CHF Pharmacotherapy Board Review Table (HFrEF Focus)

Ranking based on mortality reduction, reduction in HF hospitalization, and strength of guideline-supported evidence in chronic HFrEF (EF ≤40%).

Rank	Drug Class	Typical Starting Dose	Target Dose	Mortality Benefit	HF Hospitalization Reduction	Major Adverse Effects	Landmark Clinical Evidence
1	**ARNI (Sacubitril/Valsartan)**	24/26 mg BID or 49/51 mg BID	97/103 mg BID	★★★★★	★★★★★	Hypotension, hyperkalemia, renal dysfunction, angioedema	**PARADIGM-HF**: 20% relative reduction in CV death/HF hospitalization vs enalapril
1	**SGLT2 Inhibitors** (Dapagliflozin, Empagliflozin)	Dapagliflozin 10 mg daily; Empagliflozin 10 mg daily	Same dose	★★★★★	★★★★★	Genital infections, volume depletion, euglycemic DKA (rare)	**DAPA-HF**, **EMPEROR-Reduced**: ~25–30% reduction in CV death/HF hospitalization
1	**Evidence-Based β-Blockers** (Carvedilol, Metoprolol Succinate, Bisoprolol)	Carvedilol 3.125 mg BID; Metoprolol SR 12.5–25 mg daily	Carvedilol 25–50 mg BID; Metoprolol SR 200 mg daily	★★★★★	★★★★☆	Bradycardia, fatigue, hypotension, worsening HF during initiation	**MERIT-HF**, **COPERNICUS**, **CIBIS-II**: ~30–35% mortality reduction
1	**Mineralocorticoid Receptor Antagonists (MRA)** (Spironolactone, Eplerenone)	12.5–25 mg daily	25–50 mg daily	★★★★☆	★★★★☆	Hyperkalemia, renal dysfunction, gynecomastia (spironolactone)	**RALES**, **EMPHASIS-HF**, **EPHESUS**: ~24–30% mortality reduction
2	**ACE Inhibitors** (Enalapril, Lisinopril, Ramipril)	Enalapril 2.5 mg BID	10–20 mg BID	★★★★☆	★★★★☆	Cough, hyperkalemia, renal dysfunction, angioedema	**SOLVD-Treatment**: 16% mortality reduction
2	**ARB** (Valsartan, Candesartan)	Valsartan 40 mg BID	160 mg BID	★★★☆☆	★★★★☆	Hyperkalemia, hypotension, renal dysfunction	**CHARM-Alternative**, **Val-HeFT**
3	**Hydralazine + Isosorbide Dinitrate**	Hydralazine 25 mg TID + ISDN 20 mg TID	Hydralazine 75 mg TID + ISDN 40 mg TID	★★★★☆	★★★☆☆	Headache, hypotension, lupus-like syndrome	**A-HeFT**: 43% mortality reduction in Black patients
4	**Ivabradine**	5 mg BID	7.5 mg BID	★★☆☆☆	★★★★☆	Bradycardia, visual phenomena, AF	**SHIFT**: 26% reduction in HF hospitalization
5	**Vericiguat**	2.5 mg daily	10 mg daily	★★☆☆☆	★★☆☆☆	Hypotension, anemia	**VICTORIA**: modest reduction in composite outcome
5	**Digoxin**	0.125 mg daily	Adjust to serum level 0.5–0.9 ng/mL	No proven mortality benefit	★★★☆☆	Arrhythmias, nausea, visual disturbances	**DIG Trial**: reduced HF admissions only
6	**Loop Diuretics** (Furosemide, Bumetanide, Torsemide)	Furosemide 20–40 mg daily	Titrate to euvolemia	No mortality benefit	Symptom relief only	Hypokalemia, renal dysfunction, ototoxicity	No mortality benefit; essential for congestion management

HFpEF (EF ≥50%)

Drug Class	Evidence
SGLT2 inhibitors	Strongest evidence; **EMPEROR-Preserved**, **DELIVER** reduced HF hospitalization
Diuretics	Symptomatic relief of congestion
MRA	Modest benefit in selected patients (**TOPCAT**)
ARNI	Some reduction in hospitalization (**PARAGON-HF**)
ACEI/ARB	Primarily BP and comorbidity management
Beta-blockers	No proven mortality benefit unless another indication exists

"Fantastic Four" of Modern HFrEF Therapy

Current guidelines prioritize initiation of four foundational therapies as early as possible:

Drug Class	Mortality Benefit	Relative Risk Reduction
ARNI (or ACEI/ARB if ARNI not tolerated)	High	~20%
β-blocker	High	~35%
MRA	Moderate-High	~30%
SGLT2 inhibitor	High	~25%

Combined use of all four therapies is estimated to reduce mortality by >60% compared with traditional therapy alone.

Practical Board Exam Pearls

Clinical Scenario	Drug Choice
Newly diagnosed HFrEF	Start all four foundational agents rapidly
Persistent congestion	Increase loop diuretic
HR >70 bpm in sinus rhythm despite max β-blocker	Add ivabradine
Black patient with NYHA III–IV symptoms	Add hydralazine/isosorbide dinitrate
Post-MI with HFrEF	MRA strongly indicated
Diabetes + HFrEF	SGLT2 inhibitor regardless of HbA1c
Recurrent HF admissions despite GDMT	Consider vericiguat
AF with HFrEF needing rate control	Digoxin may be useful