Heart failure: Managing newly diagnosed and decompensated patients admitted to hospital

1. Confirmation of Diagnosis

Person with signs and symptoms suggesting heart failure

Detailed history and clinical examination

Consider aetiology for new diagnosis of heart failure or underlying cause for exacerbation of chronic heart failure and exclude treatable causes.

- Arrange other investigations:
  - CXR
  - ECG
  - FBC
  - U&Es and Creatinine
  - LFTs
  - TFTs
  - RBG
  - Cholesterol

Confirmed diagnosis of heart failure

Diagnosis confirmed by previous echocardiogram

If current echocardiogram not clinically relevant, request repeat echo, if possible performed as an in-patient

Heart failure with preserved ejection fraction / diastolic dysfunction (EF >55%)

- Update primary diagnosis on PCIS / Cerner and document in casenotes.

Confirmed diagnosis of heart failure

Diagnosis confirmed by previous echocardiogram

Heart failure due to significant left ventricular systolic dysfunction (EF ≤ 40%)

- Update primary diagnosis on PCIS / Cerner and document in casenotes

Heart failure excluded so review diagnosis

Proceed to Management of Confirmed Heart Failure
2. Inpatient management

Heart failure with preserved ejection fraction
- Referral to heart failure specialist team.
- Arrange admission to appropriate ward/unit

Heart failure due to left ventricular systolic dysfunction (EF ≤ 40%)

Refer to Heart Failure Specialist Nurse for lifestyle advice:
- Stop smoking (smoking history, if smoker in last 12 months verbal advice, NRT or referral to smoking cessation service and document all)
- Diet, exercise, symptom management, daily weights, medication, alcohol reduction / abstinence, annual flu vaccine x 1
- Give heart failure information leaflet to patient or family /carer

Fluid balance:
1. Fluid restriction 1-2 litres in 24 hours
2. Salt restricted diet
3. Start loop diuretics e.g. furosemide 40mg od or increase and titrate according to symptoms. If required slow intravenous injection initially 50mg, increased by 20mg increments (ie, to 70mg, 90mg, etc) not less than every 2 hours (doses depend upon clinical state and previous oral doses)
   - In severe cases following review from heart failure team, a thiazide (e.g. bendroflumethiazide) may be added under close supervision

Drug management:
1. Start ACE inhibitor (ACEI) and titrate upwards.
   - If ACEI not tolerated, consider angiotensin-receptor blocker in NYHA Class I-IV.
2. Add beta blockers, when heart failure stable, and titrate upwards in NYHA Class I-IV. NB: if ACE I, ARB or beta blocker is contra indicated, document reason in casenotes.
3. Add spironolactone 12.5 – 25mg od, up to 50mg od in NYHA Class III-IV. Close monitoring of U&Es & creatinine required. NB eplerenone can be used as second line only if patient has painful gynaecomastia (unlicensed)
4. Consider ivabradine in line with NICE TA 237.
5. Consider low dose digoxin if in sinus rhythm.
6. If remains symptomatic and intolerant to spironolactone, consider addition of candesartan to ACE I under specialist supervision.
7. Consider hydralazine and nitrates

End of life care:
- Refer to guidelines for referral to specialist palliative care in end stage heart failure
- Complete DS 1500
- If appropriate, initiate The Liverpool Care of the Dying Pathway (LCP)
- Ensure ICD is deactivated

Ward monitoring of heart failure patients:
- Daily weights
- Strict fluid balance
- Sitting & standing BP
- Pulse
- Daily U&Es
- Monitor for improvement or deterioration in heart failure symptoms.

a) if still symptomatic on optimal tolerated drug therapy refer to Cardiologist for consideration of biventricular pacemaker/ cardiac resynchronisation therapy (CRTP/CRTD) provided:
1. EF <35%
2. QRS > 120 ms
a) consider referral for assist devices and transplant

Discharge planning:
- Ensure heart failure discharge letter is completed in a timely manner detailing: correct primary diagnosis, echo result, medication commenced and/or discontinued, discharge blood results, discharge weight, required monitoring, and ward follow-up arrangements from acute Trust.
- Refer to heart failure specialist nurse service for follow-up
- For more information see Heart Failure Website - Heart failure - NHS Choices

Heart failure — managing newly diagnosed and decompensated patients in acute care — clinical guidelines, v1
Principal author: Dr P Saravanan
Approved by Medicines Clinical Guideline Team: July 2013
Review by: July 2016
Signs and symptoms suggesting heart failure

Signs:

Tachycardia, Gallop rhythm, crackles, raised jugular venous pressure

The main clinical signs of heart failure are due to:
- Cardiomegaly — ie, displaced apex beat, third heart sound
- Congestion — ie, oedema, jugular venous distension, pulmonary crackles
- Activation of the sympathetic nervous system — tachycardia

Symptoms:

Dyspnoea, paroxysmal nocturnal dyspnoea (PND), fatigue, oedema

The classic symptoms of heart failure are dyspnoea and fatigue. However, orthopnoea is more specific than exertional dyspnoea when diagnosing heart failure, although its low sensitivity means it has little predictive value. PND has a greater sensitivity and predictive value.

Aetiology

Ischaemic heart disease, dilated cardiomyopathy, primary valvular disease, hypertension, cardiac arrhythmias, viral infections, toxic substances (alcohol/certain medicines), anaemia, hyperthyroidism, pregnancy, congenital heart disease

Occasionally no cause of heart failure can be found (ie, idiopathic)

Treatable causes and aggravating factors

- Anaemia
- Hyperthyroidism
- Non-compliance with medication
- Other medicines — non-steroidal anti-inflammatory drugs, corticosteroids, diltiazem, verapamil, alcohol
- Fast AF
- Infection
- Uncontrolled blood pressure
- Impaired renal function
Heart failure with preserved LV systolic function — diagnosis and management

Patients with:
- Clinical symptoms and signs of heart failure
- Supporting laboratory tests (e.g., chest X-ray showing pulmonary oedema)
- A typical clinical response to treatment with diuretics

and

- Echocardiography showing ejection fraction ≥50%

can be classed as having HF with preserved LV systolic function.

It would be useful to ensure that patients have at least one of the following in echocardiography, even though presence of these criteria is not imperative to make the diagnosis:
  1) Left atrium dilatation
  2) Evidence of left ventricle hypertrophy
  3) E/A ratio* more than 1 (trans-mitral doppler)
  4) IVRT ** > 110msec or < 60Msec (restrictive filling)

* E=early passive filling of the left ventricle, A=late left ventricle filling due to atrial contraction. In normal compliant ventricles, early filling should contribute to nearly 80% of the filling, which reverses when the ventricles do not relax well (diastolic dysfunction).

** IVRT (iso-volumetric relaxation time) is the time interval between closure of the aortic valve and opening of the mitral valve. In a compliant ventricle, this is short. It is prolonged if the left ventricle does not relax well (diastolic dysfunction). It can be very short in some conditions with a very restrictive filling pattern such as infiltrative cardiomyopathies

Treatment

There are no large scale clinical trials to confirm efficacy of most medications
The mainstay of therapy is diuretics.
Admission to cardiology ward

The following patients should be admitted to a cardiology ward:

A) New diagnosis of heart failure

1) All new admissions with clinical features of heart failure with current echo showing ejection fraction ≤40%

2) Anyone with clinical features as above but an ejection fraction >40% and any of the following:

<table>
<thead>
<tr>
<th>Pulmonary oedema</th>
<th>Shown on chest X-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral pleural effusions</td>
<td></td>
</tr>
<tr>
<td>Evidence of LVH by voltage criteria</td>
<td></td>
</tr>
<tr>
<td>Evidence of ischaemic heart disease or a previous myocardial infarction — ie, Q waves in ≥ 2 contiguous leads, persistent deep T-wave inversion and dynamic ST-T changes with or without chest pain</td>
<td>Shown on ECG</td>
</tr>
<tr>
<td>Evidence of significant valve disease (at least moderate)</td>
<td>Shown on echocardiography</td>
</tr>
<tr>
<td>Evidence of significant left ventricular hypertrophy</td>
<td></td>
</tr>
<tr>
<td>Evidence of estimated PAP &gt; 45 mmHg</td>
<td></td>
</tr>
</tbody>
</table>

3) Anyone deemed by a cardiologist to have a new diagnosis of heart failure with preserved LV function

B) Patients previously known to have heart failure

If current admission relates to decompensation of heart failure as evidenced by any of the following:

- Respiratory distress (respiratory rate > 40 breaths per minute) or pulmonary oedema (determined by radiograph)
- Hypoxia (oxygen saturation < 90%)
- Anasarca or significant oedema (≥+2)
- Syncope or hypotension (systolic blood pressure ≤80 mm Hg)
- Evidence of ischaemia (chest pain with ECG changes)
- Significant recent reduction in exercise tolerance

It is useful to keep in mind that the following are the most common causes of heart failure:

- Ischaemic heart disease: 40%
- Dilated cardiomyopathy: 32%
- Valvular heart disease: 12%
- Hypertension: 11%

Referral for device therapy in heart failure

Patients can be considered for cardiac resynchronisation therapy (eg, pacemaker or defibrillator) if they have a confirmed diagnosis of heart failure — either due to ischaemic or non-ischaemic aetiology with any of the following:

- Inability to exercise at least 4 metabolic equivalents
- Impaired systolic function (ejection fraction ≤35%)
- Significant heart failure symptoms (New York Heart Association classes IV or III, or class II with significant symptoms)
- Left ventricular volume overload
- Functional mitral regurgitation
- Significant left ventricular diastolic dysfunction
A) **NYHA class III or IV symptoms** — left ventricular ejection fraction ≤ 35%, QRS duration ≥ 120ms in **Sinus Rhythm** (if the patient is in AF please, see C) and on optimal (maximal tolerated doses of) heart failure medicines.

B) **NYHA class II symptoms** — left ventricular ejection fraction ≤ 35%, QRS duration ≥ 150ms in **Sinus Rhythm** and on optimal (maximal tolerated doses of) heart failure medicines.

C) **NYHA class III or IV symptoms** — left ventricular ejection fraction ≤ 35%, QRS duration ≥ 130ms in AF with a slow ventricular rate needing a pacemaker or where AV node ablation is contemplated as a rate control strategy and they are already on optimal (maximal tolerated doses of) heart failure medicines.

D) **NYHA class III or IV symptoms** — left ventricular ejection fraction ≤ 35% and in need of a pacemaker for profound symptomatic bradycardia, where it is expected that they will use their pacemaker more than 50% of the time.

Referrals should be made to a device specialist — currently Dr.P.Saravanan, consultant cardiologist.

**Referral for cardiac transplant**

Patients can be considered for cardiac transplant if they have one or more of the following (usually they will be aged less than 65 years):

- Two or more admissions for treatment of decompensated heart failure within the last 12 months.
- Persistent clinical evidence of overt heart failure after optimised medical treatment.
- Echocardiographic evidence of right ventricular dysfunction or increasing pulmonary artery pressure on optimal treatment (aim to refer before the pulmonary arterial systolic pressure exceeds 50mmHg).
- Deteriorating renal function attributable to heart failure or inability to tolerate diuretic dosages sufficient to clear congestion without change in renal function (aim to refer before creatinine clearance falls below 50ml/min or the estimated glomerular filtration rate [eGFR] falls below 40ml/min/1.73 m2).
- Significant episodes of ventricular arrhythmia despite full drug and electrophysiology/device treatment.
ACE inhibitors: Initiation and titration in adults with left ventricular systolic dysfunction

Evidence from clinical trials suggest that patients with, or at risk of developing heart failure show an improvement in symptoms and a reduction in morbidity and mortality when treated with an ACE inhibitor (ACEI). Therefore, all patients diagnosed with heart failure due to left ventricular systolic dysfunction should be considered for an ACEI.

**Indication:** Confirmed LVSD EF <40% and no contraindication to ACE Inhibitor.

### Table 1. Contraindications and cautions for prescribing ACEI in LVSD

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral renal artery stenosis</td>
<td>Hypotension (systolic blood pressure (BP) &lt; 90mmHg</td>
</tr>
<tr>
<td>Aortic or mitral valve stenosis or outflow obstruction</td>
<td>Patients with a documented intolerance of ACEI due to symptomatic hypotension – consider re-challenging with a long acting ACEI.</td>
</tr>
<tr>
<td>Known hypersensitivity to ACEI or excipients or to any other ACEI.</td>
<td>Patients on high dose diuretics (i.e. furosemide &gt; 80mg daily)</td>
</tr>
<tr>
<td>History to angioedema of any cause</td>
<td>Breast feeding</td>
</tr>
<tr>
<td>Pregnancy / risk of pregnancy</td>
<td>Moderate to severe renal impairment (i.e. creatinine &gt; 150μmol/L or eGFR &lt; 60ml ? min / 1.73m²)</td>
</tr>
<tr>
<td>Baseline potassium &gt; 5.5mmol/L</td>
<td>Baseline potassium &gt; 5 to 5.5mmol</td>
</tr>
</tbody>
</table>

Consider referral prior to initiation

- Creatinine >200micromol/L
- Urea > 12mmol/L
- Sodium <130mmol/L
- Systolic BP < 100mmHg
- Diuretic dose > 80mg furosemide daily or bumetanide 2mg daily
- Known or suspected renal artery stenosis (e.g. peripheral vascular disease
- Frail elderly

1. **Initiation and monitoring**
   - Check baseline blood chemistry. (e.g. serum creatinine, urea, potassium, sodium and creatinine clearance) and blood pressure (BP)
   - Discontinue potassium supplements/potassium sparing diuretics and review need for concomitant nephrotoxic drugs e.g. NSAIDs
   - Review dose of diuretic therapy.
   - Start with the lowest recommended dose of ACEI and titrate as suggested below. Aim for the target dose, failing that, the maximum tolerated dose. **Some ACEI is better than no ACEI.**

2. **Dose Titration**
- BP and blood chemistry (e.g. serum creatinine, urea, potassium, sodium and creatinine clearance) should be checked within **a week** of initiation and within **two weeks** of each change of dose. Recheck at 1, 3, and 6 months after achieving maintenance dose, then 4 monthly thereafter. Reduce dose/stop according to “worsening renal function” and “symptomatic hypotension” in “problem solving” below.

- ACEI dose can be doubled at no less than **2 weekly** intervals in the community. More rapid titration may be carried out in patients in hospital with close monitoring, tolerability permitting. Smaller increments may be more clinically suitable for certain patients.

### Licensed ACEI

<table>
<thead>
<tr>
<th>Licensed ACEI</th>
<th>Starting Dose (mg)</th>
<th>Target Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramipril</td>
<td>1.25mg once daily</td>
<td>5mg twice daily or 10mg once daily</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5mg-5mg once daily</td>
<td>30-35mg once daily</td>
</tr>
</tbody>
</table>

Ramipril and lisinopril are the Trusts ACEI of choice however some patients will require titration of existing therapy.

### 3. What to do if the following problems occur:

#### 1. Angioedema

- Rare but life threatening. Discontinue therapy and seek immediate advice from accident and emergency.

#### 2. Worsening renal function

An increase in urea, creatinine and K⁺ is to be expected after initiation/titration of ACEI. If the increase is small and asymptomatic, no action is necessary. Please see the table below for recommended actions.

<table>
<thead>
<tr>
<th>Blood Chemistry</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine ↑ up to 50% above baseline or to 265µmol/L (whichever is smaller). OR K⁺ ↑ to ≤5.5 mmol/L</td>
<td><strong>No action required.</strong> Repeat blood chemistry (urea, creatinine and potassium) within 2-4 weeks.</td>
</tr>
</tbody>
</table>
| Creatinine ↑ > 50% but < 100% above baseline or between 265µmol/L and 310µmol/L (whichever is smaller). OR K⁺ ↑ to ≥ 5.5 - ≤5.9 mmol/L | **Review required- consider**
  - Stopping concomitant nephrotoxic drugs e.g. NSAID’s, non-essential vasodilators (e.g. calcium antagonists, nitrates) and if no signs of fluid retention, reduce the dose of diuretic.
  - Review causes of high potassium. Stop other agents that cause hyperkalaemia e.g. potassium sparing diuretics.
  - If despite adjusting medication the creatinine and K⁺ remain higher than above the dose of ACEI should be halved and the blood chemistry re-checked in 5-7 days. If the response to this is not satisfactory, seek specialist advice.
  - Blood chemistry should be monitored closely until K⁺ and Creatinine concentrations are stable |
| Creatinine ↑ by >100% (from baseline) or to above 310µmol/L. OR K⁺ ≥ 6mmol/l | **Discontinue ACEI and discuss with cardiologist** |

*Note: it is very rarely necessary to stop an ACEI and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.*

Heart failure — managing newly diagnosed and decompensated patients in acute care — clinical guidelines, v1
Approved by Medicines Clinical Guideline Team: July 2013 Review by: July 2016
3. Asymptomatic low blood pressure
- Does not usually warrant a change in therapy

4. Symptomatic low blood pressure
- Consider dehydration and address as appropriate
- Review diuretic dose with a view to decreasing dose if patient free of symptoms suggestive of fluid retention.
- If dizziness and light-headedness and/or confusion occur, consider stopping nitrates, calcium channel blockers and other vasodilators first, then consider reducing dose of beta-blocker
- Monitor closely and allow longer intervals between dose titrations. Consider reduction of ACEI dose to the previous tolerated dose.
- Seek specialist advice if measures do not resolve symptomatic hypotension

5. Persistent dry cough
- Review aetiology of cough e.g. due to smoking, worsening heart failure/pulmonary oedema, respiratory disease or ACEI therapy.
- Review cough tolerability vs benefits of an ACEI. Some patients may tolerate re-institution of the ACEI after a drug free period (ESC)

Rarely requires discontinuation of treatment. If significantly affecting the patient’s quality of life, an Angiotensin Receptor Blocker (ARB) should be commenced in place of the ACEI.

4. Patient information
- Explain the expected benefits to the patient –treatment can improve their symptoms, prevent their heart failure getting worse, increase survival and decrease hospital admissions
- Symptoms may not improve immediately. It may take a few weeks or months to have a full effect
- Advise patients to report principal adverse effects e.g. cough, hypotension or dizziness
- Advise patients to take the first dose at night as they may experience a first dose hypotensive effect
- Advise patients to avoid OTC NSAIDs, soluble tablets and salt substitutes high in K+
- Advise patients what to do if they forget to take a dose.

References
- Summary of product characteristics for Zestril available online at www.medicines.org.uk
- Summary of product characteristics for Innovace available online at www.medicines.org.uk
- Summary of product characteristics for Tritace available online at www.medicines.org.uk
- British National Formulary 63, March 2012
- Acknowledgments to South London Cardiac and Stroke Network, Northampton General Hospital, Kings College Hospital and St George’s Hospital & Gloucestershire Countrywide Primary Care Heart Failure Guidelines
Angiotensin II receptor blockers (ARBs): Initiation and titration in adults with left ventricular systolic dysfunction

ARBs (sartans) have a more limited evidence base and have not shown superiority over ACEI in any large scale clinical trial. There are currently no compelling indications for the use of ARBs routinely first line. Therefore, they should only be considered second line in patients truly intolerant to ACEI.

- **Candesartan** is the ARB of choice for use in heart failure and impaired LVSD (ejection fraction <40%), in the following patients: Patients previously intolerant of an ACE inhibitor, candesartan has been shown to reduce the risk of the composite outcome of cardiovascular death or CHF hospitalisation, the risk of CHF hospital admission and to improve NYHA class (CHARM alternative).  

**Indication:** Confirmed LVSD EF <40% intolerant to an ACE Inhibitor but no contraindication to an ARB.

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>- History of hypersensitivity to ARB or any excipients</td>
<td>- Hyperkalaemia (K+ &gt; 5.0mmol/L)</td>
</tr>
<tr>
<td>- Pregnancy</td>
<td>- Patients with renal impairment i.e. serum creatinine is &gt;220μmol/L or greater and/or glomerular filtration rate &lt; 15mL/min</td>
</tr>
<tr>
<td>- Breastfeeding</td>
<td>- Baseline potassium &gt; 5 to 5.5mmol/l</td>
</tr>
<tr>
<td>- Patient on both an ACEI and aldosterone antagonist</td>
<td>- Hepatic impairment</td>
</tr>
<tr>
<td>- Baseline potassium &gt; 5.5 mmol/L</td>
<td>- Patients with volume depletion such as those on high dose diuretics may lead to symptomatic hypotension therefore volume should be restored prior to administration</td>
</tr>
<tr>
<td></td>
<td>- Symptomatic or severe asymptomatic hypotension (systolic BP&lt;90mmHg)</td>
</tr>
<tr>
<td></td>
<td>- Patients taking potassium supplements or other drugs that may increase potassium</td>
</tr>
<tr>
<td></td>
<td>- Renal artery stenosis</td>
</tr>
<tr>
<td></td>
<td>- Patients on haemodialysis</td>
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<tr>
<td></td>
<td>- Haemodynamically relevant aortic or mitral valve stenosis</td>
</tr>
<tr>
<td></td>
<td>- Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>- Primary aldosteronism</td>
</tr>
</tbody>
</table>

**Table 1:** Contraindications and cautions for prescribing ARBs in LVSD

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<td>- Creatinine &gt; 200micromol/L</td>
</tr>
<tr>
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• Known or suspected renal artery stenosis (e.g. peripheral vascular disease)
• Frail elderly

1. Initiation and monitoring

• Check baseline blood chemistry. (e.g. serum creatinine, urea, potassium, sodium and creatinine clearance) and blood pressure (BP)
• Discontinue potassium supplements/potassium sparing diuretics and review need for concomitant nephrotoxic drugs e.g. NSAIDs
• Review dose of diuretic therapy.
• Start with the lowest recommended dose of ARB and titrate as suggested below. Aim for the target dose, failing that, the maximum tolerated dose. **Some ARB is better than no ARB**

2. Dose Titration

• BP and blood chemistry (e.g. serum creatinine, urea, potassium, sodium and eGFR) should be checked within **one week** of initiation and within **two weeks** of each change of dose. Recheck at 1, 3, and 6 months after achieving maintenance dose, then 4 monthly thereafter.
• Reduce dose/stop according to “worsening renal function” and “symptomatic hypotension” in “problem solving” below.
• ARB dose can be doubled at no less than 2 **weekly** intervals if appropriate. Smaller increments may be more clinically suitable for certain patients. More rapid titration may be carried out in patients in hospital with close monitoring, tolerability permitting.

<table>
<thead>
<tr>
<th>Licensed ARB</th>
<th>Starting Dose (mg)</th>
<th>Target Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan</td>
<td>4mg once daily - a lower dose of 2mg daily should be used in the elderly.</td>
<td>32mg daily</td>
</tr>
</tbody>
</table>

3. What to do if the following problems occur:

1. Angioedema
• Rare but life threatening. Discontinue therapy and seek immediate advice from accident and emergency.

2. Worsening renal function
An increase in urea, creatinine and K⁺ is to be expected after initiation/titration of ARB. If the increase is small and asymptomatic, no action is necessary. Please see the table below for recommended actions.

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Blood Chemistry & Action

<table>
<thead>
<tr>
<th>Concentrations are stable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Creatinine</strong> ↑ by &gt;100% (from baseline) or to above 310µmol/L.</td>
</tr>
<tr>
<td>OR <strong>K+ ≥ 6mmol/l</strong></td>
</tr>
</tbody>
</table>

* Note: it is very rarely necessary to stop an ARB and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.

3. Asymptomatic low blood pressure

- Does not usually warrant a change in therapy

4. Symptomatic low blood pressure

- Consider dehydration and address as appropriate
- Review diuretic dose with a view to decreasing dose if patient free of symptoms suggestive of fluid retention
- If dizziness and light-headedness and/or confusion occur, consider stopping nitrates, calcium channel blockers and other vasodilators first, then consider reducing dose of beta-blocker
- Monitor closely and allow longer intervals between dose titrations. Consider reduction of ARB dose to the previous tolerated dose.
- Seek specialist advice if measures do not resolve symptomatic hypotension

Patient information

- Explain the expected benefits to the patient – e.g. this treatment can improve their symptoms, prevent their HF getting worse, increase survival and decrease hospital admissions
- Symptoms may not improve immediately. The medication may take a few weeks or months to have a full effect.
- Advise patients to report principal adverse effects e.g. hypotension or dizziness
- Advise patients to avoid OTC NSAIDs, soluble tablets and salt substitutes high in K+
- Candesartan can be taken with or without food
- Advise patients what to do if they forget to take a dose

References

- Summary of product characteristics for Amias. Available online at www.medicines.org.uk
- British National Formulary 63, March 2012
- Acknowledgments to South London Cardiac and Stroke Network, Northampton General Hospital, Kings College Hospital and St George’s Hospital & Gloucestershire Countrywide Primary Care Heart Failure Guidelines
Loop diuretics: Initiation and titration in adults with heart failure

Diuretic therapy provides the mainstay of symptomatic management of heart failure. However, evidence is lacking demonstrating morbidity and mortality benefits. Generally loop diuretics are first line therapy when treating decompensation. The loop of choice would be furosemide with bumetanide reserved for those patients unresponsive to furosemide. Patients with refractory oedema may require combination therapy of a loop diuretic and a thiazide diuretic, although this increases the risk of provoking biochemical disturbances.

**Indication**

Loop diuretics should routinely be 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 treatments. Some patients will require diuretics as maintenance therapy.

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity to these compounds</td>
<td>Hypotension (systolic BP &lt;90mmHg)</td>
</tr>
<tr>
<td>Hypovolaemia</td>
<td>Prostatic enlargement or impaired micturation</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Gout</td>
</tr>
<tr>
<td>Severe hypokalaemia K+ &lt; 3.3 mmol/L</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Severe Hyponatraemia Na &lt; 130 mmol/L</td>
<td>Hepatic impairment*</td>
</tr>
<tr>
<td>Comatose/ precomatose states associated with liver cirrhosis</td>
<td>Renal Impairment*</td>
</tr>
<tr>
<td>Anuria</td>
<td>Pregnancy*</td>
</tr>
<tr>
<td>Renal failure due to nephrotoxic or hepatotoxic drugs</td>
<td>Breast feeding*</td>
</tr>
<tr>
<td></td>
<td>Drug interactions see list below.</td>
</tr>
<tr>
<td></td>
<td>* see BNF for details on each drug.</td>
</tr>
</tbody>
</table>

1. **Initiation and titration of loop diuretics.**

The following checks should be carried out before initiating/increasing/decreasing loop diuretics.

Patient weight, fluid status, heart rate, BP, JVP and baseline blood chemistry. (e.g. serum creatinine, urea, potassium, sodium and creatinine clearance, eGFR)

a) For mild to moderate fluid retention:

For those patients NOT PRESCRIBED diuretics:
- Start with a low dosage of furosemide e.g. furosemide 40mg PO daily and increase slowly see Table 2 overleaf until clinical improvement of signs and symptoms of congestion.

For those patients PRESCRIBED diuretic therapy:
- The patient’s diuretic dose should be increased initially for 3 days. Furosemide should generally be increased in 40mg increments, bumetanide in 1mg PO increments. See table 2 overleaf.
Table 2. Oral furosemide and bumetanide suggested dose increments (NB. 1mg of bumetanide is approximately equivalent to a 40mg dose of furosemide)

<table>
<thead>
<tr>
<th>Frusemide:</th>
<th>Bumetanide: (dose may be split am/pm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current Dose</strong></td>
<td><strong>Increase to</strong></td>
</tr>
<tr>
<td>40mg daily</td>
<td>80mg daily*</td>
</tr>
<tr>
<td>80mg daily*</td>
<td>120mg daily*</td>
</tr>
<tr>
<td>120mg daily*</td>
<td>160mg daily*</td>
</tr>
</tbody>
</table>

* diuretics are usually taken in the morning. If BP is low to allow for further titration doses can be split twice daily with the second dose taken at 2pm. For example 120mg daily could also be taken 80mg mane and 40mg at 2pm.

b) For moderate to severe fluid retention:

Consider IV Diuretic therapy:

**Furosemide** 20 to 50mg, by IV bolus, at a rate not exceeding 4mg/minute. Doses over 50mg should be given as an IV infusion (undiluted or added to sodium chloride 0.9% — the volume of infusion is not critical provided an administration rate of 4mg/minute is not exceeded). A continuous infusion can be used under specialist supervision if there is a poor response to repeat bolus doses. A suggested regimen is 10mg per hour (adjusted according to response).

**Managing resistant oedema**

A thiazide diuretic e.g. bendroflumethiazide can be used in synergy with a loop diuretic, in cases of severe fluid overload. **Bendroflumethiazide** 2.5mg, orally, daily or on alternate days. Increasing to 5mg, if indicated. This will result in a powerful diuresis and should be initiated only on advice from the **specialist heart failure service**.

For patients whose condition remains resistant, **metolazone** (now unlicensed) can be considered on the recommendation of a heart failure clinic.

**Monitoring for patients on diuretic therapy**

The patient should be reviewed daily on the ward. An adequate response to treatment would be improved symptoms and weight reduction of 0.5 kg/day. Daily U&Es and BP required. Dose of diuretic should be adjusted, particularly after restoration of dry weight, to avoid the risk of renal dysfunction and dehydration. Aim to achieve dry weight with lowest achievable dose.

It may be worth considering increasing ACEI dose or adding in spironolactone if BP and renal function permits.

Refer to algorithm on heart failure management and guidance on individual drugs

2. Reducing doses of maintenance diuretic therapy

- This should be undertaken cautiously. The dose should only be reduced from the usual maintenance only if there are signs of volume depletion and hypoperfusion i.e. evidence of significant weight loss from dry weight (> 1 kg) rising blood urea (> 5 mmol/L or > 25 per cent) and/or symptoms of dizziness (e.g. postural hypotension) or feeling “dried out”.
- The dose of diuretic should not be reduced if there is peripheral oedema or if the JVP is elevated. If the patient has a rising blood urea, falling weight and/or symptoms of dizziness/dehydration but peripheral oedema consider seeking advice from a cardiologist.
- Dose reduction should be carried out by 40mg furosemide or 1mg bumetanide increments that are the reverse of the up-titration guidelines outlined above.
3. What to do if the following problems occur:

1. **Symptomatic hypotension (systolic <100mmHg)**
   - Check blood chemistry
   - Encourage fluid intake
   - Withhold one to three diuretic doses and lower doses by one stage.
   - Counsel patients to avoid abrupt postural changes.
   - Reassess BP and hypotensive symptoms daily
   - If patient remains symptomatic, review vasodilators and if taking ramipril once a day, consider splitting
dose to twice a day

2. **Hypokalaemia – See Wirral Trust hypokalaemia guideline**
   - For hypokalaemia consider increasing ACEI/ARB. Consider addition of spironolactone if clinically indicated.
   - Monitor potassium closely.

3. **Hypomagnesaemia – See Wirral Trust hypomagnesaemia guideline**
   - Discuss with Consultant Cardiologist

4. **Hyponatraemia – See Wirral Trust hyponatraemia guideline**
   - Fluid restriction
   - Reduce or stop diuretics if possible

5. **Insufficient response or diuretic resistance**
   - Check compliance and fluid intake
   - Increase dose of diuretic as detailed above
   - Consider switching from furosemide to bumetanide
   - Administer loop diuretic twice daily or on an empty stomach
   - Discuss with the heart failure team for other options for management

6. **Hypovolaemia/dehydration**
   - Assess volume status
   - Consider diuretic dose reduction as documented above

7. **Hyperuricaemia/gout**
   - For acute gout attacks, physician to treat with colchicine and avoid NSAIDS.
   - For frequent gout attacks, consider prophylaxis with allopurinol.

8. **Increased fasting blood sugar**
   - Review for new diagnosis of diabetes

9. **Renal Failure**
   - Check for hypervolemia/dehydration
   - Exclude other nephrotoxic agents .g. NSAIDs, Trimethoprim
   - Withhold aldosterone antagonist
   - Consider a reduction of ACEI/ARB in line with individual drug guidelines
   - Discuss with renal team or heart failure team at the hospital with regards to deteriorating renal function

10. **Rash/Allergy to frusemide**
    - Bumetanide can be used in patients allergic to frusemide.

11. **Photosensitivity**
4. Patient information

- Time of the taking the loop diuretic is not fixed, however it is better to avoid taking after 4pm as this can lead to nocturia
- Report dizziness/light-headedness as this may be indicative of over treatment
- Encourage patient to self-weigh daily (after waking and voiding but before breakfast and dressing) and agree an action plan if notices a sudden weight gain.
- Report sudden or sustained weight increase or decrease (more than 1kg over 3 days) to a specialist nurse or GP
- Report any symptoms of fluid overload i.e. increased breathlessness, frothy sputum, peripheral oedema to a specialist nurse or GP
- Diarrhoea, vomiting, hot weather and poor fluid intake exacerbate dehydration. Contact GP if persists for > 2-3 days
- Gout can occur

References

- Summary of product characteristics for Burinex available online at www.medicines.org.uk
- British National Formulary 63, March 2012
- Acknowledgments to South London Cardiac and Stroke Network, Northampton General Hospital, Kings College Hospital and St George’s Hospital & Gloucestershire Countrywide Primary Care Heart Failure Guidelines
Beta blockers: Initiation and titration for adults with left ventricular systolic dysfunction

Beta-blockers reduce mortality (by about 30%) and hospital admissions (by about 20%) when added to full conventional heart failure therapy, including ACE inhibitor treatment.

**Indication** Confirmed LVSD, EF <40%, clinically stable and no contraindication to beta blocker

**Table 1. Contraindications and cautions for prescribing beta blockers in LVSD**

Beta-blocker therapy should not be withheld for any of the following reasons: increasing age, presence of peripheral vascular disease (PVD), erectile dysfunction, diabetes mellitus, interstitial pulmonary disease and chronic obstructive pulmonary disease (COPD) without reversibility.

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe bronchial asthma or severe COPD – see cautions.</td>
<td>Mild to moderate reversible airways disease – monitor peak flow prior to and following initiation and after any dose change. If concerned, seek specialist advice prior to initiation.</td>
</tr>
<tr>
<td>Uncontrolled/acute heart failure/ decompensation of heart failure/symptoms of fluid retention in the past 6 weeks</td>
<td>Renal or hepatic disease (see BNF for further details)</td>
</tr>
<tr>
<td>Prinzmetal’s angina</td>
<td>Beta-blockers may mask early signs of hypoglycaemia. Worsening control of blood glucose may occur. Monitoring is therefore necessary in patients with diabetes when beta-blockers are initiated/ titrated.</td>
</tr>
<tr>
<td>Sinus bradycardia (&lt;50bpm)</td>
<td>First degree heart block</td>
</tr>
<tr>
<td>Hypotension – (systolic BP &lt;90mmHg) or symptomatic hypotension</td>
<td>Use of concomitant medication that may increase the risk of bradycardia</td>
</tr>
<tr>
<td>Sick sinus syndrome including sino-atrial block, 2nd or 3rd degree heart block (without a pacemaker)</td>
<td></td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td></td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td></td>
</tr>
<tr>
<td>Severe peripheral circulatory disturbances/ PAD</td>
<td></td>
</tr>
<tr>
<td>Phaeochromocytoma (unless specific use with α blockers)</td>
<td></td>
</tr>
<tr>
<td>Patients treated with verapamil</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity to beta-blockers or any of the excipients</td>
<td></td>
</tr>
</tbody>
</table>

**Beta blockers licensed for LVSD available on the Wirral Trust Prescribing Formulary**

**Bisoprolol** – adjunct in stable moderate to severe heart failure with reduced systolic ventricular function (EF≤35% on echo). Bisoprolol is cardioselective and therefore should be the preferred agent if beta-blockers are used in patients with respiratory problems.
**Carvedilol** – used as an adjunct to diuretics, digoxin or ACE inhibitors in symptomatic chronic heart failure. Carvedilol works on β1, β2 and α-adreno receptors and therefore may be more effective at reducing hypertension.

**Bisoprolol is the preferred agent, with carvedilol a suitable second-line alternative**

**NICE recommends** switching stable patients who are already taking a beta-blocker for a comorbidity (for example, angina or hypertension), and who develop heart failure due to LVSD, to a beta-blocker licensed for heart failure.

1. **Initiation and Titration**

   Treatment should be initiated and titrated by those experienced in the management of heart failure

   - Introduce beta-blockers in a ‘start low, go slow manner’
   - Ensure the patient is symptomatically stable and other heart failure therapies have been mainly unchanged for 2 weeks.
   - Doses should be increased according to the dose titration schedule in Table 2 if patient remains clinically stable.
   - Aim for a target dose as detailed below. Failing that, aim for the maximum tolerated dose. **Some beta-blocker is better than no beta-blocker.**

   **Table 2. Suggested dose titration schedule for bisoprolol, carvedilol and nebivolol**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Week 0</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Week 16</th>
<th>Week 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25mg od</td>
<td>2.5mg od</td>
<td>3.75mg od</td>
<td>5mg od</td>
<td>7.5mg od</td>
<td>10mg od</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125mg bd</td>
<td>6.25mg bd</td>
<td>12.5mg bd</td>
<td>25mg bd*</td>
<td>50mg bd**</td>
<td></td>
</tr>
</tbody>
</table>

*maximum dose in patients with severe heart failure or body weight <85kg
**maximum dose for those with body weight ≥ 85kg

If a beta-blocker has been stopped for more than 2 weeks, re-introduce cautiously. Consider restarting from the initiation dose.

2. **Monitoring**

   - Monitor heart rate, blood pressure, clinical status, symptoms and signs of congestion e.g. body weight, breathlessness and oedema. An ECG is recommended in ALL patients before initiation.

   - Check blood electrolytes, urea and creatinine 1-2 weeks after initiation and 1-2 weeks after final dose titration.

   **Beta-blockers should not be stopped suddenly unless absolutely necessary due to the rebound effects (in myocardial ischaemia/infarction and arrhythmias). Ideally specialist advice should be sought before treatment discontinuation.**

3. **What to do if the following problems occur:**

   1. **Worsening symptoms/signs** (e.g. increasing dyspnoea, fatigue, oedema, weight gain >1.5kg over 3days)
• If increased congestion, double dose of diuretic and/or halve dose of beta-blocker (if increasing diuretic does not work)
• If marked fatigue (and/or bradycardia, see below) halve dose of beta blocker (rarely necessary)
• Review patient in one to two weeks. If there has been no improvement, seek specialist advice.
• If serious deterioration, halve the dose of beta-blocker or stop treatment (rarely necessary) and seek specialist advice.
• If there are worsening symptoms of airways disease, stop the beta-blocker and seek specialist advice.

2. Asymptomatic low blood pressure
• Does not usually warrant a change in therapy

3. Symptomatic low blood pressure systolic (<100mmHg)
• If combined with dizziness, light-headedness or confusion, consider discontinuing drugs such as nitrates, calcium channel blockers and other vasodilators
• If no signs/symptoms of congestion, consider reducing dose of diuretic.
• If these measures do not solve problem, seek specialist advice

4. Bradycardia (HR<50)
• If bradycardia and worsening symptoms, halve the dose of beta-blocker or if severe deterioration, stop beta-blocker (rarely necessary)
• Consider need to continue treatment with other drugs used to slow the heart (digoxin, amiodarone, diltiazem) and discontinue if co-morbidities allow.
• Arrange ECG to exclude heart block.
• Seek specialist advice.

5. 2nd or 3rd degree heart block
• Stop beta-blocker and consult specialist advice (patient may require hospital admission)

6. Impotence
• This may resolve as heart failure improves. Consider a referral to the erectile dysfunction clinic if appropriate.

Advice to patient
• Explain the expected benefits and emphasise that the treatment given is given to prevent worsening of heart failure, improve symptoms, reduce the risk of hospital admission and prolong life.
• Symptomatic improvement may take up to 3-6 months or longer to develop
• Temporary symptomatic deterioration may occur during initiation and/or up titration in approximately 20-30% of cases. Advise patients to report deterioration (fatigue, breathlessness and tiredness) and that deterioration can usually be easily managed by adjustment of other medication – patients should be advised not to stop their beta-blocker therapy without speaking to their GP or heart failure team.
• Patients should be encouraged to weigh themselves daily (after waking and voiding but before breakfast and dressing) and to consult their GP/heart failure team if they have persistent weight gain (e.g. an increase in your weight over the last 3 days by 3-4 pounds (1.5kg) or more)
• Carvedilol should be taken with food

References
• Summary of product characteristics for Cardicor. Available online at www.medicines.org.uk ,
• Summary of product characteristics for Eucardic. Available online at www.medicines.org.uk/,
• British National Formulary 63, March 2012
• Acknowledgments to South London Cardiac and Stroke Network, Northampton General Hospital, Kings College Hospital and St George’s Hospital & Gloucestershire Countrywide Primary Care Heart Failure Guidelines
Spironolactone: Initiation and titration for adults with left ventricular systolic dysfunction

The RALES study demonstrated that treatment with low dose spironolactone was associated with improved survival, reduced hospitalisations, improved NYHA class when added to standard therapy in patients with severe (NYHA class III or IV) ejection fraction < 35%.

**Indications**
Patients with LVSD (EF <35% ) who remain moderately to severely symptomatic (NYHA III-IV) despite optimal therapy (ACE inhibitor (ACEI), beta-blocker, diuretic and ± digoxin).

**Table 1. Contraindications and cautions for prescribing beta blockers in LVSD**

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anuria</td>
<td>• Porphyria</td>
</tr>
<tr>
<td>• Acute renal insufficiency</td>
<td>• Pregnancy and lactation</td>
</tr>
<tr>
<td>• Rapidly deteriorating or severe impairment of renal function (baseline SrCr &gt;200µmol/L or GFR &lt;30mls/min or urea &gt;11.2mmol/L)</td>
<td>• Hepatic impairment (Child Pugh Class A &amp; B, monitor electrolytes closely)</td>
</tr>
<tr>
<td>• Hyperkalaemia defined as (K+ &gt;5.0mmol/L at initiation)</td>
<td>• Moderate to severe renal impairment SrCr&gt;150 µmol/L</td>
</tr>
<tr>
<td>• Addison's disease</td>
<td>• Elderly – initial dose of 12.5mg daily recommended</td>
</tr>
<tr>
<td>• Hypersensitivity to spironolactone or excipients</td>
<td>• Drug interactions</td>
</tr>
<tr>
<td>• Hyponatraemia - Na+&lt;135mmol/L</td>
<td>*See back of BNF</td>
</tr>
<tr>
<td>• Co-prescription of potassium sparing diuretics, potassium supplements.</td>
<td></td>
</tr>
<tr>
<td>• Severe hepatic insufficiency Childs Pugh Class C</td>
<td></td>
</tr>
<tr>
<td>• Combination of an ACEI and ARB</td>
<td></td>
</tr>
</tbody>
</table>

**Consider referral to heart failure specialist prior to initiation:**
- Hyponatraemia (<135mmol/L)
- Symptomatic hypotension or severe asymptomatic hypotension (systolic BP<90mmHg)
- Significant renal dysfunction/renovascular disease e.g. creatinine > 221 micromol/L or urea >15mmol/L or hyperkalaemia (>5.0mmol/L)

**Table 1. Contraindications and cautions for prescribing spironolactone in LVSD**

**Initiation and Monitoring**
- Check baseline blood chemistry. (e.g. serum creatinine, urea, potassium, sodium and eGFR and liver function tests)
- Initiate 25mg once daily (For elderly patients use either 12.5mg daily or 25mg on alternate days).
- Check blood chemistry at 1, 4, 8, 12 weeks, 6, 9 and 12 months and then 6 monthly thereafter.
- For those patients started on a lower dose if blood chemistry and BP are within normal ranges at 4 weeks titrate to 25mg daily.
• Doses of 50mg daily may be advised by a specialist if heart failure symptoms deteriorate and the patients K+ level permits.

If K+ rises to ≥ 5.5mmol/L ≤ 5.9mmol/L or creatinine rises to 200µmol/L, reduce dose to 25mg alternate days and monitor blood chemistry closely.

If K+ rises to ≥ 6mmol/L, or creatinine rises above 200µmol/L, stop spironolactone and seek specialist advice.

1. What to do if the following problems occur:

1. Sodium/water depletion and/or hypovolaemia
   • Consider a reduction in the concomitant diuretic dose e.g. bumetanide or furosemide
   • Measure blood chemistry
   • Consider reducing the dose or stopping spironolactone/eplerenone

2. Symptomatic hypotension (systolic <100mmHg)
   • Measure blood chemistry
   • Assess fluid intake
   • Consider a reduction in the diuretic dose or omit a couple of doses of diuretic
   • Advise about avoiding abrupt postural changes
   • If symptoms persist or are severe, seek specialist advice

3. GI upset
   • Reduce dose or discontinue therapy

4. Hyponatraemia
   • Na< 135mmol/L, stop spironolactone/eplerenone and seek specialist advice

5. Hyperkalaemia
   • See guidance above also refer to Wirral Trust Hyperkalaemia Guideline

6. Gynaecomastia
   • Stop spironolactone - usually reversible on cessation of therapy
   • Eplerenone may be considered as an alternative to spironolactone, under specialist supervision, for patients with severe LVSD, where spironolactone is indicated but has not been tolerated usually due to the development of gynaecomastia. This is an unlicensed indication.

Patient information
• Treatment is given to improve symptoms, prevent worsening of heart failure and to prolong life.
• Symptom improvement occurs within a few weeks to a few months of starting treatment.
• Spironolactone should be taken with food
• Avoid salt substitutes (LO-SALT) and over the counter cystitis remedies high in K+.
• Avoid NSAIDs (including over the counter and topical NSAIDs)
• In the case of dehydration, diarrhoea or vomiting, withhold the spironolactone immediately and contact your GP.

References
• Summary of product characteristics for Aldactone. Available online at www.medicines.org.uk
• British National Formulary 63, March 2012
• Acknowledgments to South London Cardiac and Stroke Network, Northampton General Hospital, Kings College Hospital and St George’s Hospital & Gloucestershire Countrywide Primary Care Heart Failure Guidelines
Ivabradine: Initiation in adults with left ventricular systolic dysfunction

Ivabradine is a pure heart-rate lowering drug. The SHIFT study demonstrated that reducing heart rate with ivabradine in selected chronic heart failure patients significantly reduced heart failure related admissions and heart failure related deaths. However, no overall effect on all-cause or CV mortality was observed.

NICE TA 267 November 2012 recommends ivabradine as a treatment option for chronic heart failure patients if all of the following criteria are met:

- Patients with NYHA class II to IV stable chronic heart failure and,
- Patients who are in sinus rhythm with a heart rate of ≥ 75 beats per minute and,
- Patients 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,
- Patients have a left ventricular ejection fraction ≤ 35%.

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

Table 1: Contra-indications and cautions for prescribing ivabradine in stable LVSD patients

<table>
<thead>
<tr>
<th>Contra-indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity to the active substance or excipients</td>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td>Pregnancy or lactation</td>
<td>Second degree AV block</td>
</tr>
<tr>
<td>Resting heart rate &lt;60 bpm prior to treatment</td>
<td>Unstable heart failure, particularly NYHA class IV</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>Immediately post CVA</td>
</tr>
<tr>
<td>Pacemaker dependent (heart rate imposed exclusively by the pacemaker.</td>
<td>Unexpected deterioration in visual function, especially in patients with retinitis pigmentosa</td>
</tr>
<tr>
<td>Congenital QT syndrome</td>
<td>Hepatic insufficiency (avoid in severe hepatic impairment)</td>
</tr>
<tr>
<td>Cardiogenic shock or acute MI</td>
<td>Renal insufficiency (CrCl&lt;15ml/min)</td>
</tr>
<tr>
<td>Sino-atrial block or 3rd degree AV block</td>
<td>Mild to moderate hypotension (avoid if &lt;90/50mmHg)</td>
</tr>
<tr>
<td>Unstable or acute heart failure</td>
<td>DC cardioversion - if non-urgent wait 24 hours after last dose of ivabradine</td>
</tr>
<tr>
<td>Combination with strong cytochrome P450 3A4 inhibitors (see table 2)</td>
<td>Combination with QT prolonging agents requires close cardiac monitoring (see table 2)</td>
</tr>
</tbody>
</table>

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.

1. **Dosing**

Heart failure — managing newly diagnosed and decompensated patients in acute care — clinical guidelines, v1
Principal author: Dr P Saravanan
Approved by Medicines Clinical Guideline Team: July 2013
Review by: July 2016
Obtain baseline BP and pulse before initiation and after each change in dose

Table 2:

### Ivabradine dosing

<table>
<thead>
<tr>
<th>Initiating dose</th>
<th>5mg orally twice daily (BD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If elderly patient i.e. &gt;75 years old, or unable to tolerate the initial dose above, use the reduced starting dose:</td>
<td></td>
</tr>
<tr>
<td>Reduced starting dose</td>
<td>2.5mg orally twice daily (half of a 5mg tablet- scored)</td>
</tr>
</tbody>
</table>

2. Common Drug Interactions (See BNF for full list)

#### Table 3: Drug interactions

<table>
<thead>
<tr>
<th>Drug Interactions</th>
<th>Increased plasma ivabradine levels and risk of bradycardia. Concomitant use of ivabradine with potent CYP 3A4 inhibitors (clarithromycin, erythromycin, ketoconazole, itraconazole and fluconazole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong CYP 3A4 inhibitors</td>
<td>Increased plasma ivabradine levels. Concomitant use should be avoided.</td>
</tr>
<tr>
<td>HIV protease inhibitors</td>
<td>Increase risk of bradycardia. Avoid use of ivabradine with verapamil.</td>
</tr>
<tr>
<td>Calcium channel blockers (rate limiting – diltiazem and verapamil)</td>
<td>Concomitant use with ivabradine should be avoided. If use is unavoidable close cardiac monitoring (ECG, heart rate) is needed.</td>
</tr>
<tr>
<td>Drugs that prolong the QT interval (sotalol, amiodarone, disopyramide, quinidine, citalopram, fluoxetine)</td>
<td>Hypokalaemia in combination with ivabradine induced bradycardia may increase the risk of severe arrhythmias especially in patients with long QT syndrome.</td>
</tr>
<tr>
<td>Diuretics – potassium depleting thiazide or loop diuretics</td>
<td>Reduce ivabradine plasma levels. Concomitant use with rifampicin, barbiturates, and phenytoin may result in reduced efficacy of ivabradine; dose adjustments may be necessary.</td>
</tr>
<tr>
<td>Potent CYP 3A4 inducers</td>
<td>Reduce ivabradine levels due to increased ivabradine metabolism via CYP 3A4 enzyme induction.</td>
</tr>
<tr>
<td>St Johns Wort</td>
<td>Increase plasma ivabradine levels</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>Increase plasma ivabradine levels</td>
</tr>
</tbody>
</table>

3. Monitoring

Review for response (resting pulse and blood pressure) two weeks after treatment initiation

The dose of ivabradine should be titrated to achieve a resting heart rate of ≤ 60bpm.

#### Table 4: Ivabradine dosage adjustment recommendations based on patients resting pulse rate

<table>
<thead>
<tr>
<th>Pulse Rate</th>
<th>Dose 5mg twice daily (BD)</th>
<th>Dose 2.5mg twice daily (BD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse &lt;50bpm or symptoms of bradycardia</td>
<td>Reduce to 2.5mg BD*</td>
<td>Stop</td>
</tr>
<tr>
<td>Pulse 50-60bpm</td>
<td>Continue 5mg BD</td>
<td>Continue 2.5mg BD</td>
</tr>
</tbody>
</table>
Pulse >60bpm | Increase to 7.5mg BD | Increase to 5mg BD

*If bradycardia (pulse<50bpm) or symptoms of bradycardia persist despite dose reduction, treatment should be discontinued.

4. Problem Solving

Table 5: Common side effects of ivabradine

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Side Effects</th>
</tr>
</thead>
</table>
| Most common | Luminous phenomena (phosphenes) - visual disorder  
Blurred vision  
Bradycardia |
| Common | Headache  
Dizziness  
1st degree AV block (prolonged PQ interval on ECG)  
Ventricular extrasystoles  
Uncontrolled blood pressure |

Bradycardia is one of the most common adverse effects experienced in chronic heart failure patients (5% in the ivabradine treated group v 1% in the placebo group from the SHIFT study). In these patients dose reduction or treatment cessation should be considered. (See table 2)

Luminous phenomena - This is a transient enhanced brightness in a limited area of the visual field. They are usually triggered by sudden variations in light intensity. The onset of phosphenes is generally within the first two months of treatment after which they may occur repeatedly. Phosphenes will resolve either during or after treatment.

Ivabradine is a black triangle drug. ANY adverse effects must be reported to the Committee on Safety of Medicines (CSM). [http://yellowcard.mhra.gov.uk/](http://yellowcard.mhra.gov.uk/)

5. Patient Information

- Explain the expected benefits - treatment with ivabradine will reduce the resting heart rate and has been shown to reduce heart failure related hospitalisations and death.
- Take with food. Advise patients what to do if they miss a dose.
- Advise patients to report any adverse effects, including dizziness to the GP.
- Counsel patients about the possibility of visual disturbance and advise not to drive if visual acuity is affected, especially at night.
- Avoid in lactose intolerant patients.
- Avoid grapefruit juice

References

- Summary of product characteristics for Procoralan. Available online at [www.medicines.org.uk](http://www.medicines.org.uk)
- British National Formulary 63, March 2012
- Acknowledgments to South London Cardiac and Stroke Network
Wirral Community Heart Failure Service

All patients who have had a recent admission with either decompensating heart failure or a new diagnosis of heart failure should be referred to community heart failure services for clinical review and follow-up.

Specialists in this service work with patients, families and carers to help patients and families better understand the diagnosis and how to ensure they stay well.

Patients with a suspected but **unconfirmed diagnosis** can be referred to Wirral Heart Support for investigation and confirmation of diagnosis.

The Heart Failure Service offers:
- Confirmation of diagnosis and management plan by consultant cardiologist or GPSI in cardiology.
- Full range of diagnostic tests, including BNP, ECG and Echocardiogram
- Follow up appointments with symptom and medication review
- Clinics available at St Catherine’s Hospital and Victoria Central Health Centre
- Home visits for patients with a confirmed diagnosis who are too unwell to attend clinic
- Robust links with Wirral University Teaching Hospital NHS Foundation Trust’s Arrowe Park Hospital
- Referral to other specialist centres for expert review e.g. Device therapy, ablation.
- Access to cardiac rehabilitation through the Living Well with Heart Failure rehabilitation programme.
- Links with community nursing services, matrons and palliative care.
- Appropriate patients can be offered remote telehealth monitoring?

How you can access the service:

A **Heart Services referral form** must be completed. The service accepts referrals from GPs, practice nurses and hospital staff for patients who have been admitted with a suspected or confirmed diagnosis heart failure. (NOTE: Only Wirral health professionals are able to access this form).

Only patients with Wirral GP’s will be eligible for this service.

**Opening Times:**
Monday – Friday, 9:00am – 5:00pm
Wednesday, 9:00am – 8:00pm

**Contact:**

<table>
<thead>
<tr>
<th>Wirral Heart Services</th>
<th>Clinics are also available at:</th>
</tr>
</thead>
<tbody>
<tr>
<td>St Catherine’s Health Centre</td>
<td>Victoria Central Health Centre, Mill Lane, Wallasey And</td>
</tr>
<tr>
<td>Church Road</td>
<td>The Warrens Medical Centre, Arrowe Park Road, CH49 5PL</td>
</tr>
<tr>
<td>Tranmere</td>
<td></td>
</tr>
<tr>
<td>Wirral, CH42 0LQ</td>
<td></td>
</tr>
<tr>
<td>Tel: 0151 604 7711 - Fax: 0151 652 4004</td>
<td></td>
</tr>
</tbody>
</table>

**Related Links:**

Wirral Heart Support Centre [www.wirralheartbeat.org.uk](http://www.wirralheartbeat.org.uk)
Wirral Heart Beat is an independent charity dedicated to assisting the work of the British Heart Foundation [www.bhf.org](http://www.bhf.org)
Community Heart Failure Nurse Referral Form
Direct Line 0151 604 7711 ext 3765
Please fax this form to 0151 652 4004

Please read guidance before completing referral form:-

1. The HF Nurse Service is for patients with **confirmed heart failure** on echocardiogram
2. The referring clinician is responsible for ensuring heart failure is the main cause of admission
3. Patients with a secondary diagnosis of HF should only be referred by medical staff / HF team
4. Patients will be reviewed 2 – 4 weeks from referral, either in clinic or at home.
5. You should refer patients with uncertain diagnosis for a Specialist HF opinion and assessment
6. The patient must live in Wirral and be registered with a Wirral GP. (this excludes patients who are registered with GPs in Neston or Ellesmere Port)
7. Patients for cardiac rehabilitation should be referred in the normal manner

IF YOU REQUIRE A REVIEW WITHIN 10 WORKING DAYS
PLEASE CONTACT THE DEPARTMENT TO DISCUSS,
OTHER PATIENTS WILL BE SEEN ROUTINELY

TO DISCUSS A PATIENT PRIOR TO REFERRAL
Contact the Community Heart failure Service on 0151 604 7711 between 9.00-5.00PM,
Monday – Friday (8.00pm on Wednesdays)

ALWAYS ADVISE YOUR PATIENT TO ATTEND HIS OR HER GP OR RETURN TO HOSPITAL SHOULD THEIR SYMPTOMS WORSEN
Community Heart Failure Nurse Referral Form
Direct Line 0151 604 7711 ext 3765
Please fax this form to 0151 652 4004

<table>
<thead>
<tr>
<th>PATIENT NAME:</th>
<th>Referring Clinician:</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRN NO:</td>
<td>Print name</td>
</tr>
<tr>
<td>D.O.B:</td>
<td>Contact details</td>
</tr>
<tr>
<td>Address:</td>
<td>Date of referral:</td>
</tr>
<tr>
<td>Telephone number:</td>
<td>Expected date of discharge</td>
</tr>
</tbody>
</table>

Results of ECHOCARDIOGRAM

| Date | / | / |

Is HF the primary diagnosis? Yes/ No
Is aetiology known?
If HF is a secondary diagnosis, what is primary reason for admission?
Please comment …

Clinical Management Plan

Past medical history:

<table>
<thead>
<tr>
<th>MI / MD</th>
<th>AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Hypertension</td>
</tr>
<tr>
<td>CKD</td>
<td>Other … specify</td>
</tr>
</tbody>
</table>

HF Drug History

<table>
<thead>
<tr>
<th>ACE inhibitor</th>
<th>if not, any contraindications ?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blocker</td>
<td>if not, any contraindications ?</td>
</tr>
<tr>
<td>Diuretics</td>
<td>if not, any contraindications ?</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>if not, any contraindications ?</td>
</tr>
</tbody>
</table>

Urgent (see note regarding urgent referrals)

<table>
<thead>
<tr>
<th>Routine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitable for attendance at clinic (St Catherine’s at Birkenhead, Victoria Central at Wallasey or The Warrens Health Centre - Pensby)</td>
</tr>
<tr>
<td>Domiciliary visit required</td>
</tr>
<tr>
<td>Any History Violence, Abuse or Verbal /Physical Aggression to Health Care Staff</td>
</tr>
<tr>
<td>Is follow-up arranged with the referring team? Yes / No</td>
</tr>
</tbody>
</table>

Follow –up arrangements: