

Supplementary Table 3. Contraindications or cautions of disease-modifying agents in patients with heart failure reduced ejection fraction

Angiotensin-converting enzyme inhibitors (ACEIs)

Contraindications

- History of angioedema
- Known bilateral renal artery stenosis
- Pregnancy/risk of pregnancy
- Known allergic reaction/other adverse reaction (drug-specific)

Cautions

- Hyperkalemia with $K^+ > 5.0$ mmol/L
- Renal dysfunction with $eGFR < 30$ mL/min/1.73 m²
- Symptomatic or severe asymptomatic hypotension (SBP < 90 mm Hg)

Beta-blockers

Contraindications

- 2nd or 3rd degree AV block (in the absence of a permanent pacemaker)
- Critical limb ischemia
- Asthma (relative contraindication)
- Known allergic reaction/other adverse reaction (drug-specific)

Cautions

- Severe (NYHA class IV) HF
- Current or recent (< 4 weeks) exacerbation of HF, heart block, or HR < 50 bpm
- If persisting signs of congestion, hypotension (SBP < 90 mm Hg), raised jugular venous pressure, ascites, or marked peripheral oedema—try to relieve congestion and achieve ‘euvolemia’ before starting a beta-blocker

Mineralocorticoid receptor antagonists

Cautions

- Hyperkalemia with $K^+ > 5.0$ mmol/L
- Renal dysfunction with $eGFR < 30$ mL/min/1.73 m²

Sacubitril/valsartan (angiotensin receptor-neprilysin inhibitor)

Contraindications

- History of angioedema
- Bilateral renal artery stenosis
- Pregnancy/risk of pregnancy and breastfeeding period
- Known allergic reaction/other adverse reaction (drug-specific)
- $eGFR < 30$ mL/min/1.73 m²
- Symptoms of hypotension or a SBP < 90 mm Hg

Cautions

- A washout period of at least 36 hours after ACEI therapy is required to minimize the risk of angioedema.
- Hyperkalemia with $K^+ > 5.0$ mmol/L

Sodium-glucose co-transporter 2 inhibitors

Contraindications

- Known allergic reaction/other adverse reaction (drug-specific)
- Pregnancy/risk of pregnancy and breastfeeding period
- $eGFR < 20$ mL/min/1.73 m²
- Symptoms of hypotension or a SBP < 95 mm Hg

Cautions

- Individual risk of euglycemic ketoacidosis should be considered
- Genito-urinary and soft tissue infections
- Drug interactions to look out for: insulin, sulfonylurea derivatives, and other anti-diabetic drugs predisposing to hypoglycemia
- Adjustment of diuretics, if needed, to prevent volume depletion

eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; AV, atrioventricular; NYHA, New York Heart Association; HF, heart failure; HR, heart rate.