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ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: Addenda

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Web Table 3 Aetiology of heart failure

There is no agreed or satisfactory classification for the causes of HF, with much overlap between potential categories

Myocardial disease

1. Coronary artery disease
2. Hypertension[a]
3. Cardiomyopathy[b]
   a. Familial
      i. Hypertrophic
      ii. Dilated
      iii. Arrhythmogenic right ventricular cardiomyopathy
      iv. Restrictive
      v. Left ventricular non-compaction
   b. Acquired[c]
      i. Myocarditis (inflammatory cardiomyopathy)
         Infective
         - Bacterial
         - Spirochaetal
         - Fungal
         - Protozoal
         - Parasitic
         - Rickettsial
         - Viral

         Immune-mediated
         - Tetanus toxoid, vaccines, serum sickness
         - Drugs
         - Lymphocytic/giant cell myocarditis
         - Sarcoidosis
         - Autoimmune
         - Eosinophilic (Churg–Strauss)

         Toxic
         - Drugs (e.g. chemotherapy, cocaine)
         - Alcohol
         - Heavy metals (copper, iron, lead)

      ii. Endocrine/nutritional
         - Phaeochromocytoma
         - Vitamin deficiency (e.g. thiamine)
         - Selenium deficiency
         - Hypophosphataemia
         - Hypocalcaemia

      iii. Pregnancy

      iv. Infiltration
         - Amyloidosis
         - Malignancy

Valvular heart disease

Mitral
Aortic
Tricuspid
Pulmonary

Pericardial disease

Constrictive pericarditis
Pericardial effusion

Endocardial disease

- Endomyocardial diseases with hypereosinophilia [hypereosinophilic syndromes (HES)]
- Endomyocardial disease without hypereosinophilia [e.g. endomyocardial fibrosis (EMF)]
- Endocardial fibroelastosis

Congenital heart disease

Arrhythmia

Tachyarrhythmia
  Atrial
  Ventricular
Bradyarrhythmia
  Sinus node dysfunction

Conduction disorders

- Atrioventricular block

High output states

- Anaemia
- Sepsis
- Thyrotoxicosis
- Paget's disease
- Arteriovenous fistula

Volume overload

- Renal failure
- Iatrogenic (e.g. post-operative fluid infusion)

AV = atrioventricular; HF = heart failure.

[a]Both peripheral arterial and myocardial factors contribute to the development of heart failure.

[b]Other inherited diseases may have cardiac effects. e.g. Fabry disease.

Web Table 10: Prognostic variables in heart failure

A very large number of variables have been shown to relate to outcome in HF (and new prognostic markers are regularly identified). This table lists some of the more commonly described prognostic variables.

Demographics, history, and physical examination

- Age, sex, ethnicity, NYHA class, body mass index.
- Signs of congestion, increased jugular venous pressure, third heart sound, low systolic blood pressure, higher heart rate.
- Diabetes mellitus, renal dysfunction, depression, COPD.
- Ischaemic aetiology, history of myocardial infarction.

Routine laboratory tests

- Serum sodium
- Liver enzymes, bilirubin
- Serum creatinine/creatinine clearance/eGFR
- BUN/urea and markers of tubular injury
- Serum albumin
- Uric acid
- Haemoglobin
- Red cell distribution width
- Troponin I/T
- Urinary albumin creatinine ratio

Neurohormones, cytokines, and related factors[a]

- Plasma renin activity
- Angiotensin II
- Aldosterone
- Catecholamines
- (Big) endothelin-1
- Adrenomedullin
- Natriuretic peptides[b]
- Vasopressin/Co-peptin
- Cytokines
- sST-2
- Galectin-3
- Collagen markers

Electrical variables

- QRS width
- LV hypertrophy
- Atrial fibrillation
- Complex ventricular arrhythmias
- Heart rate variability

Imaging variables

- LV internal dimensions and fractional shortening
- Cardiothoracic ratio on chest X-ray
- Wall motion index (various[c])
- Ejection fraction
- Left atrial size
- Restrictive filling pattern/short deceleration time
- Right ventricular function (various[c])
- Inflammation (contrast-enhanced CMR), iron content (in thalassaemia: CMR)
- Amyloidosis (contrast kinetics in CMR)
- Ischaemia and viability imaging, arrhythmogenic substrates

Exercise test/haemodynamic variables (rest/exercise)

- VO_2
- VE/VCO_2 slope
- Max/peak (normal >20 mL/kg/min[d])
- 6-min walk distance (normal >600 m[d])
- Cardiac index (normal >2.5 L/min/m^2)
- LV end-diastolic pressure/pulmonary artery wedge pressure (normal <12 mmHg)

BUN = blood urea nitrogen; CMR = cardiac magenetic resonance; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; HF = heart failure; LV = left ventricular; NYHA = New York Heart Association; sST-2 = soluble ST-2; VO_2 = peak oxygen consumption.

[a]This list is not intended to be comprehensive and other circulating factors may also be associated with prognosis.

[b]Various peptides including C-terminal, N-terminal, and mid-regional are predictive of outcome.

[c]Various measures/classifications can be used, and no single threshold for normal/abnormal can be given.

[d]Functional capacity varies greatly according to prior fitness, age, and sex; values given are a guideline for older (>65 years) adults.

Web Table 11: Practical guidance on the use of angiotensin-convering enzyme inhibitors (or an angiotensin II receptor blocker) in patients with systolic heart failure[a]

WHY?

To improve symptoms and exercise capacity, reduce the risk of HF hospitalization, and increase survival

IN WHOM AND WHEN?

Indications

- Potentially all patients with HF and an EF ≤40%
- First-line treatment (along with beta-blockers and an MRA) in patients with NYHA class II–IV HF; start as early as possible in the course of disease.
- ACE inhibitors are also of benefit in patients with asymptomatic LV systolic dysfunction (NYHA class I)

Contraindications

- History of angioedema[b]
- Known bilateral renal artery stenosis
- Pregnancy/risk of pregnancy

Cautions/seek specialist advice

- Significant hyperkalaemia (K^+ >5.0 mmol/L)
- Significant renal dysfunction (creatinine >221 µmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2)
- Symptomatic or severe asymptomatic hypotension (systolic blood pressure <90 mmHg)

Drug interactions to look out for

- K^+ supplements/ K^+-sparing diuretics, e.g. amiloride and triamterene (beware combination preparations with furosemide), MRAs and renin inhibitors[c]
- NSAIDs[d]
- Trimethoprim/trimethoprim-sulfamethoxazole
- 'Low-salt' substitutes with a high K^+ content

WHERE?

- In the community for most patients
- Exceptions–see Cautions/see specialist advice

WHICH ACE INHIBITOR AND WHAT DOSE? – *see Table 14*

HOW TO USE?

- Check renal function and electrolytes
- Start with a low dose *(see Table 14)*
- Double the dose *at not less than* 2-week intervals in the community. More rapid dose up-titration may be carried out in patients in hospital or who are otherwise closely monitored, tolerability permitting
- Aim for target dose (see above) or, failing that, the highest tolerated dose
- Remember: some ACE inhibitor (or ARB) is better than no ACE inhibitor
- Re-check blood chemistry (urea/BUN, creatinine, K^+) 1–2 weeks after initiation and 1–2 weeks after final dose titration
- Monitor blood chemistry 4 monthly thereafter
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring and dose up-titration

ADVICE TO PATIENT

- Explain expected benefits
- Treatment is given to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival
- Symptoms improve within a few weeks to a few months after starting treatment
- Advise patients to report principal adverse effects, (i.e. dizziness/symptomatic hypotension, cough)–see PROBLEM SOLVING
- Advise patients to avoid NSAIDs[d] not prescribed by a physician (i.e. purchased over-the-counter) and salt substitutes high in K^+–see PROBLEM SOLVING

PROBLEM SOLVING

Asymptomatic low blood pressure

- Doses not usually require any change in therapy

Symptomatic hypotension

- Dizziness/light headedness is common and often improves with time–patients should be reassured
- Reconsider need for nitrates, calcium-channel blockers,[e] and other vasodilators and reduce dose/stop, if posible
- If no signs of symptoms of congestion, consider reducing diuretic dose
- If these measures do not solve problem, seek specialist advice

Cough

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

Worsening renal function and hyperkalaemia

- Some rise in urea (BUN), creatinine, and potassium is to be expected after an ACE inhibitor; if an increase is small and asymptomatic, no action is necessary
- An increase in creatinine of up to 50% above baseline, or 266 µmol/L (3 mg/dL)/eGFR <25 mL/min/1.73 m^2, whichever is the smaller, is acceptable
- An increase in potassium to ≤5.5 mmol/L is acceptable
- If urea, creatinine, or potassium does rise excessively, consider stopping concomitant nephrotoxic drugs (e.g. NSAIDs[d]) and other potassium supplements or retaining agents (triamterene, amiloride) and, if no signs of congestion, reducing the dose of diuretic
- If greater rises in creatinine or potassium than those outlined above persist despite adjustment of concomitant medications, the dose of the ACE inhibitor (or ARB) should be halved and blood chemistry re-checked within 1-2 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 >310 µmol/L (3.5 mg/dL)/eGFR <20 mL/min/1.73 m^2, the ACE inhibitor (or ARB) should be stopped and specialist advice sought
- Blood chemistry should be monitored frequently and serially until potassium and creatinine have plateaued

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BUN = blood urea nitrogen; EF = ejection fraction; HF, heart failure; LV = left ventricular; MRA = mineralocorticoid receptor antagonist; NSAID = non-steroidal anti-inflammatory drug; NYHA = New York Heart Association.

Note: it is very rarely necessary to stop an ACE inhibitor (or ARB), and clinical deterioration is likely if treatment is withdrawn. Ideally, specialist advice should be sought before treatment discontinuation.

[a]The recommendations in this table represent expert opinion based upon relevant clinical trials (drugs, titration schedules, target doses, patient monitoring, treatment benefits, and reported adverse effects) and clinical experience.

[b]The safety of an ARB in patients developing angioedema with an ACE inhibitor is uncertain.

[c]Renin inhibitors are not recommended in heart failure.

[d]Avoid NSAIDs unless essential.

[e]Calcium-channel blockers should be discontinued unless absolutely necessary, and diltiazem and verapamil are potentially harmful because of their negative inotropic action.

WebTable 12: Practical guidance on the use of beta-blockers in patients with systolic heart failure[a]

WHY?

To improve symptoms, reduce the risk of HF hospitalization and increase survival

IN WHOM AND WHEN?

Indications

- Potentially *all* patients with *stable* mild or moderate systolic HF (EF ≤ 40%); patients with severe HF also benefit from beta-blockers but treatment should be started under the care of a specialist
- First-line treatment, along with an ACE inhibitor and an MRA, in patients with *stabilized* HF; start as early as possible in the course of disease

Contraindications

- Asthma (COPD is not a contraindication)
- Second- or third-degree AV block (in the absence of a permanent pacemaker)

Cautions/seek specialist advice

- Severe (NYHA class IV) HF
- Current or recent (<4 weeks) exacerbation of HF (e.g. hospital admission with worsening HF), heart block, or heart rate <60 b.p.m.
- Persisting signs of congestion, hypotension/low blood pressure (systolic <90 mmHg), raised jugular venous pressure, ascites, marked peripheral oedema—try to relieve congestion and achieve 'euvolaemia' before starting beta-blocker

Drug interactions to look out for (because of risk of bradycardia/atrio ventricular block)

- Verapamil, diltiazem (should be discontinued)[b]
- Digoxin, amiodarone, ivabradine

WHERE?

- In the community in stable patients (NYHA class IV/severe HF patients and those with a current/recent exacerbation should be referred for specialist advice)
- In patients hospitalized with worsening HF–after stabilizing, relieving congestion, and, if possible, restoring 'euvolaemia'(but ideally before discharge).
- Other exceptions–see Cautions/see specialist advice

WHICH BETA-BLOCKER AND WHAT DOSE? - *see Table 14*[c]

HOW TO USE?

- Start with a low dose *(see Table 14)*
- Double the dose at *not less than* 2-week intervals (slower up-titration may be needed in some patients)
- Aim for target dose (see above) or, failing that, the highest tolerated dose
- Remember: *some* beta-blocker is better than no beta-blocker
- Monitor heart rate, blood pressure, and clinical status (symptoms, signs–especially signs of congestion, body weight)
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), and dose up-titration

ADVICE TO PATIENT

- Explain expected benefits (see WHY?) and mention possibility of *temporary* adverse effects
- Treatment is given to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival
- Symptomatic improvement may develop slowly after starting treatment, sometimes taking 3–6 months or longer
- *Temporary* symptomatic deterioration *may* occur during initiation or up-titration phase; in the long term, beta-blockers improve well-being
- Advise patient to report deterioration (see PROBLEM SOLVING) and that deterioration (tiredness, fatigue, breathlessness) can usually be easily managed by adjustment of other medication; patients should be advised not to stop beta-blocker therapy without consulting the physician
- To detect and to treat deterioration early, patients should be encouraged to weigh themselves daily (after waking, before dressing, after voiding, before eating) and to increase their diuretic dose should their weight increase, persistently (>2 days), by >1.5–2.0 kg[d]

PROBLEM SOLVING

Worsening symptoms or signs (e.g. increasing dyspnoea, fatigue, oedema, weight gain)

- If increasing congestion, increase dose of diuretic or halve dose of beta-blocker (if increasing diuretic dose does not work)
- If marked fatigue (or bradycardia–see below), halve dose of beta-blocker (rarely necessary); review patient in 1–2 weeks; if not improved, seek specialist advice
- If serious deterioration, halve dose of beta-blocker or stop this treatment (rarely necessary); seek specialist advice

Low heart rate

- If <50 b.p.m. and worsening symptoms, halve dose of beta-blocker, or, if severe deterioration, stop beta-blocker (rarely necessary)
- Review need for other heart rate-slowing drugs (e.g. digoxin, amiodarone, diltiazem, or verapamil[b])
- Arrange electrocardiogram to exclude heart block
- Seek specialist advice

Asymptomatic low blood pressure

- Does not usually require any change in therapy

Symptomatic hypotension

- If dizziness, light headedness, or confusion and a low blood pressure, reconsider need for nitrates, calcium-channel blockers,[b] and other vasodilators and reduce/stop, if possible
- If no signs or symptoms of congestion, consider reducing diuretic dose
- If these measures do not solve problem, seek specialist advice

ACE = angiotensin-converting enzyme; AV = atrioventricular; COPD = chronic obstructive pulmonary disease; HF, heart failure; LV = left ventricular; MRA = mineralocorticoid receptor antagonist; NSAID = non-steroidal anti-inflammatory drug; NYHA = New York Heart Association.

Note: beta-blockers should not be stopped suddenly unless absolutely necessary (there is a risk of a 'rebound' increase in myocardial ischaemia or infarction and arrhythmias). Ideally, specialist advice should be sought before treatment discontinuation.

[a]The recommendations in this table represent expert opinion based upon relevant clinical trials (drugs, titration schedules, target doses, patient monitoring, treatment benefits, and reported adverse effects) and clinical experience.

[b]Calcium-channel blockers should be discontinued unless absolutely necessary, and diltiazem and verapamil are potentially harmful because of their negative inotropic effect.

[c]Metoprolol tartrate should not be used in preference to an evidence-based beta-blocker in HF.

[d]This is generally good advice for all patients with HF.

Web Table 13: Practical guidance on the use of mineralocorticoid receptor antagonists in patients with systolic heart failure[a]

WHY?

To improve symptoms, reduce the risk of HF hospitalization, and increase survival

IN WHOM AND WHEN?

Indications

- Potentially all patients with persisting symptoms (NYHA Class II-IV) and an EF ≤35% despite treatment with an ACE inhibitor (or ARB) and beta-blocker

Cautions/seek specialist advice

- Significant hyperkalaemia (K^+ >5.0 mmol/L)[b]
- Significant renal dysfunction (creatinine >221 μmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2)[b]

Drug interactions to look out for

- K^+ supplements/ K^+-sparing diuretics (e.g. amiloride and triamterene; beware combination preparations with furosemide)
- ACE inhibitors/ARBs/renin inhibitors[c]
- NSAIDs[d]
- Trimethoprim/trimethoprim-sulfamethoxazole
- 'Low-salt' substitutes with a high K^+ content

Contraindication

- Eplerenone–strong CYP3A4 inhibitors, e.g. ketoconazole, itraconazole, nefazodone, telithromycin, clarithromycin, ritonavir, and nelfinavir

WHERE?

- In the community or in the hospital
- Exceptions—see Cautions/seek specialist advice

WHICH MRA AND WHAT DOSE? - *see Table 14*[e]

HOW TO USE?

- Check renal function and electrolytes (particularly K^+)
- Start with a low dose (see above)
- Consider dose up-titration after 4–8 weeks
- Check blood chemistry at 1 and 4 weeks after starting/increasing dose and at 8 and 12 weeks; 6, 9, and 12 months; 4-monthly thereafter
- If K^+ rises above 5.5 mmol/L or creatinine rises to 221 μmol/L (2.5 mg/dL)/eGFR <30 mL/min/1.73 m^2, halve dose and monitor blood chemistry closely
- If K^+ rises to >6.0 mmol/L or creatinine to >310 μmol (3.5 mg/dL) eGFR <20 mL/min/1.73 m^2, stop MRA immediately and seek specialist advice
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring, and dose up-titration

ADVICE TO PATIENT

- Explain expected benefits (see WHY?)
- Treatment is given to improve symptoms, to prevent worsening of HF leading to hospital admission, and to increase survival
- Symptomatic improvement occurs within a few weeks to a few months of starting treatment
- Avoid NSAIDs[d] not prescribed by a physician (i.e. purchased over-the-counter) and salt substitutes high in K^+
- If diarrhoea or vomiting occurs, patients should stop the MRA and contact the physician/nurse

PROBLEM SOLVING

Worsening renal function/hyperkalaemia

- See HOW TO USE?
- The main concern is hyperkalaemia (>6.0 mmol/L); although this was uncommon in RALES and EMPHASIS-HF, it has been seen more commonly in clinical practice
- Conversely, a high-normal K^+ level may be desirable in patients with HF, especially if they are taking digoxin
- It is important to avoid other K^+-retaining drugs (e.g. K^+-sparing diuretics such as amiloride and triamterene) and nephrotoxic agents (e.g. NSAIDs[d])
- The risk of hyperkalaemia and renal dysfunction when an MRA is given to patients already taking both an ACE inhibitor and ARB is higher than when an MRA is added to just an ACE inhibitor or ARB given singly; this triple combination of an ACE inhibitors, ARB and MRA is NOT recommended (see recommendations below)
- Some 'low-salt' substitutes have a high K^+ content
- Male patients treated with spironolactone may uncommonly develop breast discomfort or gynaecomastia (switching to eplerenone should be considered)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; NSAID = non-steroidal anti-inflammatory drug; NYHA = New York Heart Association.

[a]The recommendations in this table represent expert opinion based upon relevant clinical trials (drugs, titration schedules, target doses, patient monitoring, treatment benefits, and reported adverse effects) and clinical experience.

[b]It is extremely important to adhere to these cautions and doses to avoid serious hyperkalaemia.

[c]Renin inhibitors are not recommended in heart failure.

[d]Avoid NSAIDs unless essential.

[e]Cancenone is not recommended in heart failure.

Web Table 15: Practical guidance on the use of diuretics in patients with heart failure (with a reduced or preserved ejection fraction)

WHY?

To relieve breathlessness and oedema in patients with symptoms and signs of congestion

IN WHOM AND WHEN?

Indications

- Potentially all patients with symptoms and signs of congestion, irrespective of EF
- Should always be used in combination with an ACE inhibitor (or ARB), beta-blocker, and an MRA in patients with a reduced EF
- Use minimum dose necessary to maintain euvolaemia–the patient's 'dry weight' (i.e. to keep the patient free of symptoms and signs of congestion)
- Dose may need to be increased or decreased according to the patient's volume status; patients can be educated and trained to alter their own diuretic dose, according to need (based on symptoms, signs and weight changes–see Section 14)

Contraindications

- Not indicated if the patient has never had symptoms or signs of congestion
- Known allergic reaction/other adverse reaction (drug-specific)

Cautions/seek specialist advice

- Significant hypokalaemia (K^+ ≤3.5 mmol/L)–may be made worse by diuretic
- Significant renal dysfunction (creatinine >221 μmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2)–may be made worse by diuretic or patient may not respond to diuretic (especially thiazide diuretic)
- Symptomatic or severe asymptomatic hypotension (systolic blood pressure <90 mmHg)–may be made worse by diuretic-induced hypovolaemia

Drug interactions to look out for

- Combination with ACE inhibitor ARB or renin inhibitors[b]–risk of hypotension (usually not a problem)
- Combination with other diuretics (e.g. loop plus thiazide)–risk of hypovolaemia, hypotension, hypokalaemia, and renal impairment[a]
- NSAIDs[c]–may attenuate effect of diuretic

WHERE?

- In the community for most patients

WHICH DIURETIC AND WHAT DOSE? - *see Table 16*

HOW TO USE?

- Check renal function and electrolytes
- Start with a low dose *(see Table 16)*
- Adjust dose according to symptoms and signs of congestion, blood pressure, and renal function
- Re-check blood chemistry 1–2 weeks after initiation and after any increase in dose (urea/BUN, creatinine, K^+)
- When to stop up-titration, reduce dose, stop treatment–see PROBLEM SOLVING
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring, and dose adjustment (including patient training in dose adjustment)

ADVICE TO PATIENT

- Explain expected benefits
- Symptoms improve quickly–usually within days of starting treatment
- Advise patients to report principal adverse effects (e.g. thirst) (avoid excessive consumption of hypotonic fluids, which can cause hyponatraemia) and dizziness/symptomatic hypotension–see PROBLEM SOLVING
- Advise patients to avoid NSAIDs[b] not prescribed by a physician (i.e. purchased over-the-counter)–may cause diuretic resistance and renal impairment
- Patient may be trained to adjust dose based on symptoms, signs, and changes in weight (if regular weighing)
- Dose may need to be decreased if fluid loss (e.g. due to diarrhoea/vomiting, excessive sweating)

PROBLEM SOLVING

Asymptomatic low blood pressure

- Dose may be reduced if no symptoms or signs of congestion

Symptomatic hypotension

- Causing dizziness/light headedness–reduce dose if no symptoms or signs of congestion
- Reconsider need for nitrates, CCBs,[d] and other vasodilators
- If these measures do not solve problem, seek specialist advice

Hypokalaemia/hypomagnaesaemia

- Increase ACE inhibitor/ARB dose, add MRA, potassium supplements; magnesium supplements

Hyponatraemia

- *Volume depleted:* stop thiazide or switch to loop diuretic, if possible; reduce dose/stop loop diuretics if possible; *volume overloaded:* fluid restriction; increase dose of loop diuretic; consider AVP antagonist (e.g. tolvaptan if available); i.v. inotropic support; consider ultrafiltration

Hyperuricaemia/gout

- Consider allopurinol prophylaxis; for symptomatic gout use colchicine for pain relief; avoid NSAIDs

Hypovolaemia/dehydration

- Assess volume status; consider diuretic dosage reduction

Insufficient diuretic response/diuretic resistance

- Check compliance and fluid intake; increase dose of diuretic; consider switching from furosemide to bumetanide or torasemide; add MRA/increase dose of MRA; combine loop diuretic and thiazide/metolazone[a]; administer loop diuretic twice (or more times) daily or on empty stomach/consider short-term i.v. infusion of loop diuretic; consider ultrafiltration

Renal impairment (rising creatinine/BUN–urea)

- Check for hypovolaemia/dehydration; exclude use of other nephrotoxic agents, e.g. NSAIDs, trimethoprim; withhold MRA; if using concomitant loop and thiazide diuretic stop thiazide diuretic; consider reducing dose of ACE inhibitor/ARB; consider haemofiltration/dialysis

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; AVP = arginine vasopressin; BUN = blood urea nitrogen; CCBs = calcium-channel blockers; EF = ejection fraction; HF = heart failure; i.v. = intravenous; MRA = mineralocorticoid receptor antagonist; NSAIDs = non-steroidal anti-inflammatory drugs.

[a]Usually only needed for a short period–careful monitoring of blood chemistry is essential.

[B]Renin inhibitors are not recommended in heart failure.

[c]Avoid NSAIDs unless essential.

[d]CCBs should be discontinued in patients with systolic HF unless absolutely necessary, and diltiazem and verapamil are potentially harmful in patients with systolic heart failure because of their negative inotropic action.