

Heart Failure Pharmacotherapy

Based on the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

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References:

- [1] Classes of Heart Failure. American Heart Association. May 31, 2017. <https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure>
 [2] Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in Circulation. 2022 May 3;145(18):e1033]. Circulation. 2022;145(18):e895-e1032. doi:10.1161/CIR.0000000000001063

Heart Failure Categories

Stage	LVEF	NYHA Class
A At risk for HF • No HF signs/symptoms • No structural/functional heart disease • No abnormal biomarkers	HFrEF <i>(reduced EF)</i> LVEF ≤ 40%	I • No symptoms from ordinary daily activities
B Pre-HF • No HF signs/symptoms • ONE of the following: (1) Structural heart disease (2) ↑ filling pressures (3) Risk factors PLUS ↑ natriuretic peptides OR persistently ↑ cardiac troponin w/o competing diagnosis	HFimpEF <i>(improved EF)</i> LVEF > 40% <i>(upon follow up after a previous measurement of LVEF ≤ 40%)</i>	II • No symptom at rest • Ordinary daily physical activities cause HF symptoms
C Symptomatic HF • Structural heart disease AND • Current or previous HF symptoms	HFmrEF <i>(mildly reduced EF)</i> LVEF 41-49% <i>(w/ evidence of spontaneous/provokable ↑ LV filling pressures)</i>	III • No symptom at rest • Activities lighter than ordinary daily physical activities cause HF symptoms
D Advanced HF • HF symptoms interfering with normal activity and/or recurrent HF hospitalizations (despite GDMT)	HFpEF <i>(preserved EF)</i> LVEF ≥ 50% <i>(w/ evidence of spontaneous/provokable ↑ LV filling pressures)</i>	IV • Symptoms at rest • Discomfort worsens with physical activities

Goals of Therapy

Stage A
• Primary prevention of heart failure
Stage B
• Prevention of clinical heart failure
Stage C
• Reduction of mortality • Reduction of heart failure symptoms and hospitalization risk • Elimination of potential barriers to self-care
Stage D
• Provision of inotropic support until mechanical circulatory support or cardiac transplantation is available • Palliative symptom control and functional improvement (if not eligible for mechanical circulatory support or cardiac transplantation)

Pharmacotherapy Recommendations

Stage A	Stage B	Stage C (HFpEF)	Stage C (HFmrEF)	Stage C (HFimpEF)
<ul style="list-style-type: none"> Control BP in patients with hypertension SGLT2i in patients with T2DM plus: <ul style="list-style-type: none"> Established CVD or, High CV risk Manage existing comorbidities 	<ul style="list-style-type: none"> ACEi and evidence-based BB in patients with LVEF ≤ 40% <ul style="list-style-type: none"> If LVEF ≤ 40% and recent MI, use ARB if ACEi is not tolerated 	<ul style="list-style-type: none"> Diuretics as needed (loop preferred) SGLT2i may be beneficial May consider MRA, ARB/ARNi if LVEF is closer to 50% 	<ul style="list-style-type: none"> PRN diuretics (loop preferred) SGLT2i may be beneficial May consider MRA, ACEi/ARB/ARNi, and evidence-based BB particularly if LVEF is closer to HFrEF threshold 	<ul style="list-style-type: none"> Continue GDMT <ul style="list-style-type: none"> Even if asymptomatic

Stage C (HFrEF)

All patients	Specific patients
<ul style="list-style-type: none"> ARNi or ACEi or ARB <ul style="list-style-type: none"> ARNi: NYHA class II-III ACEi or ARB: NYHA class II-IV Order of preference: ARNi > ACEi > ARB 36-hour washout required when switching between ACEi and ARNi (and vice versa) Beta Blocker (evidence-based) <ul style="list-style-type: none"> Bisoprolol, carvedilol, metoprolol succinate MRA (e.g. eplerenone, spironolactone) <ul style="list-style-type: none"> NYHA class II-IV eGFR > 30 mL/min/1.73m² Serum potassium < 5 mEq/L SGLT2i <ul style="list-style-type: none"> With or without T2DM Diuretics (as needed) <ul style="list-style-type: none"> Loop diuretics preferred 	<ul style="list-style-type: none"> Hydralazine + isosorbide dinitrate <ul style="list-style-type: none"> African American patients on optimal therapy NYHA class III-IV Ivabradine <ul style="list-style-type: none"> NYHA class II-IV and LVEF ≤ 35% On GDMT including max tolerated BB NSR with resting HR ≥ 70 BPM Vericiguat <ul style="list-style-type: none"> NYHA class II-IV and LVEF < 45% Recent HF worsening ↑ BNP or NT-proBNP Digoxin <ul style="list-style-type: none"> If symptomatic despite GDMT or Unable to tolerate GDMT Potassium binders <ul style="list-style-type: none"> e.g., Patiromer, sodium zirconium cyclosilicate Patients with hyperkalemia (K⁺ ≥ 5.5 mEq/L) while on RAASi Omega-3 PUFA (may consider as an adjunct) <ul style="list-style-type: none"> NYHA class II-IV

Selected Medications That May Cause or Exacerbate HF

COX inhibitors (e.g., NSAIDs)	<ul style="list-style-type: none"> ↑ H₂O retention, ↑ vascular resistance, ↓ response to diuretics Immediate onset, major induction/precipitation of HF
Thiazolidinediones	<ul style="list-style-type: none"> Potential blockage of calcium channel Intermediate onset, major induction/precipitation of HF
Saxagliptin, Alogliptin	<ul style="list-style-type: none"> Mechanism is unclear Immediate or delayed onset, major induction/precipitation of HF
Flecainide, Disopyramide	<ul style="list-style-type: none"> Proarrhythmic, negative inotropic effects Immediate to intermediate onset, major induction/precipitation of HF
Sotalol	<ul style="list-style-type: none"> Proarrhythmic effects, beta blockade Immediate to intermediate onset, major induction/precipitation of HF
Dronedarone	<ul style="list-style-type: none"> Negative inotropic effects Immediate to intermediate onset, major induction/precipitation of HF
Doxazosin	<ul style="list-style-type: none"> Beta-1 stimulation, ↑ renin and aldosterone Intermediate to delayed onset, moderate induction/precipitation of HF
Diltiazem, Verapamil	<ul style="list-style-type: none"> Negative inotropic effects Immediate to intermediate onset, major induction/precipitation of HF
Nifedipine	<ul style="list-style-type: none"> Negative inotropic effects Immediate to intermediate onset, moderate induction/precipitation of HF

Recreated from Table 13 from the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Abbreviations

ACEi: angiotensin-converting enzyme inhibitors	BP: blood pressure	HFimpEF: heart failure with improved ejection fraction	LVEF: left ventricular ejection fraction	PRN: as needed
ARB: angiotensin (II) receptor blocker	CVD: cardiovascular disease	HFmrEF: heart failure with mildly reduced ejection fraction	MI: myocardial infarction	PUFA: polyunsaturated fatty acid
ARNi: angiotensin receptor-neprilysin inhibitors	eGFR: estimated glomerular filtration rate	HFpEF: heart failure with preserved ejection fraction	MRA: mineralocorticoid receptor antagonist	RAASi: renin-angiotensin-aldosterone system inhibitor
BB: beta-blocker	GDMT: guideline-directed medical therapy	HFrEF: heart failure with reduced ejection fraction	NT-proBNP: N-terminal prohormone of B-type natriuretic peptide	SGLT2i: sodium-glucose cotransporter-2 inhibitor
BNP: B-type natriuretic peptide	HF: heart failure	LV: left ventricular	NYHA: New York Heart Association	T2DM: type 2 diabetes mellitus