Caring for your patients with heart failure

In 2022, the American Heart Association and American College of Cardiology recommended quadruple therapy for heart failure with reduced ejection fraction patients (HFrEF).[1]

For patients with HFrEF who are not on all four medications, consider prescribing the missing guideline-directed medical therapies and titrating to target doses as tolerated. Most resources recommend adding medications one by one in the outpatient setting to improve tolerance.

Quadruple medication therapy is shown to reduce cardiovascular mortality and hospitalizations by up to 64%.[2]

Quadruple therapy includes one medication from each drug class

Drug class		Medication*	Tier†	Initial dose	Target dose
Renin-angiotensin-aldosterone system inhibitors (RAASi)	Angiotensin-converting enzyme inhibitors (ACE-I)	captopril	T3	6.25 mg 3x/day	50 mg 3x/day
		enalapril	T1	2.5 mg 2x/day	10–20 mg 2x/day
		fosinopril	T1	5–10 mg 1x/day	40 mg 1x/day
		lisinopril	T1	2.5–5 mg 1x/day	20–40 mg 1x/day
		perindopril	T2	2 mg 1x/day	8–16 mg 1x/day
		quinapril	T1	5 mg 2x/day	20 mg 2x/day
		ramipril	T1	1.25–2.5 mg 1x/day	10 mg 1x/day
		trandolapril	T1	1 mg 1x/day	4 mg 1x/day
	Angiotensin receptor blocker (ARB)	candesartan	T3	4–8 mg 1x/day	32 mg 1x/day
		losartan	T1	25–50 mg 1x/day	50–150 mg 1x/day
		valsartan	T1	20–40 mg 1x/day	160 mg 2x/day
	Angiotensin receptor-neprilysin inhibitor (ARNI)	sacubitril-valsartan	T3	49 mg sacubitril and 51 mg valsartan 2x/day (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan 2x/day)	97 mg sacubitril and 103 mg valsartan 2x/day
Beta-blockers		bisoprolol	T2	1.25 mg 1x/day	10 mg 1x/day
		carvedilol	T1	3.125 mg 2x/day	25–50 mg 2x/day
		carvedilol CR	T4	10 mg 1x/day	80 mg 1x/day
		metoprolol succinate (CR/XL)	T1	12.5–25 mg 1x/day	200 mg 1x/day
Mineralocorticoid receptor antagonists (MRA)		spironolactone	T1	12.5–25 mg 1x/day	25–50 mg 1x/day
		eplerenone (nonformulary)	NF‡	25 mg 1x/day	50 mg 1x/day
Sodium-glucose cotransporter 2 inhibitors (SGLT2)		empagliflozin	T3	10 mg 1x/day	10 mg 1x/day
		dapagliflozin	T4	10 mg 1x/day	10 mg 1x/day

* Some patients may be on a RAASi, beta-blocker or SGLT2 medication that is not optimized for heart failure. After quadruple therapy is established or maximized, please consider switching to medications optimized for HFrEF treatment (as appropriate).

† Tier level based on Super National 5 formulary (most common for individual Medicare Advantage prescription drug plans). To check individual formularies or coverage, visit **https://Provider.Humana.com**.

‡ Nonformulary

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References

1 Paul A. Heidenreich 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," *Circulation* 145, no. 18 (April 2022): e895–e1032, accessed March 6, 2024, doi: 10.1161/CIR.0000000000001063.

2. Jasper Tromp et al., "A Systematic Review and Network Meta-Analysis of Pharmacological Treatment of Heart Failure with Reduced Ejection Fraction," *JACC: Heart Failure* 10, No. 2 (February 2022): 73–84, accessed March 6, 2024, doi: 10.1016/j.jchf.2021.09.004.