Meds for HFrEF with best evidence and target doses as established by RCTs

FIRST LINE: ideally start all core meds (ARNI, ACEI or ARB; MRA; SGLT2i; and BB) simultaneously at low doses and titrate over 3 months to target doses, with caveats. See blog post for details.

ARNI (Angiotensin Receptor Neprolysin Inhibitor)
For patients with chronic symptomatic class II to IV HF with EF ≤40%, instead of ACEI or ARB.
NNT=21 vs ACEI in preventing CV hospitalization or death, though also causes symptomatic hypotension in 1 of 21 patients.

	Initial dose	Target dose	Notes
Sacubitril/valsartan (*Entresto*)	24/26mg to 49/51mg bid	97/103mg bid	Do not use in pts with history of angioedema with ACEI or ARB, recent increase in diuretic, starting SBP < 100, or in frail elders. Stop any prior ACEI x 36hr, then start 40/51mg bid and increase to 97/103 after 2-4wks OR if no prior use ACEI/ARB or GFR < 30, start at 24/26mg bid. Monitor SBP (goal >90), K (goal < 5.5), Cr (goal < 2.5)

ACE inhibitors
Not to be used with ARNI or ARB.

Captopril	6.25 mg three times daily	50 mg three times daily	If patients are unable to reach the target dose, they probably still get benefit from lower doses. Monitor for hyperkalemia, increased creatinine.
Enalapril (*Vasotec*)	2.5 mg twice daily	10 mg to 20 mg bid	
Lisinopril (*Prinivil*, *Zestril*)	2.5 to 5 mg once daily	20 to 40 mg once daily	
Ramipril (*Altace*)	1.25 to 2.5 mg once daily	10mg once daily	

ARBs
For patients who are intolerant to ACEI due to cough or angioedema, and in whom an ACEI or ARNI is inappropriate.
Patients already taking an ARB for another indication (e.g., hypertension), as an ACEI alternative.

Candesartan (*Atacand*)	4 to 8mg qd	32mg once daily	Same cautions and monitoring as for ACEI. Uptitrate by doubling the dose.
Losartan (*Cozaar*)	25 to 50mg qd	50 to 150mg qd	
Valsartan (*Diovan*)	20 to 40mg bid	160mg bid	

BBs
For stable patients with EF ≤40% with symptoms or prior symptoms. Defer initiation until HF is compensated.

Bisoprolol	1.25mg qd	10mg qd	Main adverse effects: fluid retention, worsening HF, fatigue, bradycardia, heart block, and hypotension. Monitor vitals closely during uptitration. Do not increase dose until any adverse effects have resolved. Use diuretics to manage fluid retention. Decrease dose in the event of bradycardia associated with dizziness or lightheadedness, or second- or third-degree heart block. If hypotension occurs, separate beta-blocker from other hypotensive agents (e.g., ACEI), or decrease diuretic dose. Continue beta-blocker even if it does not seem to improve heart failure symptoms.
Carvedilol (*Coreg*)	3.125mg bid	50mg bid	
Carvedilol extended release (*Coreg CR*)	10mg qd	80mg qd	
Metoprolol succinate (*Toprol XL*)	12.5mg to 25mg qd	200mg qd	
SGLT-2 Inhibitors Reduces mortality and worsening HF in class II, III, or IV HFrEF with or without DM			
Empagliflozin (*Jardiance*)	10mg qd	10mg qd	Avoid in pts with DM1 or with history of DKA, CKD4 or worse, volume depletion / hypotension
Dapagliflozin (*Farxiga*)	10mg qd	10mg qd	
Sotalgiflozin (*Impefa*)	200mg qd	400mg qd	
Aldosterone Antagonists			
Eplerenone (*Inspra*)	25mg qd (qod if eGFR 30 to 49)	50mg qd (25mg qd if eGFR 30 to 49)	Contraindicated with elevated Cr at baseline (≥ 2.5 men, ≥ 2 women), or K ≥ 5, or eGFR ≤30. Add-on to ACEI, ARB, **or** ARNI, plus beta-blocker May cause hyperkalemia. Monitor K and Cr. Watch for interactions with / make adjustments to K supplements and loop diuretics, which encourage hypoK; avoid NSAIDs and high K foods.
Spironolactone (*Aldactone*)	12.5 to 25mg qd	25 mg qd or bid	
Loop diuretics For patients with class II to IV heart failure with fluid retention or history of it, to improve symptoms and exercise tolerance, and to manage beta-blocker associated fluid retention.			
Furosemide (*Lasix*)	20 to 40mg qd or bid	max total daily dose 240mg (600mg in renal impairment)	Furosemide most common and cheapest but poorest bioavailability. Once stable, may try prn use (pt self-titration based on daily weights).

Bumetanide (*Bumex*)	0.5 to 1mg qd or bid	max total daily dose 10 mg	Furosemide or bumetanide bid might improve efficacy, but uptitrate first to max single dose before trying. Second dose afternoon, not qhs. Consider switch to bumetanide or torsemide for pts: • who require hospitalization for HF despite furosemide use. • who still have bothersome symptoms despite optimization of furosemide and other HF meds. Consider switching to torsemide rather than bumetanide; torsemide has a longer duration of action and more evidence in HF. Consider thiazide instead of loop for mild fluid retention with HTN.
Torsemide (*Demadex*)	10 to 20 mg qd	max total daily dose 200mg	
ALTERNATE FIRST LINE FOR AFRICAN AMERICANS			
Vasodilators May also use as add-on for non-African Americans if persistent HTN despite maximal doses of typical HF meds.			
Isosorbide dinitrate + hydralazine (*BiDil*)	20/37.5mg tid	40/75mg tid	Increase dose q3-5 days if tolerated
SECOND LINE / INFREQUENTLY USED MEDS			
Ivabradine	2.5 to 5mg bid	7.5mg bid	Additional therapy for persistent symptoms; most appropriate for patients in sinus rhythm with HR ≥70 bpm despite maximal beta blocker therapy.
Vericiguat	2.5mg qd	10mg qd	Additional therapy for persistent symptoms; rarely used
Digoxin	0.0625 to 0.25mg daily	Dose is based on digoxin level.	Additional therapy for persistent symptoms; rarely used