



Gateshead Network  
Commissioning Consortium



# The Management of Confirmed Left Ventricular Systolic Dysfunction (LVSD)

## VERSION CONTROL SHEET

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# **NHS SOUTH OF TYNE AND WEAR**

## **The Management of Confirmed Left Ventricular Systolic Dysfunction (LVSD)**

### **Introduction and aims of this guideline**

Heart failure is a clinical syndrome caused by a reduction in the heart's ability to pump blood around the body. The majority of the estimated 900,000 cases of heart failure in the UK are due to coronary heart disease (CHD), often with coexisting hypertension, diabetes and atrial fibrillation. It is most commonly caused by left ventricular dysfunction, but it can also result from several other diseases of the heart, such as abnormalities of the valves. In its advanced stages heart failure impairs the function of many other body systems, particularly the kidneys.

The incidence of heart failure is about one new case per 1000 population per year and is rising at about 10% per year. This increases with age and is over 10 cases per 1000 in people age 85 years and over.

Prognosis is poor with survival rates worse than those for breast or prostate cancer. Annual mortality for those with heart failure ranges from 10% to over 50% depending on severity. There are thought to be about 6,000 deaths a year due to heart failure due to coronary heart disease.

Heart failure imposes a considerable disease burden in both primary and secondary care, consuming substantial resources. Heart failure accounts for about 5% of all medical admissions to hospital and is associated with very high readmission rates – estimated to be as high as 50% over three months in severe cases.

The aim of the guideline is to support the management of heart failure patients primary care and to ensure consistency of care across NHS SoTW. The guidelines will be used to support the delivery of objectives set out in the NHS SoTW Local enhanced services for heart failure.

Implementation of the guideline will improve the overall management of heart failure patients and will result in the reduction of morbidity, mortality and hospital admissions for heart failure.

### **Development**

This guideline was developed by the heart failure sub-group of the NHS SoTW CVD strategy group.

The sub-group that developed this guideline were as follows:-

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The guidelines were distributed for wider comments to:-

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### **Audit**

An audit has been developed as part of the NHS SoTW Local Enhanced Service for heart failure which will be submitted to NHS SoTW annually by participating practices. This audit will demonstrate adherence to the guidelines.

## Equality and Diversity Statement

This (plan/service/policy) will aim to be accessible to everyone regardless of age, disability, gender, race, sexual orientation, religion/belief or any other factor that may result in unfair treatment or inequalities in health/employment.

**This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.**

**This guideline should be used in conjunction with the NICE guideline CG108: Chronic heart failure.**

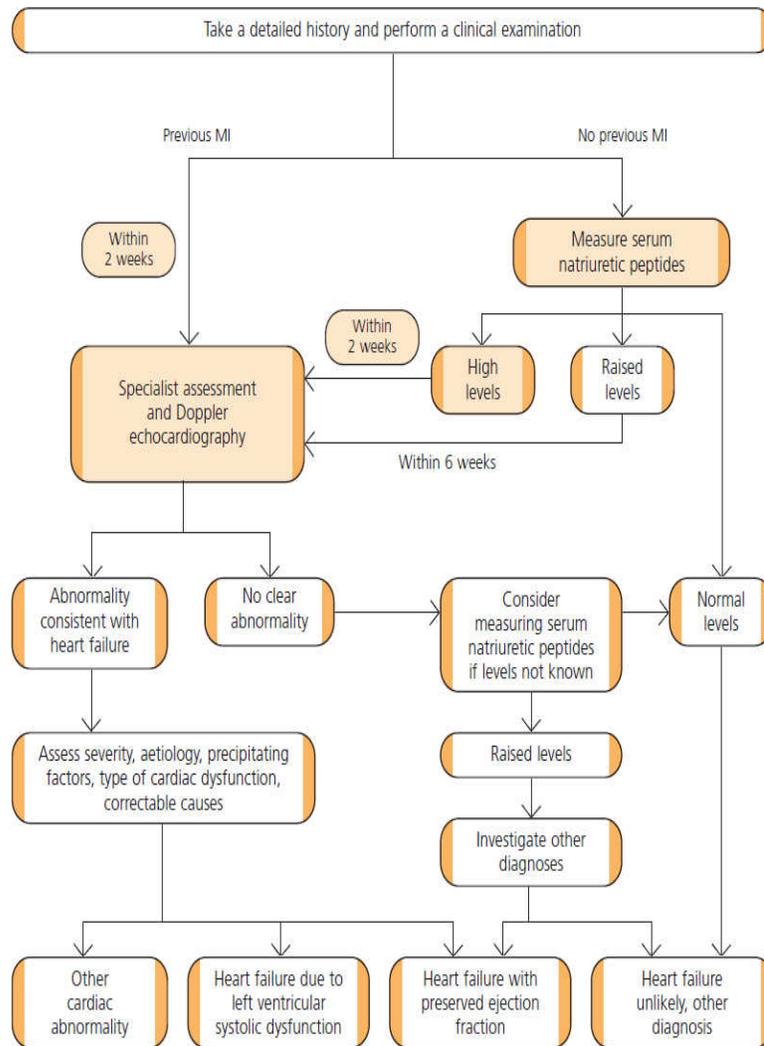
**Full details of contra-indications and cautions for individual drugs are available in the BNF or in the Summary of Product Characteristics (available in the Electronic Medicines Compendium)  
[www.emc.medicines.org.uk](http://www.emc.medicines.org.uk)**

## References

- NICE guideline CG108. Chronic heart failure. August 2010
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- Swedberg K, Komajda M, Bohm M, Borer JS, Ford I, Dubost-Brama A, Lerebours G, Tavazzi L. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. *Lancet* 2010;376:875–885.
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# Diagnosis of heart Failure

## Diagnosing heart failure



### Serum natriuretic peptides

- High levels – NTproBNP >2000 pg/ml (236 pmol/litre)
- Raised levels – NTproBNP 400–2000 pg/ml (47–236 pmol/litre)
- Normal levels – NTproBNP < 400 pg/ml (47 pmol/litre)

### Be aware that:

- very high levels of NTproBNP carry a poor prognosis.
- NTproBNP < 400 pg/ml (47 pmol/litre) in an untreated patient make heart failure unlikely.
- the level does not differentiate between heart failure due to left ventricular systolic dysfunction and heart failure with preserved ejection fraction.
- obesity or treatment with diuretics, ACE inhibitors, beta-blockers, angiotensin II receptor antagonists, and aldosterone antagonists can reduce levels
- high levels can have causes other than heart failure (left ventricular hypertrophy, ischaemia, tachycardia, right ventricular overload, hypoxaemia [including pulmonary embolism], GFR < 60 ml/minute, sepsis, COPD, diabetes, age > 70 and liver cirrhosis).

## Tests for evaluating possible aggravating factors and alternative diagnoses

- Perform an ECG.
- Consider chest X-ray
- Blood tests - (electrolytes, urea and creatinine, eGFR [estimated glomerular filtration rate], thyroid function tests, liver function tests, fasting lipids, fasting glucose, full blood count).
- Urinalysis
- Peak flow or spirometry.

## Symptoms of heart failure

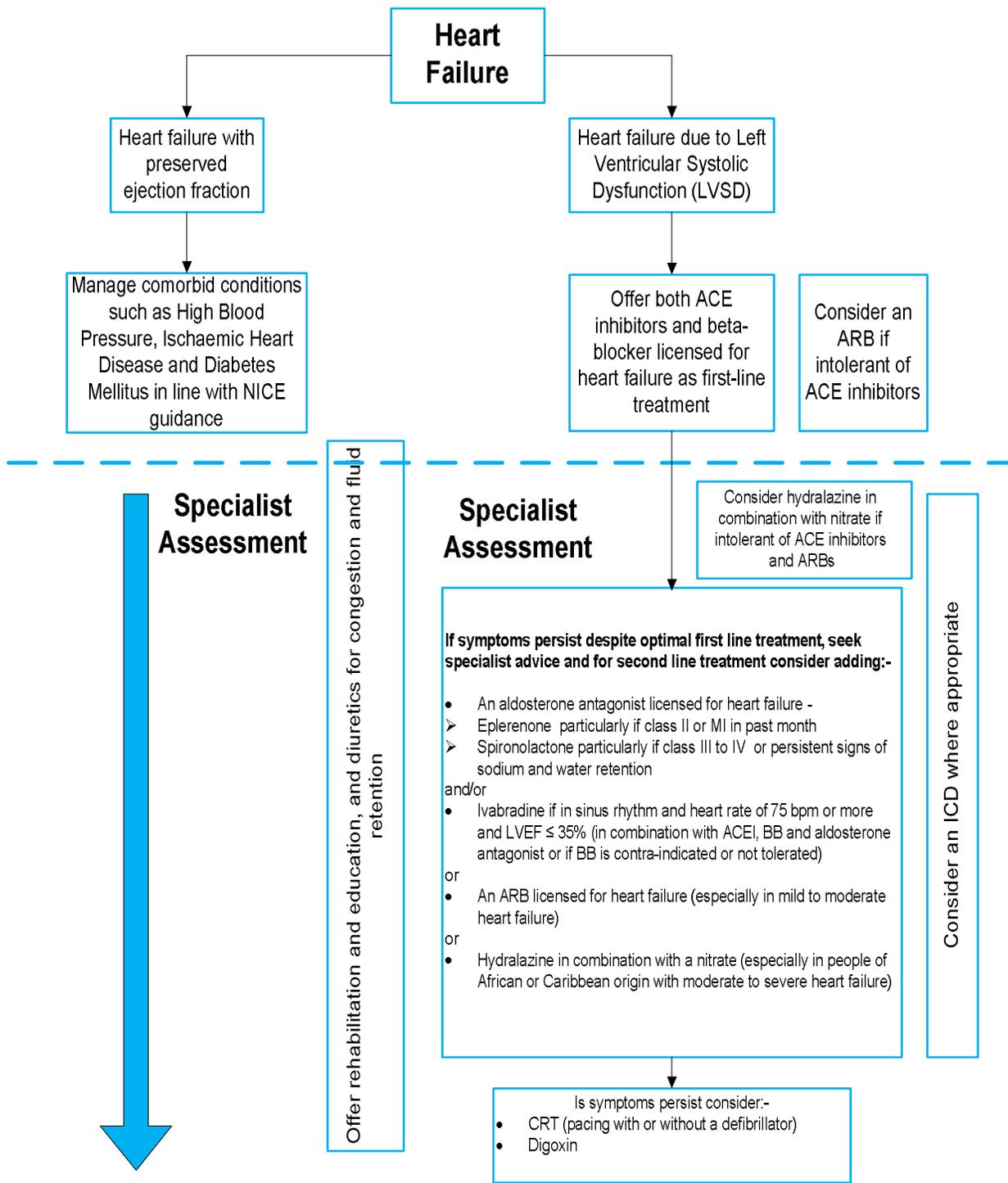
The simplest means of quantifying the severity of symptoms in heart failure is to use the New York Heart Association (NYHA) classification.

<b>Class I</b>	No limitations. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitations (asymptomatic left ventricular dysfunction).
<b>Class II</b>	Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary activity results in fatigue, palpitation, dyspnoea or angina pectoris (symptomatically ' <i>mild</i> ' heart failure).
<b>Class III</b>	Marked limitation of physical activity. Although patients are comfortable at rest, less than ordinary physical activity will lead to symptoms (symptomatically ' <i>moderate</i> ' heart failure).
<b>Class IV</b>	Inability to carry out any physical activity without discomfort. Symptoms of congestive cardiac failure are present even at rest. With any physical activity, increased discomfort is experienced (symptomatically ' <i>severe</i> ' heart failure).

It is important to remember that the commonly used abbreviation of the classification (*'mild'*, *'moderate'* and *'severe'*) refer to **symptoms** and not to **prognosis**

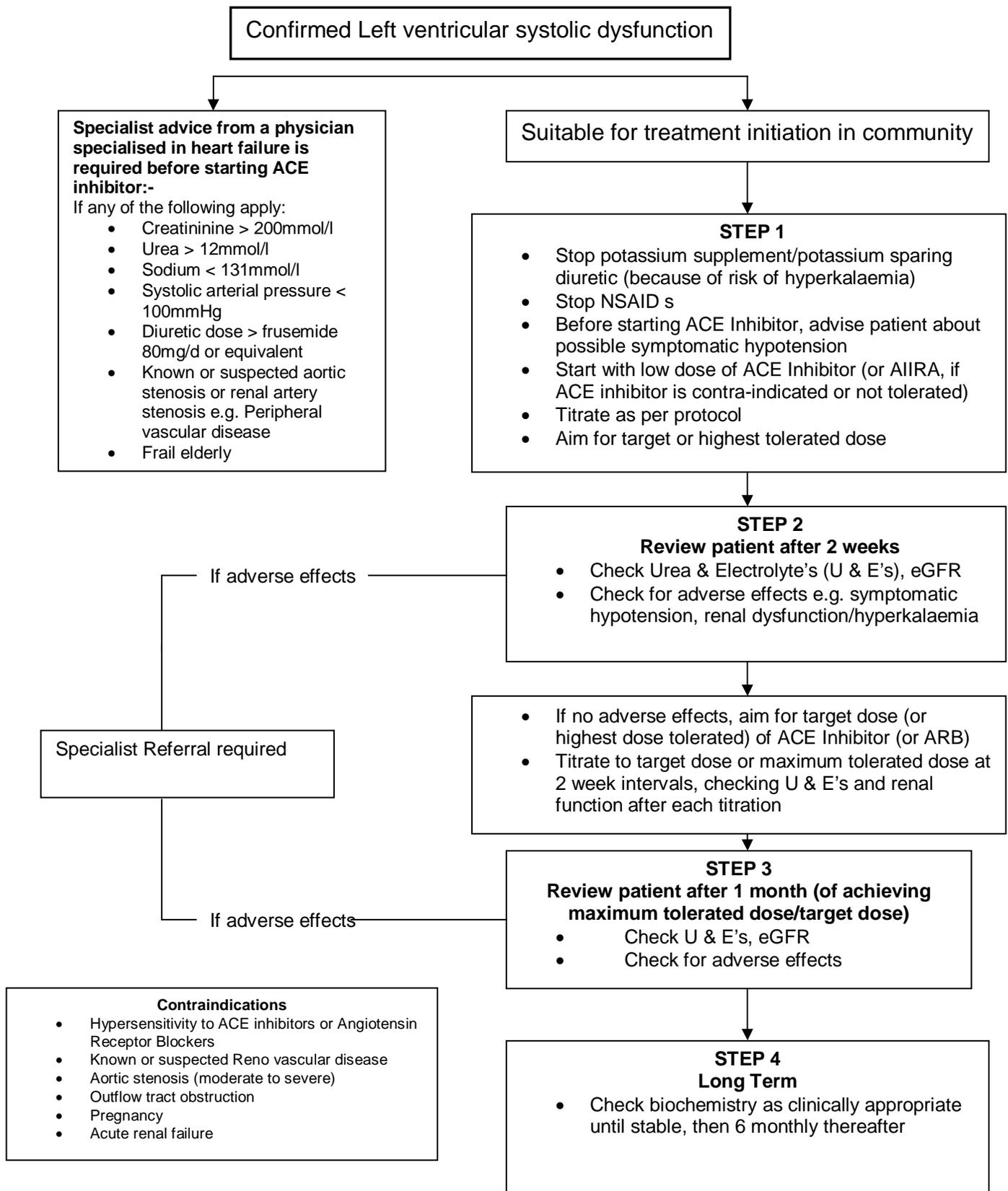
## Pharmacological treatment of symptomatic heart failure due to LVSD

Patients with symptomatic heart failure due to left ventricular systolic dysfunction should be treated with the following drugs (if tolerated and not contra-indicated) and in the sequence indicated.



## ACE Inhibitors/Angiotensin II Receptor Antagonists (AIIRA)

All patients with heart failure due to left ventricular systolic dysfunction should be considered for treatment with an ACE inhibitor. The ACE inhibitor should be started before beta-blockade is introduced but if the patient is already on a beta blocker, it is not necessary to discontinue before starting the ACE inhibitor.



## Problem solving – ACE Inhibitors (and AIIRA's)

Asymptomatic low blood pressure does not usually require any change in therapy.

### Symptomatic hypotension

- If dizziness, light-headedness and/or confusion and a low blood pressure consider discontinuing nitrates, calcium channel blockers and other vasodilators before stopping ACE inhibitor/AIIRA
- If no signs/symptoms of congestion consider reducing diuretic dose.

If these measures do not solve problem seek specialist advice.

### Cough

- Cough is common in patients with chronic heart failure, many of whom have smoking-related lung disease.
- Cough is also a symptom of pulmonary oedema which should be excluded when a new or worsening cough develops.

### Only relates to ACE inhibitors:

- ACE Inhibitor cough is characterised by a tickle starting in the back of the throat and is persistent and dry, it usually starts within 1-6 weeks (but in some patients can start months or up to a year) of starting the ACE inhibitor but rarely requires treatment discontinuation and often improves within 3-6 months of continued treatment.
- If the patient develops a troublesome dry cough which interferes with sleep and is likely to be caused by an ACE inhibitor, consider substituting an angiotensin-II receptor antagonist e.g. Candesartan for the ACE inhibitor.

### Worsening renal function

- ACEI/AIIRA therapy should not normally be started if the pre-treatment serum potassium concentration is significantly above the normal reference range (typically  $>5.0$  mmol/l).
- Stop ACEI/AIIRA therapy if the serum potassium concentration rises to above 6.0 mmol/l and other drugs known to promote hyperkalaemia have been discontinued.
- If creatinine is  $>200\mu\text{mol/l}$ , seek specialist advice before initiating ACEI/AIIRA therapy
- Following the introduction or dose increase of ACEI/AIIRA, do not modify the dose if either the GFR decrease from pre-treatment baseline is  $<25\%$  or the plasma creatinine increase from baseline is  $<30\%$ .
- If there is a fall in eGFR or rise in plasma creatinine after starting or increasing the dose of ACEI/AIIRA, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, the test should be repeated in a further 1–2 weeks. Do not modify the ACE/AIIRA dose if the change in eGFR  $<25\%$  or change in plasma creatinine is  $<30\%$
- If the eGFR change is  $\geq 25\%$  or change in plasma creatinine is  $\geq 30\%$ :-
  1. Stop NSAID, amiloride, triamterene, non-essential vasodilators (e.g. calcium channel blockers, nitrates) if prescribed and review U and E's one week
  2. If no improvement in eGFR or above not prescribed and no signs of fluid overload, reduce loop diuretic dose and review patient and U and E's in one week
  3. If no improvement in eGFR or patient not taking loop diuretics, or signs of fluid overload, reduce to lowest dose of ACE or ARB and review patient and U and E's in 2 weeks.
  4. If already on lowest dose ACE or ARB or no improvement in eGFR stop ACE or ARB and refer for specialist opinion if not already done so
- If creatinine is  $> 350\mu\text{mol/l}$ , the ACE inhibitor or ARB should be stopped and specialist advice sought.
- Blood electrolytes should be monitored closely until K<sup>+</sup> and Creatinine concentrations are stable.

### Note

**It is very rarely necessary to stop ACE inhibitor/AIIRA and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.**

## Angiotensin II Receptor Antagonists

Angiotensin II Receptor Antagonists can be considered as an alternative to ACE inhibitors in patients who are intolerant to or contra-indicated to an ACE inhibitor. ACE inhibitors and Angiotensin II Receptor Antagonists may occasionally be used together in the treatment of heart failure after optimisation of the ACE inhibitor and Beta Blocker, especially if the patient has mild to moderate heart failure (NYHA Class II – III). This combination would normally be initiated under specialist supervision.

<b>ACE inhibitor and Angiotensin II Receptor Antagonist titrations</b>		
<b>ACE Inhibitors</b>	<b>Titration</b>	<b>Target Dose</b>
<b>RAMIPRIL</b>	Initiation 1.25mgs od→ 2.5mgs bd→ 5mgs bd or 10mg od (Increase in two week increments)	5mgs BD or 10mg daily
<b>LISINOPRIL</b>	2.5mgs od→ 5mgs od→ 10mgs od→ 15mgs od → 20mgs od→ 30mgs od (Increase in two week increments)	20-30mgs daily
<b>ENALAPRIL</b>	2.5mgs od→ 5mgs od→ 10mgs od→ 5mgs od → 20mgs od (Increase in two week increments)	20mgs daily
<b>PERINDOPRIL</b>	Initiate at 2mgs od→ 4mgs od (In LVSD post MI up titrate to 8mgs daily) (Increase in two week increments)	4mgs daily

If truly intolerant to ACE Inhibitor (due to cough), consider Angiotensin II Receptor Antagonist.

New information from a meta-analysis shows the finding of a 1.2% increase in the absolute risk of new cancer diagnosis over an average of four years. It is therefore important to ensure patients are given an adequate trial of ACE Inhibitor.

<b>CANDESARTAN</b>	Initiate 4mgs od→ 8mgsod→ 16mgs od→ 32mgs od (Increase in two week increments)	32mgs daily
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## Beta Blockers

Switch stable patients who are currently taking for another co-morbidity to one which is licensed for heart failure during clinical review.

Beta Blockers are well tolerated in heart failure and should be considered for all patients with LVSD, including older patients, who do not have any contra indications

### Contra-indications

- True Bronchial Asthma
- Heart Block or heart rate < 55bpm
- Sick sinus syndrome
- Liver disease
- Hypersensitivity to beta blockers
- Metabolic acidosis
- Cardiogenic shock
- Prinzmetal angina
- Severe Peripheral arterial disease
- Pheochromocytoma

### Cautions (but beta blockers can still be initiated)

- Renal and hepatic impairment
- Diabetes
- Peripheral arterial disease
- Interstitial pulmonary disease
- COPD without reversibility
- Erectile Dysfunction
- Systolic BP < 90mmHg
- Heart rate < 60bpm
- Patients taking calcium channel blockers
- Pregnancy and lactation

### Pre-initiation checks

- Clinically stable
- ECG: heart rate >55/min
- Systolic BP >90mmHg
- No contra-indications

### Bisoprolol titration

- Starting dose 1.25mg once daily
- Target dose 10mg once daily
- Start at low dose and increase by increments of 1.25mg until 5mg, **at no less than 2 weekly intervals**
- When at 5mg, increase by 2.5mg increments at monthly intervals

### Carvedilol titration

- Starting dose 3.125mg twice daily
- Target dose 25-50mg twice daily\*
- Start at low dose and double dose **at no less than two weekly intervals**
- \*Carvedilol – maximum dose of 25mg twice daily is **severe** heart failure. In mild to moderate heart failure if weight is > 85kg – maximum dose of 50mg twice daily
- No monitoring required

### Other considerations

- **Verapamil/diltiazem (rate limiting calcium channel blockers) should be discontinued unless absolutely necessary. Diltiazem & verapamil are generally contraindicated in CHF. Verapamil should be avoided in combination with beta-blockers**
- Aim for target dose, failing that, the highest tolerated dose.
- Titration should be tailored to suit individual needs of patients. This may mean that titration schedules are slightly variable.
- Check U & E's 1-2 weeks after initiation and 1-2 weeks after final dose titration
- Nebivolol can be considered for patients over the age of 70 with mild to moderate heart failure who cannot tolerate Bisoprolol or Carvedilol
- Formularies may differ between the 3 PCTs, this must be taken into account when making drug choices

## Problem solving – Beta Blockers

### **Worsening Symptoms/Signs (Increasing dyspnoea, fatigue, peripheral oedema, weight gain)**

- If increasing congestion, increase diuretic dose for 3 days, if symptoms resolve revert to lower diuretic dose & continue with beta blocker.
- If symptoms persist consider reducing or stopping beta blocker dose temporarily.
- Wait 4 weeks before attempting to up-titrate or re-initiate beta blocker.

### **Excessive Bradycardia**

Heart rate < 55/min and:

- If symptomatic, consider stopping beta blocker
- If asymptomatic, revert to the lower beta blocker dose
- Consider stopping or reducing other rate controlling drugs (e.g. digoxin, amiodarone, diltiazem). Verapamil should be avoided in combination with beta blockers.
- Review within 1 week and seek specialist advice if bradycardia persists

Heart rate <45/min

- Stop beta blocker and obtain 12-lead ECG to exclude heart block

### **Symptomatic Hypotension (e.g. Dizziness, light-headedness, confusion)**

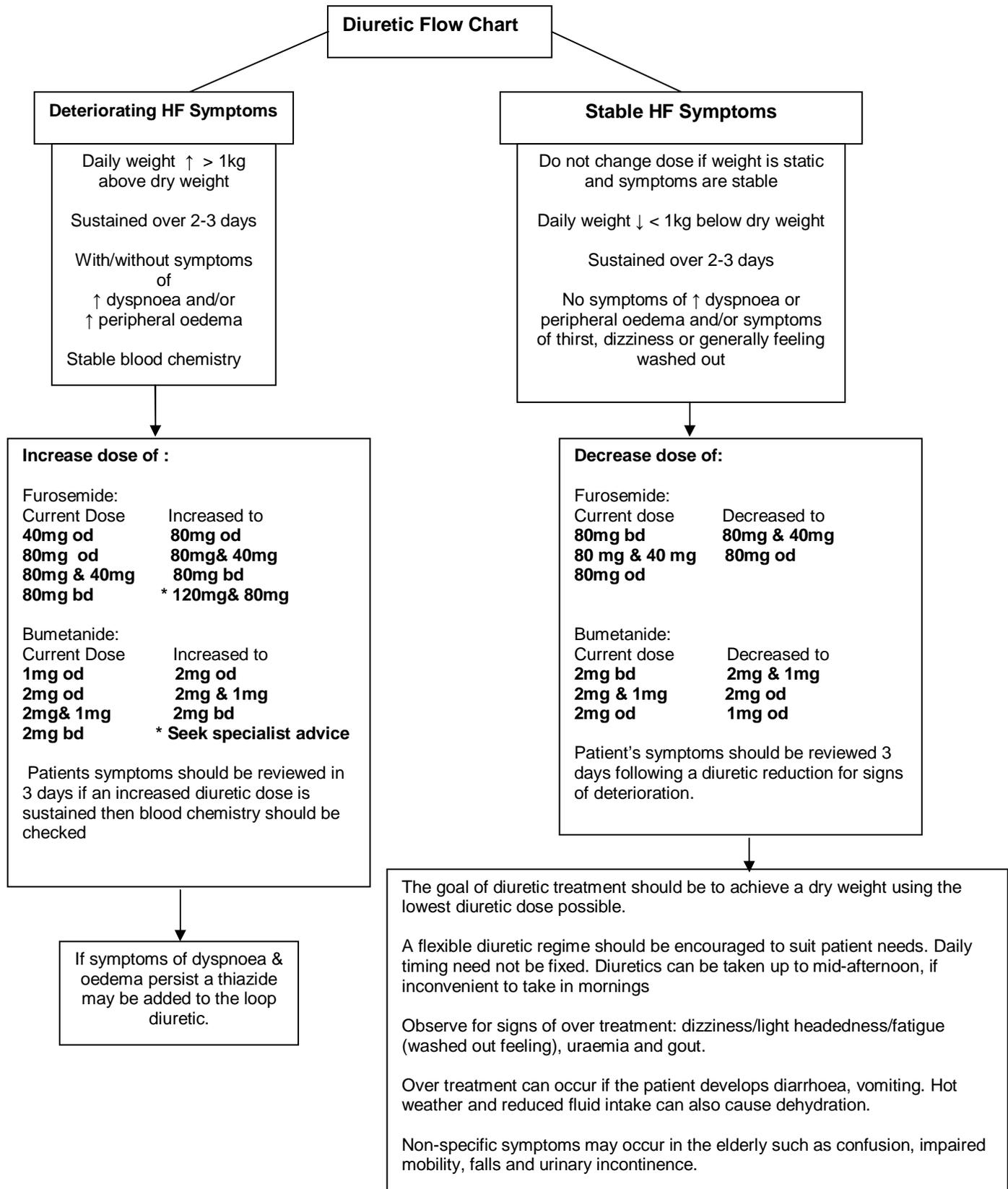
- If no signs/symptoms of congestion, consider reducing diuretic dose
- If symptoms persist, consider reducing or stopping other drugs which can lower blood pressure and have no value in heart failure.
- Consider temporarily reducing the ACE inhibitor dose
- If symptoms persist, consider reducing or stopping the beta blocker. Ideally, seek specialist advice before stopping beta blocker.
- Wait 4 weeks before attempting to up-titrate or re-initiate beta blocker.

### **Note**

**Beta Blockers should not be stopped suddenly unless absolutely necessary (Risk of a rebound increase in MI and arrhythmias).**

## Diuretics

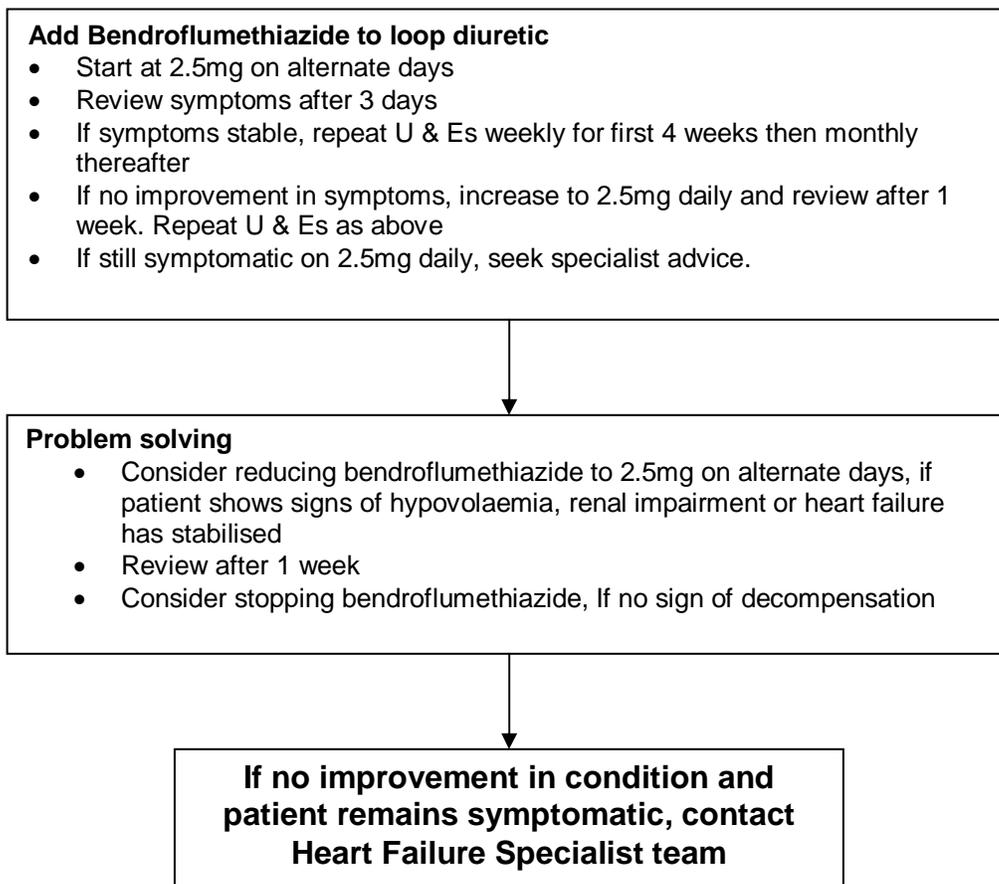
Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in patients with heart failure, and titrated (up and down) according to need following the initiation of subsequent heart failure therapies. Low to medium dose of loop diuretics should also be offered to patients with a preserved ejection fraction.



## Thiazide and thiazide-like diuretics

These diuretics may be used in combination with loop diuretics in patients with severe heart failure. Unlike loop diuretics, thiazide and thiazide-like diuretics are long acting and adjustment of the timing of dosing is not advantageous as for loop diuretics.

**Combinations of thiazide/thiazide-like diuretics and loop diuretics must be used with extreme caution and will usually be initiated by a member of the heart failure specialist team, it is advisable to seek advice from the team before considering commencing a thiazide.**



Please note: Metolazone is currently no longer available as a licensed product in the UK. Unlicensed imports of metolazone are available as a “special” but difficulties in obtaining supplies have been reported. This should be considered before prescribing <http://www.bsh.org.uk/latest-news/metolazone-withdrawal/>

## Aldosterone Antagonists (Spironolactone and Eplerenone)

### Spironolactone

Spironolactone is given to improve symptoms, prevent worsening of heart failure and to increase survival. Symptom improvement occurs within a few weeks to a few months of starting treatment. **Where an Aldosterone Antagonist is indicated in primary care, Spironolactone should be used first line.**

#### Assess suitability for treatment

- Consider if patient is still symptomatic despite optimal therapy with an ACE inhibitor and/or beta-blocker (unless contra-indicated or not tolerated), particularly if any of the following are present:-
  - NYHA III-IV
  - persistent signs of sodium & water retention
  - in patients with NYHA Class II heart failure and left ventricular systolic dysfunction (LVEF  $\leq$ 30%)
- Dose 12.5mg-25mg daily (50mg may be advised by a specialist if heart failure deteriorates and no problem with hyperkalaemia)
- Initiation should be facilitated by a heart failure specialist

#### Pre-initiation checks

- Potassium supplements & potassium sparing diuretics (e.g. Amiloride) should be discontinued 2 weeks prior to spironolactone being commenced and loop diuretics should be used as an alternative.
- Check blood chemistry before initiation
- If Serum Creatinine > 200micromol/l, Urea > 12mmol/l or Serum Potassium (K+) > 4.5mmol/l, seek specialist advice before initiation

#### Spironolactone initiation

- Start Spironolactone at 25mg on alternate days for 2 weeks then increase to 25mg once daily, if U & E's permit. (Target dose 25mg-50mg once daily)
- Check blood chemistry weekly following dose titration then at 4, 8 and 12 weeks ; 6, 9 and 12 months, then 6 monthly thereafter

#### Problem Solving

- Reduce dose to 25mg on alternate doses, if K+ rises to between 5.5 and 5.9 mmol/l or creatinine rises to 220 $\mu$ mol/l – monitor blood chemistry closely. If no improvement in U & E's after 2 weeks, consider stopping spironolactone after discussion with heart failure specialist
- Stop spironolactone and seek specialist advice, if K+ rises  $\geq$  6.0mmol/l or serum creatinine > 220 $\mu$ mol/l
- Stop spironolactone and seek specialist advise if patient develops diarrhoea, vomiting (or any other cause of sodium and water depletion) or gynaecomastia
- If patients experience significant gynaecomastia, **Eplerenone** at the same dose can be used as a replacement, clinical monitoring and treatment regimen remains the same

#### Cautions

- Elderly
- Hepatic impairment
- Renal impairment
- Acute porphyria

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#### Contra-indications

- Hyperkalaemia
- Hyponatraemia
- Addison's Disease
- Pregnancy and breast feeding

# Eplerenone

Consider starting Eplerenone:-

- if patient is still symptomatic despite optimal therapy with an ACE inhibitor and/or beta-blocker (unless contra-indicated or not tolerated) **and** has had an acute MI and clinical evidence of heart failure. Treatment should be initiated within 3-14 days of the MI.
- In patients with NYHA Class II heart failure, in addition to standard optimal therapy, to reduce the risk of cardiovascular mortality and morbidity in adult patients with NYHA class II (chronic) heart failure and left ventricular systolic dysfunction (LVEF  $\leq$ 30%)

Initiation should be facilitated by a heart failure specialist.

If patient has an acute MI and is taking spironolactone for a concomitant condition, they should continue with the spironolactone or switch to eplerenone.

## Initiation and Monitoring

- Potassium supplements & potassium sparing diuretics (e.g. Amiloride) should be discontinued
- For Post MI heart failure patients: Starting dose 25mg once daily 3-14 days after acute MI, then increase to 50mg once daily within 4 weeks, taking into account potassium levels
- For patients with NYHA class II heart failure: Starting dose 25mg once daily and titrate to a target dose of once daily preferably with 4 weeks, taking into account potassium levels
- Serum Potassium should be monitored before initiation eplerenone, at 1 week, 1 month, 3 month, 6 month, 9 month, 12 month after initiation, then 6 monthly thereafter. This is particularly important in the elderly, in patients with diabetes and in patients with renal impairment.
- Frequent and regular monitoring of serum potassium is recommended in patients with mild-moderate hepatic impairment.
- Patients with a serum potassium  $>5.0$ mmol/L should not be started on Eplerenone.

## Problem Solving

Dose adjustment may be required if the serum potassium level fluctuates. If serum potassium (mmol/l) is:-

- 5.0-5.4 – no dose adjustment is required
- 5.5-5.9 – decrease dose – 50mg daily to 25mg daily; 25mg daily to 25mg every other day; 25mg every other day to withhold
- $\geq 6.0$  - Withhold - Restart at 25mg every other day when potassium levels fall below 5.0mmol/L

## Drug Interactions

- Do not prescribe with strong CYP3A4 inducerse.g. (e.g. Itraconazole, Ketoconazole, titoonavir, nelfinavir, Clarithromycin, telithromycin and nefazadone)
- Lithium, cyclosporin and tacrolimus should be avoided during treatment with eplerenone.
- Care should be taken with the co-administration with potassium supplements, trimethoprim, ACE inhibitors or angiotension-II receptor antagonists as this may increase the risk of hyperkalaemia.
- Co-administration with alpha I blockers, tricyclic antidepressants, neuroleptics, amifostine or baclofen may increase the risk of postural hypotension.
- Care should be taken when prescribing with NSAIDs, as this may lead to acute renal failure especially in at-risk patients (elderly and/or dehydrated patients).
- Care should also be taken when co-administrating digoxin, warfarin, CYP3A4 inhibitors and CYP3A4 inducers.

## Contra-indications

- Severe hepatic insufficiency (Child-Pugh Class C)
- Hypersensitivity to eplerenone or the excipients
- Concomitant potassium sparing diuretics and potassium supplements
- Concomitant strong CYP3A4 inducers

## Cautions

- Patients at risk of developing hyperkalaemia
- Impaired renal function
- Impaired hepatic function
- Pregnant or lactating women

## Ivabradine

**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.**

### Assess suitability for treatment

Consider if NYHA class II to IV stable chronic heart failure with systolic dysfunction and:-

- who are in sinus rhythm with a heart rate of 75 beats per minute (bpm) or more and
- who are given ivabradine in combination with standard therapy including beta-blocker therapy, ACE inhibitors and aldosterone antagonists, or when beta-blocker therapy is contraindicated or not tolerated and
- with a left ventricular ejection fraction of 35% or less

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

### Initiation and Monitoring of Ivabradine

- Starting dose is 5 mg twice daily.

After two weeks of treatment:-

- If resting heart rate is persistently above 60 bpm, increase to 7.5 mg twice daily, or
- If resting heart rate is persistently below 50 bpm or if symptoms related to bradycardia (such as dizziness, fatigue or hypotension), decrease to 2.5 mg twice daily (one half 5 mg tablet twice daily)
- If heart rate is between 50 and 60 bpm, the dose of 5 mg twice daily should be maintained.

In patients aged 75 years or more, consider a lower starting dose of 2.5 mg twice daily (i.e. one half 5 mg tablet twice daily) before up-titration if necessary.

### Problem Solving

If during treatment, heart rate decreases persistently below 50 beats per minute (bpm) at rest or the patient experiences symptoms related to bradycardia,

- titrate dose downward to the next lower dose in patients receiving 7.5 mg twice daily or 5 mg twice daily.

If heart rate increases persistently above 60 beats per minute at rest:-

- titrate dose to the next upper dose in patients receiving 2.5 mg twice daily or 5 mg twice daily.

Treatment must be discontinued if heart rate remains below 50 bpm or symptoms of bradycardia persist

Ivabradine can cause visual disturbances, especially where sudden variations in light intensity may occur. Patient should be advised regarding driving, especially when driving at night and when operating machinery

### Drug Interactions

- Contra-indicated in combination with strong cytochrome P450 3A4 inhibitors such as azole antifungals (ketoconazole, itraconazole), macrolide antibiotics (clarithromycin, erythromycin, josamycin, telithromycin), HIV protease inhibitors (nelfinavir, ritonavir) and nefazodone
- Not recommended in combination with rate-limiting calcium channel blockers such as verapamil or diltiazem
- Grapefruit juice should be restricted when taking Ivabradine
- Precaution with use in moderate CYP3A4 inhibitors and CYP3A4 inducers (see spc for full details <http://www.medicines.org.uk/EMC/medicine/17188/SPC/Procoralan/#INDICATIONS>)

### Contra-indications

Hypersensitivity to Ivabradine  
resting heart rate below 60bpm prior to treatment  
cardiogenic shock; acute MI; unstable angina severe  
hypotension (< 90/50 mmHg)  
severe hepatic insufficiency  
sick sinus syndrome; sino-atrial block  
Unstable or acute heart failure  
pacemaker dependent (heart rate imposed exclusively by the pacemaker)  
AV-block of 3<sup>rd</sup> degree  
Pregnancy and lactation

### Cautions

- Creatinine clearance < 15ml/min
- Moderate hepatic impairment
- NYHA Class IV patients
- Mild to moderate hypotension
- Should not be initiated in patients with a pre-treatment resting heart rate < 60bpm

Not recommended in patient with:-

- AF and other cardiac arrhythmias (including QT prolongation)
- AV-block of 2nd degree

## Other Drugs

### Hydralazine/Nitrate combination

Consider in patients who remain symptomatic despite optimal therapy with an ACE inhibitor and a beta-blocker or are intolerant of ACE inhibitors/Angiotensin II Receptor Antagonist, particularly if the patient is of African or Caribbean origin. **Seek advice of a physician with specialist interest in heart failure.**

#### Dose

Hydralazine 37.5 – 75mg three times a day plus Isosorbide Dinitrate 20 - 40mg three times a day (or equivalent dose of isosorbide mononitrate)

#### Cautions

Severe renal failure (dose reduction may be required), severe hepatic impairment

#### Contra-indications

Systemic Lupus Erythematosus, symptomatic hypotension, cor pulmonale, pregnancy and breast-feeding

## Digoxin

Consider starting if, worsening or severe heart failure due to left ventricular systolic dysfunction despite first- and second-line treatment for heart failure

#### Dose

62.5 – 125mcg once daily

#### Monitoring

Routine monitoring of digoxin levels is not recommended.

A digoxin concentration measured within 8–12 hours of the last dose may be useful to confirm a clinical impression of toxicity or non-adherence. The serum digoxin concentration should be interpreted in the clinical context as toxicity may occur even when the concentration is within the 'therapeutic range'

Check plasma digoxin levels if:

- Digoxin toxicity is suspected (nausea & vomiting, headache, confusion, visual symptoms, arrhythmias)
- Patient is commenced on other drugs which are known to alter digoxin levels e.g. macrolide antibiotics, amiodarone, diltiazem, verapamil (see BNF for full list of interactions)
- Patient has poor or worsening renal function

Blood potassium concentrations should also be monitored regularly and hypokalaemia avoided (predisposes to digitalis toxicity)

#### Cautions

Sick sinus syndrome; thyroid disease; reduce dose in elderly and renal impairment; pregnancy; hypertrophic obstructive cardiomyopathy.

#### Contraindications

Complete heart block; 2<sup>nd</sup> degree AV block; supraventricular arrhythmias caused by Wolff-Parkinson-White syndrome, ventricular tachycardia or fibrillation, myocarditis and constrictive pericarditis

## **Non-surgical device treatment of heart failure with reduced ejection fraction (systolic heart failure)**

The following guidelines are simplified version of those in the European Society of Cardiology's guidelines on non-surgical device treatment. They are intended to highlight patients that should be referred to the HF team for further assessment.

### **Implantable cardioverter-defibrillator**

Approximately half of the deaths in patients with HF, especially in those with milder symptoms, occur suddenly and unexpectedly, and many, if not most, of these are related to ventricular arrhythmias (whereas others may be related to bradycardia and asystole). Prevention of sudden death is therefore an important goal in HF. While the key disease-modifying neurohumoral antagonists mentioned earlier reduce the risk of sudden death, they do not abort it. Specific antiarrhythmic drugs do not decrease this risk (and may even increase it). For this reason, ICDs have an important role to play in reducing the risk of death from ventricular arrhythmias.

Refer to Heart failure team for consideration for ICD in Primary Prevention if

- They are currently experiencing or have recently experienced symptomatic heart failure optimised on medical therapy
- They have a left ventricular ejection fraction of <35% despite optimal therapy
- They are expected to live at least 12 months
- LVSD due to all aetiologies will benefit

### **Cardiac resynchronization therapy**

Cardiac resynchronisation therapy can improve symptoms and outcomes in patients with symptomatic heart failure.

Cardiac resynchronisation therapy with a pacing device (CRT-P) is recommended as a treatment option for people with heart failure who fulfill all the following criteria:-

- They are currently experiencing or have recently experienced New York Heart Association (NYHA) class II-III symptoms
- They are expected to live at least 12 months
- They are in sinus rhythm or have an atrial arrhythmia:
  - **either** with a QRS duration of > 150 ms and RBBB
  - **or with a QRS duration of > 120 ms and LBBB**
- They have a left ventricular ejection fraction of 35% or less despite optimal therapy

### **ECG monitoring of patients with LVSD**

Patients with symptomatic LVSD should have an annual ECG to identify those who may benefit from assessment for ICD or CRT.

### **Drugs which can lead to deterioration of heart failure**

Patients with heart failure are usually elderly and may have co-morbid conditions which will lead to polypharmacy. A number of commonly used drugs may lead to a clinical deterioration of heart failure, in particular:-

- NSAIDs can lead to fluid retention and renal impairment
- 'Over the counter' analgesic drugs containing NSAIDs and aspirin
- St John's Wort, liquorice and some herbal and homeopathic remedies
- Most calcium channel antagonists (except amlodipine and felodipine which should be used only for angina or uncontrolled hypertension)
- Corticosteroids- by causing sodium and water retention
- Tricyclic antidepressant drugs- may depress cardiac function and have pro-arrhythmic effect
- Lithium, as levels can be affected by changes in diuretic doses. Lithium levels should be checked each time U & Es are done.
- Erythromycin and some antifungal agents- prolongation of QT interval; may precipitate ventricular arrhythmias.
- Pioglitazone and Rosiglitazone should not be used in patients with heart failure or a history of heart failure. The incidence of heart failure is increased when these drugs are combined with insulin.
- Doxazosin should be used with caution in heart failure as can lead to deterioration of symptoms.
- Ensure side effects/interactions of any new drugs are checked in BNF prior to commencement.

## **Non pharmacological management of heart failure**

### **Exercise**

It is important that patients are encouraged to be as active as possible. Many patients are reluctant to exercise due to breathlessness.

Basic exercise recommendations are:-

- Walking, cycling/static bike and gentle resistance exercise.
- Gentle resistance exercise at home using stairs, lifting weights (for example, tins of beans), and squats can be encouraged.
- Initially aim for slow gentle progression aiming to achieve initially 15minutes - once achieved a gradual increase to 30minutes x 5 weekly.
- Current Government guidelines advocate 30minutes x 5 weekly. (This can be achieved in 5/10/15/20minute blocks). Patients should be able to exercise but be able to hold a conversation through their exercise. All breathlessness should resolve on resting.

### **AVOID**

- Swimming, jogging, heavy lifting, and gymnasium work unless referred via Cardiac Rehabilitation Team.

### **Contra-Indications for Exercise**

- MI – previous 3/52
- Moderate/severe Aortic Stenosis
- Acute Infection
- Progressive worsening of exercise tolerance
- Worsening of symptoms
- NYHA IV
- Complex ventricular arrhythmia at rest or exercise induced
- Decrease in systolic blood pressure during exercise
- Resting Heart Rate  $\geq 100$ beats per minute

Heart Failure Rehabilitation Group is accessible via secondary care or the heart failure specialist nurses

### **Smoking**

Patients should be strongly advised not to smoke. Referral to stop smoking services should be considered

### **Alcohol**

- Patients with alcohol-related heart failure should abstain from drinking alcohol
- Alcohol consumption should be discussed with all heart failure patients and advice given with regard to limits depending on the clinical circumstances

### **Sexual activity**

Healthcare professionals should be prepared to broach sensitive issues with patients, such as sexual activity, as these are unlikely to be raised by the patient

**Vaccination**

All heart failure patients should be offered an annual influenza vaccination and vaccination against pneumococcal disease (frequency will depend on other co-morbid condition, refer to pneumococcal vaccination guidelines)

**Air travel**

Air travel will be possible for the majority of patients with heart failure depending on their clinical condition at the time of travel

**Driving regulations**

Heavy Goods Vehicle and Public Service Vehicle license: physicians should be up to date with the latest Driver and Vehicle Licensing Authority guidelines. Check the website for regular updates: [www.dft.gov.uk/dvla](http://www.dft.gov.uk/dvla)