





Cumulative risk reduction in all-cause mortality if all four evidence-based medical therapies are used: Relative risk reduction 72.9%, Absolute risk reduction: 25.5%, NNT = 3.9, over 24 months



Foundational Drugs for Treating HFrEF (LVEF < 40%)

	COR	LOE	Recommendations
RAAS Inhibitors	1	Α	In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality
	1	Α	In patients with previous or current symptoms of chronic HFrEF, the use of ACEi is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible
	1	B- R	In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality
Beta blockers	1	А	In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality is recommended to reduce mortality and hospitalizations
MRAs	1	А	In patients with HFrEF and NYHA class II to IV symptoms, an MRA is recommended to reduce morbidity and mortality, if eGFR >30 mL/min/ 1.73 m2 and serum potassium is <5.0 mEq/L
SGLT2 Inhibitors	1	А	In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes



Ivabradine (2a) In patients with LVEF ≤ 35% with NYHA II-III; NSR with HR \geq 70 bpm at rest on maximally tolerated Beta-Blockers. Initial dose: 5 mg BID Target dose: 7.5 mg BID Vericiquat (2b) In patients with LVEF ≤ 45%; recent HFH or IV diuretics; elevated NP levels. Initial dose: 2.5 mg QD Target dose: 10 mg QD **Additional** Digoxin (2b) Medical In patients with symptomatic HF despite GDMT or Therapies after unable to tolerate GDMT. Initial dose: 0.125-0.25 mg QID (follow monogram) **GDMT** Target dose: titrate to achieve serum concentration 0.5- < 0.9 ng/ml **Optimization** PUFA (2b) In patients with HF and NYHA II-IV Dose: 1 gram daily of n-3PUFA (850-880 mg of EPA and DHA) Potassium binders (2b) In HF patients with hyperkalemia (≥ 5.5 mEg/L) while taking RAASi. Medications: Patiromer; sodium zirconium cyclosilicate

Abbreviations: DHA indicates docosaexaenoic acid; EPA, eicosapentaenoic acid; GDMT, guideline-directed medical therapy; HF, heart failure; HFH, heart failure hospitalization; HR, heart rate; IV, intravenous; LVEF, left ventricular ejection fraction; NP, natriuretic peptide; NSR, normal sinus rhythm; NYHA, New York Heart Association; PUFA, polyunsaturated fatty acid; and RAASi, renin-angiotensin-aldosterone system inhibitors.



Foundational Drugs for Treating HFpEF

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SGLT2i

COR	LOE	Recommendations	
2b	B-R	In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.	
2b	B-R	In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.	
2a	B-R	In patients with HFpEF, SGLT2is can be beneficial in decreasing HF hospitalizations and cardiovascular mortality	

HFpEF by the Guidelines



