U.S. Department of Veterans Affairs
Veterans Health Administration
PBM Academic Detailing Services

A QUICK REFERENCE GUIDE (2022)

Managing Heart Failure in Primary Care

Classification of heart failure (HF)[1]

Acronym	Classification	Ejection fraction (EF) (%)	Description
HFrEF	**HF with reduced EF**	≤ 40	Previously referred to as "systolic HF." Guideline-directed medical therapy (GDMT) should be initiated and optimized as tolerated.
HFpEF	**HF with preserved EF**	≥ 50*	Previously referred to as "diastolic HF." Diagnosis of exclusion. Evidence-based therapies are limited.
HFmrEF	**HF with mildly reduced EF**	41-49*	Trend toward treating like HFrEF. No major clinical trials in this population; it is unclear whether characteristics and outcomes are more like HFpEF.
HFimpEF	**HF with improved EF**	Previously ≤ 40 and a subsequent measurement > 40	Continue GDMT for HFrEF, if tolerating. Further data needed to determine best management strategy.

*With evidence of spontaneous or provokable increased left ventricular filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement); EF = ejection fraction

New York Heart Association (NYHA) functional classification of HF

NYHA Class I	NYHA Class II	NYHA Class III	NYHA Class IV
No limitation of physical activity/ symptoms with ordinary physical activity; no symptoms at rest	Slight limitation of physical activity/symptoms with ordinary physical activity; no symptoms at rest	Marked limitations of physical activity/symptoms with less than ordinary physical activity; no symptoms at rest	Unable to carry on physical activity without symptoms of HF; symptoms even at rest

Management of heart failure by stage[1]

Stage	Description	NYHA class	Management strategy
A	At risk for HF, but without current or previous signs of HF, without structural or functional heart disease, or abnormal biomarkers (e.g., patients with HTN, diabetes, obesity, ASCVD, exposure to cardiotoxic agents, genetic variant or family history of cardiomyopathy)	None	Prevent HF by treating risk factors. Encourage healthy lifestyle (i.e., physical activity, healthy dietary patterns, maintaining normal weight). Avoid smoking.
B	Pre-HF: without current or previous symptoms or signs of HF but evidence of one of the following: • Structural heart disease **or** • Evidence of increased filling pressures **or** • Risk factors plus increased natriuretic peptide levels or persistently elevated cardiac troponin in the absence of competing diagnoses	None	Continue to treat risk factors. Monitor for development of HF symptoms. Start ACEI or ARB (if cough or angioedema with ACEI) **and** BB (i.e., carvedilol, metoprolol succinate, bisoprolol) if reduced EF ≤40%.
C	Current or previous symptoms or signs of HF	I–IV	Evidence-based pharmacotherapy to reduce symptoms and improve outcomes; diuretics as needed.
D	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT	IV	Refer to specialist and establish patient specific goal for care; continue GDMT as tolerated.

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta blocker; HTN = hypertension; NYHA = New York Heart Association; ASCVD = atherosclerotic cardiovascular disease ; HF = heart failure; GDMT = guideline directed medical therapy

Guideline recommended options for the management of heart failure with reduced ejection fraction (HFrEF)[2-5]

GDMT medication option*	Patient considerations	Cautions / contraindications	CV mortality	HF hospitalization
Evidence-based beta blocker	• All patients unless contraindicated (e.g., cardiogenic shock, heart block without a pacemaker) • Target doses not required prior to adding other medications.	Use caution in patients with: • Asthma — use a beta$_1$ selective option • Severe reversible airway disease • Heart block or severe bradycardia (unless patient has a pacemaker) • Long QT syndrome with history of torsades de pointes • Raynaud phenomenon	↓	↓

ARNI /ACEI/ ARB	• Choose ONE agent for all patients unless contraindicated (not to combine medication classes).
	  • ACEI/ARB preferred if NYHA Class I
	  • ARNI preferred if Class II-III
	• Target doses not required prior to adding other medications.
		• ACEI and ARNI contraindicated in patients with history of angioedema. ARB can be used on an individual basis after angioedema.
		• ALL should be avoided in bilateral renal artery stenosis and pregnancy; use caution in unilateral artery stenosis.
		• **ARNI cannot be given within 36 hours of an ACEI** or with aliskiren in patients with diabetes.
		• Use caution in patients with hyperkalemia, symptomatic hypotension and acute kidney injury.
			↓	↓

Mineralo-corticoid receptor antagonist	• NYHA class II-IV • K+ ≤ 5 mEq/L prior to initiation • eGFR ≥ 30 mL/min/1.73m^2 • Target doses not required prior to adding other medications.	• Caution when used with medications or foods that can increase serum potassium and in situations that could lead to dehydration (e.g., diuresis, diarrhea). • Avoid in pregnancy.	↓	↓
SGLT-2 inhibitor	• NYHA class II-IV • eGFR ≥ 25 mL/min/1.73m^2 for initiating dapagliflozin • eGFR ≥ 20 mL/min/1.73m^2 for initiating empagliflozin • Do not need to be at target doses of other medications before adding.	• Use with caution in low eGFR. • Avoid in patients on dialysis and in pregnancy. • See card on clinical pearls for using SGLT-2 inhibitors on page 5.	↓ to a lesser extent	↓
Hydralazine/ isosorbide dinitrate	• NYHA class III-IV • Persistently symptomatic Black patients despite concomitant use of ARNI/ACEI/ARB, beta blocker, SGLT-2 inhibitor, and MRA • Patients unable to take ACEI/ARB/ ARNI	• **Do not** use with PDE-5 inhibitors, in patients who are allergic to organic nitrates or symptomatic hypotension. • Patients on ISDN were excluded from trials evaluating vericiguat.	↓	↓
Ivabradine	• NYHA class II-III **and** • EF ≤ 35% **and** • Resting HR ≥ 70 beats per minute in normal sinus rhythm on maximally tolerated BB or patient unable to tolerate BB or has contraindications to BB	• Contraindicated in patients with acute decompensated heart failure, significant hypotension, sick sinus syndrome, clinically significant bradycardia, severe hepatic impairment, if HR maintained by pacemaker, strong CYP3A4 inhibitors, and atrial fibrillation.	No reduction	↓
Vericiguat	• NYHA class II-IV • Following HF hospitalization or outpatient use of IV diuretics	• Do not use in patients on other soluble guanylate cyclase (sGC) stimulators (e.g., riociguat). • Concomitant use of PDE-5 inhibitors is not recommended. • Patients on long acting nitrates, including ISDN, were excluded from trials evaluating vericiguat. • Avoid in pregnancy.	No reduction	↓

*Choices are not mutually exclusive, and no order is inferred; NYHA = New York Heart Association; GDMT = guideline-directed medical therapy; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta blocker; EF = ejection fraction; SGLT-2 = sodium-glucose co-transporter-2; HR = heart rate; ARNI = angiotensin receptor blocker/neprilysin inhibitor; eGFR = estimated glomerular filtration rate; PDE = phosphodiesterase; IV = intravenous; MRA = mineralocorticoid receptor antagonist; CYP = cytochrome P; IDSN = isosorbide dinitrate

continued from page 2 (Guideline recommended options for the management of HFrEF)

GDMT medication option*	Patient considerations	Cautions / contraindications	CV mortality	HF hospitalization
Diuretic (e.g., furosemide, torsemide, bumetanide)	• NYHA class II-IV • Maintain euvolemia • Persistent volume overload	• Avoid in anuria, hepatic coma, and severe states of electrolyte depletion. • Avoid if hypersensitivity to furosemide, bumetanide, or torsemide. Use ethacrynic acid in these patients.	No reduction	↓
Digoxin	• Symptomatic heart failure already optimized or unable to tolerate other heart therapies • Use with caution in patients with renal dysfunction • Target trough level 0.5–0.9 ng/mL	• Avoid in patients with myocarditis, hypomagnesemia, hypokalemia, Wolf-Parkinson-White syndrome, acute myocardial infarction, amyloidosis, trough > 2 ng/mL, or symptoms of toxicity (i.e., nausea, vomiting, diarrhea, abdominal pain, visual disturbances, anorexia). • Low body weight and chronic kidney disease may increase risk of digoxin toxicity.	No reduction	↓

*Choices are not mutually exclusive, and no order is inferred; NYHA = New York Heart Association; GDMT = guideline-directed medical therapy; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta blocker; EF = ejection fraction; SGLT-2 = sodium-glucose co-transporter-2; HR = heart rate; ARNI = angiotensin receptor blocker/neprilysin inhibitor; eGFR = estimated glomerular filtration rate; PDE = phosphodiesterase; IV = intravenous; MRA = mineralocorticoid receptor antagonist; CYP = cytochrome P; IDSN = isosorbide dinitrate

Medications for patients with HFrEF[1,2,6-10]

Medication	Starting daily dose (mg)	Target daily dose (mg)*	Comments	Monitor
Angiotensin receptor blocker/neprilysin inhibitor (ARNI)				
Sacubitril/valsartan	**Sacubitril 24/valsartan 26 BID** For patients not on ACEI or ARB, on low doses [e.g., ≤10 mg enalapril, ≤20 mg lisinopril, ≤100 mg losartan or ≤ 160 mg valsartan], CrCl < 30 mL/min, moderate hepatic impairment [Child-Pugh class B], or age ≥ 75 **Sacubitril 49/valsartan 51 BID** Switching from ACEI or ARB at standard doses	Sacubitril 97/valsartan 103 BID	If switching from ACEI, allow a 36-hour washout period before initiating sacubitril/valsartan. No washout needed if switching from an ARB.	Serum K+ and renal function at baseline, 2-4 weeks after initiation and during titration
Angiotensin converting enzyme inhibitor (ACEI)				
Captopril	6.25 TID	50 TID	ARNI preferred over ACEI in NYHA Class II-III Use ACEI prior to ARB	Serum K+ and renal function at baseline, 2-4 weeks after initiation and during titration Side effects (e.g., cough)
Enalapril	2.5 BID	10-20 BID		
Fosinopril	5-10	40		
Lisinopril	2.5-5	20-40		
Ramipril	1.25-2.5	10		

*Unless specified, use highest tolerated dose while maintaining adequate blood pressure; PIONER-HF trial started doses at the higher dose in patients with SBP ≥120 mm Hg; In subsequent weeks, doses increase if patients were able to maintain BP (i.e., SBP >100-110 mm Hg).[11] ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; K+ = potassium; HFrEF = heart failure with reduced ejection fraction; BID = twice daily; TID = three times daily; NYHA=New York Heart Association; Please see VA National Formulary for current list of formulary medications **VA Formulary Advisor (vanf.app)**

continued from page 3 (Medications for patients with HFrEF)

Medication	Starting daily dose (mg)	Target daily dose (mg)	Comments	Monitor
Angiotensin receptor blocker (ARB)				
Losartan	25-50	150	Use ACEI prior to ARB. ARNI preferred over ARB in NYHA Class II-III.	Serum K+ and renal function at baseline, 2-4 weeks after initiation and during titration
Valsartan	40 BID	160 BID*		
Candesartan	4-8	32*		
Beta blocker				
Carvedilol IR	3.125 BID	Patient weight <187 lbs: 25 BID; ≥187 lbs: 50 BID	Avoid in advanced heart block, severe bradycardia (unless pacemaker present), cardiogenic shock, severe reversible airway disease. Metoprolol tartrate not recommended. Convert tartrate to succinate (e.g., 50 mg tartrate BID = 100 mg succinate daily).	HR/BP Worsening HF
Metoprolol succinate	12.5–25	200		
Bisoprolol	1.25	10		
Sodium-glucose co-transport 2 (SGLT-2) inhibitors				
Dapagliflozin	10	10	Recommended in chronic kidney disease (eGFR ≥ 20 for empagliflozin, eGFR ≥ 25 for dapagliflozin). Do not use in severe renal impairment. Evaluate fluid status and if concerned about hypovolemia consider adjusting diuretic when initiating. See card on clinical pearls for using SGLT-2 inhibitors on page 5 for more information.	Glucose levels in patients with diabetes BP and BMP
Empagliflozin	10	10		
Mineralocorticoid receptor antagonists (MRA)				
Spironolactone†	12.5–25 CrCl < 50: 12.5 daily or every other day	25 daily or BID CrCl < 50: 12.5–50 daily	Avoid starting if: eGFR ≤ 30; or K+ ≥ 5 mEq/L. After started if: K+ increase > 5.5 mEq/L or worsening renal function, hold until K+ < 5. Consider restart at lower dose 72 hours after resolution. Discontinue if unable to maintain K+ < 5.5 mEq/L. If concomitant potassium supplements, stop or adjust when initiating or titrating MRA.	Regular checks of K+ and renal function should be performed according to clinical status, approximately 1 week, then 4 weeks, then every 6 months after initiating or intensifying MRA, with more frequent testing if clinically appropriate (e.g., patient that is clinically unstable of fluctuating renal function). Look for gynecomastia and ask about mastalgia, if appropriate.
Eplerenone†	25 CrCl < 50: 25 mg every other day	50 CrCl < 50: 25 daily		
Vasodilators				
Hydralazine	25 TID	75 TID (225 total daily dose)	In combination with isosorbide dinitrate	BP
Isosorbide dinitrate	20 TID	40 TID (120 total daily dose)	DO NOT use with PDE inhibitors and vericiguat. Common side effects including flushing, hypotension, nausea, and headache. These can be minimized by utilizing a slow titration schedule; starting with ½ tablet three times daily may increase tolerability.	BP
Hydralazine 37.5 mg / Isosorbide 20 mg	1 tablet TID	2 tablets TID		BP

†For those at high risk of hyperkalemia or who have marginal renal function (eGFR 30–49 mL/min/1.73 m^2), an initial regimen of every-other-day dosing is advised; K+ =potassium; BID = twice daily; TID = three times daily; NYHA=New York Heart Association; IR = immediate release; HR = heart rate; BP = blood pressure; eGFR = estimated glomerular filtration rate; BMP = basic metabolic panel; CrCl = Creatinine clearance mL/min; HFrEF = heart failure with reduced ejection fraction; Please see VA National Formulary for current list of formulary medications **VA Formulary Advisor (vanf.app)**

continued from page 4 (Medications for patients with HFrEF)

Medication	Starting daily dose (mg)	Target daily dose (mg)	Comments	Monitor
Other medications used in heart failure				
Ivabradine*†	2.5-5 BID	7.5 mg BID (dependent on HR; see comments)	Adjust dose after two weeks based on resting HR . HR > 60: increase dose by 2.5 mg (given twice daily) up to max dose of 7.5 mg twice daily. HR 50–60: maintain dose. HR < 50 or symptoms of bradycardia: decrease dose by 2.5 mg (given twice daily).	HR
Vericiguat†	2.5	10	If SBP ≥ 100 mm Hg, increase dose every 2 weeks. Decrease dose if SBP < 90 mm Hg.	BP
Digoxin	0.125 (requires renal dose adjustment)	—	Use lower dose in older patients, those with small frame/low BMI, or patients with chronic kidney disease/ impairment.	Target trough: 0.5–0.9 ng/mL at least 6-12 hours after last dose

*Unless specified, use highest tolerated dose while maintaining adequate HR; †Initiation preferred by cardiology; BID = twice daily, BP = blood pressure; HR = heart rate; SBP = systolic blood pressure; BMI = body mass index; Please see VA National Formulary for current list of formulary medications **VA Formulary Advisor (vanf.app)**

Diuretics for patients with HF

Medication	Starting daily dose (mg)	Maximum daily dose (mg)	Comments	Monitor
Furosemide*	20–40 daily or BID	600	Approximate oral conversion: Furosemide 40 mg ≈ Torsemide 10-20 mg ≈ Bumetanide 1mg = Ethacrynic acid 50 mg IV to PO: Furosemide 1:2 Bumetanide 1:1	Serum K+, Mg, renal function, volume status Thiazide diuretics can increase the risk of gout.
Bumetanide	0.5–1 daily or BID	10		
Torsemide	10–20 daily	200		
Metolazone*	2.5–10 daily**	20		
Ethacrynic acid	50 mg daily	400		

*Should be taken on an empty stomach; **Can be used for sequential nephron blockade when given once with a loop diuretic; K+ potassium; BID = twice daily; Mg = magnesium; IV = intravenous; PO = by mouth; Please see VA National Formulary for current list of formulary medications; **VA Formulary Advisor (vanf.app)**

Clinical pearls for using SGLT-2 inhibitors[12,13]

Diabetes / DKA	• Do not use in type 1 diabetes mellitus. • Educate patient on symptoms. If diabetic ketoacidosis (DKA) suspected, stop SGLT-2 inhibitor and take appropriate action. • DKA can occur in the setting of euglycemia in patients on a SGLT- 2 inhibitor. Increased risk in setting of very low-carbohydrate diet, excessive alcohol, extreme exercise, major surgery, periods of starvation/prolonged fasting, and/or excessive insulin dose reductions. • Educate patient to temporarily hold SGLT-2 inhibitor if any predisposing situations or symptoms that may increase risk of DKA occur (e.g., prolonged fasting, vomiting, trouble breathing, abdominal pain, and/or acute febrile illness). • Monitor patients on insulin and/or sulfonylureas when starting, especially if at or below HbA1c goal, or if a history of hypoglycemia.
Renal effects	• Renal, major adverse CV event (MACE), and heart failure benefits still observed at lower eGFRs. • Initial decline in eGFR expected. If early decline due to dehydration, then consider reducing and/or withholding diuretics or other medications (e.g., ACEI, ARB) and/or assess for other causes (follow patient closely). If initial decline > 30%, discontinue SGLT-2 inhibitor and evaluate further.

continued from page 5 (Clinical pearls for using SGLT-2 inhibitors)

Heart failure	• Assess loop diuretic dose and if not hypervolemic, may consider dose reduction of loop diuretic with initiation of SGLT-2 inhibitors in selected patients. • If diuretic dose reduced, provide clear instructions when to resume previous diuretic dose if symptoms of hypervolemia or worsening heart failure along with a low threshold to call team if problems/questions.
Blood pressure	• Caution with lower BP, especially if systolic BP is around 100 mm Hg or less. • Advise patient to keep well hydrated.
Infection history	• Assess history of genital mycotic infections and personal hygiene and/or problems with urinary flow. • Consider temporarily stopping therapy in patients with active genital or urinary tract infections until after patient has been appropriately treated for infectious etiology. • Counsel on proper hygiene, signs, and symptoms of infection, and to notify provider/seek medical advice if symptoms of infection. • Patients with severe obesity, indwelling urinary catheters (e.g., Foley), or very poor personal hygiene may be at higher risk of Fournier's gangrene. • For patients with recurrent urinary tract infections (UTI) consider infectious diseases consultation.
Follow-up	• Consider follow-up with a BMP (including bicarbonate) within ~4-6 weeks. If at higher risk of adverse events, closer follow-up of tolerability (+/- BMP in 1-2 weeks) may be warranted. • Repeat BMP periodically based on initial results and underlying disease state(s). • Assess blood sugar control (if patient has diabetes), BP, weight, and tolerability at follow-up.

Refer to prescribing information for more specific guidance; DKA = diabetic ketoacidosis; CV = cardiovascular; eGFR = estimated glomerular filtration rate; ACEI = angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP = blood pressure; BMP = basic metabolic panel

Heart failure medications in chronic kidney disease (CKD)[14,15]

CKD Stage 3 (eGFR ≥30 ≤59ml/min/1.73m^2)

- ARNI, ACEI, or ARB recommended.
- Beta blocker recommended.
- Mineralocorticoid receptor antagonist (MRA) recommended if HF symptoms persistent despite ACEI (or ARB) and beta blocker.
- Do not use MRA if K+ > 5, or SCr > 2.5 for males or SCr > 2.0 for females.
- Vericiguat recommended as indicated.
- Ivabradine recommended as indicated.
- Digoxin recommended as indicated (renal dose adjustment required).

CKD Stage 4 and 5 (eGFR <30 mL/min/1.73m^2)

- ACEI or ARB might be considered with careful monitoring of renal function and electrolytes.
- ACEI or ARB are safe to use in patients on dialysis.
- ARNI may be considered, but has not been extensively studied in this population.
- Beta blocker recommended.
- Avoid MRA.
- Vericiguat recommended as indicated, but has not been studied in eGFR < 15.
- Ivabradine may be considered.
- Digoxin recommended as indicated (renal dose adjustment required).

Hydralazine / isosorbide dinitrate does not require adjustment for renal impairment.

Medications for the treatment of heart failure with preserved ejection fraction (HFpEF)[8,16-19]

Treatment options	Recommendations	Medication considerations
BP control	• Hypertension should be controlled to prevent morbidity.*	• When selecting medication, consider other co-morbidities and the potential benefits. • No class of antihypertensive is contraindicated on the basis of HFpEF.
SGLT-2 inhibitor	• Helps reduce heart failure related hospitalizations regardless of diabetes.	• Reasonable if NYHA class II-IV

*In accordance to clinical practice guidelines; GDMT = guideline directed medical therapy, SBP = systolic blood pressure, ACEI = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, eGFR = estimated glomerular filtration rate

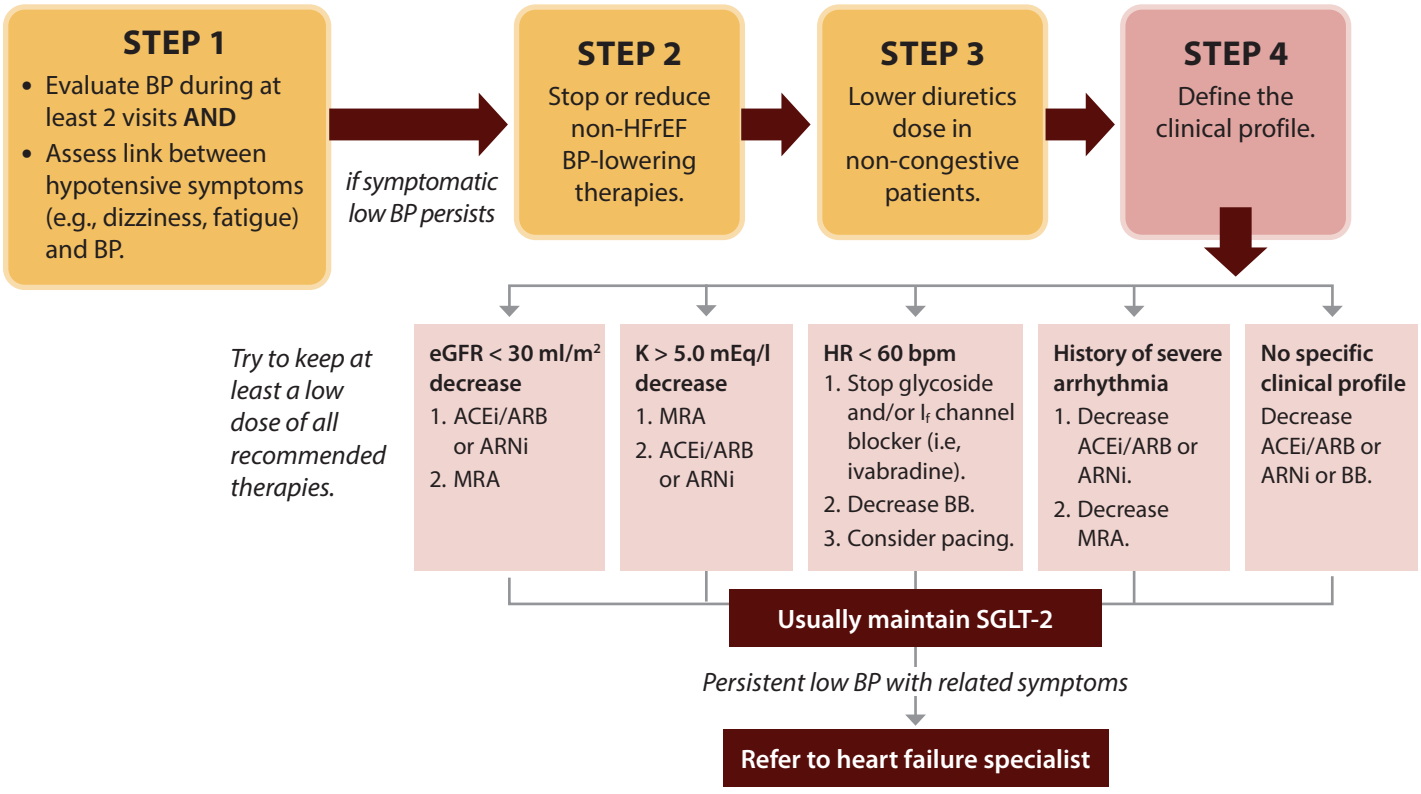
continued from page 6 (Medications for patients with HFpEF)

Treatment options	Recommendations	Medication considerations
Sacubitril/valsartan	• Might help reduce heart failure related hospitalization (p=0.05).	• May be reasonable: - Women - EF < 57% - Hospitalization in the past 9 months
Mineralocorticoid receptor antagonists	• Might help reduce heart failure related hospitalization. • Subgroup analysis of the North American population suggests benefit in the composite of death, aborted cardiac death, and heart failure hospitalizations.	• May be reasonable: - Age 50 or older - HF hospitalization within the last year or elevated BNP - Creatinine < 2.5 mg/dL, - Potassium < 5.0 mEq/L - eGFR > 30ml/min/1.73m^2 and stable
Angiotensin receptor blockers	• Might help reduce hospitalizations.	• May be reasonable and provide additional benefits: - Hypertension - Albuminuria
Fluid management	• Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF.	• Loop diuretics are preferred in symptomatic patients. • If minimal edema, can consider thiazide particularly if concomitant hypertension.

*In accordance to clinical practice guidelines; GDMT = guideline directed medical therapy; SBP = systolic blood pressure; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate

Management of patients with HFrEF and hypotension[20,21]

Assess blood pressure (BP) both supine and standing. Patients with a hypotensive emergency or cardiogenic shock should receive urgent admission.



ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta blocker; EF = ejection fraction; SGLT-2 = sodium-glucose co-transporter-2; HR = heart rate; ARNI = angiotensin receptor blocker/neprilysin inhibitor; eGFR = estimated glomerular filtration rate; BP = blood pressure: K = potassium.

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