NOVARTIS

ENTRESTO® (sacubitril/valsartan)
50, 100, 200 mg film-coated tablets

Basic Succinct Statement (BSS)

Version 1.2

CODE: BSS RD 10 JUL 2017; APPR 03 DEC 2018

This material is only meant for Healthcare Professionals

ENTRESTO® tablets

Important note: Before prescribing, consult full prescribing information.

Presentation: Tablets: film-coated tablets containing 50 mg, 100 mg, or 200 mg Entresto (sacubitril/valsartan)® as sodium salt complex.

Indications: ♦ Entresto is indicated in adult patients for treatment of symptomatic chronic heart failure with reduced ejection fraction. ♦ Entresto is administered in combination with other heart failure therapies (e.g. beta blockers, diuretics and mineralocorticoid antagonists) as appropriate, in place of an ACE inhibitor or ARB.

Dosage and administration:

♦**Adults:** The recommended starting dose of Entresto is 100 mg twice daily. Double the dose every 2-4 weeks to the target of 200 mg twice daily, as tolerated by the patient. A starting dose of 50 mg twice daily and slow dose titration (doubling every 3-4 weeks) are recommended for patients not currently taking an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), and should be considered for patients previously taking low doses of these agents.
♦**Geriatric patients**: Dose should be in line with the renal function of the elderly patient.
♦**Pediatric patients:** Entresto has not been studied.
♦**Renal impairment:** No dose adjustment is required in patients with mild renal impairment. Starting dose of 50 mg twice daily and caution is recommended in patients with moderate to severe renal impairment.
♦**Hepatic impairment:** No dose adjustment is required in patients with mild hepatic impairment. Starting dose of 50 mg twice daily is recommended in patients with moderate hepatic impairment. Entresto is contraindicated in patients with severe hepatic impairment, biliary cirrhosis or cholestasis.
♦**Method of administration:** For oral use. May be administered with or without food.

Contraindications: ♦Hypersensitivity to the active substances or to any of the excipients. ♦Concomitant use with ACE inhibitors. Entresto must not be administered until 36 hours after discontinuing ACE inhibitor therapy. ♦Known history of angioedema related to previous ACE inhibitor or ARB therapy. ♦Hereditary or idiopathic angioedema. ♦Concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m^2). ♦Severe hepatic impairment, biliary cirrhosis and cholestasis. ♦Second and third trimester of pregnancy.

Warnings and precautions:

♦**Dual blockade of the Renin-Angiotensin-Aldosterone System (RAAS):** Entresto is contraindicated with an ACE inhibitor due to the risk of angioedema. Entresto must not be initiated until 36 hours after taking the last dose of ACE inhibitor therapy. If treatment with Entresto is stopped, ACE inhibitor therapy must not be initiated until 36 hours after the last dose of Entresto. Entresto is contraindicated with aliskiren-containing products in patients

with diabetes mellitus or in patients with renal impairment (eGFR <60 ml/min/1.73 m^2). Entresto should not be co-administered with an ARB due to the angiotensin II receptor blocking activity of Entresto.

♦**Hypotension:** Treatment should not be initiated unless SBP is ≥100 mmHg. If hypotension occurs, temporary down-titration or discontinuation of Entresto is recommended. Dose adjustment of diuretics, concomitant antihypertensives and treatment of other causes of hypotension (e.g. hypovolaemia) should be considered. Sodium and/or volume depletion should be corrected before starting treatment with Entresto.

♦**Impaired and worsening renal function:** ♦Down titration of Entresto should be considered in patients who develop a clinically significant decrease in renal function. Caution should be exercised when administering Entresto in patients with severe renal impairment.

♦**Hyperkalemia:** Treatment should not be initiated if the serum potassium level is >5.4 mmol/l. Monitoring of serum potassium is recommended, especially in patients who have risk factors such as renal impairment, diabetes mellitus or hypoaldosteronism or who are on a high potassium diet or on mineralocorticoid antagonists. If patients experience clinically significant hyperkalaemia adjustment of concomitant medicinal products, or temporary down–titration or discontinuation is recommended. If serum potassium level is >5.4 mmol/l discontinuation should be considered.

♦**Angioedema:** If angioedema occurs, Entresto should be immediately discontinued and appropriate therapy and monitoring should be provided until complete and sustained resolution of signs and symptoms has occurred. Entresto must not be re-administered. Patients with a prior history of angioedema were not studied. As they may be at higher risk for angioedema, caution is recommended if Entresto is used in these patients. Entresto must not be used in patients with a known history of angioedema related to previous ACE inhibitor or ARB therapy or with hereditary or idiopathic angioedema. Black patients may have increased susceptibility to develop angioedema.

♦**Patients with renal artery stenosis:** Caution is required in patients with renal artery stenosis and monitoring of the renal function is recommended.

♦**Patients with NYHA functional classification IV:** Caution should be exercised when initiating Entresto in patients with NYHA functional classification IV due to limited clinical experience in this population.

♦**B-type natriuretic peptide (BNP):** BNP is not a suitable biomarker of heart failure in patients treated with Entresto because it is a neprilysin substrate.

♦**Patients with hepatic impairment:** Caution is recommended when using in moderate hepatic impairment patients. Entresto is contraindicated in patients with severe hepatic impairment, biliary cirrhosis or cholestasis (Child-Pugh C classification).

Adverse drug reactions:

Very common (≥10%)*:* Hyperkalemia, hypotension, renal impairment.

Common (1 to 10%): Anaemia, hypokalemia, hypoglycaemia, dizziness, headache, syncope, vertigo, orthostatic hypotension, cough, diarrhea, nausea, gastritis, renal failure, fatigue, asthenia.

Uncommon (0.1 to 1%)*:* Hypersensitivity, dizziness postural, pruritus, rash, angioedemia.