**DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)**

# Management of Chronic Heart Failure with Reduced Ejection Fraction (HFrEF) in primary care

## Diagnosis

- Patients with suspected heart failure should receive a range of basic tests including NTproBNP. NTproBNP >400 ng/L suggests possible heart failure- refer to rapid access heart failure referral clinic for specialist assessment, including transthoracic echocardiography (ECHO) to confirm diagnosis. See Shared care pathology guideline

## Initial management

- Give people specific advice on salt (<6g/day) & fluid intake and address risk factors (e.g. smoking, obesity, cardiotoxic drugs including illicit drugs, hypertension, diabetes, AF). Offer a personalised exercise-based cardiac rehabilitation programme.

- All patients with HFrEF should be considered for an ACE inhibitor and beta blocker. Introducing one drug at a time, and once the person is stable on the first drug (usually an ACEi) then adding the second drug. Aim for the target dose of ACEi and beta blocker; or, failing that, the maximum tolerated dose.

- Patients with HFrEF who have ongoing symptoms of heart failure despite optimal treatment, should be given mineralocorticoid receptor antagonists (MRA) spironolactone as first line option.

- The safety and efficacy of combining an ACEi, an ARB and MRA is uncertain and the use of these three drugs together is not recommended due to high risk of hyperkalaemia and renal dysfunction.

## Monitoring

- All patients with heart failure are at risk of renal impairment and hyperkalaemia. It is very important to monitor renal function and electrolytes - 6 monthly in stable patients, and more frequently when there is change in drug treatment and/or an acute change in the patient's condition.

- Monitor response to titration of medications closely in CKD taking into account increased risk of hyperkalaemia. If eGFR <45ml/min/1.73m$^2$ consider lower doses and/or slower titration of dose of ACEi or ARB, MRA & digoxin.

- Heart failure monitoring (minimum 6 monthly for stable patients) should also include a clinical assessment (functional capacity, fluid status, cardiac rhythm, cognitive & nutritional status), review of medication (e.g. stop NSAID, calcium channel blockers such as verapamil, diltiazem) and side effects.

## Further drug treatments & referral

- Sacubitril valsartan is a treatment option to be used as per NICE TA 388. Treatment is initiated by specialist and may be continued by GP. This should not be co-administered with an ACEi or an ARB. Due to risk of angioedema patients who commence treatment will have their ACEi discontinued at least 36 hours before treatment is started.

- Dapagliflozin or empagliflozin is recommended as an 'add on' treatment option for heart failure as per NICE TA679/TA773. Treatment with SGLT2i for heart failure is initiated by the specialist and stabilised before transferring the patient to primary care. **Not to be used in patients with type 1 diabetes**. See p.8 for further detail.

- Specialist advice should be sought for patients who do not respond to treatment or deteriorate after having been stable for a number of years on optimum pharmacological treatment with an unaccountable cause.

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**Glossary**

| | |
|---|---|
| ACEi | angiotensin converting enzyme inhibitor |
| ANRi | Angiotensin Receptor-Neprilysin Inhibitor |
| ARB | angiotensin receptor blockers |
| CCB | Calcium channel blockers |
| BNP | B-type natriuretic peptide |
| eGFR | estimated glomerular filtration rate |
| ECG | Electrocardiogram |
| FBC | full blood count |
| HFREF | heart failure with reduced ejections fraction |
| HR | heart rate |
| ICD | implantable cardiovascular defibrillators |
| LFT | liver function test |
| LVEF | left ventricular ejection fraction |
| MRA | mineralocorticoid receptor antagonist |
| NTproBNP | N-terminal proB-type natriuretic peptide |
| RAS | renin–angiotensin system |
| SBP | systolic blood pressure |
| SGLT2i | Sodium/glucose cotransporter-2 inhibitors |
| TFT | thyroid function test |
| U&Es | serum urea & electrolytes |
| UTI | Urinary tract infection |

| Document update | Date updated |
|---|---|
| Metolazone brand Xaqua DNP | Aug 2022 |
| Xaqua preferred brand for new patients | Sept 2022 |
| MHRA drug safety warning on metolazone added | January 2023 |
| Updated email address for South HF team referrals | July 2024 |

**References**


1. BNF via https://www.medicinescomplete.com/
2. SIGN 147- Management of chronic heart failure. March 2016
3. NICE TA 267 Ivabradine for treating chronic heart failure
4. NICE Clinical Knowledge Summaries (CKS)- Chronic Heart Failure
5. NICE NG106 Chronic heart failure in adults: diagnosis and management
6. NICE TA 388 Sacubitril valsartan for treating symptomatic chronic HFrEF
7. NICE TA 679 Dapagliflozin for treating heart failure with reduced ejection fraction
8. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure



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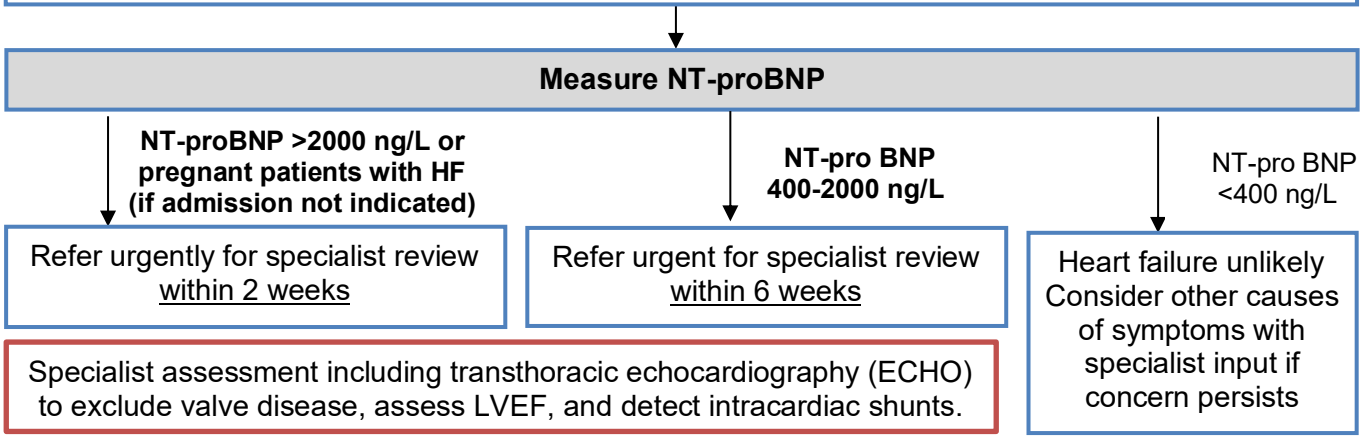
## 1. Introduction

This guideline is based on NICE NG106 Chronic heart failure in adults: diagnosis and management, and aims to improve diagnosis and treatment for people with heart failure in primary care, with emphasis on the pharmacological treatment of Heart failure with reduced ejection fraction (HFrEF). HFrEF is defined as heart failure with a left ventricular ejection fraction (LVEF) below 40%

## 2. Investigation/ Diagnosing heart failure

See Derbyshire shared care pathology guideline – cardiology- Heart failure

- Take a detailed history and perform a clinical examination to evaluate for possible aggravating factors and to exclude other conditions with similar presentations
- Patients with suspected chronic heart failure should receive a range of basic tests. The investigations chosen will vary depending on the presentation but should usually include:
  - **NTproBNP** (note this is shown as 'BNP' on clinical reporting system in Derbyshire)
  - **12-lead ECG**
  - **chest X-ray**
  - **other blood tests (U&E, FBC, TFT, LFT, HAB1c (or fasting blood glucose), lipids)**
  - **urinalysis**
  - **peak flow or spirometry**




- NTproBNP >400 ng/L suggests possible heart failure – refer to rapid access heart failure referral clinic at UHDB & CRH for specialist assessment, including transthoracic echocardiography (ECHO), to confirm diagnosis.
- Be aware that obesity, African or African–Caribbean family origin, or treatment with diuretics, ACE inhibitors, beta‑blockers, ARBs or MRAs can reduce levels of NT-proBNP levels
- While awaiting referral and if symptoms are severe to warrant treatment (but not admission) start a loop diuretic e.g. furosemide 20-40mg per day. Stop if possible oral NSAIDs (including OTCs) or calcium channel blockers (e.g. verapamil, diltiazem)
- The basis for historical diagnoses of heart failure should be reviewed, and only patients whose diagnosis is confirmed should be managed in accordance with this guideline.

**New York Heart Association (NYHA) Functional Classification of Heart Failure**

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

## 3. Management of chronic heart failure with reduced ejection fraction (HFrEF)- overview

**General management**

- Stop aggravating drugs if possible (oral NSAID, negatively inotropic CCB)
- Specific advice on fluid intake &salt in diet (<6g/day)
- Address risk factors (smoking, alcohol, cardiotoxic drugs including illicit drugs, obesity, hypertension, diabetes, Atrial Fibrillation)
- Follow local guidelines on primary/secondary prevention of coronary heart disease
- Advise pneumococcal, influenza and other relevant vaccination
- Offer a personalised, exercise-based cardiac rehabilitation programme
- Offer personal record (care plan) – for therapy, weight, risk factors etc.

**Monitoring**

- Clinical assess and monitor U&Es & eGFR every 6 months when patient clinically stable and on stable doses of medication
- eGFR 30-45 ml/min/1.73 $m^2$- consider lower doses or slower titration of ACEI or ARBs, MRAs, sacubitril valsartan & digoxin

**Diuretics to relieve symptoms and signs of congestion & fluid retention** (oedema, lung crackles, raised JVP, pulmonary congestion on chest X-ray)

consider ICD[1] implantation (NICE TA 314)

**Patient with HFrEF**

Start one drug at a time. Up-titrate to max. tolerated evidence-based doses

**ACEi** (or ARB if not tolerated) check U&E, BP at baseline & 1-2 weeks after initiation & dose titration

**Beta Blocker** start low, go slow check heart rate, BP & clinical status

**Still symptomatic** — No

**Add MRA antagonist**- spironolactone 25mg daily or alternate days
stop $K^+$ supplements/ $K^+$ sparing diuretics;
ensure **no** hypovolaemia, baseline $K^+$ <5 mmol/l, creatinine <220umol/l;
monitor U&E closely starting at 5-7 days post initiation

**Still symptomatic** — No

**Specialist assessment**

**EF <40%**

NOT type1 diabetics, eGFR see table p.8

**Dapagliflozin or empagliflozin** (NICE TA679/ TA773 **as add on** Specialist initiation, monitor eGFR

**EF <35%**

Able to tolerate ACEI (or ARB)

**Sacubitril/Valsartan** (NICE TA388) to replace ACEI (or ARB) Specialist initiation, monitor U&E, BP

Sinus rhythm, HR ≥75 bpm

Ivabradine (NICE TA 267) as add on Specialist initiation

QRS duration ≥120 msec

Evaluate need for CRT[2] (NICE TA 314)

**Treatments may be combined if indicated**

**Resistant symptoms**

Yes → Advice from specialist heart failure team consider digoxin or Hydralazine + nitrate[4]

LVAD[3], or heart transplant

No → **No further action required**
**Consider reducing diuretic dose**

1. Implantable cardioverter defibrillators. 2. cardiac re-synchronisation therapy. 3. left ventricular assist device. 4. Especially if of African-Caribbean descent

## 4. First line Drug treatments for HFrEF

- All patients with HFrEF should be offered treatment with an ACEi and a Beta-blockers licensed for use in heart failure.
- Start one drug at a time- ACEi is usually initiated first, but there may be clinical reasons for starting a BB first e.g. additional anti-anginal treatment needed
- Always stop negatively inotropic CCBs (diltiazem, verapamil) if possible.
- In HF a systolic blood pressure of 90 is often well tolerated. There is no need to reduce drug doses if the patient is without related symptom. If it is necessary to reduce drug doses then consider reducing diuretic first as it is often necessary to reduce the diuretic to "make room" for ACEi, BB and MRA.
- Aim for the target dose of ACEi and beta-blocker. But some is better than none and a little of both is better than lots of one and none of the other.
- **Close monitoring is required during initiation and ongoing drug treatment**, especially in patients with CKD (increased risk of hyperkalaemia).

| **Angiotensin converting enzyme inhibitor (ACEi)** | | | **Angiotensin receptor blockers (ARB)** |
|---|---|---|---|
| **Place of therapy** | All patients with HFrEF should be offered for treatment with an ACEi, unless C/I. | | ARB is an alternative for patients intolerant of ACEi (e.g. due to cough*). |
| **Initiation** | Start at the appropriate low dose and titrated upwards at short intervals (eg. every 2 weeks) up to the maximum tolerated or target dose. | | |
| **Caution** | Seek specialist advice before initiation in following groups:<br>• Cr>221µmol/l, K+>5mmol/l or $Na^+$<130mmol/l<br>• Systolic BP<90mmHg<br>• diuretic dose>80mg furosemide/ day or equivalent<br>• known or suspected artery stenosis (e.g. severe peripheral vascular disease)<br>• pregnancy (C/I in 2nd and 3rd trimester) | | |
| **Monitoring** | Monitor U&E, eGFR & BP at baseline, 1-2 weeks after initiation and 1-2 weeks after each dose increment.<br>Once dose stable, monitor monthly for 3 months and then at least every 6 months, and at any time the person becomes acutely unwell. | | |
| **Abnormal results** | **A rise in urea, creatinine and potassium is to be expected after initiation of an ACEi/ ARB**<br>• ↑ creatinine up to 50% above baseline or 266 micromol/l, whichever is smaller; or ↑ potassium <5.5mmol/l is acceptable<br>• Greater rises in creatinine or potassium than those outlined above persist<br>o adjustment of concomitant medications (e.g. stopping of NSAIDs) and other potassium supplements/ retaining agents (e.g. amiloride, spironolactone), reduce diuretic dose (if there are no signs of congestion).<br>o Half the dose of ACEi/ ARB and recheck U&E & eGFR within 1-2 weeks.<br>o Seek specialist advice if response still unsatisfactory. ↑ creatinine by >100% or to above 310 micromol/l; or ↑ potassium to ≥5.5 mmol/l - Stop ACEi/ ARB and seek specialist advice. | | |
| **notes** | Combination use of medicines blocking renin-angiotensin hormone system (RAS) (MHRA 2014)<br>• Combination use of drugs from different classes of the RAS blocking agents (ACEi, ARBs and aliskiren) is not usually recommended; however, some evidence suggests that the benefits of ACEi+ARB combination may outweigh the risks in a selected group of heart failure patients for whom other treatments are unsuitable.<br>• Candesartan is licensed as add-on therapy to ACEi for people with symptomatic HF despite optimal therapy.<br>• Combination of ACEi, beta-blocker and ARB may be considered for persistently symptomatic patients –initiated only by a specialist<br>• **The combination of ACE+ARB+MRA together is not recommended.** | | |
| | **Lisinopril** | **Ramipril** | **Candesartan** (ARB of choice for HF) | **Losartan** |
| **Starting dose** | 2.5mg once daily | 2.5mg once daily | 4mg once daily | 12.5mg- 50mg once daily |
| **Target dose** | 20-35mg once daily | 10mg daily or 5mg twice daily | 32mg once daily | 150mg once daily |

*Cough is common in heart failure. ACE inhibitors cause cough in some patients. The effect of ACEi on survival is more certain than that of ARB. Do not rule out ACEi until absolutely certain that the drug is causing the cough.

<table>
<tr><th colspan="3">Beta-blockers (BB)</th></tr>
<tr><td>Place of therapy</td><td colspan="2">Beta-blockers licensed for use in heart failure should be offered in patients with symptomatic HFrEF after diuretic, and usually after ACEi.<br>Patients existing on BB for concomitant condition (e.g. angina, hypertension) who develop HF should continue with a BB licensed for HF.</td></tr>
<tr><td>Initiation</td><td colspan="2">• Before starting BB patient should have stable chronic HF without acute failure during the past 6 weeks, and a mainly unchanged basic therapy during the past 2 weeks.<br>• ‘Start low, go slow’ - assess HR, BP & clinical status (signs & symptoms especially of congestion, body weight) after starting and at each dose titration. It is sometimes necessary to leave it a lot longer than the suggested two weeks before increasing the dose.<br>• Sometimes the improvement in symptoms with beta-blockers is immediate. Sometimes it is necessary to encourage a patient to go through a period of symptom worsening before they feel better.</td></tr>
<tr><td>Caution</td><td colspan="2">Absolute C/I :<br>• Acute heart failure or during episodes of heart failure decompensation requiring i.v. inotropic therapy or cardiogenic shock<br>• AV block of second or third degree (without a pacemaker) or Sinoatrial block or Sick sinus syndrome<br>• Symptomatic/severe bradycardia with less than 60 beats/min before start of therapy or Symptomatic/severe hypotension (SBP <90mmHg)<br>• Severe bronchial asthma or severe COPD* or Late stages of peripheral arterial occlusive disease / Raynaud’s syndrome<br>• Untreated phaeochromocytoma or metabolic acidosis<br>* Some of the above may be relative C/I e.g. NICE recommends offering a selective BB in COPD patients without reversibility – if unsure contact a cardiologist. BB are usually well tolerated in COPD. Rhonchi are present periodically in HF and COPD. Do not stop the BB unless for certain it is causing bronchospasm.<br><br>Do not stop BB abruptly. Gradually halving dose every week if discontinuation is necessary.<br>The only indications to stop bisoprolol therapy abruptly are: severe symptomatic hypotension, acute pulmonary oedema, cardiogenic shock, severe symptomatic bradycardia, 2nd or 3rd degree AV block.</td></tr>
<tr><td>Monitoring</td><td colspan="2">Monitor heart rate, blood pressure, and clinical status (for symptoms and signs of heart failure) after each dose increase<br>The SPC recommends that after initiation of treatment and dose increases patients should be observed over 4 hours (BP, HR, signs of increasing HF). Locally this is not considered to be necessary. Return home to the supervision of a responsible, forewarned adult would be adequate.</td></tr>
<tr><td rowspan="2">Abnormal results</td><td colspan="2">Low Heart rate (<50 beats/min) with worsening symptoms, and the patient is symptomatic:<br>• Review the need for other heart rate slowing drugs e.g. digoxin, amiodarone, diltiazem/ verapamil; halve the dose of BB, or if there is severe deterioration, stop BB (rarely necessary).<br>• Arrange an ECG to exclude heart block& seek specialist advice.<br>• No further increase in bisoprolol dose should be made without specialist advice, if the pulse (or apex beat if in AF) drops below 50 bpm and/or the SBP is less than 90mmHg, or there is symptomatic hypotension or bradycardia above these levels.</td></tr>
<tr><td colspan="2">Worsening shortness of breath<br>• Temporarily half titration. Increase diuretic dose and review in 2 weeks.<br>• Resume titration if breathlessness reverted to prior level.<br>• Alternatively, temporarily reduce bisoprolol dose and prolong intervals between subsequent titration if breathlessness settles.<br>• Ivabradine is an alternative option after specialist initiation (NICE TA267).</td></tr>
<tr><td></td><td>Bisoprolol</td><td>Carvedilol</td></tr>
<tr><td>Starting dose</td><td>1.25mg once daily</td><td>3.125mg twice daily</td></tr>
<tr><td>Target dose</td><td>10mg once daily<br>Increase from 1.25 mg to 2.5 mg to 3.75 mg to 5 mg at 1-2week intervals;<br>Increase from 5mg to 7.5mg to 10mg at 4 weeks intervals</td><td>25mg BD for patients <85 kg; 50mg BD for patients >85 kg<br>Titrate the dose by doubling every 2 weeks.</td></tr>
</table>

| Diuretics | | |
|---|---|---|
| **Place of therapy** | Loop diuretics routinely used for the relief of congestive symptoms and fluid retention. | |
| **Initiation** | Titrated up and down according to need following the initiation of subsequent heart failure therapies.<br>Aim for the lowest dose needed to relieve symptoms | |
| **Monitoring** | Check U&E & eGFR 1-2 weeks after starting treatment and after each dose titration.<br>If stable then once every 6 months. | |
| **Notes** | Diuretic resistance (after specialist initiation and assessment)<br>Thiazide and thiazide-like diuretics (metolazone brand Xaqua) can be added to loop diuretics to create a synergistic and potent diuresis in patients who are failing to adequately respond to increasing doses of loop diuretics. See metolazone traffic light classification and MHRA Jan 2023 for further information. This combination can be effective and avoid the need for hospitalisation but is not without risk thus should be initiated and managed by a specialist, and on-going care only handed to primary care when stable. | |
| | **Furosemide** | **Bumetanide** (2nd line option if lack of efficacy with furosemide) |
| **Starting dose** | 20-40mg per day | 1mg per day |
| **Usual dose** | 40-80mg (up to 240mg) per day<br>Usually once daily in the morning, but can be given morning & lunch | Up to 5mg/day; higher doses may be required- monitor closely |

| Mineralocorticoid receptor antagonist (MRA) | | |
|---|---|---|
| **Place of therapy** | Add MRA in patients with HFrEF who remain symptomatic despite optimal therapy with ACEi and BB.<br>**Do not use ACE+ARB+MRA together.** | |
| **Initiation** | stop K+ supplements/ K+ sparing diuretics; ensure no hypovolaemia, baseline K+ <5 mmol/l, creatinine <220µmol/l | |
| **Caution** | Spironolactone is C/I in serum potassium >5mmol/l, creatinine >220µmol/l (or CKD stage >3), or known acute liver disease.<br>Caution if body weight <50kg. | |
| **Monitoring** | (Locally suggested) U&E at baseline, 5-7days post initiation/ dose titration, then at 4,8 & 12 weeks, then 6monthly thereafter (3monthly or more if clinical reasons for ↑ risk of renal impairment) | |
| **Abnormal results** | Persistent hyperkalaemia<br>• half dose of MRA & recheck biochemistry. Liaise with heart failure specialist nurses.<br>• If intolerant of spironolactone or potassium > 5.5 mmol/l or creatinine > 220 µmol/l- Reduce dose to 25 mg alternate days.<br>If still problems - stop spironolactone<br>If potassium > 5.9 mmol/l or creatinine to 310µmol/l - stop spironolactone immediately and seek specialist advice. | |
| | **spironolactone** | **Eplerenone**<br>2nd line if spironolactone not suitable (usually specialist recommendation for male <50years of age due to gynaecomastia risk). |
| **Starting dose** | 25mg daily or 25mg on alternate days | 25mg once daily |
| **Usual dose** | Depend on symptoms and biochemistry stability. 12.5mg once daily or 25mg on alternate days to 25-50mg once daily | 50mg once daily usually within 4 weeks |

5. **Other drug treatments for HFrEF** (after specialist assessment and initiation)

| **Sodium/glucose cotransporter-2 inhibitors (SGLT2i)** | | |
|---|---|---|
| | **Dapagliflozin** (NICE TA679) | **Empagliflozin** (NICE TA773) |
| **Place of therapy** | **Add-on** to optimised standard care with<br>• ACEi or ARB + BB + MRA if tolerated, or<br>• Sacubitril/valsartan + BB + MRA if tolerated<br>It is not a requirement to swap ACEi/ARB to ARNI before commencing SGLT2i.<br>Clinician should weigh benefits and risks in each individual case. | |
| **JAPC classification** | **GREEN** specialist initiation & stabilisation | |
| **Initiation criteria (for info)** | LVEF<40%, no hypovolaemia; **NOT type 1 diabetics**, eGFR >30 ml/min/1.73$^2$<br>Specialist may advise using dapagliflozin or empagliflozin for HFrEF in some patients with eGFR <30ml/min/1.73$^2$ on case-by-case basis, assessing risk vs benefit. Liaise with specialist when considering stopping treatment due to poor renal function | |
| **Dose for HFrEF** | **10mg once daily** with/without food.<br>Dapagliflozin is not recommended in eGFR<15ml/min/1.73$^2$. Severe hepatic impairment- start at 5 mg daily and increase to 10 mg if well tolerated. | 10mg once daily with/without food.<br>Empagliflozin is not recommended in eGFR<20 ml/min/1.73$^2$. Not recommended in severe hepatic impairment |
| **Caution** | • Correction of hypovolaemia may require reduction or withdrawal of diuretics and review of fluid intake. In euvolaemic patients who require a regular diuretic it may be appropriate to reduce diuretic by ~40mg furosemide equivalent.<br>• Systolic BP <95mmHg<br>• History of recurrent urinary tract infections or candida | |
| **Baseline monitoring by specialist** | • U&Es including renal and hepatic function at initiation<br>• Blood pressure and volume status at and after initiation<br>• Re-check renal function and blood pressure 4 weeks after initiation<br>  ○ at 4 weeks there is an expected dip in eGFR of up to 20% for which there is no reason to withdraw SGLT2i<br>• For type 2 diabetics, check:<br>  ○ HbA1c level (in last 3 months), if no recent changes in diabetic therapy<br>  ○ if recent therapy change- need an up-to-date HbA1c<br>• Consider factors in the patient history that may predispose to ketoacidosis before initiation | |
| **Handover to GP from HF specialist** | Diabetic and HF patients<br>Emphasise to the GP that SGLT2i has been added *primarily* for heart failure prognosis and symptoms and that the medication should be continued even if HbA1c is not reduced and should not be stopped inadvertently- see initiation/dosing info above<br>Non- diabetic patients with HF<br>Emphasise to the GP that this has been started for heart failure prognosis and symptoms and not because the patient is diabetic and that the medication should not be stopped inadvertently- see initiation/dosing info above | |
| **GP ongoing Monitoring** | Monitor renal function- annual GFR and when<br>• starting concomitant medicines that may reduce renal function and periodically thereafter.<br>• GFR <60mL/min- check at least 2-4 times per year<br><br>Carefully monitor volume status during intercurrent conditions that may lead to volume depletion (e.g. gastrointestinal illness):<br>• physical examination including BP<br>• blood tests including U&Es & haematocrit | |
| **MHRA drug safety warning** | • **Risk of diabetic ketoacidosis (DKA)**, MHRA April16<br>  ○ discuss the risk factors for DKA and inform patients of the signs and symptoms; advise them to seek immediate medical advice if they develop any of these<br>  ○ discontinue treatment with the SGLT2i immediately if DKA is suspected or diagnosed *(GP/hospital to test for raised ketones in patients with signs and symptoms of DKA, even if plasma glucose levels are near-normal or normal.)* | |

| | |
|---|---|
| | ○ do not restart treatment with any SGLT2i in patients who experienced DKA during use, unless another cause for DKA was identified and resolved<br>○ interrupt treatment with the SGLT2i in patients who are hospitalised for major surgery or acute serious illnesses; treatment may be restarted once the patient's condition has stabilised<br>• Risk of lower-limb amputation, MHRA Mar17<br>○ Canagliflozin may increase the risk of lower-limb amputation in patients with type 2 diabetes. Evidence does not show an increased risk for dapagliflozin/ empagliflozin, but the risk may be a class effect.<br>○ advise patients receiving any SGLT2i about the importance of routine preventive foot care and adequate hydration.<br>• Reports of Fourniers gangrene, MHRA Feb19<br>○ Fournier's gangrene is a rare but serious and potentially life-threatening infection- if suspected, stop the SGLT2i and urgently start treatment<br>○ urogenital infection or perineal abscess may precede necrotising fasciitis<br>○ advise patients to seek urgent medical attention if they experience severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise<br>• Monitor ketones in blood during treatment interruption, MHRA Mar 2020 |
| **Patients with type2 diabetes and heart failure** | • Although SGLT2 inhibitors have a low risk of hypoglycaemic events, reducing blood glucose levels via this mechanism could potentially predispose patients taking other anti-glycaemic medication (particularly insulin or sulphonylureas) to hypoglycaemia**.**<br>• **Concomitant medication for glycaemic control must be reviewed in line with HbA1c target**. **Liaise with primary care/specialist diabetes services**:<br>○ Glitazones are contraindicated in heart failure and should be stopped.<br>○ Patients on metformin alone will likely tolerate SGLT2i without reduction in metformin although dose reduction of insulin and sulfonylureas is often necessary<br>○ It may also be relevant to consider stopping or swapping other hypoglycaemic therapies depending on baseline glycaemic control and personalised target.<br>○ Caution if there is a history of previous/frequent hypoglycaemia.<br>○ SGLT2i may be prescribed as part of the regimen for glycaemic control in line with local diabetes guideline. Consider additional glucose-lowering treatment if GFR persistently <45ml/min.<br>• Existing alternative SGLT2i (canagliflozin) for the management of type 2 diabetes in patients with HFrEF- continue in line with the licence OR switch to dapagliflozin or empagliflozin – an informed decision should be undertaken between clinician and patient.<br>• **Dapagliflozin or empagliflozin is primarily for heart failure prognosis and the medication should be continued even if HbA1c is not reduced** |
| **Patient counselling** | **Inform patients signs and symptoms of DKA** (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat), and advise them to **seek immediate medical advice if they develop any of these.**<br><br>**Temporarily withhold SGLT2 inhibitor** in patients who<br>• are hospitalised for major surgery or acute serious illnesses (MRHA 2020)<br>• are not eating or drinking<br>• has inter-current conditions that may lead to volume depletion (e.g. vomiting/ diarrhoea)<br>• have major infection<br><br>Specific information and education for heart failure and diabetics with heart failure starting SGLT2i should be provided e.g.<br>• Forxiga (dapagliflozin)/ in HFrEF patient information leaflet<br>• TREND Diabetes Type2 diabetes and diabetic ketoacidosis patient information leaflet |

| ARNi | Sacubitril/ valsartan |
|---|---|
| **NICE criteria** | NICE TA388 NYHA class II-IV symptoms **and** LVEF ≤ 35% **and** already taking a stable dose of ACEi or an ARB (>4 weeks). |
| **JAPC classification** | **GREEN** specialist initiation & stabilisation |
| **Initiation criteria** | eGFR>30ml/min/1.73$^2$, $K^+$ <5.5mmol/l, and systolic BP>99bpm |
| **Dose** | **Discontinue ACEi for 36 hours before initiating sacubitril/valsartan to minimise the risk of angioedema.**<br>Starting dose one 49/51mg tablet twice daily; ↑ at 2-4 weeks to target dose one 97/103mg tablet twice daily as tolerated by the patient.<br>Consider starting dose of 24mg/26mg twice daily for patients with SBP ≥100-110 mmHg and in patients with moderate renal impairment (eGFR 30-60 ml/min/1.73 m$^2$) |
| **Caution/ MHRA drug safety** | • Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg.<br>• SBP ≤95 mmHg or symptomatic hypotension, hyperkalaemia, or renal dysfunction:- Adjust concomitant medicinal products and/or temporary down–titration, or discontinue sacubitril/valsartan. |
| **GP Monitoring** | **Once stable, monitor blood pressure, U&E every 6 months** |

| HCN channel blocker | Ivabradine |
|---|---|
| **NICE criteria** | NICE TA267 NYHA II-IV stable HFrEF with LVEF ≤35% **and** sinus rhythm with a HR ≥75 bpm **and** given in combination with standard therapy (BB, ACEi & MRA), or when BB is C/I or not tolerated. |
| **JAPC classification** | **GREEN** specialist initiation & stablisation |
| **Initiation criteria** | Heart rate ≥75 bpm and blood pressure >90/50 mmHg |
| **Dose** | Starting dose 5 mg twice daily with food. Only increase dose to 7.5 mg twice daily after 3-4 weeks and if the 5 mg dose is well tolerated but insufficient.<br>Reduce to 2.5 mg (half 5mg tablet) twice daily if resting HR persistently below 50 bpm or if the patient has symptoms of bradycardia.<br>Stop ivabradine if resting HR remains <50 bpm or symptoms of bradycardia persist. |
| **Caution/ MHRA drug safety** | MHRA June 2014- Emerging clinical trial evidence of increased cardiovascular risk.<br>• The starting dose of ivabradine is 5 mg twice daily. The maintenance dose should not exceed 7.5 mg twice daily.<br>• Carefully monitor patients for bradycardia or its symptoms.<br>• Avoid concomitant use of ivabradine with heart rate-reducing calcium channel blockers such as verapamil or diltiazem. |
| **GP Monitoring** | Monitor Heart rate and symptoms of bradycardia - dizziness, fatigue, hypotension. |

| **Digoxin** |
|---|
| • Digoxin is recommended for worsening or severe heart failure in sinus rhythm despite 1st & 2nd line treatment, or patients with AF and heart failure.<br>• Digoxin has no survival advantage in heart failure but is sometimes useful for treating symptoms.<br>• Caution- in the real world of elderly heart failure patients, drug interactions, intercurrent illnesses, and transient disturbance of renal function can lead to life-threatening hyperkalaemia or digoxin toxicity. |
| **Antiplatelet and Statin** |
| • Consider prescribing an antiplatelet to people with atherosclerotic arterial disease- clopidogrel 75mg daily for ischemic stroke/ PAD; aspirin 75mg once daily for secondary prevention CVD<br>• A statin (atorvastatin as per local lipid guideline is indicated in patients with atherosclerotic arterial disease or has a 10-year risk of CV disease >10%. |
| **Sodium zirconium cyclosilicate (Lokelma)- RED** |
| Specialist option may include sodium zirconium cyclosilicate for treatment of chronic hyperkalaemia as per NICE TA599 |

## 6. Information for patients

Give patient appropriate **lifestyle advice**, as well as **advice on their medications** (see appendix 2&3 patient information sheet for ACEi & BB in heart failure).

### Exercise

Regular low-intensity physical activity is recommended for people with stable heart failure. All patients should be encouraged to exercise as much as their symptoms allow. Ensure the person has been referred to a supervised exercise-based rehabilitation programme.

### Salt & fluid intake

The kidneys avidly retain salt in heart failure, and this results in congestion.

- Advise the person to avoid excessive salt intake. Adult daily intake should not exceed 6 g of salt each day (2.5 g of sodium each day).
- Salt substitutes e.g.'Lo Salt' contains significant amount of potassium and should be avoided.
- Formal fluid restriction is difficult to achieve with any accuracy at home. Patients with hyponatraemia should be encouraged to be careful about the amount of fluid they drink. Occasionally it is necessary to limit the patient to less than 2 litres per day.
- Further information can be found on British Heart Foundation website.

**What to do if acutely unwell (e.g., diarrhoea & vomiting)**

Provide sick day guidance (Medicines and your kidneys PIL) on temporary cessation of medicines to patients deemed at high risk of acute Kidney Injury (AKI), based on an individual risk assessment.

Patients should be counselled to maintain fluid intake, contact their GP, and temporarily stop taking ACEi/ARB, diuretics, MRA, sacubitril valsartan, or dapagliflozin, usually for 24-48 hours, until they have had a blood test or once they are better and taking oral fluids.

### Weight monitoring

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

### Alcohol & smoking

For patients with alcoholic cardiomyopathy (in which alcohol has a toxic effect on the myocardium) complete abstinence is essential. For everyone else the recommendation is to not regularly drinking more than 14 units per week. Smoking should be strongly discouraged in all patients.

## 7. Further resources

- British Heart foundation https://www.bhf.org.uk/
  - Your guide to heart failure (downloadable); Heart failure personal record (downloadable)
  - Living with heart failure; Medicines for my heart (downloadable)
- NHSE AKI Programme (Think Kidneys)- Acute Kidney injury resources for primary care
- Open access e-learning package for primary care http://www.uhl-library.nhs.uk/aki_gp/index.html
- https://www.pumpingmarvellous.org/
- https://www.heartfailurematters.org/
- Live Life Better Derbyshire – support for smoking cessation, weight management, mental wellbeing etc.

## 8. Referral

Management of heart failure should be seen as a shared responsibility between patient and healthcare professional. Consider referral to a specialist heart failure nurse if appropriate: (see appendix 1 referral form)
The Community Heart Failure Nursing Service
South 01332 564879 (London Road Team); 01332 789 205 (RDH Team)
DCHST.heartfailuresouth@nhs.net
North Tel: 01246 253061 DCHST.heartfailurenorth@nhs.net

**Appendix 1 DCHS Heart Failure Specialist Services**

Derbyshire Community Health Services NHS
NHS Foundation Trust

# DCHS Heart Failure Specialist Service

# GP Referral Criteria and Contact Details

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

- ☐ Aged 18+ (unless referred by consultant Cardiologist)
- ☐ Registered with a GP in Derby & Derbyshire CCG
- ☐ With a diagnosis of Left Ventricular Systolic Dysfunction (LVSD) which MUST be confirmed by echo, angio or other cardiac imaging
- ☐ The patient has been asked and agrees to the heart failure nurse being involved in their care

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

- ☐ Patient has had a recent hospital admission with worsening heart failure
- ☐ Initiation/titration of ACEi and/or Beta Blocker is problematic (specify issues on page 2)
- ☐ Patient is not symptom controlled despite GP changes to medications and follow up review (specify issues on page 2)
- ☐ Patient has advanced heart failure or complex palliative care needs (specify on page 2)
- ☐ Patient/carer struggling with self management strategies

**Urgency:**

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

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

## The Community Heart Failure Nursing Service

| Heart failure Team (North) | Heart failure Team (South) |
|---|---|
| (Covering GPs in Chesterfield, North East and High Peak and Dales areas)<br><br>Heart Failure Nurse Services<br>Welbeck Suite, Walton Hospital<br>Whitecotes Lane<br>Chesterfield<br>S30 3HW<br><br>Tel: 01246 253061<br>Monday to Friday 9 – 4pm<br>(excl. bank holidays)<br>DCHST.heartfailurenorth@nhs.net | (Covering GPs in Erewash, Amber Valley, Derbyshire Dales and City areas)<br><br>Heart Failure Nurse Services<br>Florence Nightingale Community Hospital<br>London Road<br>Derby, DE12QY<br><br>01332 564879 (London Road Team)<br>Monday to Friday 9 – 4pm<br>(excl. bank holidays)<br>01332 789 205 (RDH Team)<br>Monday to Sunday – 8am-4pm<br>dchst.heartfailuresouth@nhs.net |

# DCHS Heart Failure Specialist Service
# GP Referral Form for patients with LVSD

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

**Patient Details**

| | | | | |
|---|---|---|---|---|
| Name | | D.O.B. | | Male / Female |
| Address | | | | |
| | | NHS No | | |
| Postcode | | Telephone | | |

**GP Details**

| | |
|---|---|
| Name | |
| Address | |
| Tel | |

**Referrer's Details (if not GP)**

| | | | |
|---|---|---|---|
| Name | | Title | |
| Tel | | | |

**TPP GP PRACTICES PLEASE COMPLETE -** consent to access the patient record ***before*** we see them is enormously helpful, please make sure your share is open also

| | | | |
|---|---|---|---|
| Pt. consents to IN share with GP | Y / N | Pt. consents to OUT share with GP | Y / N |
| Pt. consents to IN share with HFSN | Y / N | Pt. consents to OUT share with HFSN | Y / N |

**Investigations**

The patient should have had at least a NT-proBNP ("BNP") and echo along with U&Es. Please provide some details on these tests. If they have had a recent ECG this information is invaluable too

| | Date | Result/comment |
|---|---|---|
| NTproBNP | | |
| Echo | | |
| Trends in U&E | | |
| ECG | | |

**Current Condition and REASON FOR REFERRAL – MUST BE COMPLETED**

| Brief history of illness. (Please also include any factors that may affect staff safety including if there are communication/memory issues and the patient prefers us to contact a nominated other party): |
|---|
| |

**Important information**

| Other in patient medical issues /events/ medical intolerance | |
|---|---|
| | |
| No of acute admissions in last year | |

**Current Medications**

| Drug | Dose | Frequency | Start Date if Known |
|---|---|---|---|
| | | | |

**Appendix 2 Patient Information leaflet- ACEi**

## PATIENT INFORMATION SHEET FOR ACE INHIBITORS IN HEART FAILURE

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

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

### Why ACE Inhibitors?

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

### How do they work in Heart Failure?

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

### Side Effects

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

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

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

***Cough*** - This is also a quite common side effect. Cough is also a symptom of heart failure and so the ACE Inhibitor is not always the cause of the cough. If your cough is particularly troublesome tell your Doctor/Heart Failure Nurse so that if necessary your dose can be lowered or an alternative medicine tried.

***Swelling of your lips and throat*** - This is extremely rare. If this happens to you it is vital that you dial 999 and get medical help immediately.

***Starting the Treatment***

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

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

**Taking Your First Dose or Increasing Your Dose**

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

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

| ACE inhibitor | Starting dose | Target dose |
|---|---|---|
| Lisinopril | 2.5mg once daily | 20-35mg once daily |
| Ramipril | 2.5mg once daily | 5mg twice daily or 10mg once daily |
| Enalapril | 2.5mg twice daily | 20mg twice daily |

**Ongoing Care**

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

**Where to get Help and Advice**

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

Your GP, who you can contact in the usual way.
Your Heart Failure Nurse: Chesterfield link - **01246 253061**
Derby link - **01332 564879 (London Road Team); 01332 789 205 (RDH Team)** Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.

## Appendix 3 Patient Information leaflet- beta-blockers

## PATIENT INFORMATION SHEET FOR BETA-BLOCKERS IN HEART FAILURE

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

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

### Why Beta-blockers?

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

### How do They Work in Heart Failure?

**There are 2 main benefits for taking Beta-blockers in heart failure.**

Firstly they work by slowing the heart beat down which takes some of the work load off the heart and allows more time for the heart to fill with blood in between each heart beat.

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

### Side Effects

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

### Starting the Treatment

The 2 main Beta-blockers we use in heart failure are called Bisoprolol and Carvedilol.

If we were to block the action of adrenaline on the heart all at once then the function of the heart may get worse. For this reason beta-blockers are started at very low doses to allow the heart to get used to their actions. The dosage is then built up slowly over the next few months. You will get benefit even from the lower doses but the full benefit is gained at the higher doses and may take 3 – 6 months to take effect.

Start with a low dose (see starting and target doses) and double the dose at not less than two-weekly intervals. Aim for the target dose or, failing that, the highest tolerated dose.

| Beta blocker | Starting dose | Target dose |
|---|---|---|
| Bisoprolol | 1.25mg once daily | 10mg once daily |
| Carvedilol | 3.125mg twice daily | 25-50mg twice daily |

**Taking Your First Dose**

It is recommended that you are supervised either at home by a family member or at your GP Practice/ Clinic for 3-4 hours after taking your first dose. This is to ensure that in the rare event of any problems they are spotted immediately. Plan a quiet few hours and ensure that for the first week taking a beta-blocker that you are not too busy.

**Important Information**

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

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

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

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

***Increase in weight*** – You will already have been asked to weigh yourself daily to monitor your heart failure. This is especially important if we change your treatment. If your weight increases over 2-3 days by 1-2 kgs (3-4lbs) then follow the flexible diuretic regime below to help clear or prevent any excess fluid from building up in your body:-

- If you already take 40mgs Furosemide once a day increase to 80mgs once a day for 3 days, then go back to your 40mgs dose.
- If you are taking 80mgs Furosemide once a day increase to 80mgs twice a day for 3 days, then go back to your 80mg dose.
- If you are already taking 80 mgs twice a day please seek help from the person who initiated your beta-blocker dose.

**Ongoing Care**

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

**Where to get Help and Advice**

**It is best to seek advice from the person/service that has initiated and is increasing your Beta- blocker dose**

Your GP who you can contact in the usual way
Your Heart Failure Nurse:
Chesterfield link - **01246 253061**
Derby link - **01332 564879 (London Road Team); 01332 789 205 (RDH Team)**
Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.