Worcestershire NHS
Acute Hospitals NHS Trust

WORCESTERSHIRE COUNTY AREA PRESCRIBING COMMITTEE

GUIDELINES FOR TREATMENT OF CHRONIC HEART FAILURE CAUSED BY LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and/or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

These guidelines are designed to be used to guide in the management of patients with chronic heart failure in both primary and secondary care.

This guideline is for use by the following staff groups:

All staff responsible for the management of patients with heart failure

Lead Clinician(s)

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Dr D Abban	Consultant Cardiologist
Dr D Wilson	Consultant Cardiologist

Approved by Worcestershire Area Prescribing Committee :	April 2017
Review Date: This is the most current document and is to be used until a revised version is available	3rd August 2020

Key amendments to this guideline

Date	Amendment	By:
April 2009	Guideline approved by Worcestershire Area Prescribing Committee	
June 2011	Addition of BNP added to guideline	D Abban
June 2011	Amendment approved at Cardiology Meeting June 2011	D Abban
Feb 2013	Update, NICE guidance 2010/ESC guidelines 2012	K Smith/Dr Abban
06/05/2014	Telephone numbers on appendix 1 updated for south office	Jamie-Rae Tanner
06/08/2015	Document extended for 12 months as per TMC paper approved on 22nd July 2015	TMC
August 2016	Document extended for 12 months as per TMC paper approved on 22nd July 2016	TMC
August 2017	Further Extension as per TMC paper approved on 22nd July 2015	TMC
July 2016	Major re write/update and addition of ARNIs, Guidelines specified to relate only to patients with at least moderate LVSD	Dr Taylor/K Ridout
December 2017	Sentence added in at the request of the Coroner	

TABLE OF CONTENTS

Medical Therapy Guidelines to treat Chronic Heart Failure secondary to Left Ventricular Dysfunction for use in Primary Care

Introduction

These guidelines are primarily designed to be used as a protocol for the nurses in the heart failure service to use in the management of patients with chronic heart failure in primary care. However as they also represent best practice for the management of heart failure (and are in accordance with the latest NICE and ESC guidance) they will provide a useful guide to all individuals in primary and secondary care who are responsible for the care of an individual with heart failure.

Competencies Required

Experienced nurses working within the Heart Failure Service who have either undergone or are working towards specific training in the management of patients with chronic heart failure, with a recognized non-medical independent prescribing qualification.

Patients Covered

Patients with a confirmed diagnosis of heart failure due to left ventricular systolic dysfunction (LVSD) within Worcestershire. LVSD must be at least moderate to be the likely cause of their heart failure.

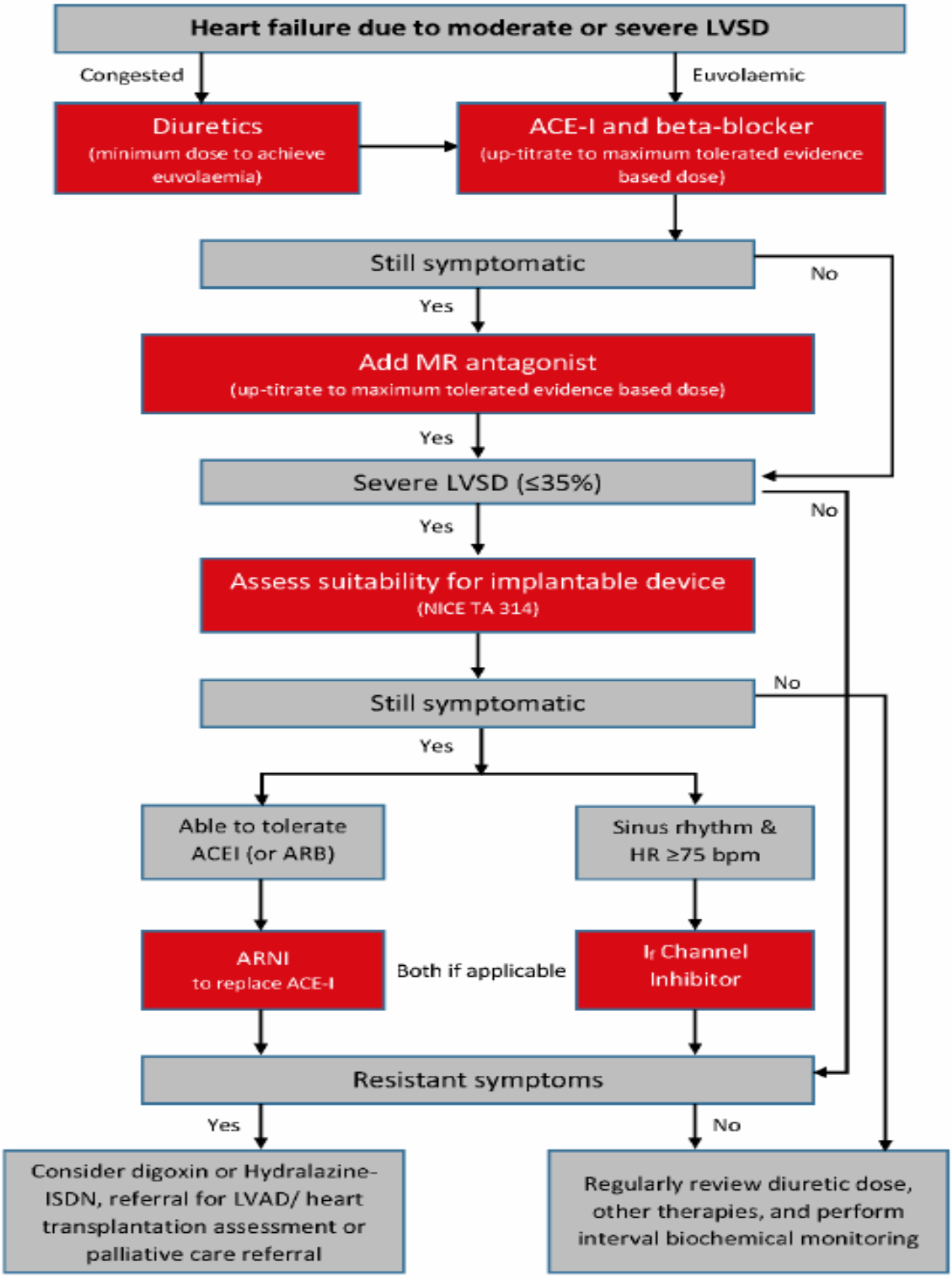
Left ventricular systolic function (as assessed by any imaging modality) is a continuum ranging from normal function to severe impairment. The majority of the proven benefit for the prognostic therapies in this guideline document are based on population with at least moderate left ventricular systolic function. Whilst there may be a role for some medical therapies to delay the onset of heart failure in patients with mild LVSD this is an area of medicine that requires further research. More importantly when the patients with mild LVSD are symptomatic, the mild LVSD is unlikely to be the cause of their symptoms, and when heart failure does exist it is often due to other factors such as impaired LV relaxation or arrhythmias. In many cases a patients symptoms are not due to heart failure but co-existing lung disease, anaemia, obesity, deconditioning or other causes.

Accordingly this document only covers patients with at least moderate LVSD.

However, patients with heart failure due to causes other than LVSD are prone to fluid overload and require diuretic therapy and the principles herein remain a useful guide for the management of diuretic therapy. Similarly, ACEi and beta blockers may have a role in preventing reverse remodelling post myocardial infarction and again the principles herein will be a useful practical guide.

List of Abbreviations

ACE-I	Angiotensin converting enzyme inhibitor
ARB	Angiotensin receptor blocker
ARNI	Angiotensin receptor-neprilysin inhibitor
If	Funny channel
LVSD	Left ventricular systolic dysfunction
MRA	Mineralocorticoid receptor antagonist
NYHA	New York Heart Association


Heart failure due to moderate or severe LVSD
Congested
Euvolaemic
Diuretics
(minimum dose to achieve euvolaemia)
ACE-I and beta-blocker
(up-titrate to maximum tolerated evidence based dose)
Still symptomatic
No
Yes
Add MR antagonist
(up-titrate to maximum tolerated evidence based dose)
Yes
Severe LVSD (≤35%)
No
Yes
Assess suitability for implantable device
(NICE TA 314)
Still symptomatic
No
Yes
Able to tolerate ACEI (or ARB)
Sinus rhythm & HR ≥75 bpm
ARNI
to replace ACE-I
Both if applicable
If Channel Inhibitor
Resistant symptoms
Yes
No
Consider digoxin or Hydralazine-ISDN, referral for LVAD/ heart transplantation assessment or palliative care referral
Regularly review diuretic dose, other therapies, and perform interval biochemical monitoring

The Use Of Loop Diuretic Therapy In Heart Failure

Introduction

Diuretics should be used routinely for the relief of 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.

(NICE Guidelines 2010)

Thiazide diuretics or Metolazone can be considered in addition to a loop when the clinical response to a loop in isolation is insufficient.

Contraindications

- Known allergic reaction (drug specific)

Cautions (seek specialist advice)

- K+ ≤3.5 mmol/L – may be made worse by diuretic.
- Significant renal dysfunction Cr ≥ 221 umol/L or eGFR <30. It is important to appreciate that a further deterioration in renal function is likely and patient will need close biochemical monitoring. Patient may not respond to usual doses of loop diuretic (and do not use thiazide diuretic).
- Symptomatic or severe asymptomatic hypotension (SBP <90 mmHg) – may be made worse by diuretic-induced hypovolaemia.
- Drug interactions to look out for:
  - NSAID – may attenuate effects of diuretic.
  - Combination with ACE inhibitors or ARB or renin inhibitors – risk of hypotension (usually not a problem).
  - Combination with other diuretics (e.g. loop plus thiazide) – risk of hypovolaemia, hypotension, hypokalaemia, and renal impairment.
- Diabetes: Loop diuretics may exacerbate diabetes (but hyperglycaemia less likely than with thiazides)
- Hepatic impairment - hypokalemia induced by loop diuretics can precipitate hepatic encephalopathy)

Common Side Effects (see current BNF for full list)

- Electrolyte imbalance
- Metabolic alkalosis
- Postural hypotension
- Pancreatitis
- Acute urinary retention
- Blood disorders (including bone-marrow depression, thrombocytopenia and leucopenia)
- Tinnitis and deafness (usually with high parenteral doses)
- Hyperuricaemia
- Worsening renal impairment, especially in the elderly
- Temporary increase in serum cholesterol and triglyceride levels

Section A - Patient Selection Criteria

- All patients with clinical evidence of congestion (irrespective of LVEF)
- Patient has none of the documented contraindications

Section B - Patient Advice

- □ Explain benefits of therapy. Treatment is given to relieve breathlessness and oedema
- Loop diuretics are usually best taken before breakfast and/or between 12:00 and 13:00 hrs on an empty stomach (to ensure a consistent and prompt effect).

- Timing of taking the loop diuretic is not fixed, however it is better to avoid taking after 6pm as this can lead to nocturia.
- Advise patients how to recognize overtreatment (dizziness and/or lightheadedness) or under treatment (increased breathlessness, frothy sputum, increasing peripheral oedema) and to report these promptly to specialist nurse or GP
- and advise them to report sudden sustained weight increase or decrease (more than 1kg over 3 days) to specialist nurse or GP
- Gout can occur
- Advise patient to self-weigh daily (after waking and voiding but before breakfast and dressing), educate patient to alter their own diuretic dose according to need and agree an action plan.
- Advise patient to avoid NSAIDS not prescribed by a physician, as these will counteract
- treatment and risk further deterioration in renal function.
- Ideally avoid soluble analgesia, antacids and any other medications with high sodium content

Section C – Initiation, Titration and Managing Adverse Effects During Titration

In the majority of cases Furosemide is the first line diuretic of choice

Name	**Initiation Dose**	**Usual maximum dose***	**Titrate up in steps of****
Loop diuretics			
Furosemide	40mg	120mg b.d.	40mg
Bumetanide	1mg	5mg o.d. (can be split)	1mg
Thiazides			
Bendroflumethiazide	2.5mg	10mg o.d.	2.5mg
Thiazide-like diuretics			
Metolazone	2.5mg	5mg b.d.	2.5mg

*When higher doses are considered this should be discussed with the patient's cardiologist.
**Larger titrations may be required if heart failure continues to worsen. The patient should be monitored closely and discussed with cardiologist.

- Check renal function and electrolytes before use
- Start with a low dose (see initiation dose above)
- Adjust dose according to symptoms and signs of congestion, blood pressure, and renal function..
- In congested patients aim an effective dose for a patient to achieving positive diuresis with a simultaneous reduction of body weight by 0.75-1.0 kg per day.
- Identify the patients ideal 'dry weight' (i.e. to keep the patient free of symptoms and signs off congestion – euvolaemia)
- For maintenance use minimum dose necessary to maintain the patient's 'dry weight'
- Dose may need to be increased or decreased according to the patient's volume status (Remember that excessive diuresis is more dangerous than oedema itself)
- Recheck blood chemistry 1-2 weeks after initiation and after any increase in dose (urea/BUN, creatinine, K+)

If insufficient response/diuretic resistance

- Check compliance and re-assess daily fluid intake
- Increase dose of diuretic

- Consider switching from furosemide to bumetanide or torasemide (these have greater bioavailability)
- Add a MRA/increase dose of MRA
- Add a thiazide or metolazone (these work synergistically)
  (NB only consider a thiazide if eGFR >30ML/min/1.73m2)
  Metolazone is no longer licensed for use in the UK, but is available as a 'special order' product from community pharmacies. Please be aware that it may take longer to source than previously)

  If still congested consider semi-elective admission for short term i.v diuretic administration.

- **PROBLEM SOLVING**

• Asymptomatic low blood pressure:
- dose may be reduced, but only if no symptoms or signs of congestion.
• Symptomatic hypotension (Causing dizziness/light headedness)
- reduce dose if no symptoms or signs of congestion.
- reconsider need for nitrates, CCBs and other vasodilators.
- if these measures do not solve problem, seek specialist advice.
• Hypokalaemia/hypomagnaesaemia:
- Increase ACE-I/ARB dose.
- add MRA, potassium supplements; magnesium supplements.
• Hyponatraemia
- Management depends on assessment of patients volume status.
- If Volume depleted:
- reduce dose/stop loop diuretics if possible.
- stop any thiazide diuretics
- If Volume overloaded:
- fluid restriction.
- increase dose of loop diuretic.
- discuss with cardiologist appropriateness /need for inpatient treatment, i.v. inotropic support, ultrafiltration..
• Hyperuricaemia/gout:
- consider allopurinol prophylaxis.
- for symptomatic gout use colchicine for pain relief.
- avoid NSAIDs.
• Hypovolaemia/dehydration:
- if volume status suggests hypovolaemia then reduce the diuretic dosage.
• Renal impairment (rising creatinine/urea):
- check for hypovolaemia/dehydration.
- exclude use of other nephrotoxic agents, e.g. NSAIDs, trimethoprim.
- withhold MRA.
- if using concomitant loop and thiazide diuretic stop thiazide diuretic.
- consider reducing/temporarily witholding ACE inhibitor/ARB.

The Use of Ace Inhibitors in Heart Failure

Introduction

Given in adequate doses, ACE inhibition significantly reduces mortality, hospital admissions for heart failure and risk of further acute myocardial infarction. All patients with heart failure due to LVSD should be considered for an ACE inhibitor as 1st line therapy (along with beta-blockers). Clinical judgement should be used to decide which to start first (NICE 2010).

Angiotensin II receptor antagonists should be used in treating heart failure only if the patient is intolerant of an ACE inhibitor due to persistent intolerable cough or angioedema. Angiotensin II antagonists may not be any safer than ACE Inhibitors in patients with renovascular disease (NICE 2010).

ACE inhibitor / ARB therapy should be initiated at the appropriate dose and titrated upwards at short intervals (no less than 2 weekly) until optimum tolerated dose or target dose is achieved.(ESC 2016)

Contraindications

Absolute contraindications include:

- Hypersensitivity to ACE inhibitors (including angioedema)
- Bilateral renal artery stenosis

(If patient has Angioedma with an ACE inhibitor it is reasonable to challenge with an ARB)

Cautions

- Patients with peripheral vascular disease or generalized atherosclerosis are more likely to have clinically silent renovascular disease (in patients with severe bilateral renal artery stenosis ACE inhibitors and ARBs reduce or abolish glomerular filtration, and are likely to cause severe and progressive failure)
- Use with care in patients with severe or symptomatic aortic stenosis and hypertrophic cardiomyopathy (risk of hypotension) – Do not use if critical aortic stenosis.
- Use cautiously if SBP <90mmHg. However low BP (particularly when asymptomatic) is **not** a contraindication to treatment
- Avoid Non-steroidal anti-inflammatory drugs, as these increase the risk of renal damage
- The concurrent use of potassium-sparing diuretics, potassium-containing salt substitutes and trimethoprim increases the risk of hyperkalemia

Side Effects

The most common side effects include: cough, hypotension, renal insufficiency, hyperkalaemia, angioedema, rash, gastro intestinal disturbance, taste disturbance, hypoglycemia, jaundice or marked elevations of hepatic enzyme (discontinue if jaundice or marked elevations of hepatic enzymes occur during treatment).

Section A - Patient Selection Criteria (Ace Inhibitors)

- All patients with a confirmed left ventricular systolic dysfunction (moderate or severe) on echocardiogram – there is also evidence of benefit in patients with asymptomatic LVSD.
- Creatinine <221 umol/l (in patients with worse baseline function, specialist advice should be sought before commencing)
- Patient has no contraindications to initiation of ACE inhibitor therapy (see contraindications)
- Do not start ACE Inhibitors in patients with possible haemodynamically significant valve disease until assessed by a specialist.

Note: ACE inhibitors should be considered in patients with a previous myocardial infarction even if they do not have the LV systolic dysfunction, in order to prevent or delay the onset of HF. However this is beyond the scope of this guidance document.

Section B – Patient Advice

- Explain benefits of therapyTreatment is given to
  - Improve symptoms
  - Prevent worsening of HF leading to hospital admission
  - Increase survival
- Symptomatic benefit (when seen) is within a few weeks to a few months after starting treatment.
- Advise patients to report principal adverse effects (i.e dizziness/symptomatic hypotension, cough)
- Warn patients that postural dizziness is common particularly early in therapy. Encourage patient not to discontinue medication without seeking medical advice.
- Explain the need for close blood test monitoring
- Advise patients to avoid purchased over the counter NSAIDS and salt substitutes high in K+

Section C - Managing Adverse Effects During Titration

Ramipril and Perindopril are currently the ACE Inhibitor of choice and Candesartan is the ARB of choice for the Area Prescribing Committee.

Name	**Initiation Dose**	**Target Dose**
ACE inhibitors		
Ramipril	2.5mg od	10mg od
Lisinopril*	2.5mg/5mg	35mg od
Perindopril Erbumine	2mg od	4mg od (may be on higher doses if also being used for hypertension or post MI)
ARBs		
Candesartan	4mg od	32mg od
Valsartan	40mg bd	160mg bd
Losartan	25mg od	150mg od

*Beware in patients with renal impairment as relies totally on glomerular filtration for excretion

- Check baseline renal function and electrolytes
- Start with suggested initiation dose (see below for exceptions)
- Double the dose at not less than 2-week intervals in the community (More rapid dose up-titration may be carried out in the hospital in-patient setting)
- Aim for target dose (see above) or, failing that, the highest tolerated dose
- Remember: some ACE inhibitor is better than no ACE inhibitor
- Re-check renal biochemistry 7-10 after initiation and 7-10 days after each dose titration.
- Once at tolerated maximum dose monitor blood chemistry 4 monthly thereafter
- See Problem Solving for when to stop up-titration, reduce dose or stop treatment
- In the following conditions a lower start dose, and slower up titrations may be warranted at the discretion of the prescribing clinician:
- Severe heart failure (NYHA class IV)
- Receiving high dose diuretic therapy (e.g. > 80mg furosemide daily or equivalent)

- Hypovolaemia.
- Hyponatraemia (<130mmol/l)
- Pre –existing symptomatic hypotension (<90mmHg)
- Unstable heart failure
- High-dose vasodilator therapy
- Valve disease as primary cause
- Unknown cause of heart failure

PROBLEM SOLVING

- Asymptomatic low blood pressure
- Does not usually require any change in therapy

- Symptomatic hypotension
- Dizziness/light headedness is common and often improves with time: offer reassurance
- Reconsider need for nitrates, calcium-channel blockers, other vasodilators and reduce dose/stop, if possible

- If no signs or symptoms of congestion, consider reducing diuretic dose
- If these measures do not solve problem then consider splitting dose or reducing dose.

- Cough
- Cough is common in patients with HF, many of whom have smoking-related lung disease
- Cough is also a symptom of pulmonary oedema, which should be excluded when a new worsening cough develops
- ACE inhibitor-induced cough does not always require treatment discontinuation
- When a troublesome cough does develop (e.g. one stopping the patient from sleeping) and can be proved to be due to ACE inhibition (i.e. recurs after ACE inhibitor withdrawal and re-challenge), substitution of an ARB is recommended

- Worsening renal function and hyperkalaemia
- Some rise in urea, creatinine, and potassium is to be expected after an ACE inhibitor; if an increase is small and asymptomatic, no action is necessary
- An increase in creatinine of up to: 50% above baseline, or 266 µmol/L / or eGFR <25 mL/min/1.73 m2 - whichever is the smaller, is acceptable
- An increase in potassium to ≤5.5 mmol/L is acceptable
- If creatinine, or potassium do rise above these levels, consider stopping concomitant nephrotoxic drugs (e.g. NSAIDs) and other potassium supplements or agents that cause hyperkalaemia and if no signs of congestion, reducing the dose of diuretic.If no other adjustments required, or these rises persist despite adjustment of concomitant medications, the dose of the ACE inhibitor (or ARB) should be halved and blood chemistry re-checked within 7-10 days; if there is still an unsatisfactory response, specialist advice should be sought.
- If potassium rises to >6.0 mmol/L or creatinine increases by >100% or to >310 µmol/L (3.5 mg/dL) or eGFR <20 mL/min/1.73 m2, the ACE inhibitor (or ARB) should be stopped and specialist advice sought.
- Blood chemistry should be monitored frequently and serially until potassium and creatinine have plateaued.

THE USE OF BETA BLOCKERS IN HEART FAILURE

INTRODUCTION

Beta blockers licensed for use in heart failure should be initiated in patients with heart failure due to left ventricular systolic dysfunction after diuretic and with ACE inhibitor therapy (regardless of whether or not symptoms persist).
Offer beta-blockers licensed for heart failure to all patients with heart failure due to left ventricular systolic dysfunction (regardless of whether or not symptoms persist), including patients who:

- Are older
- have peripheral vascular disease
- have erectile dysfunction
- have diabetes mellitus
- have interstitial pulmonary disease and
- have chronic obstructive pulmonary disease without reversibility

(NICE Guidelines 2010)
Switch stable patients who are already taking a beta-blocker for a comorbidity (for example, angina or hypertension), and who develop heart failure due to left ventricular systolic dysfunction, to a beta-blocker licensed for heart failure. (NICE 2010)

CONTRAINDICATIONS

- 2nd or 3rd degree AV block (in absence of a pacemaker)
- Critical limb ischaemia
- Known allergic reaction /adverse event (drug-specific)

Asthma is a relative contra-indication. A cardio-selective beta-blocker can be trialed under close medical supervision by a consultant (after consideration of the risks for and against their use). Clarify the accuracy of the diagnosis of asthma; COPD is not a contra-indication.
In the following situations appropriate specialist advice should be sought before commencing Beta blockade:

- NHYA Class IV Heart failure – Risk of decompensation
- History of Prinzmetal's angina / vasospastic angina.
- Myasthenia gravis
- Portal hypertension (risk of deterioration in liver function)
- History of hypersensitivity – may increase sensitivity to allergens and result in more serious hypersensitivity response also may reduce response to adrenaline

CAUTIONS

- Symptoms of hypoglycaemia and thyrotoxicosis may be masked
- History of chronic obstructive airways disease (introduce cautiously and monitor lung function)
- If persisting signs of congestion: raised jugular venous pressure, ascites, marked peripheral; try to relieve congestion and achieve 'euvolaemia' before starting a beta-blocker.
- Use cautiously if pre-existing first degree AV block/ sinus node disease or on other rate limiting medication such as Verapamil*, Diltiazem*, Digoxin, Amiodarone or Ivabradine.

**Non-dihydropyridine calcium channel blockers should be discontinued in heart failure caused by reduced ejection fraction due to their negative inotropic effects.*

SIDE-EFFECTS (see current BNF for full list)

Bradycardia, worsening heart failure, hypotension, conduction disorders, bronchospasm, peripheral vasoconstriction (including exacerbation of intermittent claudication and Raynaud's phenomenon), gastrointestinal disturbances, fatigue, sleep disturbances, headache, exacerbation of psoriasis, alopecia, dizziness

SECTION A - PATIENT SELECTION CRITERIA

- Confirmed left ventricular systolic dysfunction on echocardiogram (moderate or severe) regardless of aetiology.
- Patient has none of the above documented contraindications

Patients with severe (NYHA class IV) symptoms benefit from beta-blockers but treatment can precipitate a decompensation and should be initiated by a specialist with due consideration of need for inpatient initiation.
If Heart rate less than 60bpm prior to treatment then specialist should decide on appropriateness of beta-blockade.

SECTION B - PATIENT ADVICE

- Explain the known benefits of the therapy:
- Treatment is given to improve symptoms,
- To prevent worsening of HF leading to hospital admission
- To increase survival.
- Symptomatic improvement may develop slowly after starting treatment, sometimes taking 3–6 months or longer.
- Temporary symptomatic deterioration may occur during initiation or up-titration phase
- Advise patient to weigh themselves daily (after waking and voiding but before breakfast and dressing) and agree an action plan if they do have sudden weight gain
- Take with food (Carvedilol)
- Advise not to drive if they feel faint or dizzy
- Warn patients who wear contact lenses of possible dry eyes
- Encourage patient never to stop beta blockers before seeking advice from GP or Heart Failure Nurse
- Advise patients with COPD to report any increased wheeze.

SECTION C – INITIATION, TITRATION AND MANAGING ADVERSE EFFECTS DURING TITRATION

DO NOT START A BETA- BLOCKER WHILST THE PATIENT IS DECOMPENSATED. WAIT UNTIL THE PATIENT HAS BEEN ADEQATELY OFF-LOADED.
Bisoprolol is currently the beta-blocker of choice for the Area Prescribing Committee / County Cardiac Network.

- Start with the recommended initiation dose
- The higher initiation doses can be used in stable patients (Minimal symptoms, HR >60bpm, SBP >100mmHg, not congested) with none of the cautions above.
- Increase the dose at not less than 2-week intervals by the recommended incremental dose (slower up-titration may be needed in some patients when cautions apply).
- Aim for target dose, or failing that, the highest tolerated dose (remember: some beta-blocker is better than no beta-blocker).
- Monitor heart rate, blood pressure, and clinical status (symptoms, signs of congestion, body weight).
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING.

Name	**Initiation Dose**	**Increment dose**	**Target Dose**
Bisoprolol	1.25-2.5mg od	2.5mg	10mg od
Carvediolol	3.125 -6.25 mg bd	6.25mg	25mg bd*
Metoprolol**	12.5mg-25mg bd	25 mg	100mg bd
Nebivolol	1.25mg-2.5mg od	2.5mg	10mg od

*Target dose of Carvediolol is 50mg bd if body weight > 85kg
** This is an off-label use, but consistent with an evidenced based approach demonstrated to be clinically effective in MERIT-HF

PROBLEM SOLVING
Asymptomatic low blood pressure

- Does not usually require any change in therapy

Worsening symptoms: (increased dyspnoea, fatigue, oedema, weight gain).

- If worsening congestion increase dose of diuretic or halve dose of beta-blocker (if increasing diuretic dose does not work).
- If marked fatigue consider reducing beta-blocker (rarely necessary and if required usually only temporarily)
- Review patient in one week if no improvement discuss with GP/Cardiologist
- If serious deterioration in condition halve or stop dose and seek advice from appropriate physician

Bradycardia: (< 50 bpm)

- If bradycardic with worsening symptoms, halve dose or, if there is severe deterioration in symptoms stop beta blocker
- Review need /appropriateness of any other rate-limiting drugs.
- Consider checking digoxin level if appropriate
- If heart rate < 45 bpm record ECG to document rhythm (?AV block)
- A 12 lead ECG should be recorded in the event of **any** symptomatic bradycardia.
- Asymptomatic sinus bradycardia or 1st degree AV block does not require reduction or cessation of beta blockade

Symptomatic hypotension: (< 90 mmHg associated with dizziness, fainting, confusion)

- Check blood chemistry to exclude other causes for symptoms
- Consider stopping any vasodilatory drugs (e.g.nitrates, calcium channel blockers)
- Consider temporary reduction in ACE Inhibitor
- If no signs or symptoms of congestion, consider reducing diuretic dose
- If unresolved reduce dose or stop beta blocker after seeking advice

THE USE OF MINERALOCORTOCOID ANTAGONISTS (MRA) IN HEART FAILURE

INTRODUCTION

Patients with heart failure due to left ventricular systolic dysfunction, who remain symptomatic (NHYA Class II-IV) despite treatment with an ACE inhibitor (or ARB) and a beta blocker, should be prescribed a MRA.

The RALES mortality trial showed that low dose Spironolactone together with ACE inhibitor and diuretic therapy markedly and progressively improved survival of patients in advanced heart failure, irrespective of aetiology (RALES 1999). More recently, the EMPHASIS-HF and EPHESUS trials have confirmed this is the case with Eplerenone.

CONTRAINDICATIONS

- Known allergic reaction during previous exposure (drug specific)
- Addison's disease

CAUTIONS

- Hyperkalaemia and significant renal dysfunction are relative contraindications:
- Seek specialist advice if K+ > 5.0 mmol/L or Creatinine 221 umol/L or eGFR <30 mL/min/1.73m$_2$
- Avoid Non-steroidal anti-inflammatory drugs, as these increase the risk of renal damage
- The concurrent use of potassium-sparing diuretics, potassium-containing salt substitutes, renin inhibitors and trimethoprim increases the risk of hyperkalemia
- Significant acute porphyria
- Strong Cytochrome P450 3A4 inhibitors (e.g. ketoconazole, clarithromycin, ritonavir, nelfinavir will increase the risk of hyperkalaemia / renal dysfunction (Eplenerone only)

SIDE EFFECTS (see current BNF for full list)

Side effects include: Gastro-intestinal disturbances, gynaecomastia (less common with eplerenone), lethargy, headache, confusion, rashes, hyperkalaemia (discontinue), hyponatraemia (especially when used with a loop diuretic), atrial fibrillation (eplerenone), arterial thrombosis (eplerenone) hepato-toxicity, blood disorders.

SECTION A - PATIENT SELECTION CRITERIA

- Patients with heart failure due to left ventricular systolic dysfunction (any aetiology), who remain symptomatic (NHYA Class II-IV) despite treatment with an ACE inhibitor (or ARB) and a beta blocker
- Patient has none of the above contraindications

SECTION B - PATIENT ADVICE

- Explain the known benefits: to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival.
- Symptomatic improvement occurs within a few weeks to a few months of starting treatment.
- Avoid NSAIDs not prescribed by a physician (i.e. purchased over-the-counter) and salt substitutes high in K+.

• Warn of the possible side effects – particularly gynaecomastia (with Spironolactone) and signs of sodium and water depletion

- If diarrhoea/vomiting occurs or there is infection with fever leading to intense sweating patients should be aware the risk of dehydration and electrolyte imbalance and contact their nurse / physician.

SECTION C - INITIATION, TITRATION AND MANAGING ADVERSE EFFECTS DURING TITRATION

Spironolactone is currently the MRA of choice for the Area Prescribing Committee / County Cardiac Network

Eplerenone should be used in patients with previous intolerance of Spironolactone because of gynaecomastia, and continued in patients already taking it

Name	**Initiation Dose**	**Target Dose**
Spironolactone	25mg od	25-50mg
Eplerenone	25mg od	50mg od

- Check renal function and electrolytes
- Start with initiation dose.
- Consider dose up-titration after 4–8 weeks.
- If asymptomatic after starting Spironolactone 25mg then further increments not required.
- Check blood chemistry at 7-10 days after starting/increasing dose and at 1,2,3, 6, 9, and 12 months; 4-monthly thereafter.

PROBLEM SOLVING

Renal Dysfunction:

- If K+ rises above 5.5 mmol/L or creatinine rises by, >50% from baseline, above 221 µmol/L or eGFR <30 mL/min/1.73 m2, halve dose (12.5 mg OD or 25mg alternate days are reasonable options) and monitor blood chemistry closely.

- If K+ rises to >6.0 mmol/L or creatinine to >310 µmol (3.5 mg/dL) eGFR <20 mL/min/1.73 m2, stop MRA immediately and seek specialist advice.

Gynaecomastia (10% in the RALES study)

Male patients may need to be discontinue Spironolactone if they experience breast discomfort or significant breast tissue increase.

These patients should be switched to Eplerenone.

THE USE OF IVABRADINE IN STABLE HEART FAILURE DUE TO LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

Ivabradine is now indicated in stable Chronic Heart Failure NYHA II-IV class with systolic dysfunction, in patients in sinus rhythm and whose heart rate is **≥75bpm**, in combination with standard therapy including beta- blockers, or when beta- blocker therapy is contraindicated or not tolerated, and who have an ejection fraction of 35% or less. (Based on results of the SHIFT study).

➢ **Ivabradine should be initiated only by a heart failure specialist after 4 weeks of stable optimal standard therapy; (NICE TA267).**

CONTRAINDICATIONS

- Severe bradycardia
- Cardiogenic shock
- Acute myocardial infarction
- Immediately after cerebrovascular accident
- Sick-sinus syndrome, sino-atrial block, 2nd and 3rd degree heart block
- Patients with pace-maker
- Congenital QT syndrome

CAUTIONS

- Monitor for atrial fibrillation or other arrhythmias
- Hypotension (avoid if severe)
- Retinitis pigmentosa
- No safety data available for the drug's use if eGFR <15

SIDE-EFFECTS (see current BNF for full list)

Main side-effects include: bradycardia, first-degree heart block, ventricular extrasystoles; headache, dizziness; visual disturbances including phosphenes and blurred vision; *less commonly* nausea, constipation, diarrhoea, palpitations, supraventricular extrasystoles, dyspnoea, vertigo, muscle cramps, eosinophilia, hyperuricaemia, and raised plasma-creatinine concentration.

SECTION A - PATIENT SELECTION CRITERIA

- Patients with heart failure due to left ventricular systolic dysfunction (any aetiology), who remain symptomatic (NHYA Class II-IV) despite 4 weeks of stable optimum tolerated treatment with an ACE inhibitor (or ARB), a beta blocker and an MRA.
- LVEF ≤35%,
- Patients must be in sinus rhythm with a heart rate of ≥75bpm
- Patient has none of the above contraindications

SECTION B - PATIENT ADVICE

Explain the known benefits: to prevent worsening of heart failure, reduce hospital admissions and improve survival.

Warn of possible side effects – especially bradycardia and advise to report any symptoms of bradycardia (syncope, dizziness, fatigue etc).

SECTION C - INITIATION, TITRATION AND MANAGING ADVERSE EFFECTS DURING TITRATION

The usual recommended starting dose of ivabradine is 5 mg twice daily (2.5mg bd in those over 75 years old). After two weeks of treatment, the dose can be increased to 7.5 mg twice daily if resting heart rate is persistently above 60 bpm (beats per minute) or decreased to 2.5 mg twice

daily if resting heart rate is persistently below 50 bpm, or in case of symptoms related to bradycardia such as dizziness, fatigue or hypotension. If heart rate is between 50 and 60 bpm, the dose of 5 mg twice daily should be maintained.

PROBLEM SOLVING

Bradycardia:

- Review other medications that may be causing bradycardia
- Check ECG to exclude arrhythmia

Treatment must be discontinued if heart rate remains below 50 bpm or symptoms of bradycardia persist. (Procoralan SPC, Servier).

AF or any other arrhythmia:

- Treatment with ivabradine must be discontinued if persistent AF or any other arrhythmia develops during treatment

Visual changes:

- Usually transient, and gradually disappear after a few months of treatment
- If persistent or causing discomfort consider discontinuation

THE USE OF ANGIOTENSIN RECEPTOR NEPRILYSIN INHIBITORS (ARNI) IN HEART FAILURE

INTRODUCTION

Sacubitril/Valsartan is the first in class for this agent and consists of an angiotensin receptor blocker (ARB) combined with a neprilysin inhibitor as a single molecule.

These drugs MUST NOT be co-prescribed with an ACE inhibitor or another ARB. Sacubitril Valsartan should always be prescribed using the generic name to avoid concomitant prescribing of ACE-I or additional ARB therapy.

When compared to an ACE inhibitor, this combination drug was shown to reduce the risk of CV death or first hospitalisation for heart failure (ARR 4.7%) and reduce the risk of all-cause mortality (ARR 2.8%) in selected populations.

CONTRAINDICATIONS

- Systolic Blood pressure < 100mmHg
- Hypersensitivity to the active substances or to any of the excipients listed.
- Concomitant use with ACE inhibitors.

- Sacubitril valsartan must not be administered until 36 hours after discontinuing ACEi therapy.
- Known history of angioedema related to previous ACE inhibitor or ARB therapy.
- Hereditary or idiopathic angioedema.
- Concomitant use with aliskiren (a direct renin inhibitor) in patients with either diabetes mellitus or renal impairment (eGFR <60 ml/min/1.73 m2).
- Severe hepatic impairment, biliary cirrhosis and cholestasis.
- Second and third trimester of pregnancy.
- Treatment should not be initiated if the serum potassium level is >5.4 mmol/l.

CAUTIONS

- Avoid abrupt withdrawal (especially if concurrent ischaemic heart disease)
- Hypotension (symptomatic hypotension more likely if age >65yrs, renal disease, SBP<112)
- This drug can cause deteriorating renal function. Down-titration should be considered in patients who develop a clinically significant decrease in renal function.
- Use may be associated with an increased risk of hyperkalaemia. Monitoring of serum potassium is recommended and if clinically significant hyperkalaemia adjustment of concomitant medicinal products, or temporary down–titration or discontinuation is recommended. If serum potassium level is >5.4 mmol/l discontinuation should be considered.
- Angioedema: 0.4% risk but likely higher in black patients. If angioedema occurs discontinue drug and do not re-administer.
- Renal artery stenosis: close monitoring of renal function recommended
- BNP is not a suitable biomarker of heart failure in patients treated with this drug as its breakdown is reduced.
- Patients with moderate hepatic impairment (Child Hugh B or ALT/AST >2x ULN) are likely to have greater exposure and safety is not established.

SIDE EFFECTS

The most clinically significant side effects are symptomatic hypotension, deteriorating renal function, cough, angioedema. See the BNF for a full list of possible adverse effects.

SECTION A - PATIENT SELECTION CRITERIA

In accordance with NICE TA388 and the local APC patients must meet all of the following criteria for licensed use of sacubitril valsartan:

- New York Heart Association (NYHA) class II to IV symptoms
- Left ventricular ejection fraction ≤ 35%
- Taking a stable dose of an ACE inhibitor or an ARB, **which has been stopped**
- Systolic blood pressure >100mmHg
- No contra-indications to treatment

SECTION B – PATIENT ADVICE

- Explain benefits of therapy, and drugs place in treating patients with heart failure.
- Warn of possible side effects, particularly – hypotension, dizziness, cough.
- Advise of the risk and warning symptoms of angioedema - swelling of your face, lips, tongue, and throat, and inform patient to get emergency medical help if they have these symptoms or trouble breathing.
- Explain the need for close blood test monitoring.
- Encourage patient not to discontinue medication without seeking medical advice.
- Warn patients of the danger of taking concomitantly with an ACEi or ARB and encourage patient to carry alert card

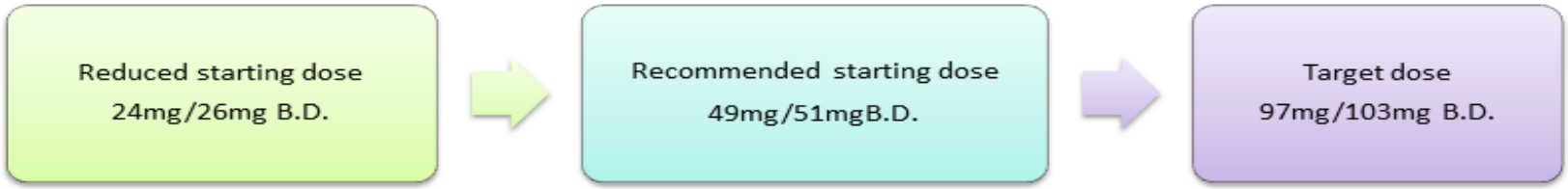
SECTION C – INITIATION AND TITRATION

Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team. In Worcestershire county the drug needs to be initiated under the guidance of a consultant cardiologist with monitoring by the heart failure team. Once the patient has been stable on the maximum tolerated dose for 1 month on-going prescription and monitoring can continue in primary care.
The flowchart overleaf guides dose initiation and up-titration.

Practical Guide to Sacubitril / Valsartan initiation and dose titration

Sacubitril valsartan should always be prescribed using the generic name to avoid concomitant prescribing of ACE-I or additional ARB therapy

The first dose of Sacubitril Valsartan must not be used until at least 36hours post the final dose of ACEi therapy



Start at the **reduced starting dose** if:
- Previously only on a low dose of an ACEi / ARB
- Baseline SBP 100-110mmHg
- Moderate renal impairment (eGFR 30-60)
- Moderate liver impairment (AST/ALT >2x ULN)

These patients should move to the next steps at 3-4 week intervals (if clinically tolerated).

Start at the **recommended starting dose**
If previously stable on at least:

Lisinopril	10mg	Candesartan	16mg
Perindopril	4mg	Irbesartan	150mg
Ramipril	5mg	Losartan	50mg
		Valsartan	160mg

These patients should move to the next step at 2-4 week intervals (if clinically tolerated).

Patients should move to the next stepped dose up (at the appropriate time point) providing they do not experience:
- hyperkalaemia (K+>5.4 mmol/L)
- significant deterioration in renal function
- symptomatic hypotension

THE USE OF DIGOXIN IN HEART FAILURE

INTRODUCTION

Cardiac glycosides are indicated in atrial fibrillation in order to control ventricular rate and thereby improve ventricular rate, function and any degree of symptomatic heart failure.
In sinus rhythm, digoxin is recommended to improve the clinical status of patients with persisting heart failure symptoms due to left ventricular systolic dysfunction despite first and second line treatment. The starting dose for patients in heart failure (in sinus rhythm) is 62.5micrograms to 125micrograms once daily.
The primary benefit and indication for digoxin in heart failure is to reduce symptoms.
(DIG trial/Nice 2010, ESC 2016)

CONTRAINDICATIONS

- Intermittent complete heart block and second degree AV block
- Myocarditis, constrictive pericarditis
- Supraventricular arrhythmias associated with accessory conducting pathways e.g. Wolff-Parkinson White syndrome
- Ventricular tachycardia or fibrillation
- Hypertrophic obstructive cardiomyopathy (unless concomitant atrial fibrillation and heart failure (but use with caution)

CAUTIONS

- Sick sinus syndrome
- Recent myocardial infarction
- Thyroid disease
- Reduce dose in the elderly and in renal impairment
- Avoid hypokalaemia, hypomagnesaemia, hypercalcaemia
- Pregnancy
- Amiodarone, erythromycin, verapamil and poor renal function commonly increase plasma digoxin levels and the maintenance dose of digoxin should be reduced.

SIDE EFFECTS (see current BNF for complete list)

Main side effects (most are associated with excessive dosage): anorexia, nausea, vomiting, diarrhoea, abdominal pain, visual disturbances, headache, fatigue, drowsiness, confusion, delirium, hallucinations, depression, arrhythmias, AV block, rash, intestinal ischaemia, gynaecomastia, thrombocytopenia.

(BNF Sep 2012)

SECTION A - PATIENT SELECTION CRITERIA

- Worsening or severe (symptomatic) heart failure (NYHA class III –IV) due to left ventricular systolic dysfunction despite all other appropriate first and second line therapies and device therapy (when appropriate).
- Patients with atrial fibrillation requiring rate control.
- Patient has none of the documented contraindications.

If the patient does not fit into the above criteria, consider discussion with appropriate physician.

SECTION B - PATIENT ADVICE

- Explain the known benefits of digoxin therapy.
- Warn of possible side effects.
- Encourage the patient not to discontinue medication without seeking medical advice.

SECTION C - MANAGING ADVERSE EVENTS DURING TITRATION

Digoxin toxicity – Can arise with any dose of digoxin but is more common when the 'therapeutic' concentration is exceeded. However measurement of digoxin concentration is not a reliable guide therefore routine serum levels are not required. Watch for the following symptoms and STOP the drug, at least temporarily if any of these occur. An urgent serum digoxin concentration should be measured and advice from appropriate physician sought.

- Anorexia
- Nausea and vomiting
- Xanthopsia (yellow tint to vision)
- Symptomatic bradycardia
- Ventricular arrhythmias

In elderly patients the symptoms and signs may be less specific but may include:

- Confusion (new onset or increasing)
- Deteriorating mobility and falls

Raised Plasma digoxin levels – Commonly increase because of deteriorating renal function and drug interactions (see BNF for full list of interactions).

- **Amiodarone** – will cause a gradual increase in digoxin levels. Halve digoxin dose when starting amiodarone
- **Erythromycin** – will cause a rapid increase in digoxin levels and an alternative should be used whenever possible.
- **Poor renal function** (including diarrhoea/vomiting and any other cause) - Monitor renal function closely. Omit or reduce digoxin doses until clinically stable again.
- **Digoxin induced arrhythmias** – common in hypokalaemic patients.
- **Changes to drug therapy** – particularly important when changes to diuretic and ACE therapy are made.

Blood sample for digoxin levels should be taken at least 8 hours after the last dose
(Based on Glasgow/Gloucester Guidelines

Palliative Care Treatment for Heart Failure

Palliative Care is extremely important in failure. It is most applicable for those patients with NYHA class 3 and 4 Heart Failure. Heart failure management can be considered in three stages:

Stage 1. Chronic disease management (NHYA I-III)
The therapies discussed so far in this document represent those required in this phase. The goals of care include active monitoring, effective therapy to prolong survival, symptom control, patient and carer education and supported self-management.

Stage 2. Supportive and palliative care (NHYA III-IV)
Patients entering this stage of their disease should be considered for advanced heart failure therapies such as transplant / LVAD if appropriate*
After this relatively stable primary phase needing routine chronic disease management; patients enter a secondary phase of decline requiring increased utilization of medical and hospital care. At this point the goals of care should shift to maintaining optimal symptom control and quality of life. Prognostic therapies are no longer as important.
Identification of when to concentrate on palliative treatment is difficult. Prognostic scores which may help to identify those with reduced survival include:
HF Survival Score: http://www.heartfailurerisk.org/
Seattle HF Score: https://depts.washington.edu/shfm/
However these only consider some parameters and practically the following are probably more useful indications that the focus of care should shift.
- recurrent episodes of decompensation within 6 months despite optimal tolerated therapy
- progressive renal dysfunction
- Persisting hyponatraemia
- a greater than 5% non-fluid-related weight loss (cachexia)
- escalating diuretic dose requirements
- the occurrence of malignant arrhythmias
- chronic poor quality of life or intractable NYHA class IV symptoms,

Shared care with close liaison between specialist palliative care services, the HF team and/or the primary care physician s likely to lead to optimally managed and coordinate patient's care.
Care might shift to a palliative focus over time rather than a focus on disease modification. Good communication is a paramount aspect of care delivery with the patient and family understanding the rationale for a change in focus of care.
Key aspects of treatment include:

Symptom assessment and control.
- Morphine (with an antiemetic when high doses are needed) can be used to reduce breathlessness, pain and anxiety
- Diuretic management: increased to relieve severe congestion or down titrated due to excessive thirst.
- Reducing HF drugs that reduce blood pressure to maintain sufficient oxygenation and reduce the risk of falls.
- Stopping non-essential therapies e.g. cholesterol lowering drugs, osteoporosis treatments.

Common Medication Contraindicated for use in Heart Failure

Consider stopping or reducing down to the lowest effective dose any of the following medication in patients with heart failure, following consideration of past medical history and concomitant medical conditions and if necessary after discussion with an appropriate medical professional:

- NSAIDs (diclofenac, ibuprofen, indomethacin, ketorolac, naproxen, and piroxicam) and COX2 inhibitors (etoricoxib and rofecoxib) – can cause fluid retention and are associated with an increased risk of hospital admission due to heart failure. (Note – the same applies to aspirin when used as an analgesic)
- Steroids (prednisolone and dexamethasone) – can cause hypertension in a dose related manner due to increased peripheral resistance and sodium and water retention. Although usually only used in cases of important likely benefit, because of their well-known adverse effects.
- Diltiazem and Verapamil – have negative ionotropic effects which may further worsen cardiac function.
- Nifedipine and Nicardipine - have a negative safety profile in heart failure (Note - amlodipine and felodipine, may be used to treat hypertension but may compromise attaining optimal dosage of ACEIs/ARBs, beta-blockers and aldosterone antagonists.)
- Pioglitazone - May cause fluid retention and heart failure by increasing renal sodium

reabsorption.

- Flecainide and dronedarone (anti-arrhythmics) –may increase the risk of ventricular arrhythmias, worsen heart failure and increase risk of mortality and hospital admissions.
- Moxonidine – increases risk of heart failure mortality.

Common Medication to be used with Caution in Heart Failure

- Tricyclic Antidepressants (e.g amitriptyline) - can prolong QT interval and cause

arrhythmias as well as risk of hypotension.

- Trimethoprim-sulfamethoxazole (Septrin) – can increase the risk of hyperkalaemia and AKI when used alongside ACE inhibitors.
- Theophylline – tachycardia and atrial arrhythmia can occur even when used at therapeutic levels in heart failure. Close monitoring is required if this is to continue.
- PDE-5 inhbitiors (Sildenafil, vardenafil, tadalafil) – are vasodilators so can precipitate hypotension (especially if used alongside GTN/nitrates). Note – Sildenafil is sometimes used in pulmonary hypertension.
- Over the counter medicines including: Those with high salt content which may cause fluid retention, e.g. effervescent preparations and some antacids. Decongestants for coughs and colds such as pseudoephedrine may increase workload on the heart. Laxatives taken with a large amount of water such as bulk-forming agents.
- Caution with some herbal/homeopathic remedies – seek advice if unsure.

Management of Heart Failure in Pregnancy and Breastfeeding

Some of the commonly used medication used in heart failure is contraindicated for use in pregnancy and/or breastfeeding, and some may be used with caution. There is limited data for the use of drugs in pregnancy and breastfeeding and the consensus is that medication should only be used where the perceived benefits outweigh the risks. Due to limited data it is often difficult to determine if the risk is associated with maternal clinical condition alone or medication. Use and choice of heart failure medication in pregnancy and breastfeeding will depend upon maternal clinical condition, gestation, maternal co-morbidities and other potential risks to the baby or mother. All women of child bearing age with heart failure should be reviewed by a heart failure specialist ideally prior to conception for optimization of medical therapies and to discuss risks. aiscussing management of pregnancy in all women of child-bearing age with heart failure. Below list the potential risks associated with the main classes of heart failure drugs:

Loop diuretics – Furosemide and bumetanide are generally contraindicated in pregnancy as are associated with maternal hypovolaemia and reduced placental perfusion. However there are no reports of teratogenicity with either, and they have been used for pulmonary congestion when essential. Both are considered to be safe in breastfeeding as excretion into breast milk is likely to be too small to be harmful. Furosemide is the preferred option due to most experience, short half life and high protein binding. Note - loop diuretics may theoretically inhibit lactation.

ACE inhibitors – All are relatively contraindicated in pregnancy and only used if essential. Use in the 1st trimester has been associated with neonatal cardiac malformation, CNS malformation, including neural tube defects and renal defects. Use in the 2nd or 3rd trimesters has been associated with oligohydramnios, renal tubular dysgenesis, intrauterine growth restriction including under-development of neonatal cranial and leg bones, poor lung and bladder maturation, patent ductus arteriosis and compression of the umbilical cord, which may result in reduced neonatal blood flow. There is limited evidence for the safe use of ACE inhibitors in breastfeeding with premature and newborn infants theoretically at risk from profound hypotension and renal toxicity when exposed via breast milk. Captopril and enalapril are the preferred choices in breastfeeding.

ARB's – All are contraindicated in pregnancy unless essential. The risks associated with ARB use in pregnancy is similar to ACE inhibitors. Information on the use in breastfeeding is very limited, therefore are not recommended as ACE inhibitors are considered safer.

Beta-blockers – None have shown any teratogenic risk, but use in pregnancy has been associated with intra-uterine growth restriction, neonatal hypoglycaemia, bradycardia and hypotension. Labetalol is commonly used in pregnancy for maternal hypertension. Consider continuation of chronic beta blocker therapy in stable asymptomatic women, where there are no adverse effects on the neonate. Of the three beta-blockers licensed for use in heart failure; metoprolol is excreted into breast milk though infants have shown very low serum levels so is likely to be safe and no adverse events have been reported. Carvedilol is highly protein bound so presents a low risk in breastfeeding, however experience is lacking so other agents are preferred. Bisoprolol has relatively low protein binding and moderately high renal excretion so presents a higher risk for accumulation in breastfed infants. Again there is little experience of bisoprolol use in breastfeeding, so other agents are preferred. (Note - Propranolol is considered the preferred choice in breastfeeding however is not licensed for use in heart failure).

Mineralocorticoid Receptor Antagonists – Spironolactone and Eplerenone are contraindicated in pregnancy unless potential benefits outweigh the risks. Spironolactone has been shown to be teratogenic in animal studies but limited data suggests use in breastfeeding is safe. There is no safety data for the use of Eplerenone in pregnancy or breastfeeding so avoidance is advised.

Ivabradine – Contraindicated in pregnancy and breastfeeding as toxicity shown in animal studies and is present in significant amounts in breast milk.

ARNI – Contraindicated in pregnancy and breastfeeding as toxicity shown in animal studies and is present in significant amounts in breast milk.

NOTE – Although digoxin is no longer a recommended treatment for heart failure it is generally safe in pregnancy and breastfeeding so may be a useful agent. Also isosorbide diniatrate plus hydralazine is the preferred vasodilator therapy during pregnancy if essential. There is a large volume of evidence supporting the safety of hydralazine in pregnancy, but there is limited evidence for the safety of isosorbide dinitrate. There is limited safety data for the use of this combination in breastfeeding, but as ACE inhibitors are considered compatible with breastfeeding, so are generally restarted post-partum.
Useful reference sources for drug use in pregnancy or breastfeeding:Best use of medicines in pregnancy - http://www.medicinesinpregnancy.org/
Specialist Pharmacy Service – Safety in Lactation - https://www.sps.nhs.uk/?s=&cat%5B0%5D=266&cat%5B1%5D=3008
These are not an exhaustive lists. If you have any concerns/queries with concomitant medication you may contact the Medicines Information Helpline for further advice (based at Worcester Royal Hospital) on 01905 760611 or email wah-tr.druginfo@nhs.net. Opening hours are Mon-Fri 9am – 5pm.

Monitoring Tool

STANDARDS	%	Clinical Exceptions
All patients with confirmed LVSD should be on maximum tolerated Angiotensin Converting Enzyme Inhibitor (ACE I) or Angiotensin Receptor Blocker (ARB) therapy	100	Contraindicated, Intolerant
All patients with confirmed LVSD should be on maximum tolerated beta blocker therapy	100	Contraindicated, Intolerant
All patients with confirmed LVSD still symptomatic on ACE I and Beta-blockers should receive Spironolactone or Eplerenone	100	Contraindicated. Intolerant

How will monitoring be carried out? Local Athena database, paper audit tool

When will monitoring be carried out? Yearly

Who will monitor compliance with the guideline? Heart Failure Specialist Nurses

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