First Line HF medication management.

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The Four Pillars of Heart Failure

Consider additional therapies

First Line treatment of Heart Failure (HF-REF) should be an ACE inhibitor and Beta Blocker, clinical judgement should be used to determine which commences first.

The recommendation to prescribe an ACE-inhibitor to all people with heart failure with reduced ejection fraction (HF-REF) is based on the evidence and efficacy in reducing mortality and morbidity in NICE guidelines, (NICE, 2018) and the European Society of Cardiology (ESC,2021).

An ARB should be used as an alternative for people with HF-REF who cannot tolerate the side effects of ACE inhibitors.

ACE inhibitors

Ramipril, Lisinopril,Perindopril, Enalapril BD

- U&E and renal function:- before and 2 weeks after starting an ACE inhibitor, and after each dose increment. If K+ >5.5 half the dose, > 6 stop.
- If AKI occurs, don't stop completely(reduce dose), these are not nephrotoxic medications. Expected to have 25% increase in creatinine level.
- During initiation, renal dysfunction can occur due to a drop in renal perfusion pressure and subsequent decrease in glomerular filtration. This is attributed to the drug's preferential vasodilation of the renal efferent arteriole, which impairs the kidney's ability to compensate for low perfusion states. (Nih.Gov 2018).
- Contraindication:- Aortic stenosis. Previous angioedema
- Low dose and titrate upwards at short intervals (for example, every 2 weeks) until the target or maximum tolerated dose is reached.

ACE inhibitor titration

DRUG	Low starting dose	Normal starting dose	Usual maintenance dose	Max Dose
Ramipril	1.25mg OD	1.25-3.5mg OD	2.5mg – 10mg OD	10mg OD
Lisinopril	2.5mg OD	10mg OD	20mg OD	35mg OD
Perindopril	2mg OD	4mg OD	4 – 8mg OD	8mg OD
Enalapril	2.5mg OD	5mg OD	20mg OD	40mg OD

Lower starting doses are required for people who are more prone to the adverse effects of ACE inhibitors (such as elderly, frail or renally impaired).

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Common side effects of ACE inhibitor

- Cough
- Reduced renal function, including low sodium and raised potassium.
- Runny nose
- Skin rash
- Dizziness
- Nausea, Vomiting, Diarrhoea.
- Headache
- Feeling tired
- Vertigo
- Hypotension
- Increased Falls risk
- Dry mouth

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Less common side effect of ACE

- Angioedema
- Chest Pain
- Extreme hypotension
- Depression
- Confusion
- Photosensitivity
- Jaundice

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ARB titration

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- Candesartan, Losartan, Valsartan
- Only if the patient develop adverse events with ACEI.
- Combination of ACEI and ARB NOT recommended.
- Continue to titrate up to MAX dose unless patient feels unwell, BP too low or renal function becomes impaired.

DRUG	Low starting dose	Usual starting dose	Usual maintenance dose	Maximum Dose
Candesartan	4mg OD	8mg OD	8mg OD	32mg OD
Losartan	12.5mg OD	25mg OD	25-50mg OD	100mg OD
Valsartan	40mg OD	80mg OD	80-160mg OD	320mg OD

Side effects of ARB

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Common

. Abdominal pain

. Back pain

. Nausea, dizziness, headache

. Hypotension & postural hypotension

. Decrease in renal function, hyperkalaemia

Uncommon

. Angioedema

. Skin reactions

Thrombocytopenia

Tips for management of patient symptoms on ACE or ARB.

- If the cough is mild to try and cope with the ACE rather than switching immediately to ARB as slightly better for LV function.
- Only titrate or initiate one drug at a time to observe for adverse reactions.
- Although usually prescribed OD, dose can be split to help with dizziness or prevent interactions with other medications
- Taking at bedtime, helps for side effects to wear off by morning.
- Use alongside antihistamines if skin rashes mild.
- Try to avoid taking at same time as diuretics if BP low
- Consider reducing Loop diuretic if renal impairment occurs and if needing to titrate ACEi further.

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Beta-Blockers.

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Bisoprolol, Nebivolol, Metoprolol, Carvedilol.

Introduce beta-blockers in a **'start low, go slow'** manner. Assess heart rate and clinical status after each titration. Measure blood pressure before and after each dose increment of a beta-blocker

Do not withhold treatment with a beta-blocker solely because of age or the presence of peripheral vascular disease, erectile dysfunction, diabetes, interstitial pulmonary disease or chronic obstructive pulmonary disease.

Switch people- who are already taking a beta-blocker such as Atenolol, Propranalol for angina, anxiety, hypertension, to a beta-blocker licensed for heart failure as above.

Beta Blocker

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The table represents examples of titration of beta blockers

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 12
Bisoprolol (OD)	1.25mg	2.5mg	3.75mg	5mg	5mg	5mg	5mg	7.5mg	10mg
Carvedilol (BD)	3.125mg	3.125mg	6.25mg	6.25mg	12.5mg	12.5mg	25mg	25mg-50mg (if >85kg)	
Nebivolol (OD)	1.25mg	1.25mg	2.5mg	2.5mg	5mg	5mg	10mg		

With **all of us** in mind.

Metoprolol

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In the event of patients with Respiratory conditions who are breathless with betablockers, consider changing to Metoprolol to see if better tolerated before stopping Betablockers entirely. Two weekly titration as below.

Metoprolol	**12.5mg BD**	**25mg bd**	**50mg bd**	**100mg bd Max dose**	

Beta Blocker - Side effects.

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- Heart block/Bradycardia (symptomatic)
- PVD
- Erectile disfunction
- Dizziness
- Asthma/ Bronchospasm
- Aggravation of skin disorders ie psoriasis
- Tiredness
- Nightmares/lucid dreams
- Depression
- Abdominal discomfort
- Dry eyes

Top tips for Beta-blocker use

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- In AF patients require higher heart rate and recommended rate should be 70-80 bpm.
- Over beta-blocking can cause heart to struggle maintaining cardiac output.
- Consider splitting dose if BP low and not having at same time as ACEi.
- If patient symptomatic, try at night.
- If patients experience palpitations in afternoon move betablocker to lunchtime.
- Refer to Erectile Dysfunction specialist team if required.
- Does not require routine bloods, just regular manual pulse checks and BP.
- If heart rate low reduce in first instance but if very bradycardic (<45bpm) stop.

Mineralocorticoid receptor antagonists (MRA) (Spironolactone, Eplerenone)

Offer an MRA, in addition to an ACE inhibitor (or ARB) and beta-blocker, to people who have **heart failure with reduced ejection fraction** if they continue to have symptoms of heart failure.

Gynecomastia, consider Eplerenone.

Other common side effects – hyperkalaemia, hypotension, diarrhoea, hyponatremia

Eplerenone first line MRA post MI. (Awaiting 3-month ECHO post MI for stunning)

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Top Tips with MRAs

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- Monitor U&E for potassium levels 10-14 days post commencing and at any dose changes.
- If patient's potassium low, consider increasing dose as Loop will reduce potassium further.
- Will affect BP monitor every visit and if taking alongside Loop diuretic split timings and give MRA at lunchtime.
- Males may report sensitivity to nipple area. Early signs of gynecomastia.
- In elderly patients consider starting at 12.5mg daily.

Sodium-glucose co transporter 2 inhibitors (SGLT2 inhibitors) Dapagliflozin, Empagliflozin in heart failure

SGLT2 inhibitors are recommended in patients with/without type 2 diabetes with heart failure with reduced ejection fraction

It helps to reduce hospitalization for HF, Major adverse cardiac event(MACE), CVD death.

In patients with type 2 diabetes with CKD (estimated glomerular filtration rate 30 to ≤60 mL $min^{-1}[1.73\ m]^{-2}$ or urinary albumin-to-creatinine ratio >30 mg/g, particularly >300 mg/g) to prevent the progression of CKD therefore give better renal protection.

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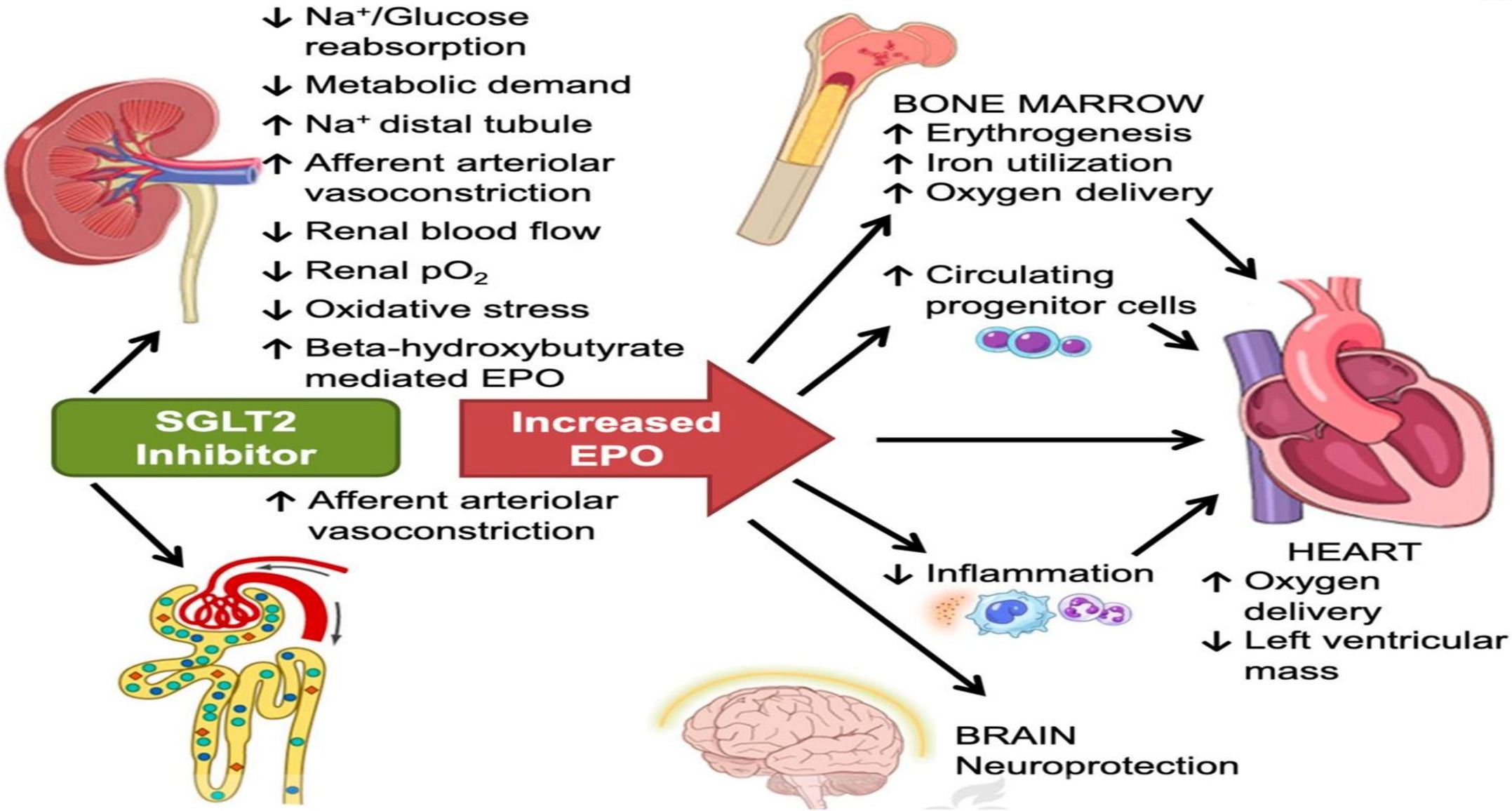
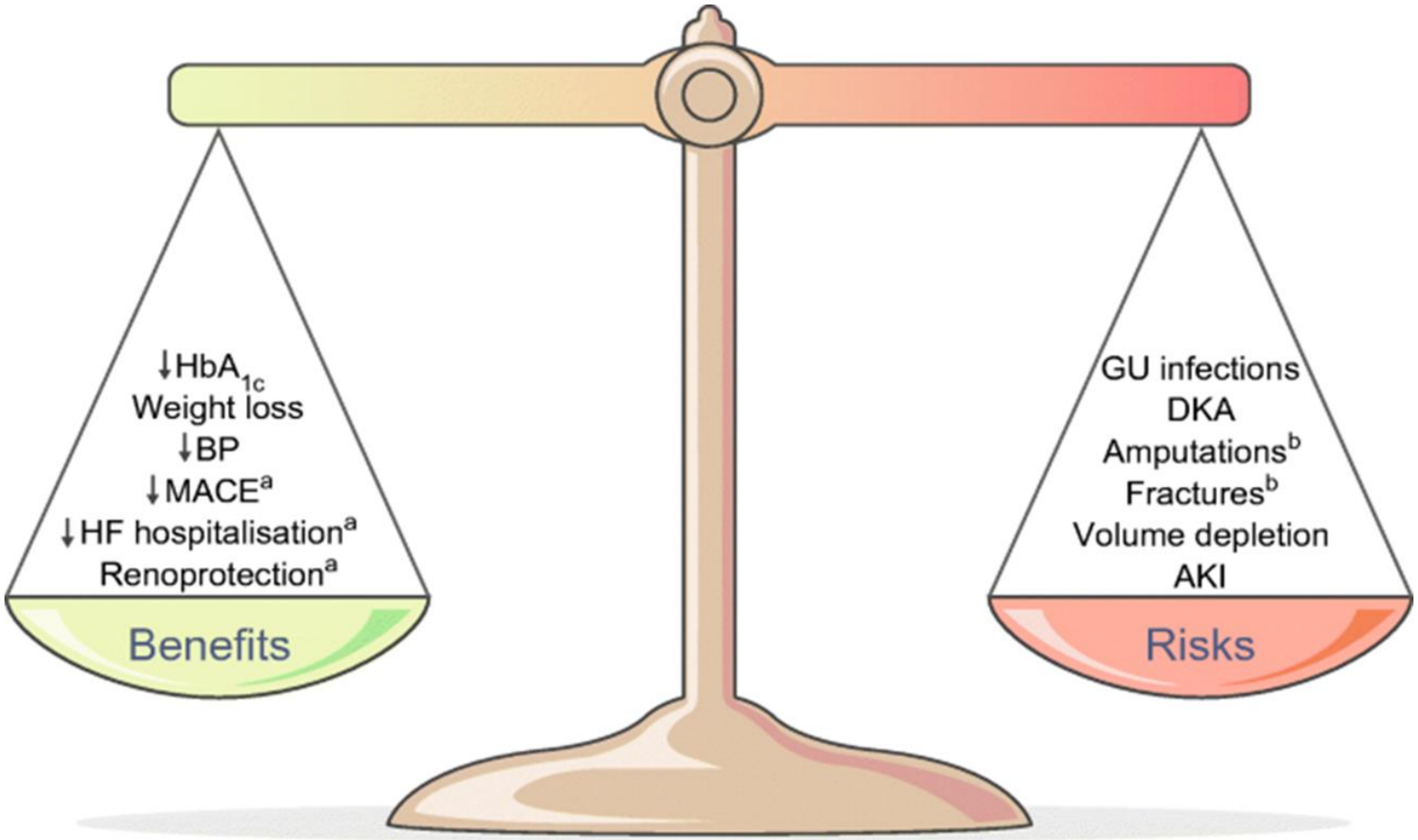

↓ Na⁺/Glucose reabsorption
↓ Metabolic demand
↑ Na⁺ distal tubule
↑ Afferent arteriolar vasoconstriction
↓ Renal blood flow
↓ Renal pO_2
↓ Oxidative stress
↑ Beta-hydroxybutyrate mediated EPO
SGLT2 Inhibitor
↑ Afferent arteriolar vasoconstriction
Increased EPO
BONE MARROW
↑ Erythrogenesis
↑ Iron utilization
↑ Oxygen delivery
↑ Circulating progenitor cells
↓ Inflammation
HEART
↑ Oxygen delivery
↓ Left ventricular mass
BRAIN
Neuroprotection

Adverse Effects



Top Tips for SGLT2i

- Dose in Heart Failure 10mg daily, no need for further titration.
- Leave bloods for 1 month post initiation as worsening of renal function is initially expected but does resolve by week 4.
- NOT for use with Type 1 Diabetes – complete contraindication.
- Monitor for Thrush and UTI symptoms and encourage excellent genital hygiene.
- SGLT2i are effective at lowering BP - monitor for low readings.

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Patient self – monitoring.

- Weigh self-daily initially, to obtain base weight. If puts on 4lbs over couple of days inform team. Increase in pitting oedema.
- Record BPs and Heart Rate (HR) at home to bring to clinic as can have false reading (White Coat) in clinic.
- Eat healthy diet and monitor fluid intake to 2litres daily unless instructed by HFSN or Cardiologist.
- Record symptoms for likely patterns.
- Avoid NSAIDs in HF.
- Low Salt intake NO LOSALT.
- Sick days – D&V stop Loop, MRA and SGLT2i.

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Case Study One

82 y o female with mild LVSD and AF.

Meds: Bisoprolol 1.25mg od, Ramipril 1.25mg od, Apixaban 2.5mg bd, Frusemide 20mg od.

Vital Signs: HR 75 irregular, BP 145/78 no deficit on standing, eGFR 72.

Oedema has improved but remains in ankles

Chest clear

PLAN: ?

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PLAN:

Patient is in Atrial Fibrillation, so HR is stable and ok at this level.

BP remains elevated consider increasing Ramipril

Consider increasing Loop for ankle oedema after next review.

Monitor bloods and BP 2 weeks post to assess renal function and effect of change.

If responds well to therapy continue to increase ACE until optimised as per maximum dose or patient tolerance.

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Case Study Two

55 y o male

POST STEMI – mild LVSD, waiting 3-month post MI ECHO to assess LV for stunning.

Meds: Bisoprolol 1.25mg od, Ramipril 1.25mg od, Eplerenone 12.5mg od, Atorvastatin 80mg on, Aspirin 75mg od, Ticagrelor 90mg bd.

Vital signs: HR 64 regular, BP 128/78 no deficit on standing.

Mild oedema to sockline continues

Bloods Na 138, K 3.4, Creatinine 78, Urea 6.0, eGFR >90.

PLAN?

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PLAN

- In view of oedema and low potassium increase Eplerenone to 25mg od.
- Review bloods, BP and oedema level 2 weeks post increase.
- If oedema remains and potassium in normal range, consider then adding in low dose loop diuretic.

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Case Study Three

- 88 y o male
- Mild LVSD, COPD, T2DM, HTN
- Meds: Bisoprolol 7.5mg od, Ramipril 5mg BD, Fostair, Salbutamol, Carbocysteine, Metformin 500mg bd, Atorvastatin 40mg on.
- Vital Signs: 132/74, HR 49 Reg,
- Patient reports lethargy and sleepy. Increased cough, Nil oedema noted.
- PLAN: ?

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PLAN:

- Check manual pulse for rate and rhythm
- 12 Lead ECG as soon as possible
- Reduce Betablocker by 2.5mg
- Reassess in 1 week and if remains low reduce further unless patient has pacemaker insitu.
- If HR improved but cough remains, consider changing to Metoprolol or consider reducing ACE if dry cough.

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ADVICE AND GUIDANCE

- Advice and guidance at BHNFT is currently available for support in managing heart failure from Cardiology via the e- referral System (eRS)
- Please include:
  - Current signs & symptoms, NYHA score
  - Latest echo findings
  - BP
  - Heart rate/rhythm
  - U&E
  - eGFR/ACR
  - Current medication including dose

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ANY QUESTIONS ?