



Entresto[®]
(sacubitril/valsartan) tablets

24/26mg • 49/51mg • 97/103mg

How to prescribe ENTRESTO[®] to your patients

Dosing and Titration Guide

INDICATION

ENTRESTO is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.

ENTRESTO is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.

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 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.

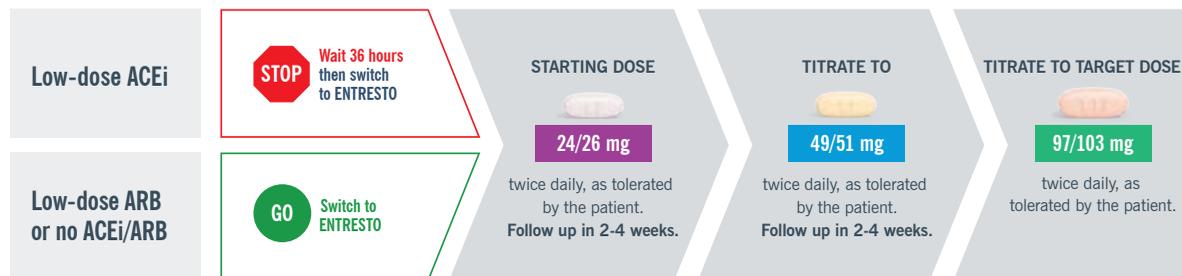
ENTRESTO is contraindicated with concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor. ENTRESTO is contraindicated with concomitant use of aliskiren in patients with diabetes.

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.

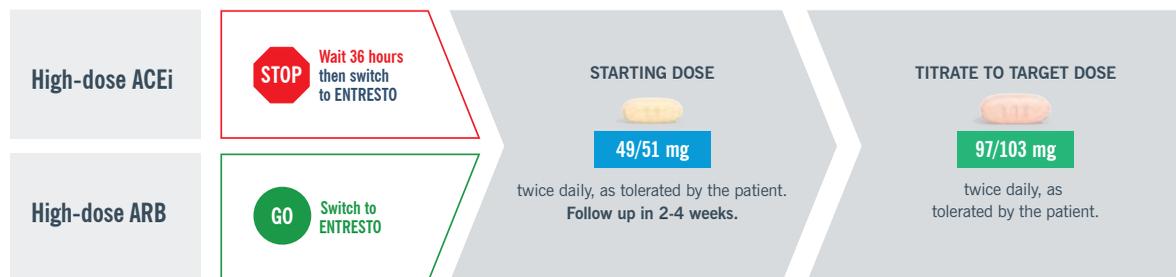
Please see additional Important Safety Information on next two pages, and [click here](#) for full Prescribing Information, including Boxed WARNING.

A straightforward approach to initiating ENTRESTO

Choose initial dose based on current treatment and titrate to the target dose¹



- **Low-dose ACEi:** total daily dose of ≤ 10 mg of enalapril or therapeutically equivalent dose of another ACEi (eg, lisinopril ≤ 10 mg; ramipril ≤ 5 mg)²
- **Low-dose ARB:** total daily dose of ≤ 160 mg of valsartan or therapeutically equivalent dose of another ARB (eg, losartan ≤ 50 mg; olmesartan ≤ 10 mg)²



- **High-dose ACEi:** total daily dose of > 10 mg of enalapril or therapeutically equivalent dose of another ACEi (eg, lisinopril > 10 mg; ramipril > 5 mg)²
- **High-dose ARB:** total daily dose of > 160 mg of valsartan or therapeutically equivalent dose of another ARB (eg, losartan > 50 mg; olmesartan > 10 mg)²
- ENTRESTO is contraindicated with concomitant use of an ACEi and in patients with a history of angioedema related to previous ACEi or ARB therapy¹
- Avoid use of ENTRESTO with an ARB, because ENTRESTO contains the angiotensin II receptor blocker valsartan¹

ENTRESTO may be administered with or without food.¹

Unless your patient is on a high ACEi or ARB dose, start ENTRESTO at 24/26 mg twice daily and double the dose every 2 to 4 weeks, as tolerated by the patient¹

IMPORTANT SAFETY INFORMATION, CONT'D

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.

Please see additional Important Safety Information on each page, beginning on page 1, and [click here](#) for full Prescribing Information, including Boxed WARNING.

References: 1. ENTRESTO [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; November 2017. 2. Senni M, McMurray JJV, Wachter R, et al. Initiating sacubitril/valsartan (LCZ696) in heart failure: results of TITRATION, a double-blind, randomized comparison of two uptitration regimens [published online ahead of print May 12, 2016]. *Eur J Heart Fail.* 2016;18(9):1193-1202. doi:10.1002/ehf.548.

ACEi=angiotensin-converting enzyme inhibitor; ARB=angiotensin II receptor blocker.

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For patients with severe renal impairment (eGFR <30 mL/min/1.73m²) or moderate hepatic impairment (Child-Pugh B classification)¹

- Follow the same approach as for patients switching from a LOW dose of an ACEi or ARB (or not currently taking an ACEi or ARB)

No starting dose adjustment is needed for mild or moderate renal impairment.

No starting dose adjustment is needed for mild hepatic impairment. Use in patients with severe hepatic impairment is not recommended.

IMPORTANT SAFETY INFORMATION, CONT'D

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 m²).

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, 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%).

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