The 2021 CCS/CHFS Heart Failure Guidelines Update is here[1]*

Are your patients being treated with guideline-recommended therapy?

PrENTRESTO® (sacubitril/valsartan) is indicated for the treatment of heart failure with reduced ejection fraction (HFrEF) in patients with NYHA Class II or III, to reduce the incidence of cardiovascular death and heart failure hospitalization.[2]

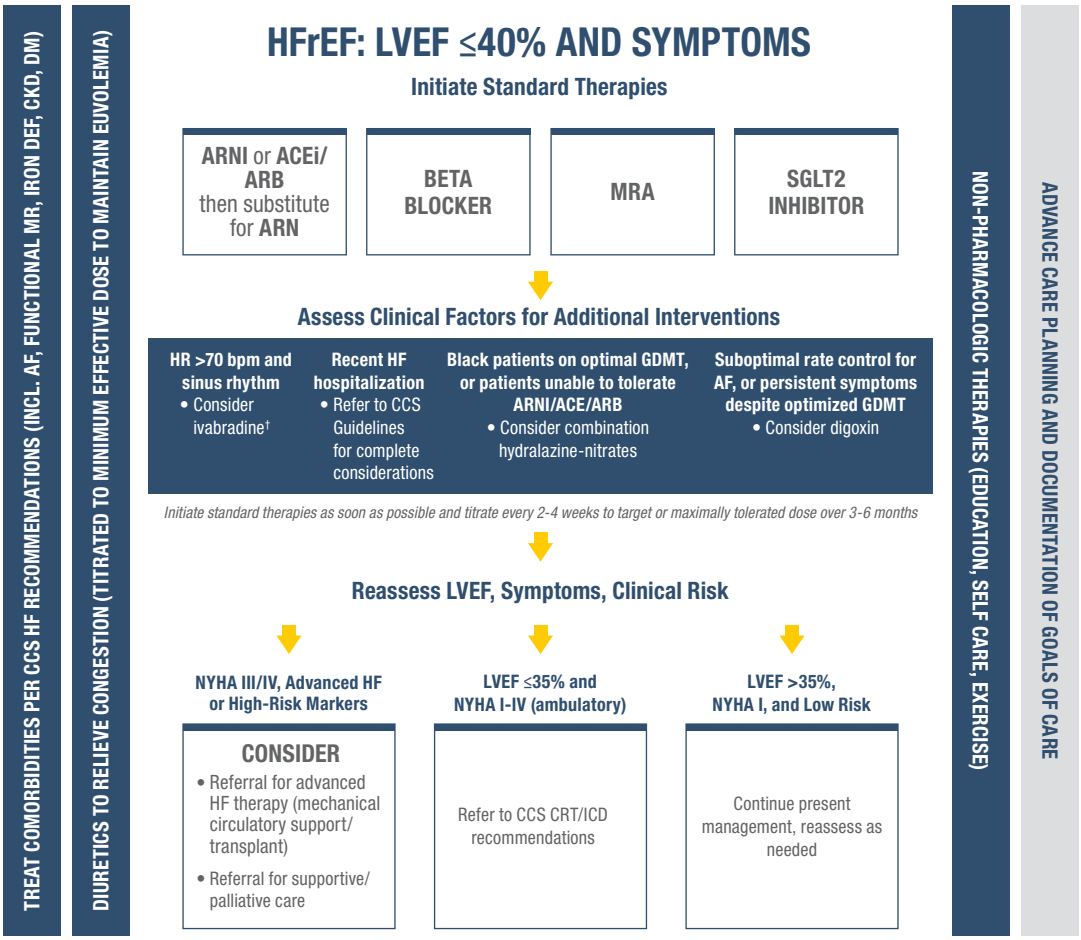
ENTRESTO® should be administered in combination with other heart failure therapies, in place of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB).[2]

* Please consult guidelines for complete recommendations.

CCS=Canadian Cardiovascular Society; CHFS=Canadian Heart Failure Society; HFrEF=heart failure with reduced ejection fraction.

PrEntresto®
sacubitril/valsartan

Updated treatment algorithm for the management of HFrEF from the 2021 CCS/CHFS Heart Failure Guidelines Update[1]*



> "Standard therapies are applicable to most patients with HFrEF for reducing cardiovascular mortality and hospitalization for HF."[1]

> "Every attempt should be made to initiate and titrate therapies with the goal of medication optimization by 3–6 months after a diagnosis of HFrEF."[1]

* Please consult guidelines for complete recommendations.
† Ivabradine is indicated in patients with HFrEF and HR ≥77 bpm in sinus rhythm.
ACEi=angiotensin converting enzyme inhibitor; AF=atrial fibrillation; ARB=angiotensin receptor blocker; ARNI=angiotensin receptor-neprilysin inhibitor; CCS=Canadian Cardiovascular Society; CHFS=Canadian Heart Failure Society; CKD=chronic kidney disease; CRT=cardiac resynchronization therapy; DM=diabetes mellitus; GDMT=guideline-directed medical therapy; HFrEF=heart failure with reduced ejection fraction; HR=heart rate; ICD=implantable cardioverter defibrillator; LVEF=left ventricular ejection fraction; MR=mitral regurgitation; MRA=mineralocorticoid receptor antagonist; NYHA=New York Heart Association; SGLT=sodium glucose transport.

2021 CCS recommendation*

ARNI: Recommended as a standard therapy for HFrEF

"The 2021 CCS HF Guidelines recommend ARNI as a standard therapy for HFrEF, in combination with other standard therapies."[1]

2021 CCS recommendation*

"We recommend that an ARNI be used in place of an ACEi or ARB, in patients with HFrEF, that remain symptomatic despite treatment with appropriate doses of GDMT... (was assigned strong recommendation, high-quality evidence)."[1]

Sacubitril-valsartan is the only available ARNI indicated in HFrEF.[1,3]

*Please consult guidelines for complete recommendations.

ACEi=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; ARNI=angiotensin receptor-neprilysin inhibitor; CCS=Canadian Cardiovascular Society; GDMT=guideline-directed medical therapy; HHF=heart failure hospitalization; HFrEF=heart failure with reduced ejection fraction.

Additional resources

CCS Guidelines and Position Statement Library

All guidelines and position statements from the CCS can be accessed at **ccs.ca/guidelines-and-position-statement-library**

The 2021 CCS/CHFS Heart Failure Guidelines Update can be accessed at **www.onlinecjc.ca/article/S0828-282X(21)00055-6/fulltext** or by scanning the following QR code with your smartphone camera:

CCS Pocket Guides

The CCS also provides pocket guides to serve as quick reference tools for their essential diagnostic and treatment recommendations.

Their 2021 Heart Failure pocket guide can be accessed at **ccs.ca/pocket-guides** or by scanning the following QR code with your smartphone camera:

Clinical use:
- ENTRESTO® should be administered in combination with other heart failure therapies, in place of an ACEi or ARB.
- ENTRESTO® should be initiated, and up-titration conducted, by a physician experienced with the treatment of heart failure.
- No dosage adjustment is required in patients over 65 years. However, ENTRESTO® has been studied in a limited number of patients above the age of 80 years. Caution is required in these patients.
- The safety and efficacy of ENTRESTO® in pediatric patients (<18 years of age) has not been established.

Contraindications:
- Recent symptomatic hypotension prior to initiation of treatment with ENTRESTO® (sacubitril/valsartan)
- Concomitant use with any drug formulation containing an ACEi, due to potential enhanced risk of angioedema. **ENTRESTO® must not be administered until at least 36 hours have elapsed following discontinuation of ACEi therapy**
- Known history of angioedema related to previous ACEi or ARB therapy
- History of hereditary or idiopathic angioedema
- As for any formulation containing an ACEi or ARB, use of ENTRESTO® together with aliskiren-containing drugs is contraindicated in patients with diabetes mellitus, whether Type 1 or 2, or in patients with moderate to severe renal impairment, i.e., eGFR <60 mL/min/1.73 m^2
- Pregnant and nursing women
- Hypersensitivity to the active substances, sacubitril or valsartan, or to any of the excipients

Most serious warnings and precautions:

Use of ARB in pregnancy: When used in pregnancy, ARBs can cause injury to or even death of the developing fetus. When pregnancy is detected, ENTRESTO® should be discontinued as soon as possible.

Use of ACEi: ENTRESTO® must not be administered with an ACEi due to the risk of angioedema.

Use of ARB: ENTRESTO® should not be administered with any other drug formulation containing an ARB, due to the angiotensin II receptor blocking activity of ENTRESTO® by its valsartan moiety.

NT-proBNP monitoring: Due to the action of sacubitril on BNP levels, only NT-proBNP may be a suitable biomarker for the monitoring of heart failure patients treated with ENTRESTO®.

Use of medications known to raise serum potassium levels: Caution should be exercised when co-administering ENTRESTO® with medications known to raise serum potassium levels (e.g., potassium-sparing diuretics, potassium supplements).

Other relevant warnings and precautions:
- ENTRESTO® should not be co-administered with any other drug formulation containing an ARB.
- Caution when co-administering ENTRESTO® with direct renin inhibitors such as aliskiren.
- Angioedema: Caution is recommended in patients with a prior history of any angioedema and in black patients.
- Symptomatic hypotension: ENTRESTO® is not recommended in patients with systolic blood pressure <100 mmHg at the time of treatment initiation.
- Hyperkalemia: Measure serum potassium before instituting ENTRESTO®, and during treatment, as appropriate, taking into account the patient's predisposition to develop hyperkalemia. Patients with serum potassium >5.2 mmol/L prior to initiation of treatment with ENTRESTO® have not been studied. Careful monitoring of serum potassium is recommended in patients with severe renal impairment, diabetes mellitus, hypoaldosteronism, or a high potassium intake in their diet.
- Decreases in renal function in susceptible individuals. Closely monitor serum creatinine, and down-titrate or interrupt ENTRESTO® in patients who develop a clinically significant decrease in renal function. Before initiation of therapy and during treatment, assess renal function, as appropriate.
- Caution in patients with renal artery stenosis, if ENTRESTO® is to be used. Careful monitoring of renal function should be carried out.
- Advising women of child-bearing potential to use contraception during treatment with ENTRESTO® and for one (1) week after their last dose.
- Nursing women: Because of the potential risk for adverse drug reactions in breastfed newborns, ENTRESTO® is not recommended during breastfeeding.
- A starting dose of 24 mg sacubitril/26 mg valsartan twice daily is recommended in patients with moderate hepatic impairment (Child-Pugh B). ENTRESTO® is not recommended in patients with severe hepatic impairment (Child-Pugh C).
- ENTRESTO® is not recommended in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2).

For more information:

Please consult the Product Monograph at www.novartis.ca/EntrestoMonograph for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-363-8883 or via medinfo.canada@novartis.com.

References: 1. McDonald M, Virani S, Chan M *et al.* CCS/CHFS Heart Failure Guidelines Update: Defining a New Pharmacologic Standard of Care for Heart Failure With Reduced Ejection Fraction. *Can J Cardiol* 2021;37(4):531-546. **2.** ENTRESTO® Product Monograph. Novartis Pharmaceuticals Canada Inc. July 13, 2021. **3.** Novartis Data on File – First and only. 2021.

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Pr Entresto® sacubitril/valsartan

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REVIEWED BY PAAB

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