MANAGEMENT OF HEART FAILURE with Reduced Ejection Fraction (HFREF)

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

- Aim for the target dose of ACE inhibitor and beta blocker; or, failing that, the maximum tolerated dose.

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

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

- Monitoring renal function has a very important role in heart failure management. This should be done 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/1.73m² consider lower doses and/or slower titration of dose of ACEI or ARB, MRA & digoxin.

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

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

- Sacubitril valsartan is a treatment option to be used as per NICE TA 388. Treatment with sacubitril/valsartan is initiated by specialist and may be continued under shared care. Patients who commence treatment will have their ACE or ARB discontinued at least 36 hours before treatment is started. (See appendix 3 for further details)

- Dapagliflozin is recommended as a treatment option as per NICE TA679. Treatment with dapagliflozin should be initiated by the specialist and stabilised before transferring the patient to primary care. Not to be used in patients with type 1 diabetes. Counsel patients on sick day rule. (See management algorithm and appendix 4 for further details, including Patient information leaflets by Trent Diabetes, or PIL produced by manufacturer which can be downloaded from forxiga.co.uk website by a Healthcare professional)

- Specialist advice should be sought for patients who deteriorate after having been stable for a number of years on optimum pharmacological treatment with an unaccountable cause.
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<th>Date updated</th>
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<tr>
<td>p.3/4 updated to remove recommendation to refer all heart failure to specialist team</td>
<td>April 2019</td>
</tr>
<tr>
<td>Dapagliflozin as per NICE TA679, prescribing information added</td>
<td>April 2021</td>
</tr>
</tbody>
</table>

Key

ACEi       angiotensin converting enzyme inhibitor
ARB        angiotensin receptor blockers
BNP        B-type natriuretic peptide
cRT        cardiac resynchronisation therapy
eGFR       estimated glomerular filtration rate
ECG        Electrocardiogram
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
TFT         thyroid function test
U&Es       serum urea & electrolytes
Definition
Heart failure with reduced ejection fraction (HFREF) - heart failure with an ejection fraction below 40%

1. Key recommendations

Investigation/diagnosis
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
  - ECG
  - chest X-ray
  - Blood tests: renal function (electrolytes, creatinine, eGFR), FBC, TFT, LFT, HbA1c, lipids
  - urinalysis
  - peak flow or spirometry

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.

Transthoracic echocardiography should be performed to exclude important valve disease, assess the systolic function of the left ventricle and detect intracardiac shunts.

Monitoring
All patients with heart failure are at risk of renal impairment and hyperkalaemia. This is a consequence of common co-morbidities (e.g. diabetes), drug treatment, or just of the heart failure itself. Monitoring renal function has a very important role in heart failure management.

- Measure at frequent intervals when there is a change in drug treatment or an acute change in the patient’s condition. Heart failure treatment, especially the combination of ACEi and MRA puts the patient at risk of acute decline in renal function and hyperkalaemia.
- Check renal function every 6 months when patients are clinically stable and on stable doses of medication.
- In the event of intercurrent illness, especially diarrhoea and vomiting, all patients should be counselled to contact their GP and to stop the ACEi and MRA (normally for 48 hours), until they have had a blood test or once they are better and taking oral fluids. See appendix 5 ‘Medicines and your Kidneys’ patient information leaflet on sick day rules.

Monitoring (minimum of 6 monthly for stable patients) should include:
  - a clinical assessment of functional capacity, fluid status, cardiac rhythm, and cognitive and nutritional status
  - a review of medication, including need for changes (e.g. cessation of negatively inotropic calcium channel antagonists e.g. verapamil, diltiazem) and possible side effects
  - U&Es and eGFR
  - In patients that do not respond to treatment, an assessment and referral for escalation of therapy may be required either to a HF specialist nurse service or cardiology.

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

Supporting patients and carers
Management of heart failure should be seen as a shared responsibility between patient and healthcare professional. Consider referral to a specialist heart failure nurse if appropriate: (see appendix 4 referral form)
- Chesterfield link - 01246 253061
- Derby link - 01332 564879
2. Investigation/Diagnosing heart failure

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

NT-pro BNP
\[<400 \text{ ng/L} \rightarrow \text{Heart failure unlikely consider other diagnosis}\]
\[400-2000 \text{ ng/L} \rightarrow \text{Refer for urgent Echo To be done within 6 weeks}\]
\[>2000 \text{ ng/L or pregnant patients with HF (if admission not indicated)} \rightarrow \text{Refer for urgent Echo To be done within 2 weeks}\]

Upon confirmation of HF GP can commence appropriate treatment
Seek specialist advice/referral if any problem arises

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 serum natriuretic peptides. Therefore, when questioning the diagnosis in patients on treatment either stop their medication for three days before taking the test or leave on treatment and get an ECHO.

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)

NEW YORK CLASSIFICATION

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

- Patient with symptomatic HFREF
  - Therapy with ACEi and beta-blocker (Up-titrate to maximum tolerated evidence-based doses)
  - Still symptomatic
    - Yes: Add MRA antagonist (up-titrate to maximum tolerated evidence-based)
      - Yes: Still symptomatic
        - Yes: EF <40%
          - eGFR>30ml/min: Dapagliflozin 10mg OD as add on to ACEI/ARB, BB ±MRA
          - Able to tolerate ACEI (or ARB): Sacubitril/Valsartan ² to replace ACE-I (or ARB)
          - QRS duration >120 msec: Evaluate need for CRT³
          - Sinus rhythm, HR ≥75 bpm: Ivabradine⁴
        - No: EF <35%
          - Specialist assessment
    - No
  - These above treatments may be combined if indicated
  - Resistant symptoms
    - Yes: Consider digoxin or H-ISDN⁵ or LVAD⁶, or heart transplantation
    - No: No further action required

1. Consider an ICD in line with ‘Implantable cardiovascular defibrillators for arrhythmias’ (NICE TA 314).
2. Sacubitril/Valsartan for treating chronic heart failure as per NICE TA388.

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3. Consider CRT in line with ‘Cardiac resynchronisation therapy for the treatment of heart failure’ (NICE TA 314).
4. Ivabradine for treating chronic heart failure as per NICE TA 267.
5. Hydralazine in combination with nitrate (especially in people of African or Caribbean origin with moderate to severe heart failure).
6. LVAD- left ventricular assist device.

4. Drug therapy

All patients with HFREF should be offered treatment with an ACEi and a Beta-blockers licensed for use in heart failure (even if rendered asymptomatic with diuretic and ACEi), but only start one drug at a time. ACEi is usually (but not necessarily) initiated first, but there may be clinical reasons for starting a beta-blocker first e.g. additional anti-anginal treatment needed.

Close monitoring is required during initiation and ongoing drug treatment.
Monitor response to titration of medications closely in CKD taking into account increased risk of hyperkalaemia. If eGFR <45ml/min/1.73m² consider lower doses and/or slower titration of dose of ACEI or ARB, MRA & digoxin.

Diuretics

- Diuretics should be routinely used for the relief of congestive symptoms and fluid retention in patients with heart failure, and titrated (up and down) according to need, following the initiation of subsequent heart failure therapies.
- The lowest dose required to relieve symptoms/congestion is the optimum dose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>Usually given once a day in the morning, but can be given twice daily (morning and lunchtime) for additional diuresis. Starting dose 20-40mg per day. Usual dose 40-80mg (up to 240mg) per day.</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>2nd line option if lack of efficacy with furosemide. Starting dose 1mg per day to usual daily dose of up to 5mg/day.</td>
</tr>
</tbody>
</table>

- Check renal function and serum electrolytes 1-2 weeks after starting treatment and after each dose titration. If stable then once every 6 months.

Diuretic resistance (after specialist initiation and assessment)

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

ACE inhibitors

- All patients with HFREF should be offered for treatment with an ACEi.
- ACEi therapy should be initiated at the appropriate low dose and titrated upwards at short intervals (eg. every 2 weeks) until the maximum tolerated or target dose is achieved.

Table 1 – starting and target dose for ACEi.

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

- Blood biochemistry (urea, creatinine and electrolytes) should be measured at baseline, 1-2 weeks after initiation and at 1-2 weeks after each dose increment.
- Monitor blood pressure before and after each dose increase. (NICE NG106)
- Once the dose is stable, repeat renal biochemistry after 1 month, and then continue to monitor U&Es and adverse effects at least every 6 months. More frequent monitoring will be dependent on the persons clinical condition, medication regimen or co-morbidities.
Change in renal function:
- A rise in urea, creatinine and potassium is to be expected after initiation of an ACEi.
- An increase in creatinine up to 50% above baseline or 266 micromol/l, whichever is smaller is acceptable; an increase in potassium <5.5mmol/l is acceptable
- If greater rises in creatinine or potassium than those outlined above persist despite adjustment of concomitant medications (e.g. stopping of NSAIDs) other potassium supplements/retaining agents (triamterene, amiloride, spironolactone/ eplerenone) and, if there are no signs of congestion, reducing the dose of diuretic. The dose of the ACE inhibitor should be halved and blood urea, creatinine and electrolytes rechecked within one to two weeks; if there is still an unsatisfactory response specialist advice should be sought.
- If potassium rises to ≥5.5 mmol/l or creatinine increases by >100% or to above 310 micromol/l the ACE inhibitor should be stopped and specialist advice sought.
- Blood urea, creatinine and electrolytes should be monitored frequently and serially until potassium and creatinine have plateaued.

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

Table 2 – starting and stable dose for ARB.

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

- Monitor renal biochemistry, adverse effects, and BP as per advice for ACEi above.

Combination use of medicines blocking renin-angiotensin hormone system (RAS)
- Although the [MHRA 2014](https://www.mhra.gov.uk) advised that the combination use of medicines from two classes of the RAS blocking agents (this includes ACEi, ARBs and aliskiren) is not recommended, there are some patients with heart failure may have a medical need for treatment with an ACEi and ARB. There is some evidence that the benefits of this combination use may outweigh the risks (hyperkalaemia, hypotension, impaired renal function) in a selected group of people with heart failure for whom other treatments are unsuitable.
- Candesartan is a RAS blocking agent licensed as add-on therapy to ACEi for people with symptomatic heart failure who require such a combination despite optimal therapy.
- The triple combination of ACEi, beta-blocker and ARB may be considered for persistently symptomatic patients – to be initiated only by a specialist.
- **The combination of ACE+ARB+MRA together is not recommended.**
First-Line Management of Heart Failure due Reduced Ejection Fraction

Echocardiogram has confirmed HFREF
(mild, moderate or severe; or measured LV ejection fraction less than 40%)

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

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

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

If truly intolerant due to cough of ACEi (except renal dysfunction or hyperkalaemia)
- Start angiotensin receptor antagonist - and titrate doses at intervals of two weeks.
- Check renal biochemistry according to guidelines given above for ACEi.

Once established on ACEi or ARB +/- diuretic
Start titrating Beta blocker- (bisoprolol)

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

NB. ACEi is usually (but not necessarily) initiated first, but there may be clinical reasons for starting a beta-blocker first e.g. additional anti-anginal treatment needed. Use clinical judgement.

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Beta-blockers

- Beta-blockers licensed for use in heart failure should be initiated in patients with symptomatic heart failure due to HFREF after diuretic and usually ACEi therapy (even if rendered asymptomatic with diuretic and ACEi).
- Beta-blockade therapy for heart failure should be introduced in a ‘start low, go slow’ manner, with assessment of heart rate, blood pressure, and clinical status after each titration.
- Patients who develop heart failure due to left ventricular systolic dysfunction and who are already on treatment with a beta-blocker for a concomitant condition (for example, angina, hypertension) should continue with a beta-blocker licensed for heart failure treatment.

Table 3 – starting and target dose for beta blockers

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

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

- Assess heart rate & clinical status (symptoms, signs especially of congestion, body weight) after starting and at each dose titration, and measure blood pressure before and after each dose increment.

Low Heart rate:
If the heart rate is <50 beats/min with worsening symptoms and the patient is symptomatic:

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

Starting bisoprolol in heart failure
The following conditions should be satisfied before starting bisoprolol:

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

(Some of the above may be relative contraindications e.g. NICE recommends the offering of a selective beta-blocker in COPD patients without reversibility – if unsure contact a cardiologist.)
Bisoprolol titration
The treatment with bisoprolol has to be initiated with a titration phase

<table>
<thead>
<tr>
<th>Dose</th>
<th>Duration</th>
<th>Increase to</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.25mg daily</td>
<td>for two weeks</td>
<td>2.5mg once daily for two weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>if well tolerated increase to</td>
</tr>
<tr>
<td>2.5mg daily</td>
<td>for two weeks</td>
<td>3.75mg once daily for two weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>if well tolerated increase to</td>
</tr>
<tr>
<td>3.75mg daily</td>
<td>for four weeks</td>
<td>5mg once daily for four weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>if well tolerated increase to</td>
</tr>
<tr>
<td>5mg daily</td>
<td>for four weeks</td>
<td>7.5mg once daily for four weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>if well tolerated increase to</td>
</tr>
<tr>
<td>7.5mg daily</td>
<td></td>
<td>10mg once daily for the maintenance therapy</td>
</tr>
</tbody>
</table>

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

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

Mineralocorticoid receptor antagonist (MRA)
- Patients with HFREF who remain symptomatic despite optimal therapy should be prescribed spironolactone at a dose of 12.5mg once daily or 25mg on alternate days to 25-50 mg once daily. Target dose is dependent on symptoms and biochemistry stability.
- Eplerenone may be used if spironolactone not suitable (usually male <50years of age due to gynaecomastia risk). Starting dose 25mg once daily with titrated target dose of 50mg once daily usually within 4 weeks.
- Patients with heart failure taking spironolactone should have blood potassium and creatinine levels monitored for signs of hyperkalaemia and/or deteriorating renal function. If hyperkalaemia is a problem then the dose of spironolactone should be halved and biochemistry rechecked. For baseline and continuous monitoring see flowchart on page 11 for recommendations.
- The use of ACE+ARB+MRA together is not recommended
**Algorithm for the use of mineralocorticoid receptor antagonist in Heart Failure due to Reduced Ejection Fraction (HFREF)**

<table>
<thead>
<tr>
<th>Confirmed HFREF and ongoing symptoms of heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitable for initiation of Spironolactone?</td>
</tr>
</tbody>
</table>

**No**

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

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

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

**Yes**

- Indications for Spironolactone after
  - Already on optimum treatment with ACEi, beta-blocker and diuretic
  - **No** evidence of hypovolaemia

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

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

*This monitoring is by local agreement with Derbyshire cardiologists/specialists
**target dose dependent on symptoms and stability of biochemistry.

If spironolactone not suitable (usually male <50 years of age) due to gynaecomastia risk, eplerenone maybe used, usually on recommendation by specialist.

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

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

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

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

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

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

5. 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.

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

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

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

9. ACE inhibitors can often be up-titrated more quickly than recommended. Beta-blockers should always be bumped up slowly. It is sometimes necessary to leave it a lot longer than the suggested two weeks before increasing the dose. Sometimes the improvement in symptoms with beta-blockers is immediate. Sometimes it is necessary to encourage a patient to go through a period of symptom worsening before they feel better.
**Ivabradine** (as per NICE TA 267)

Ivabradine is GREEN after consultant or specialist (with access to a multidisciplinary heart failure team) initiation following a period of 4 weeks on optimised standard therapy with ACEI, beta-blocker and MRA.

- **NICE criteria:**
  - New York Heart Association (NYHA) class II to IV stable chronic heart failure with systolic dysfunction with a left ventricular ejection fraction of 35% or less and
  - who are in sinus rhythm with a heart rate of 75 beats per minute (bpm) or more and
  - who are given ivabradine in combination with standard therapy including beta-blocker therapy, ACEi and aldosterone antagonists, or when beta-blocker therapy is contraindicated or not tolerated.

**MHRA June 2014**, advice for healthcare professionals regarding posology and monitoring:

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

**Sacubitril/ valsartan** (as per NICE TA 388 for treating symptomatic chronic HFREF)

JAPC classified AMBER (February 2019), initiated by cardiology specialist but may be continued in primary care under shared care guideline. (See appendix 3)

- **NICE criteria for initiation:**
  - New York Heart Association (NYHA) class II to IV symptoms and
  - left ventricular ejection fraction of 35% or less and
  - Who are already taking a stable dose of ACEi or an ARB.
- Treatment should not be initiated in patients with serum potassium level >5.4 mmol/l or with SBP <100 mmHg.
- Usual starting dose is one (49/51mg) tablet, twice daily with the dose doubled at 2 to 4 weeks to the target dose of one (97/103mg) twice daily, as tolerated by the patient.
- A starting dose of 24mg/26mg twice daily should be considered for patients with SBP ≥100 to 110 mmHg and in patients with moderate renal impairment (eGFR 30-60 ml/min/1.73 m²)
- **Patients on an ACE inhibitor should have the ACE inhibitor discontinued for 36 hours before initiating sacubitril/valsartan to minimise the risk of angioedema.**
- Periodic blood pressure monitoring (no less than annually) and renal function 3 monthly once stable is recommended. As with ACE inhibitors renal function is measured as baseline and 2-4 weeks after each dose change.

**Tolerability issues & action**

<table>
<thead>
<tr>
<th>Issues</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>SBP ≤95 mmHg or symptomatic hypotension</td>
<td>Adjustment of concomitant medicinal products and/or Temporary down–titration or Discontinuation of sacubitril/valsartan</td>
</tr>
<tr>
<td>hyperkalaemia</td>
<td></td>
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<tr>
<td>renal dysfunction</td>
<td></td>
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</table>
Dapagliflozin NICE TA679 – for treating heart failure with reduced ejection fraction.
JAPC has classified dapagliflozin as GREEN specialist/consultant initiation and stabilisation before transfer to primary care.

**NICE criteria for initiation:**
Dapagliflozin is recommended for use only if used as an add-on to optimised standard care with:
- ACEi or ARB with BB and if tolerated MRA or
- Sacubitril valsartan with BB and if tolerated MRA
- Usual dosage is 10mg once daily with or without food
- For patients with severe hepatic impairment, a starting dose of 5 mg is recommended. This may be increased to 10 mg if well tolerated.

MHRA warning for SGLT2 inhibitors include:
- risk of diabetic ketoacidosis April 2016, June 2015
- reports of Fourniers gangrene, Feb 2019
- increased risk of lower-limb amputation, Mar 2017
- monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness, Mar 2020

See appendix 4 for further prescribing details.

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

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

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

**5. Lifestyle advice**
Appropriate lifestyle advice is probably as important as pharmacological therapy

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

**Salt & fluid intake**
The kidneys avidly retain salt in heart failure and this results in congestion. Advise to reduce intake for people with high levels of salt and/or fluid consumption (aim for salt intake of less than 6g per day) and continue to review the need to restrict salt or fluid. Salt substitutes e.g. 'Lo Salt' contains some sodium and a 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.

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

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

Smoking
Should be strongly discouraged in all patients

References
1. BNF via https://www.medicinescomplete.com/ [accessed 14/11/18]
3. NICE TA 267 Ivabradine for treating chronic heart failure
4. NICE Clinical Knowledge Summaries (CKS)- Chronic Heart Failure [accessed 15/11/18]
5. NICE NG106 Chronic heart failure in adults: diagnosis and management
6. NICE TA 388 Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction
7. NICE TA 679 Dapagliflozin for treating heart failure with reduced ejection fraction

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

Further Resources
British Heart Foundation patient information leaflet ‘Medicines for my heart’
https://www.bhf.org.uk/informationsupport/treatments/medication

NHS England AKI Programme (Think Kidneys):
www.thinkkidneys.nhs.uk

Open access e-learning package for primary care:
http://www.uhl-library.nhs.uk/aki_gp/index.html

NICE AKI guidelines (CG169):
https://www.nice.org.uk/guidance/cg16
APPENDIX 1

PATIENT INFORMATION SHEET FOR ACE INHIBITORS IN HEART FAILURE

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

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

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

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

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

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

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

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

Swelling of your lips and throat - This is extremely rare. If this happens to you it is vital that you dial 999 and get medical help immediately.
**Starting the Treatment**
There are a number of different ACE Inhibitors available for you: ramipril, lisinopril, and enalapril are just a few. As with many medications it is important to increase your dose slowly and ensure that you tolerate the dose well at every step.

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

**Taking Your First Dose or Increasing Your Dose**
It is not unusual to feel slightly dizzy for a few days after starting or increasing your ACE Inhibitor. We do advise that you plan a more restful day if possible. If you do experience dizziness please read through the notes above for advice.

The two most commonly used ACE Inhibitors are ramipril and lisinopril. The charts below describe how your dose will increase. Not everyone is able to tolerate the target dose and some people need their dose increasing more slowly than described here.

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

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

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

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

Your GP, who you can contact in the usual way.
Your Heart Failure Nurse: Chesterfield link - **01246 253061**
Derby link - **01332 564879**
Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.
APPENDIX 2

PATIENT INFORMATION SHEET FOR BETA-BLOCKERS IN HEART FAILURE

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

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

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

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

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

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

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

Taking Your First Dose
It is recommended that you are supervised either at home by a family member or at your GP Practice/ Clinic for 3-4 hours after taking your first dose. This is to ensure that in the rare event of any problems they are spotted immediately. Plan a quiet few hours and ensure that for the first week taking a beta-blocker that you are not too busy.
### 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 - **Tel 01332 564879**

Your Hospital Doctor via hospital switchboard and the ward or clinic you attended.
APPENDIX 3 - Algorithm for the use of sacubitril/valsartan by specialist/consultant in heart failure due to reduced rejection fraction (HREF)

At diagnosis does patient have EF<35%  
(Consider if an updated echo is needed)  
   Yes →  
  No → Not Appropriate for Sacubitril/Valsartan

Is the patient in NYHA Class II-IV  
   Yes →  
  No → Not Appropriate for Sacubitril/Valsartan

Has pt been considered for or stable on Beta-blocker  
   Yes →  
  No → Delay Sacubitril/Valsartan until beta-blocker has been tried

Is patient on an optimised dose of ACEi/ARB  
   Yes →  
  No → Titratre to optimised level before considering sacubitril/Valsartan

Is patient stable dose of ACEi/ARB for >4 weeks  
   Yes →  
  No → Ensure 4 week period of stabilisation

Has the patient been trialled with spironolactone  
   Yes →  
  No → Delay Sacubitril/Valsartan until a MRA has been tried

Is eGFR>30ml/min/1.73m²  
   Yes →  
  No → Not Appropriate for Sacubitril/Valsartan

Is K+<5.5mmol/l  
   Yes →  
  No → Not Appropriate for Sacubitril/Valsartan

Is sBP>99bpm  
   Yes →  
  No → Not Appropriate for Sacubitril/Valsartan

Sacubitril/Valsartan indicated  
Check no absolute contra-indications or caution and review co-administration warnings.
APPENDIX 4 - Algorithm for the use of SGLT2 inhibitors in heart failure due to reduced ejection fraction (HFREF) (Specialist initiation). Use diabetic guideline if using primarily to treat diabetes

Does patient have EF<40% (Consider if an updated echo is needed)

Yes

Is the patient in NYHA Class II-IV

Yes

Has ACEi/ARB/ARNI been considered, and if appropriate, tried and optimised

No

Titrate to stable optimised dose before considering SGLT2i

Yes

Has beta-blocker been considered, and if appropriate, tried and optimised

No

Titrate to stable optimised dose before considering SGLT2i

Yes

Has MRA been considered, and if appropriate, tried and optimised

No

Titrate to stable optimised dose before considering SGLT2i

Yes

Is eGFR>30 (for dapagliflozin)

No

Not Appropriate for SGLT2i

Yes

Correct hypovolaemia before considering SGLT2i

Yes

Is there ABSENCE of signs/symptoms of hypovolaemia

No

Not Appropriate for SGLT2i

Yes

Is the patient a diabetic

Type 2

SGLT2i likely indicated

Doses of hypoglycaemics may need adjusting-Liaise with primary care/specialist diabetes services to review before prescribing SGLT2i

Type 1

STOP! SGLT2i contraindicated

SGLT2i indicated
Prescribing notes:
Dapagliflozin is licensed for the treatment of heart failure with reduced ejection fraction (with or without type diabetes).
- NYHA II-IV
- ejection fraction ≤40%

Dapagliflozin may be prescribed as an add-on to the standard heart failure treatment
- ACEi or ARB with BB and if tolerated MRA or
- Sacubitril valsartan (ARNI) with BB and if tolerated MRA
- It is not a requirement to swap ACEi/ARB to ARNI before commencing SGLT2i. Clinician should weigh benefits and risks in each individual case.

For the treatment of heart failure dapagliflozin may be used in patients with renal impairment (GFR>30ml/min)

Management of patients with Heart failure and type 2 diabetes
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.

Medication prescribed for glycaemic control must be reviewed in line with the patient’s HbA1c target.

In patients treated with dapagliflozin for heart failure and type 2 diabetes, consider additional glucose-lowering treatment if GFR persistently <45ml/min.

In patients with HFREF and type 2 diabetes dapagliflozin may be prescribed as part of the regimen for glycaemic control in line with national and local Derbyshire management of type 2 diabetes.

In patients with type 2 diabetes it is recommended to liaise with primary care/specialist diabetes services:
- Glitazones are contraindicated in heart failure and if still being used should be stopped.
- Patients on metformin alone will likely tolerate SGLT2 inhibition without reduction in metformin although dose reduction of insulin and sulphonylureas is often necessary to minimize the risk of hypoglycaemia.
- It may also be relevant to consider stopping or swapping other hypoglycaemic therapies depending on baseline glycaemic control and personalised target.
- There is a history of previous/frequent hypoglycaemia
- Refer to Derbyshire diabetes guidelines: management of Type 2 Diabetes.pdf

In patients with HFREF who are already prescribed an alternative SGLT2 inhibitor (e.g. empagliflozin, canagliflozin) for the management of type 2 diabetes this may be continued in line with the licence for the prescribed product (or may be switched to dapagliflozin – a clinical decision should be undertaken between clinician and patient).
Contraindications
- Hypersensitivity to the active substances or to any of the excipients
- Type 1 diabetes
- eGFR<30ml/min/1.73m²
- any history of diabetic ketoacidosis
- pregnancy or breastfeeding
- <18 years, not recommended

Cautions
- Correction of hypovolaemia may require reduction or withdrawal of diuretics and review of fluid intake. In euvoelaemic patients who require a regular diuretic it may be appropriate to reduce diuretic by ~40mg furosemide equivalent.
- systolic BP <95mmHg
- For patients with severe hepatic impairment, a starting dose of 5 mg is recommended. This may be increased to 10 mg if well tolerated.
- History of recurrent urinary tract infections or candida

Baseline monitoring for dapagliflozin by specialist:
- U&Es including renal and hepatic function at initiation
- Blood pressure and volume status at initiation
- Re-check renal function and blood pressure 4 weeks after initiation
  - at 4 weeks there is an expected dip in eGFR of up to 20% for which there is no reason to withdraw SGLT2i
- Blood pressure and volume status should be checked after initiation
- For type 2 diabetics, check:
  - HbA1c level (in last 3 months), if no recent changes in diabetic therapy
  - if recent therapy change, need an up to date HbA1c
- Before initiating dapagliflozin, factors in the patient history that may predispose to ketoacidosis should be considered.

Handover to GP from Heart failure specialist

Diabetic and HF patients
When advising primary care that an SGLT2i has been started in a diabetic patient with heart failure, emphasise to the GP that this 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 unless eGFR falls below 30ml/min/1.73m².
- Diabetic guidelines – for continued therapy with SGLT2i, it must show a HbA1c reduction ≥5.5 mmol/mol (0.5%) in 6 months or the SGLT2i stops if eGFR <45 ml/min/1.73m² and can only be started if eGFR >60 ml/min/1.73m² due to efficacy in lowering A1c. The SGLT2i should not be stopped inadvertently.

Non-diabetic patients with HF
When advising primary care that an SGLT2i has been started in a non-diabetic patients with heart failure, emphasise to the GP that this has been added for heart failure prognosis and symptoms and not because the patient is diabetic and that the medication should not be stopped unless eGFR falls below 30ml/min/1.73m².
Continued monitoring for dapagliflozin by GP
Monitoring of renal function (SPC)
- Annual GFR
- Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter.
- For renal function with GFR < 60 mL/min, at least 2 to 4 times per year.

In case of intercurrent conditions that may lead to volume depletion (e.g. gastrointestinal illness), careful monitoring of volume status is recommended:
- physical examination
- blood pressure measurements
- Laboratory tests including haematocrit and electrolytes

Temporary interruption of treatment with dapagliflozin is recommended for patients who develop volume depletion until the depletion is corrected

Common Co-administration Cautions for SGLT2inhibitors
Interactions with most medications with which there is an interaction will result in either:
- hypotension due to blood pressure lowering effect
- hypoglycaemia due to blood glucose reduction. See Interactions | BNF content published by NICE for specifics.

Patient counselling and advice

Risk of diabetic ketoacidosis (DKA)
Inform patients of the 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. 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.

With intercurrent illness:
Temporarily withhold dapagliflozin (or any other SGLT2 inhibitor) in patients who
- are hospitalised for major surgery or acute serious illnesses (MRHA 2020): blood ketone levels should be monitored (and be normal before restarting)
- also consider stopping in any other hospital admission until patient well/stable -if unsure withhold and seek advice from senior member of the team
- are not eating or drinking
- with inter-current conditions that may lead to volume depletion (e.g. vomiting/diarrhoea)
- have major infection

Treatment may be restarted once the patient's condition has stabilised and they are eating normally for at least 24 hours (providing no new contra-indications exist -see above)

Specific information and education for heart failure and diabetics with heart failure starting SGLT2i should be provided (eg patient information leaflet by Trend diabetes, or PIL produced by manufacturer which can be downloaded by healthcare professionals from forxiga.co.uk)
APPENDIX 5 DCHS Heart Failure Specialist Service

DCHS Heart Failure Specialist Service

GP Referral Criteria and Contact Details

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

- □ Aged 18+ (unless referred by consultant Cardiologist)
- □ Registered with a GP in Derbyshire County or Derby City PCT
- □ 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, faxed or emailed to:

The Community Heart Failure Nursing Service

<table>
<thead>
<tr>
<th>Heart failure Team (North)</th>
<th>Heart failure Team (South)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Covering GPs in Chesterfield, North East and High Peak and Dales areas)</td>
<td>(Covering GPs in Erewash, Amber Valley, Derbyshire Dales and City areas)</td>
</tr>
<tr>
<td>Heart Failure Nurse Services</td>
<td>Heart Failure Nurse Services</td>
</tr>
<tr>
<td>Welbeck Suite, Walton Hospital</td>
<td>Junction 10 level 5</td>
</tr>
<tr>
<td>Whitecotes Lane</td>
<td>Derbyshire Royal Infirmary</td>
</tr>
<tr>
<td>Chesterfield</td>
<td>London Road</td>
</tr>
<tr>
<td>S30 3HW</td>
<td>Derby, DE12QY</td>
</tr>
<tr>
<td>Tel: 01246 253061</td>
<td>Tel 01332 258131</td>
</tr>
<tr>
<td>Monday to Friday 9 – 4pm</td>
<td>Monday to Friday 9 – 4pm</td>
</tr>
<tr>
<td>(excl. bank holidays)</td>
<td>(excl. bank holidays)</td>
</tr>
<tr>
<td><a href="mailto:DCHST.heartfailurenorth@nhs.net">DCHST.heartfailurenorth@nhs.net</a></td>
<td><a href="mailto:DCHST.heartfailuresouth@nhs.net">DCHST.heartfailuresouth@nhs.net</a></td>
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</table>
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 (pg 1).

**Patient Details**

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

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>Tel</th>
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<tr>
<td>Referrer’s Details (if not GP)</td>
<td>Name</td>
<td>Title</td>
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</table>

**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

<table>
<thead>
<tr>
<th>Date</th>
<th>Result/comment</th>
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<tbody>
<tr>
<td>BNP</td>
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<tr>
<td>Echo</td>
<td></td>
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<tr>
<td>Trends in U&amp;E</td>
<td></td>
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<tr>
<td>ECG</td>
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**Current Condition and REASON FOR REFERRAL – MUST BE COMPLETED**

Brief history of illness. (Please also include any factors that may affect staff safety 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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Start Date if Known</th>
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**APPENDIX 6** Medicines and your kidney patient information leaflet
Why have I been given this leaflet?

The medicines you are taking are named on the front cover of this leaflet.

These tablets are good for your medical condition. However, if your body becomes short of fluid (dehydration), this medicine can sometimes stop your kidneys from working as they should.

The most common reasons for becoming dehydrated are:

- Vomiting
- Diarrhoea
- High temperatures or fevers
- Not being able to drink normally

If you do develop diarrhoea, vomiting or high fevers, try to drink more.

What should I do with my medicines if I become dehydrated?

If you:

- are not able to drink a normal amount of fluid,
- develop diarrhoea or vomiting or
- develop fevers,

you should temporarily stop taking the medicine(s) named on the front of the leaflet. This is to help protect your kidneys.

Once you are better and can drink normally, you should restart your medicine. For most people this is within 48 hours.

If you remain unwell for longer than this, contact your doctor. It is important to seek medical advice if your symptoms last for more than 48 hours.

Is there anything else I should do when I am dehydrated?

You can take paracetamol for pain relief or for a high temperature.

Avoid anti-inflammatory drugs (a type of pain killer) whilst you’re dehydrated. Examples of these medicines are Ibuprofen, Diclofenac or Naproxen.

To find out more about dehydration and your kidneys, see the NHS Choices website at www.nhs.uk

Seek advice from your doctor, pharmacist or nurse if you have any questions about your medicine and its use, or this leaflet.

NHS 111 is available 24 hours a day, 365 days a year, to provide health information.

Just call 111.

Who is giving you this advice?

This advice comes from consultant kidney specialists to try and prevent patients developing kidney problems.

The leaflet has been produced by East Midlands Cardiovascular Strategic Clinical Network based on a leaflet developed by colleagues at Royal Derby Hospital.

Produced May 2015

www.thinkkidneys.nhs.uk

Medicines and Your Kidneys

PATIENT INFORMATION LEAFLET

You have been given this leaflet because you take the following medicine(s):

[Please circle the medicine]

- ACE inhibitors: medicine names ending in "pril" e.g. CAPTOPRIL, ENALAPRIL, LISINOPRIL, PERINDOPRIL, RAMIPRIL
- ARB’s: medicine names ending in "sartan" e.g. CANDESARTAN, IRBESARTAN, LOSARTAN, VALSARTAN
- NSAIDS: anti-inflammatory pain killers e.g. IBUPROFEN, DICLOFENAC, NAPROXEN
- METFORMIN a medicine for diabetes

OTHER (please state):