

## **Practical Guidance on how to use Heart Failure Medications**

This document outlines the evidence, indications, contraindications and practical tips when using commonly prescribed heart failure drugs. Please refer to the BNF SPC for more detailed information.

### **ACE-i/ARBs**

#### ***Why?***

Reduces mortality and hospitalisation – evidence for ACEi includes CONSENSUS, which showed all cause mortality reduced by 40% at 6 months, and SOLVD-TREATMENT, which showed a 26% reduction in all-cause mortality and HF hospitalization rate. CHARM-alternative provided evidence for ARB, showing a combined reduction in CV mortality or HF hospitalisation rate of 23%.

#### ***Dose Targets***

- Ramipril 5mg bd
- Perindopril 8mg od
- Lisinopril 35mg od
- Enalapril 20mg bd (non-formulary –historical use)
- Candesartan 32mg od
- Losartan 100mg od
- Valsartan 160mg bd (non-formulary-historical use)

#### ***Contra-indications***

- History of angioedema
- Known bilateral renal artery stenosis
- Pregnancy/risk of pregnancy
- Severe aortic stenosis (no need to stop if already established but do not start)

#### ***Cautions/Specialist advice***

- Potassium >5mmol/l
- Significant renal dysfunction (eGFR<30ml/min/1.73m<sup>2</sup>)
- Blood pressure <90mmHg systolic
- Beware of drug interactions – risk of hyperkalaemia when combined with potassium-sparing diuretics/MRAs. Hyperkalaemia also a potential risk when combined with trimethoprim.

#### ***Problem-solving***

- Asymptomatic low blood pressure does not usually require any change in therapy
- Symptomatic hypotension is common and often improves with time; need for nitrates and calcium-channel blockers should be reviewed and the doses of these reduced/stopped if appropriate. Diuretic dose could also be reduced if no signs/symptoms of congestion.

- Cough: establish if pre-dates ACEi (overlap in population with HF/population with smoking-related lung disease.) Cough is also a symptom of pulmonary oedema, which should be excluded in a patient with a new worsening cough. If troublesome, consider substitution with an ARB.
- Worsening renal function: accept an increase in creatinine of up to 50% above baseline or  $266\mu\text{mol/l}$  or  $\text{eGFR} < 25\text{ml/min}/1.73\text{m}^2$ , whichever is smaller
- Hyperkalaemia: an increase to  $\leq 5.5\text{mmol/l}$  is acceptable
- If creatinine or potassium does rise excessively, consider stopping concomitant nephrotoxic drugs/if no signs of congestion, reducing dose of diuretic.  
If  $\text{K} > 5.5\text{mmol/l}$  or creatinine increases  $> 100\%$  or to  $> 310\mu\text{mol/l}$ , STOP drug and seek specialist advice.

## **Beta blockers**

### ***Why?***

Multiple studies have shown reduction in all-cause mortality, with reductions of around 34% (COPERNICUS, CIBIS-II and MERIT-HF). Evidence also for reduction in cardiovascular mortality or hospitalisation (by 21% in CIBIS II) and decrease risk of sudden death by 41% in MERIT-HF.

### ***Dose Targets***

- Bisoprolol 10mg od
- Carvedilol 25mg bd
- Nebivolol 10mg od

### ***Contra-indications***

- Second or third degree AV block (in the absence of a permanent pacemaker)
- Critical limb ischaemia
- Asthma – this is a relative contra-indication and if cardio-selective beta-blockers are used, it is not necessarily an absolute contra-indication. Please seek specialist advice if needed.

### ***Problem solving***

- If  $\text{HR} < 50$ , halve dose of beta blocker
- Asymptomatic low blood pressure does not usually require a change in therapy
- Symptomatic hypotension: need for nitrates and calcium-channel blockers should be reviewed and the doses of these reduced/stopped if appropriate. Diuretic dose could also be reduced if no signs/symptoms of congestion.

## **MRAs**

### ***Why?***

Use of spironolactone in the RALES trial resulted in a 30% reduction in all-cause mortality and a reduction in cardiac hospitalization rate by 35%. The EMPHASIS-HF trial showed a reduction in all-cause mortality by 24% and HF hospitalisation rate by 42%.

### ***Dose Targets***

- Spironolactone 50mg od
- Eplerenone 50mg od

### ***Cautions/seek specialist advice***

- Potassium >5mmol/L
- Significant renal dysfunction – creatinine >221µmol/l or eGFR <30ml/min/1.73m<sup>2</sup>
- Beware of interactions with other drugs that increase potassium, and potential interaction with trimethoprim

### ***Problem-solving***

- If K rises to above 5.5mmol/l or creatinine rises to >221µmol/l or eGFR <30ml/min/1.73m<sup>2</sup>, halve dose and monitor carefully
- If K<sup>+</sup> rises to >6.0 mmol/L or creatinine to >310 µmol (3.5 mg/dL) eGFR <20 mL/min/1.73 m<sup>2</sup>, stop MRA immediately and seek specialist advice
- Male patients may rarely develop breast discomfort or gynaecomastia with spironolactone; if this occurs, please consider referral to secondary care to switch to eplerenone.
- Prescribing guidance available on formulary website [HERE](#)

## **Ivabradine**

### ***Why?***

In patients with an EF of ≤ 35%, ivabradine decreased the combined CV mortality or HF hospitalisation rate by 18%.

***Dose Target:*** 7.5mg bd

### ***Contra-indications***

- Severe liver or renal dysfunction
- Pregnancy or breastfeeding
- Persistent/continuous AF (will not have an effect)
- Resting HR <70bpm

### ***Cautions/seek specialist advice***

- Moderate liver dysfunction
- Chronic retinal diseases
- Interactions with drugs that are strong inhibitors of p450 (e.g. antifungal azoles, macrolide antibiotics, HIV protease inhibitors)

### ***Problem solving***

- If HR persistently <50bpm on treatment, reduce dose or stop
- Visual phenomena are usually transient and disappear during the first few months of treatment. However, if they are problematic to the patient, it should be stopped
- Shared Care Protocol available on formulary website [HERE](#)

### **Sacubitril with valsartan (Entresto)**

#### ***Why?***

The PARADIGM-HF study showed that compared to ACEi, use of Entresto showed a risk reduction in all cause mortality by 16%, cardiovascular mortality by 20% and heart failure hospitalisation by 21%.

NICE TA388 states it is recommended in patients with NYHA class II to IV symptoms AND LVEF  $\leq$ 35% AND who are already on a stable dose of ACEi/ARB (but note this would have to be stopped for 36 hrs prior to initiating)

**Dose Target:** sacubitril 97mg/valsartan 103mg (one tablet) bd

#### ***Contraindications***

- Use of ACE-i – do not initiate until at least 36 hours after discontinuation of ACE-i
- Concomitant use of ARB
- Systolic BP <100mg
- Severe liver impairment

Shared care protocol available on formulary website [HERE](#)

### **Digoxin**

#### ***Why?***

The DIG trial showed a 28% risk reduction in hospitalisation for heart failure and a trend towards decrease in the risk of death

#### ***Cautions***

- Increased risk of digoxin toxicity if patient has hypercalcaemia, hypokalaemia or hypomagnesaemia

- Should not be used in the elderly at a long-term dose >125mcg if eGFR <30ml/minute/1.73m<sup>2</sup> due to increased risk of toxicity
- Interactions with other drugs which may increase risk of digoxin toxicity– see BNF but note these include macrolide antibiotics, colecalciferol, some antifungals, amiodarone and aminophylline

### **SGLT2 inhibitors** (refer to dapagliflozin & empagliflozin guidance)

#### **Why?**

Recent studies (DAPA-HF, EMPEROR-Reduced) have shown the beneficial effects of SGLT2 inhibitors in patients with chronic heart failure both with and without pre-existing type 2 Diabetes Mellitus. There does appear to be both a mortality benefit as well as reduction in heart failure admissions and improvement in renal function.

Consider adding a SGLT2i to optimal medical treatment for **symptomatic chronic heart failure** (NYHA class II,III, IV) in patients with an **ejection fraction of <50% and NTproBNP > 600pg/ml** (or > 900 pg/ml if in AF) **or** >400 pg/ml if hospitalised in last 12 months for HF with eGFR≥15ml/min/1.73m<sup>2</sup> (dapagliflozin) or eGFR≥20ml/min/1.73m<sup>2</sup> (empagliflozin).

#### **Recommended drug and doses:**

Dapagliflozin 10 mg once daily refer to NICE guidelines (<https://www.nice.org.uk/guidance/TA679>)

#### **Or**

Empagliflozin 10mg once daily refer to NICE guidelines (<https://www.nice.org.uk/guidance/ta773>)

#### **Cautions/Seek Specialist advice**

Avoid if

- symptomatic hypotension or BP <95mmHg
- eGFR < 15 ml/min/1.73m<sup>2</sup> (dapagliflozin) or eGFR < 20 ml/min/1.73m<sup>2</sup> (empagliflozin)

#### **Potassium Binders**

Refer to adult treatment pathway for potassium binders (sodium zirconium cyclosilicate and patiomer calcium) for persistent hyperkalaemia for patients with chronic kidney disease (stages 3b-5) or heart failure [here](#) (TLS Amber specialist initiated for this indication).

#### **References:**

1. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure – Web Addenda - [https://www.escardio.org/static-file/Escardio/Guidelines/ehw128\\_Addenda.pdf](https://www.escardio.org/static-file/Escardio/Guidelines/ehw128_Addenda.pdf)
2. British National Formulary <https://bnf.nice.org.uk/>