ACC/AHA/HFSA Guideline for the Management of Heart Failure

Select Recommendations for Risk Reduction

Derived From:

Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 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 online ahead of print April 1, 2022]. *J Am Coll Cardiol*. doi: 10.1016/j.jacc.2021.12.012

Copublished in *Circulation*. doi: 10.1161/CIR.0000000000001063

Copublished in *J Card Fail*. doi: 10.1016/j.cardfail.2022.02.010

American College of Cardiology
www.acc.org

The American Heart Association
professional.heart.org

Full-text guidelines available in *Circulation*, *JACC* and *JCF*.

Top 10 Take-Home Messages:

1. **Guideline-directed medical therapy (GDMT) for heart failure (HF) with reduced ejection fraction (HFrEF) now includes 4 medication classes that includes sodium-glucose cotransporter-2 inhibitors (SGLT2i).**
2. **SGLT2 inhibitors have a Class of Recommendation 2a in heart failure with mildly reduced ejection fraction (HFmrEF). Weaker recommendations (Class of Recommendation 2b) are made for ARNi, ACEi, ARB, MRA and beta blockers in this population.**
3. **New recommendations for HFpEF are made for SGLT2 inhibitors (Class of Recommendation 2a), MRAs (Class of Recommendation 2b) and ARNi (Class of Recommendation 2b). Several prior recommendations have been renewed including treatment of hypertension (Class of Recommendation 1), treatment of atrial fibrillation (Class of Recommendation 2a), use of ARBs (Class of Recommendation 2b) and avoidance of routine use of nitrates or phosphodiesterase-5 inhibitors (Class of Recommendation 3-No benefit).**
4. **Improved LVEF is used to refer to those patients with previous HFrEF who now have an LVEF >40%. These patients should continue their HFrEF treatment.**
5. **Value statements were created for select recommendations where high-quality, cost-effectiveness studies of the intervention have been published.**
6. **Amyloid heart disease has new recommendations for treatment including screening for serum and urine monoclonal light chains, bone scintigraphy, genetic sequencing, tetramer stabilizer therapy, and anticoagulation.**
7. **Evidence supporting increased filling pressures is important for the diagnosis of HF if the LVEF is >40%. Evidence for increased filling pressures can be obtained from non-invasive (e.g., natriuretic peptide, diastolic function on imaging) or invasive testing (e.g., hemodynamic measurement).**
8. **Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF. A heart failure specialty team reviews HF management, assesses suitability for advanced HF therapies, and uses palliative care including palliative inotropes where consistent with the patient's goals of care.**
9. **Primary prevention is important for those at risk for HF (stage A) or pre-HF (stage B). Stages of HF were revised to emphasize the new terminologies of "at risk" for HF for stage A and pre-HF for stage B.**
10. **Recommendations are provided for select patients with HF and iron deficiency, anemia, hypertension, sleep disorders, type 2 diabetes, atrial fibrillation, coronary artery disease, and malignancy.**

Note: The numbering of the following tables and figures may differ from that of the Clinical Practice Guideline.

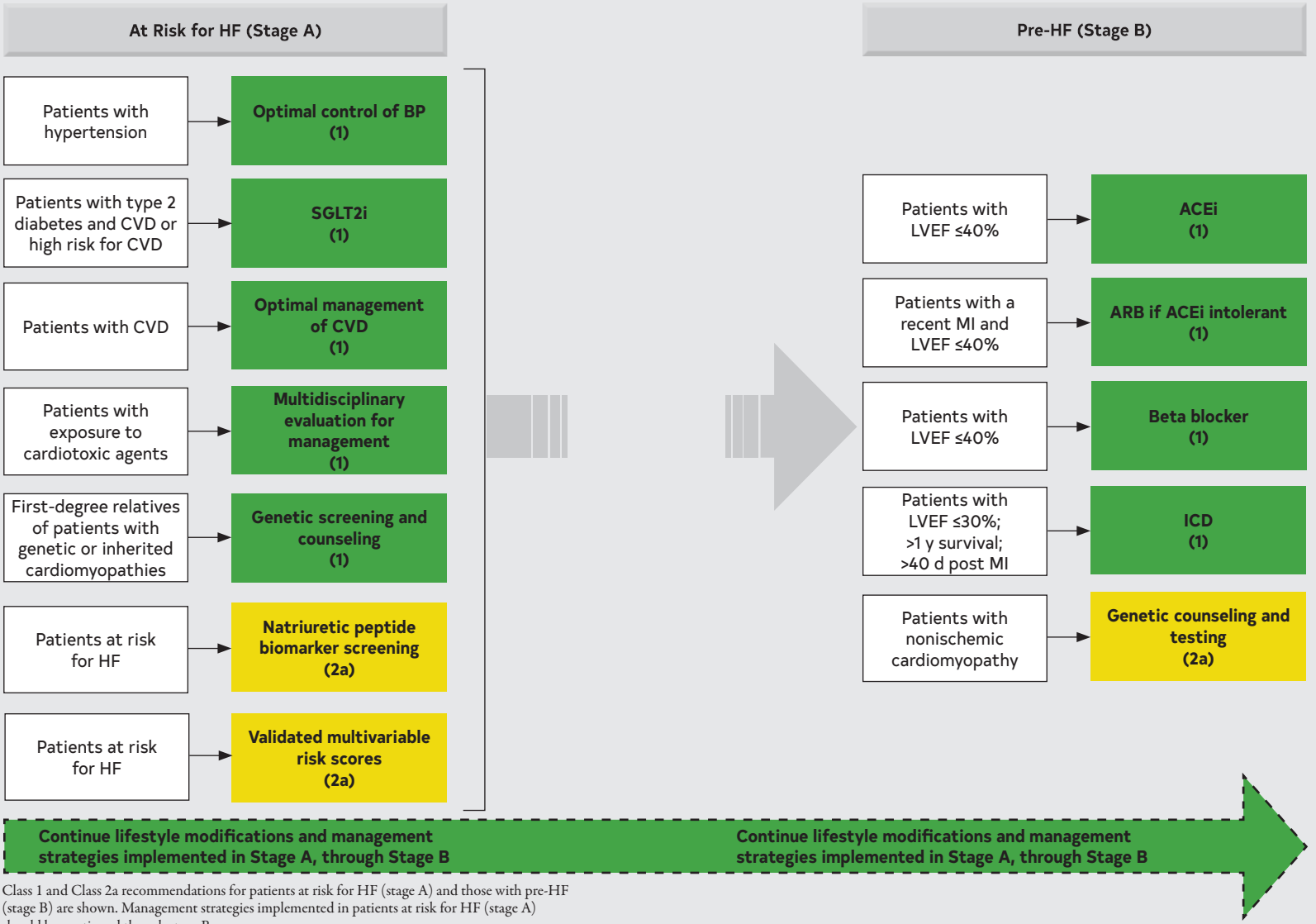
Colors in tables and figures correspond to Class of Recommendations and Level of Evidence tables.

Table 1. Stages of HF

Stages	Definition and Criteria
Stage A: At Risk for HF	At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (e.g., patients with hypertension, atherosclerotic CVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy).
Stage B: Pre-HF	No symptoms or signs of HF and evidence of 1 of the following:
	*Structural heart disease** • Reduced left or right ventricular systolic function » Reduced ejection fraction, reduced strain • Ventricular hypertrophy • Chamber enlargement • Wall motion abnormalities • Valvular heart disease
	*Evidence for increased filling pressures** • By invasive hemodynamic measurements • By noninvasive imaging suggesting elevated filling pressures (e.g., Doppler echocardiography)
	Patients with risk factors and • *Increased levels of BNPs* or* • *Persistently elevated cardiac troponin* in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary embolus, or myopericarditis
Stage C: Symptomatic HF	Structural heart disease with current or previous symptoms of HF.
Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.

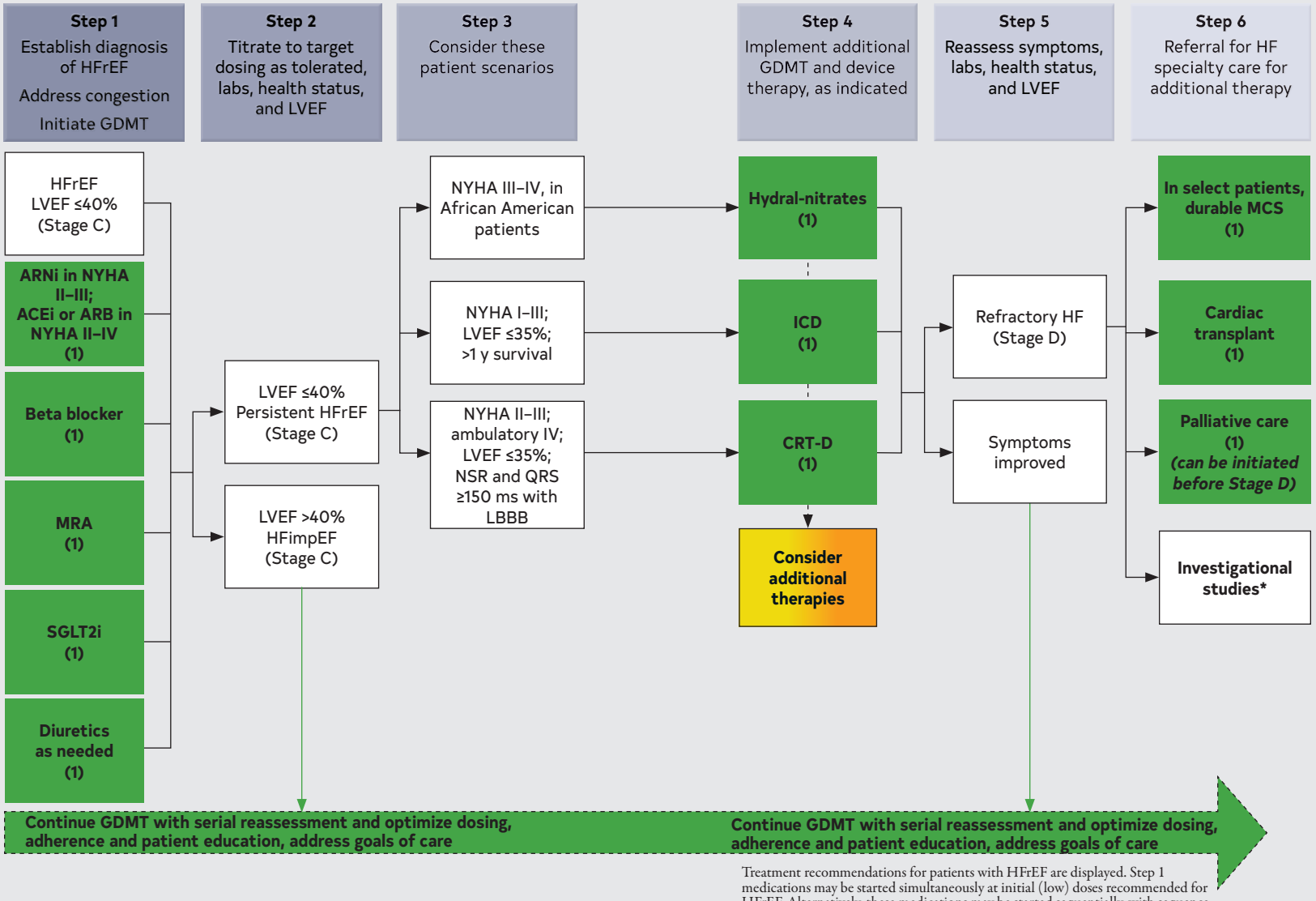
* For thresholds of cardiac structural, functional changes, elevated filling pressures, and biomarker elevations, refer to Appendix 3 (in the primary guideline).

Figure 1. Recommendations (Class 1 and 2a) for Patients at Risk of HF (Stage A) and Those With Pre-HF (Stage B)



Class 1 and Class 2a recommendations for patients at risk for HF (stage A) and those with pre-HF (stage B) are shown. Management strategies implemented in patients at risk for HF (stage A) should be continued though stage B.

Figure 2. Treatment of HFrEF Stages C and D



Treatment recommendations for patients with HFrEF are displayed. Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF. Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication. Medication doses should be increased to target as tolerated.

* Participation in investigational studies is appropriate for stage C, NYHA class II and III HF.

5. Stage A (Patients at Risk for HF)

5.1. Patients at Risk for HF (Stage A: Primary Prevention)

COR	LOE	Recommendations
1	A	1. In patients with hypertension, blood pressure should be controlled in accordance with GDMT for hypertension to prevent symptomatic HF.
1	A	2. In patients with type 2 diabetes and either established CVD or at high cardiovascular risk, SGLT2i should be used to prevent hospitalizations for HF.
1	B-NR	3. In the general population, healthy lifestyle habits such as regular physical activity, maintaining normal weight, healthy dietary patterns, and avoiding smoking are helpful to reduce future risk of HF.
2a	B-R	4. For patients at risk of developing HF, natriuretic peptide biomarker-based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of LV dysfunction (systolic or diastolic) or new-onset HF.
2a	B-NR	5. In the general population, validated multivariable risk scores can be useful to estimate subsequent risk of incident HF.

7.3. Pharmacological Treatment for HFrEF

7.3.4. Sodium-Glucose Cotransporter 2 Inhibitors

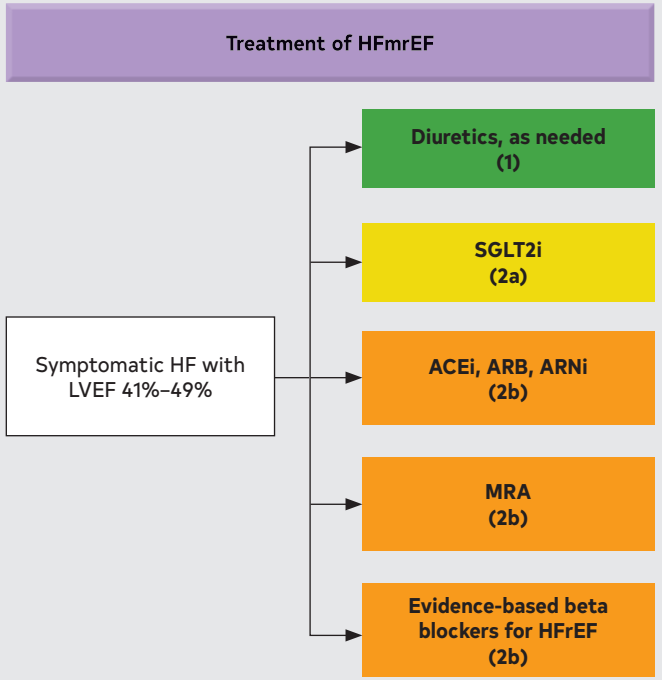
COR	LOE	Recommendations
1	A	1. In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.
Value Statement: Intermediate Value (A)		2. In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value.

7.6. Mildly Reduced EF (HFmrEF) and Improved EF (HFimpHF)

7.6.1. HF With Mildly Reduced Ejection Fraction

COR	LOE	Recommendations
2a	B-R	1. In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.
2b	B-NR	2. Among patients with current or previous symptomatic HFmrEF (LVEF, 41%–49%), use of evidence-based beta blockers for HFrEF, ARNi, ACEi, or ARB, and MRAs may be considered to reduce the risk of HF hospitalization and cardiovascular mortality, particularly among patients with LVEF on the lower end of this spectrum.

Figure 3. Recommendations for Patients With Mildly Reduced LVEF (41%–49%)



Medication recommendations for HFmrEF are displayed.

7.7. Preserved EF (HFpEF)

7.7.1. HF With Preserved Ejection Fraction*

COR	LOE	Recommendations
1	C-LD	1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity.
2a	B-R	2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.
2a	C-EO	3. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	4. 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	5. In selected patients with HFpEF, the use of ARB may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.
2b	B-R	6. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.
3: No-Benefit	B-R	7. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QOL is ineffective.

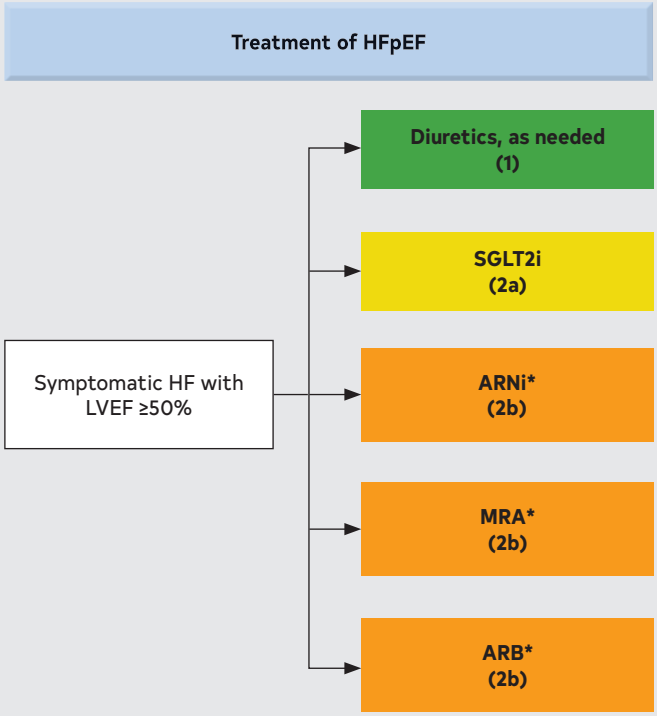
* See Section 7.2 ("Diuretics and Decongestion Strategies in Patients with HF") and Section 10.2 ("Management of Atrial Fibrillation (AF) in HF") for recommendations for use of diuretics and management of AF in HF.

10. Comorbidities in Patients With HF

10.1. Management of Comorbidities in Patients With HF

COR	LOE	Recommendations
		Management of Diabetes
1	A	1. In patients with HF and type 2 diabetes, the use of SGLT2i is recommended for the management of hyperglycemia and to reduce HF-related morbidity and mortality.

Figure 4. Recommendations for Patients With Preserved LVEF (≥50%)



Medication recommendations for HFpEF are displayed.
* Greater benefit in patients with LVEF closer to 50%.

Table 2. Drugs Commonly Used for HFrEF (Stage C HF)

Drug	Initial Daily Dose(s)	Target Dose(s)	Mean Doses Achieved in Clinical Trials
ACEi			
Captopril	6.25 mg 3 times daily	50 mg 3 times daily	122.7 mg total daily
Enalapril	2.5 mg twice daily	10–20 mg twice daily	16.6 mg total daily
Fosinopril	5–10 mg once daily	40 mg once daily	NA
Lisinopril	2.5–5 mg once daily	20–40 mg once daily	32.5–35.0 mg total daily
Perindopril	2 mg once daily	8–16 mg once daily	NA
Quinapril	5 mg twice daily	20 mg twice daily	NA
Ramipril	1.25–2.5 mg once daily	10 mg once daily	NA
Trandolapril	1 mg once daily	4 mg once daily	NA
ARB			
Candesartan	4–8 mg once daily	32 mg once daily	24 mg total daily
Losartan	25–50 mg once daily	50–150 mg once daily	129 mg total daily
Valsartan	20–40 mg once daily	160 mg twice daily	254 mg total daily
ARNi			
Sacubitril-valsartan	49 mg sacubitril and 51 mg valsartan twice daily (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan twice daily)	97 mg sacubitril and 103 mg valsartan twice daily	182 mg sacubitril and 193 mg valsartan total daily
Beta blockers			
Bisoprolol	1.25 mg once daily	10 mg once daily	8.6 mg total daily
Carvedilol	3.125 mg twice daily	25–50 mg twice daily	37 mg total daily
Carvedilol CR	10 mg once daily	80 mg once daily	NA

Table 2. Drugs Commonly Used for HFrEF (Stage C HF) *(cont'd)*

Drug	Initial Daily Dose(s)	Target Dose(s)	Mean Doses Achieved in Clinical Trials
Metoprolol succinate extended release (metoprolol CR/XL)	12.5–25 mg once daily	200 mg once daily	159 mg total daily
Mineralocorticoid receptor antagonists			
Spironolactone	12.5–25 mg once daily	25–50 mg once daily	26 mg total daily
Eplerenone	25 mg once daily	50 mg once daily	42.6 mg total daily
SGLT2i			
Dapagliflozin	10 mg once daily	10 mg once daily	9.8 mg total daily
Empagliflozin	10 mg once daily	10 mg once daily	NR
Isosorbide dinitrate and hydralazine			
Fixed dose combination	20 mg isosorbide dinitrate and 37.5 mg hydralazine 3 times daily	40 mg isosorbide dinitrate and 75 mg hydralazine 3 times daily	90 mg isosorbide dinitrate and ~175 mg hydralazine total daily
Isosorbide dinitrate and hydralazine	20–30 mg isosorbide dinitrate and 25–50 mg hydralazine 3–4 times daily	120 mg isosorbide dinitrate total daily in divided doses and 300 mg hydralazine total daily in divided doses	NA
I_f Channel inhibitor			
Ivabradine	5 mg twice daily	7.5 mg twice daily	12.8 total daily
Soluble guanylate cyclase stimulator			
Vericiguat	2.5 mg once daily	10 mg once daily	9.2 mg total daily
Digoxin	0.125–0.25 mg daily (modified according to monogram)	Individualized variable dose to achieve serum digoxin concentration 0.5–<0.9 ng/mL	NA

CLASS (STRENGTH) OF RECOMMENDATION

CLASS 1 (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS 2a (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

CLASS 3: No Benefit (MODERATE) — **Benefit = Risk**

(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS 3: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A

- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R — **(Randomized)**

- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR — **(Nonrandomized)**

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD — **(Limited Data)**

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO — **(Expert Opinion)**

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; RCT, randomized controlled trial.

Abbreviations

CRT-D, cardiac resynchronization therapy with defibrillation; **CVD**, cardiovascular disease; **EF**, ejection fraction; **GDMT**, guideline-directed medical therapy; **HF**, heart failure; **HFimpEF**, heart failure with improved ejection fraction; **HFmrEF**, heart failure with mildly reduced ejection fraction; **HFpEF**, heart failure with preserved ejection fraction; **HFrEF**, heart failure with reduced ejection fraction; **ICD**, implantable cardioverter-defibrillator; **IFE**, immunofixation electrophoresis; **LBBB**, left bundle branch block; **LV**, left ventricular; **LVEF**, left ventricular ejection fraction; **MCS**, mechanical circulatory support; **MI**, myocardial infarction; **MRA**, mineralocorticoid receptor antagonist; **NYHA**, New York Heart Association; **QOL**, quality of life; **RCT**, randomized controlled trial; **SGLT2i**, sodium-glucose cotransporter-2 inhibitors

Boehringer Ingelheim

Lilly

The printing and distribution of this educational resource was supported by Boehringer Ingelheim Pharmaceuticals, Inc.

Source

Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 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 online ahead of print April 1, 2022]. *J Am Coll Cardiol*. doi: 10.1016/j.jacc.2021.12.012

Copublished in *Circulation*. doi: 10.1161/CIR.0000000000001063

Copublished in *J Card Fail*. doi: 10.1016/j.cardfail.2022.02.010

Disclaimer

This guideline update provides clinicians with practical guidance for managing patients with heart failure. This publication contains some discussion of the use of products in populations and of outcomes that are not consitent with product labeling.

This pocket guide attempts to define principles of practice that should produce high-quality patient care. It is applicable to specialists, primary care, and providers at all levels. This pocket guide should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation. Neither IGC, the medical associations, nor the authors endorse any product or service associated with the distributor of this clinical reference tool.

GuidelineCentral.com®
TEL: 407.878.7606 • FAX: 407.878.7611
Order additional copies at GuidelineCentral.com

AHAHF02223_RR3

PC-US-127096