicinal products and or
2. Temporary down–titration or
3. Discontinuation of sacubitril/valsartan is recommended.

Periodic blood pressure monitoring (no less than annually) and renal function 3 monthly once stable is recommended. As with ACE inhibitors renal function is measured as baseline and 2-4 weeks after each dose change.

Digoxin
Digoxin is recommended for:
- Worsening or severe heart failure in sinus rhythm despite first and second line treatment
- Patients with atrial fibrillation and any degree of heart failure.

Aspirin and a statin
Aspirin (75mg once daily) is indicated if the person has atherosclerotic arterial disease. A statin atorvastatin (as per local lipid policy) is indicated in patients with atherosclerotic arterial disease or has a 10 year risk of CV disease >10%.

LIFESTYLE ADVICE
Appropriate lifestyle advice is probably as important as pharmacological therapy

Exercise
Regular aerobic and probably resistive exercise improves symptoms and quality of life. Meta-analyses suggest improvement in survival. Cardiac rehabilitation for heart failure patients is now available but all patients should be encouraged to exercise as much as their symptoms allow.

Salt restriction
The kidneys avidly retain salt in heart failure and this results in congestion. Where possible salt should be avoided. ‘Lo Salt’ contains some sodium and a significant amount of potassium. It should be avoided.

Weight monitoring
Obesity is a cause of heart failure and contributes towards the metabolic syndrome and obstructive sleep apnoea both of which exacerbate heart failure. Loss of fat weight can greatly improve symptoms. Fat weight rarely changes by more than a few hundred grams per day. Wet weight may change by as much as 2 Kg per day. Hospital admission is often preceded by a period of weight gain (salt and water retention). Hospital admission may be prevented by increasing the diuretic dose in response to weight gain. Similarly, in hot weather, weight loss signals the need to reduce the dose of diuretic.

Alcohol
For patients with alcoholic cardiomyopathy (in which alcohol has a toxic effect on the myocardium) complete abstinence is essential. For all others modest alcohol consumption is harmless.

Smoking
Should be strongly discouraged in all patients

Fluid restriction
Formal fluid restriction is difficult to achieve with any accuracy at home. Patients with hyponatraemia should be encouraged to be careful about the amount of fluid they drink. Occasionally it is necessary to limit the patient to less than 2 litres per day.

Patients should be made aware of Acute Kidney injury resources www.thinkkidneys.nhs.uk and PIL and sick day guidance
Prescribing tips

1. Medications with prognostic benefit, especially ACE inhibitors, are less well tolerated when the patient is volume contracted due to overenthusiastic diuresis. It is often necessary to reduce the diuretic to "make room" for the ACEI, beta-blocker and MRA (aldosterone) antagonist.

2. Aim for the minimum dose of diuretic required to reduce congestion

3. Aim for the target dose of ACEI and beta-blocker. But some is better than none and a little of both is better than lots of one and none of the other.

4. In heart failure a systolic blood pressure of 90 is often well tolerated. There is no need to reduce drug doses if the patient is without related symptoms. If it is necessary to reduce drug doses then consider reducing diuretic first.

5. If hypotension is a problem cut out any drugs that will lower BP but add nothing to the treatment of the heart failure eg CCBs, alpha-blockers.

6. Always stop the negatively inotropic CCBs (diltiazem, verapamil) if possible. They are associated with impaired survival. Long acting dihydropyridines (amlodipine, felodipine) have a neutral effect on mortality in heart failure

7. Cough is common in heart failure. ACE inhibitors cause cough in some patients. The effect of ACE inhibitors on survival is more certain than that of angiotensin receptor blockers. Do not rule out ACE inhibitors until you are absolutely certain that the drug is causing the cough.

8. Beta-blockers are usually perfectly well tolerated in COPD. Rhonchi are present periodically in heart failure and COPD. Do not stop the beta-blocker unless you are absolutely certain it is causing bronchospasm.

9. ACE inhibitors can often be up-titrated more quickly than recommended. Beta-blockers should always be bumped up slowly. It is sometimes necessary to leave it a lot longer than the suggested two weeks before increasing the dose. Sometimes the improvement in symptoms with beta-blockers is immediate. Sometimes it is necessary to encourage a patient to go through a period of symptom worsening before they feel better.

10. ACE inhibitors are not contraindicated in renal impairment. They are contraindicated when the presence of renovascular disease results in a decline (>50% increase in creatinine) in renal function with initiation of ACE inhibitor therapy. Check U&E one week after starting ACEI. Check sooner and more frequently where there is pre-existing renal impairment. Also beware hyperkalaemia (K+ >5.5 mmol/L)

11. Spironolactone is indicated for patients with symptomatic heart failure despite optimum treatment with ACE inhibitors and beta-blockers. If the criteria for prescribing are met, spironolactone is the preferred option to digoxin.

12. Digoxin has no survival advantage in heart failure but is sometimes useful for treating symptoms. In the Real World of elderly heart failure patients, drug interactions, intercurrent illnesses, and transient disturbance of renal function can lead to life-threatening hyperkalaemia or digoxin toxicity, so it is appropriate always to be cautious.
APPENDIX 1

PATIENT INFORMATION SHEET FOR ACE INHIBITORS IN HEART FAILURE
You have been recommended by your Doctor/Heart Failure nurse to start a drug called an Angiotensin Converting Enzyme Inhibitor or ACE Inhibitor as part of your treatment for your heart failure. Symptoms improve within a few weeks to a few months of starting treatment. Below is some information you need to know about this drug.

If you have any questions or concerns about your ACE Inhibitor please contact the Doctor/Heart Failure Nurse who commenced you on this therapy via the methods at the end of this information sheet.

Why ACE Inhibitors?
Research has shown that ACE Inhibitors help people with heart failure live longer and improve symptoms. This is especially true if they are added to the other recommended therapies - Diuretics (water tablets) and Beta Blockers. ACE Inhibitors can increase your ability to be active and sometimes they can reduce the amount of diuretics you need.

How do they work in Heart Failure?
ACE Inhibitors work by preventing some of the effects of the blood pressure hormone angiotensin. This hormone is produced by the body in response to the heart’s reduced function and tries to make the heart work harder, but in so doing often causes more damage. Angiotensin has a strong constricting effect on blood vessels, which makes life even harder for your heart. The ACE Inhibitor blocks its production allowing arteries to widen and relax. This also helps to control high blood pressure. However they are still effective for heart failure even if blood pressure is not high.

Side Effects
ACE Inhibitors tend to be tolerated better than many of the other medicines that people with heart failure are prescribed. The following are some of the side effects you may experience.

Dizziness - ACE Inhibitors can cause a drop in blood pressure especially when first taking them and also if you take other heart medications. In most cases this improves over a few days. Mild dizziness is not uncommon. If you feel faint then lay down. If you are concerned or if the dizziness does not settle seek advice either from the heart failure nurse or your doctor. Dizziness on waking can be improved if you try the following:  
- before sitting up flex and point your toes to work your calf muscles about 10 times  
- sit on the side of the bed for a minute before standing and continue to flex and point your toes.

Altered Kidney Function - ACE Inhibitors can cause problems with kidney function and your potassium level. For this reason you will have a blood test to monitor kidney function before starting your medication, after any dose increase and regularly while you take the medication. Please make sure you attend for your blood tests.

Cough - This is also a quite common side effect. Cough is also a symptom of heart failure and so the ACE Inhibitor is not always the cause of the cough. If your cough is particularly troublesome tell your Doctor/Heart Failure Nurse so that if necessary your dose can be lowered or an alternative medicine tried.
**Swelling of your lips and throat** - This is extremely rare. If this happens to you it is vital that you dial 999 and get medical help immediately.

**Starting the Treatment**
There are a number of different ACE Inhibitors available for you: ramipril, lisinopril, and enalapril are just a few. As with many medications it is important to increase your dose slowly and ensure that you tolerate the dose well at every step.

Patients are usually started with a low dose and dose doubled not less than two weekly intervals. Some healthcare professionals with experience in the use of ACE inhibitors may wish to uptitrate more rapidly taking into account risk of adverse effects and need for close monitoring. Also, not everyone is able to tolerate the target dose of ACE Inhibitor. A smaller dose that is well tolerated will certainly offer great benefits.

**Taking Your First Dose or Increasing Your Dose**
It is not unusual to feel slightly dizzy for a few days after starting or increasing your ACE Inhibitor. We do advise that you plan a more restful day if possible. If you do experience dizziness please read through the notes above for advice. The two most commonly used ACE Inhibitors are ramipril and lisinopril. The charts below describe how your dose will increase. Not everyone is able to tolerate the target dose and some people need their dose increasing more slowly than described here.

Your Doctor/Heart Failure Nurse will advise you at every stage about what dose to take and when your blood test is due.

<table>
<thead>
<tr>
<th>ACE inhibitor</th>
<th>Starting dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril</td>
<td>2.5mg twice daily</td>
<td>20mg twice daily</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5mg once daily</td>
<td>20mg once daily</td>
</tr>
<tr>
<td>Ramipril</td>
<td>2.5mg once daily</td>
<td>5mg twice daily or 10mg once daily</td>
</tr>
</tbody>
</table>

**Ongoing Care**
It is important for anyone with a heart problem to have his or her blood pressure and kidney function (this is a blood test) monitored regularly. This is especially true if you are taking ACE Inhibitors. This is usually undertaken at your GP surgery.

**Where to get Help and Advice**
It is best to seek advice from the person/service that has initiated and is increasing your ACE Inhibitor dose

Your GP, who you can contact in the usual way.
Your Heart Failure Nurse: Chesterfield link - 01246 253061
Derby link - 01332 258131
Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.
APPENDIX 2

PATIENT INFORMATION SHEET FOR BETA-BLOCKERS IN HEART FAILURE

You have been recommended by your Doctor/Heart Failure nurse to start a drug called a Beta-blocker as part of your treatment for your heart failure. Below is some information you need to know about the drug.

If you have any questions or concerns about your beta-blockers please contact the Doctor/Heart Failure Nurse who commenced you on this therapy via the methods at the end of this information sheet.

Why Beta-blockers?
Large research trials have shown that Beta-blockers help people with heart failure live longer and have a better quality of life if added to standard treatment for heart failure such as Diuretics and Ace Inhibitors.

How do They Work in Heart Failure?
There are 2 main benefits for taking Beta-blockers in heart failure.
Firstly they work by slowing the heart beat down which takes some of the work load off the heart and allows more time for the heart to fill with blood in between each heart beat.

Secondly they reduce the action of some hormones that can have a damaging effect on the heart. One particular hormone called adrenaline is released into the system to help a struggling heart pump faster and harder. In the long term high levels of adrenaline are toxic to the heart and causes abnormal heart rhythms and worsening heart failure.

Side Effects
One major side effect of Beta-blockers is that they can sometimes make asthma worse. This means that we have to take extra care when using beta blockers for anybody with asthma but those patients with Chronic Obstructive Pulmonary Disease (COPD) do tend to tolerate beta blockers quite well. Beta-blockers can make people feel lethargic and tired and also cause cold hands and feet. Tiredness is a feature of heart failure anyway. These side effects are usually short- lived whilst your body gets used to the new tablets but if they persist it is important to report this to your doctor or nurse.

Starting the Treatment
The 2 main Beta-blockers we use in heart failure are called Bisoprolol and Carvedilol. If we were to block the action of adrenaline on the heart all at once then the function of the heart may get worse. For this reason beta-blockers are started at very low doses to allow the heart to get used to their actions. The dosage is then built up slowly over the next few months. You will get benefit even from the lower doses but the full benefit is gained at the higher doses and may take 3 – 6 months to take effect.
Start with a low dose (see starting and target doses) and double the dose at not less than two-weekly intervals. Aim for the target dose or, failing that, the highest tolerated dose.

Taking Your First Dose
It is recommended that you are supervised either at home by a family member or at your GP Practice/ Clinic for 3-4 hours after taking your first dose. This is to ensure that in the rare event of any problems they are spotted immediately. Plan a quiet few hours and ensure that for the first week taking a beta-blocker that you are not too busy.
<table>
<thead>
<tr>
<th>Beta blocker</th>
<th>Starting dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25mg once daily</td>
<td>10mg once daily</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125mg twice daily</td>
<td>25-50mg twice daily</td>
</tr>
</tbody>
</table>

**Important Information**
It is very important **not** to stop taking beta-blockers suddenly unless advised by your doctor as this can cause serious problems for your heart.

**After starting the tablet and with each increase in dose some people experience the following side effects:**

**Dizziness** – Mild dizziness is not uncommon. If you feel faint then lay down. If you are concerned or if the dizziness does not settle seek advice either from the heart failure nurse or your doctor.

**Increased shortness of breath** – 1 in 3 people notice their heart failure symptoms get slightly worse over the 1st week or so. If it is just **slightly worse** then persevere, as this will usually improve after a week or two. If you **definitely feel much worse** seek advice from the heart failure nurse or your doctor. Do not stop taking the drug without advice.

**Increase in weight** – You will already have been asked to weigh yourself daily to monitor your heart failure. This is especially important if we change your treatment. If your weight increases over 2-3 days by 1-2 kgs (3-4lbs) then follow the flexible diuretic regime below to help clear or prevent any excess fluid from building up in your body:-
- If you already take 40mgs Furosemide once a day increase to 80mgs once a day for 3 days, then go back to your 40mgs dose.
- If you are taking 80mgs Furosemide once a day increase to 80mgs twice a day for 3 days, then go back to your 80mg dose.
- If you are already taking 80 mgs twice a day please seek help from the person who initiated your beta-blocker dose.

**Ongoing Care**
It is important for anyone with a heart problem to have his or her blood pressure and pulse monitored regularly. This is especially true if you are taking beta-blockers. This is usually undertaken at your GP surgery.

**Where to get Help and Advice**
**It is best to seek advice from the person/service that has initiated and is increasing your Beta- blocker dose**
Your GP who you can contact in the usual way
Your Heart Failure Nurse:
Chesterfield link  - 01246 253061
Derby link  - 01332 258131
Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.
APPENDIX 3
Algorithm for the use of sacubitril/valsartan by specialist/consultant in heart failure due to reduced rejection fraction (HREF)

At diagnosis does patient have EF<35% (Consider if an updated echo is needed) → No → Not Appropriate for Sacubitril/Valsartan
- Yes → Is the patient in NYHA Class II-IV → No → Not Appropriate for Sacubitril/Valsartan
- Yes → Has pt been considered for or stable on Beta-blocker → No → Delay Sacubitril/Valsartan until beta-blocker has been tried
- Yes → Is patient on an optimised dose of ACEi/ARB → No → Titrate to optimised level before considering sacubitril/Valsartan
- Yes → Is patient stable dose of ACEi/ARB for >4 weeks → No → Ensure 4 week period of stabilisation
- Yes → Has the patient been trialled with spironolactone → No → Delay Sacubitril/Valsartan until a MRA has been tried
- Yes → Is eGFR>30 → No → Not Appropriate for Sacubitril/Valsartan
- Yes → Is K+<5.5 → No → Not Appropriate for Sacubitril/Valsartan
- Yes → Is sBP>99 → No → Not Appropriate for Sacubitril/Valsartan
- Yes → Sacubitril /Valsartan indicated

Check no absolute contra-indications or caution and review co-administration warnings.
APPENDIX 4

DCHS Heart Failure Specialist Service

GP Referral Criteria and Contact Details

Referral Criteria please tick to confirm (must meet ALL of the following):

- Aged 18+ (unless referred by consultant Cardiologist)
- Registered with a GP in Derbyshire
- With a diagnosis of Heart Failure with Reduced Ejection Fraction (HFREF) which MUST be confirmed by echo, angio or other cardiac imaging
- The patient has been asked and agrees to the heart failure nurse being involved in their care

With one or more of the following (please tick which apply):

- Patient has had a recent hospital admission with worsening heart failure
- Initiation/titration of ACEi and/or Beta Blocker is problematic
- Patient is not symptom controlled on current medication
- Patient has advanced heart failure or complex palliative care needs
- Patient/carer struggling with self-management strategies

Urgency:

- URGENT (2-3 days), patient is continuing to deteriorate and admission likely imminent (FULL info AND PHONE CALL from clinician to team/office is VITAL)
- SOON (within 2 weeks) patient has had a recent decompensation, is stable but not improving or is slowly deteriorating (complete referral form and email through)
- ROUTINE (2-4 weeks), patient is stable even if NYHA III/IV but not on optimum treatment (complete referral and email or post)

A referral form must completed and can be posted, faxed or emailed to:

The Community Heart Failure Nursing Service

<table>
<thead>
<tr>
<th>Heart failure Team (North)</th>
<th>Heart failure Team (South)</th>
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<tbody>
<tr>
<td>(Covering GPs in Chesterfield, North East and High Peak and Dales areas)</td>
<td>(Covering GPs in Erewash, Amber Valley, Derbyshire Dales and City areas)</td>
</tr>
<tr>
<td>Heart Failure Nurse Services Welbeck Suite, Walton Hospital Whitecotes Lane Chesterfield S30 3HW</td>
<td>Heart Failure Nurse Services Junction 10 level 5 Derbyshire Royal Infirmary London Road Derby, DE1 2QY</td>
</tr>
<tr>
<td>Tel: 01246 253061 Fax: 01246 565053 Monday to Friday 9 – 4pm (excl. bank holidays) <a href="mailto:DCHST.heartfailurenorth@nhs.net">DCHST.heartfailurenorth@nhs.net</a></td>
<td>Tel 01332 258131 Monday to Friday 9 – 4pm (excl. bank holidays) <a href="mailto:DHFT.derbyhfteam@nhs.net">DHFT.derbyhfteam@nhs.net</a></td>
</tr>
</tbody>
</table>
DCHS Heart Failure Specialist Service
GP Referral Form for patients with HFREF

GP practices are encouraged to send a copy of patient summary information - to include GP and Patient Contact Data, Past Medical History, Current Prescriptions, known Allergies/Intolerances and recent blood tests, then just complete the Investigations and Current Condition sections (pg 1).

### Patient Details

<table>
<thead>
<tr>
<th>Name</th>
<th>D.O.B.</th>
<th>Male / Female</th>
<th>Address</th>
<th>NHS No</th>
<th>Postcode</th>
<th>Telephone</th>
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### GP Details

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>Tel</th>
<th>Fax</th>
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### Referrer's Details (if not GP)

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Tel</th>
<th>Fax</th>
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### TPP GP patients, consent to share record (TPP GP PRACTICES MUST COMPLETE)

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<th>Pt. consents to OUT share with GP</th>
<th>Pt. consents to IN share with HFSN</th>
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<td>Y / N</td>
<td>Y / N</td>
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### Investigations

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<th>Result</th>
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<td>BNP</td>
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<td>ECG</td>
<td>Please append copy of latest ECG</td>
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<td>CXR</td>
<td></td>
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<td>Echo</td>
<td>Please append copy of latest echo report NB MUST have echo evidence of HFREF Absence of echo or imaging or proof of HFREF – Hospital letter clearly stating this, may delay how quickly patient is seen.</td>
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<tr>
<td>Last U&amp;E</td>
<td>Na</td>
</tr>
<tr>
<td>Trends in U&amp;E</td>
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### Current Condition and REASON FOR REFERRAL – MUST BE COMPLETED

Brief history of illness. (Please also include any factors that may affect staff safety):
### Important information

| Other in patient medical issues /events/ medical intolerance |

### No of acute admissions in last year

### Current Medications

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<tr>
<th>Drug</th>
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References
1. BNF 68 September 2014- March 2015
3. NICE TA 267 Ivabradine for treating chronic heart failure
4. NICE Clinical Knowledge Summaries (CKS)- Chronic Heart Failure
5. NICE TA 388 Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction

Consultees
Derbyshire Clinical Effectiveness team
Derbyshire Guideline Group
DCHS Heart Failure specialists (Mandie Santon, Christine Laithwaite and Martin Melville)
Dr Mubarak Ahamed DTHFT consultant cardiologist
Dr Justin Cooke CRHFT consultant cardiologist
Dr Robert Mcintosh DTHFT consultant cardiologist

Resources
NHS England AKI Programme (Think Kidneys):
www.thinkkidneys.nhs.uk
Open access e-learning package for primary care:
http://www.uhl-library.nhs.uk/aki_gp/index.html
NICE AKI guidelines (CG169):
https://www.nice.org.uk/guidance/cg16