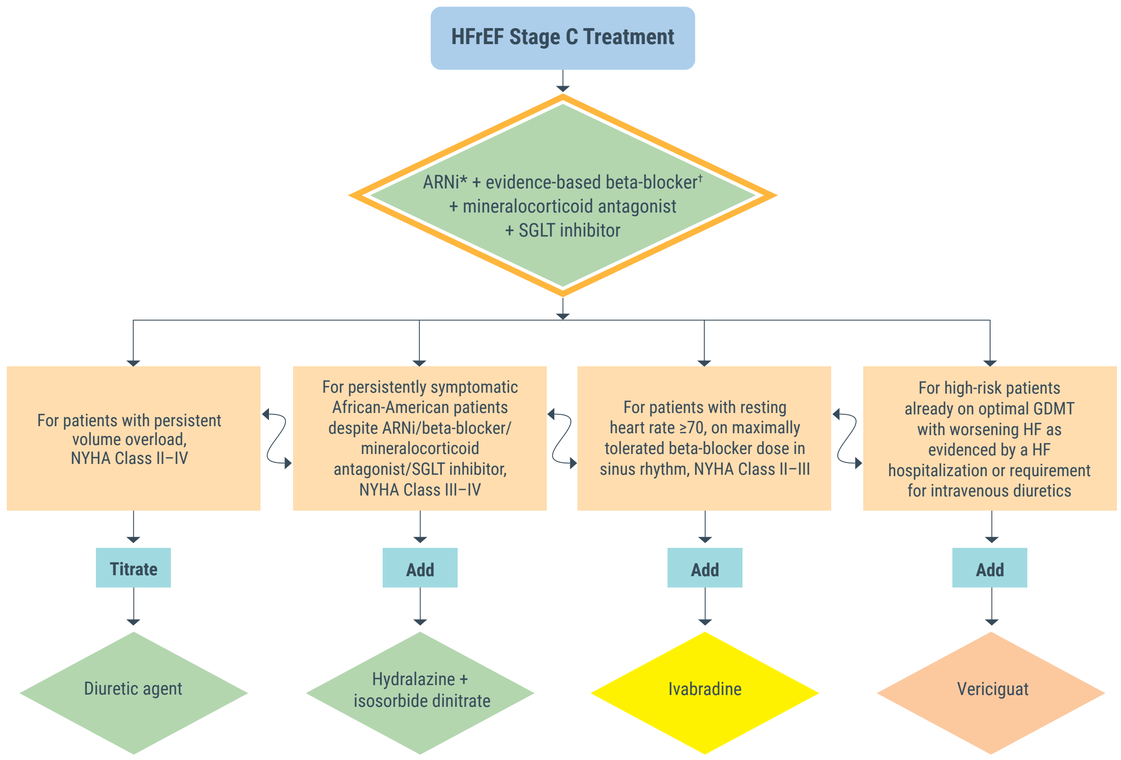
The 2024 ACC Expert Consensus Decision Pathway for the treatment of HFrEF recommends ARNi as the only first-line RASi[1]*

2024 ECDP for HFrEF: Treatment Algorithm for Guideline-Directed Medical Therapy[1]



Colors correspond to ACC/AHA Class of Recommendation. Green = Class 1 (strong); Yellow = Class 2a (moderate); Orange = Class 2b (weak).

*ACE inhibitors/ARBs should only be considered in patients with contraindications, intolerance, or inaccessibility to ARNi.
†Carvedilol, metoprolol succinate, or bisoprolol.

ACC, American College of Cardiology; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; ECDP, Expert Consensus Decision Pathway; GDMT, guideline-directed medical therapy; NYHA, New York Heart Association; RASi, renin-angiotensin system inhibitor; SGLT, sodium-glucose cotransporter.

Adapted from the *Journal of the American College of Cardiology*; 2024; Maddox TM, Januzzi JL Jr, Allen LA, et al. 2024 ACC Expert Consensus Decision Pathway for treatment of heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee; with permission from Elsevier.

*The 2024 ACC ECDP HFrEF treatment algorithm no longer includes ACE inhibitors/ARBs as a primary first-line treatment. When making a recommendation to initiate an ARNi (either as a switch or as de novo treatment), the ECDP Writing Committee recommends the decision occur within a framework of shared decision-making. For instance, ACE inhibitors/ARBs should be considered in patients with contraindications, intolerance, or inaccessibility to ARNi.[2]

AHA, American Heart Association; HFSA, Heart Failure Society of America.

First-line RASi therapy: ARNi is preferred for all appropriate HFrEF patients[1]

- ARNi is the only recommended first-line RASi* along with beta blocker, mineralocorticoid antagonist, and SGLT inhibitor for all appropriate HFrEF patients

In the ECDP, ENTRESTO®, a fixed combination of an angiotensin receptor blocker and a neprilysin inhibitor, is referred to as an ARNi.[1]

A de novo ARNi approach is preferred to ACE inhibitor or ARB pretreatment, with close follow-up, serial assessments (blood pressure, electrolytes, and kidney function), and consideration of risk of angioedema or hypotension.[1]

When making the transition from an ACE inhibitor to an ARNi, a 36-hour washout period should be strictly observed to avoid angioedema. This delay is not required when switching from an ARB to an ARNi.[1]

The ACC ECDP recommends that regardless of the sequencing of agents, careful initiation and titration of GDMT should be early and as rapid as possible with the goal to use the 4 key medication classes (ARNi, beta blocker, mineralocorticoid antagonist, and SGLT inhibitor) in each patient.[1]

The 2024 ACC ECDP for HFrEF reinforces the 2022 AHA/ACC/HFSA HF Guideline recommendation to replace well-tolerated ACE inhibitor/ARB with ARNi for NYHA Class II–III HFrEF patients. ACE inhibitor/ARB should be considered in patients with contraindications, intolerance, or inaccessibility to ARNi.[1,3]

Please see the **2024 ACC ECDP** for full guidance on GDMT optimization.

Make ENTRESTO the essential first-line RASi for your appropriate HFrEF patients

INDICATION

ENTRESTO is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.

LVEF is a variable measure, so use clinical judgment in deciding whom to treat.

IMPORTANT SAFETY INFORMATION

WARNING: FETAL TOXICITY

- **When pregnancy is detected, discontinue ENTRESTO as soon as possible**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus**

Entresto® (sacubitril/valsartan) tablets
24/26mg • 49/51mg • 97/103mg

Please see additional **Important Safety Information** on the next page, and **tap here** for full **Prescribing Information**, including **Boxed WARNING**.

IMPORTANT SAFETY INFORMATION (cont)

ENTRESTO® is contraindicated in patients with hypersensitivity to any component. ENTRESTO is contraindicated in patients with a history of angioedema related to previous angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy.

ENTRESTO is contraindicated with concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor. ENTRESTO is contraindicated with concomitant use of aliskiren in patients with diabetes.

Angioedema: ENTRESTO may cause angioedema. Angioedema associated with laryngeal edema may be fatal. ENTRESTO has been associated with a higher rate of angioedema in Black patients and in patients with a prior history of angioedema. ENTRESTO should not be used in patients with hereditary angioedema. If angioedema occurs, discontinue ENTRESTO immediately, provide appropriate therapy, and monitor for airway compromise. ENTRESTO must not be re-administered.

Hypotension: ENTRESTO lowers blood pressure and may cause symptomatic hypotension. Patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with high doses of diuretics), are at greater risk. Correct volume or salt depletion prior to administration of ENTRESTO or start at a lower dose. If hypotension persists despite dose adjustment of diuretics, concomitant antihypertensive drugs, and treatment of other causes of hypotension (e.g., hypovolemia), reduce the dosage or temporarily discontinue ENTRESTO. Permanent discontinuation of therapy is usually not required.

Impaired Renal Function: Decreases in renal function may be anticipated in susceptible individuals treated with ENTRESTO. In patients whose renal function depends upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with ACE inhibitors and angiotensin receptor antagonists has been associated with oliguria, progressive azotemia and, rarely, acute renal failure and death. Closely monitor serum creatinine, and down-titrate or interrupt ENTRESTO in patients who develop a clinically significant decrease in renal function.

ENTRESTO may increase blood urea and serum creatinine levels in patients with bilateral or unilateral renal artery stenosis. In patients with renal artery stenosis, monitor renal function. Avoid use with aliskiren in patients with renal impairment (eGFR <60 mL/min/1.73 m^2).

In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, with ENTRESTO may result in worsening of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically.

Hyperkalemia: Hyperkalemia may occur with ENTRESTO. Monitor serum potassium periodically and treat appropriately, especially in patients with risk factors for hyperkalemia such as severe renal impairment, diabetes, hypoaldosteronism, or a high potassium diet. Dosage reduction or interruption of ENTRESTO may be required.

Concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium, may lead to increases in serum potassium.

ARBs: Avoid use of ENTRESTO with an ARB, because ENTRESTO contains the angiotensin II receptor blocker valsartan.

Lithium: Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists. Monitor serum lithium levels during concomitant use with ENTRESTO.

Common Adverse Events: In a clinical trial of patients with heart failure with reduced ejection fraction, the most commonly observed adverse events with ENTRESTO vs enalapril, occurring at a frequency of at least 5% in either group, were hypotension (18%, 12%), hyperkalemia (12%, 14%), cough (9%, 13%), dizziness (6%, 5%), and renal failure/acute renal failure (5%, 5%). No new adverse reactions were identified in a trial of the remaining indicated population.

Please see additional **Important Safety Information** on the previous page, and **tap here** for full **Prescribing Information**, including **Boxed WARNING**.

References: 1. Maddox TM, Januzzi JL Jr, Allen LA, et al. 2024 ACC Expert Consensus Decision Pathway for treatment of heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2024. Epublished doi:10.1016/j.jacc.2023.12.024 **2.** American College of Cardiology, CardioSmart. *Heart Failure*. Accessed March 14, 2024. https://www.cardiosmart.org/topics/heart-failure **3.** 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 *J Am Coll Cardiol*. 2023;81(15):1551]. *J Am Coll Cardiol*. 2022;79(17):e263-e421. doi:10.1016/j.jacc.2021.12.012

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