HOSPIMAX
Maximising Life

Product Description:

Each film coated tablet contains

- SacuAct 25: Sacubitril 12mg + Valsartan 13mg
- SacuAct 50: Sacubitril 24mg + Valsartan 26mg

General Information:

Heart is a hollow, muscular organ that pumps blood through the body by contracting and relaxing. One of the primary functions of the human heart is to pump blood throughout the body.

Heart Failure – It is a clinical pathological syndrome characterized by failure of the heart to generate enough cardiac output to meet the minimum metabolic needs of the body tissues.
Left-sided heart failure:

- **Systolic failure:** The left ventricle loses its ability to contract normally. This is also known as heart failure with reduced ejection, or **HFrEF**. When this occurs, **the heart is pumping less than or equal to 40% EF.**
- **Diastolic failure:** The left ventricle loses its ability to relax normally because the muscle has become stiff. This is also known as heart failure with preserved ejection, or **HFpEF**. **When this occurs, the heart is pumping greater than or equal to 50%.**
- **Heart failure with mid-range ejection fraction (HFmrEF) is a newer concept.** In this type of heart failure, the **left ventricle pumps between 41% and 49% EF**. This places people with HFmrEF between the HFrEF and HFpEF groups.

Sacubitril: Sacubitril is a neprilysin inhibitor used in combination with valsartan as an adjunct 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.

Valsartan: Valsartan also affects the renin-angiotensin aldosterone system (RAAS), which plays an important role in hemostasis and regulation of kidney, vascular, and cardiac functions. Pharmacological blockade of RAAS via AT1 receptor blockade inhibits negative regulatory feedback within RAAS, which is a contributing factor to the pathogenesis and progression of cardiovascular disease, heart failure, and renal disease.

Mode of Action:

Sacubitril is a neprilysin inhibitor and ***Valsartan*** an angiotensin receptor blocker.
The cardiovascular and renal effects of **SacuAct** in heart failure patients are attributed to the increased levels of peptides that are degraded by neprilysin, including natriuretic peptides such as BNP and ANP, and the simultaneous inhibition of the effects of angiotensin II by valsartan through blockade of the AT1 receptor.

Indications:

To reduce the risk of cardiovascular death and hospitalization in patients with Chronic Heart Failure.

Contraindications:

- Concomitant use with any drug formulation containing an angiotensin-converting enzyme inhibitor, due to potential enhanced risk of angioedema
- SacuAct must not be administered until at least 36 hours have elapsed following discontinuation of Angiotensin Converting Enzyme Inhibitors therapy
- Known history of angioedema related to previous Angiotensin Converting Enzyme Inhibitor or Angiotensin Receptor Blocker therapy
- History of hereditary or idiopathic angioedema
- As for any formulation containing an ACEi or ARB, use of SacuAct 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/1.73m^2
- Pregnancy
- Hypersensitivity to the active substances, sacubitril or valsartan, or to any of the excipients

Drug-Food Interactions:

SacuAct may be administered with or without food.

Dosage and Administration:

Initiating dose: 49/51 mg sacubitril/valsartan BD OR lower dose 24/26 mg BID

Maximum dose: 97/103 mg BID (sacubitril/valsartan)

- In patients not currently taking an ACE inhibitor or an angiotensin II receptor blocker (ARB) and for patients previously taking low doses of these agents, start Sacubitril / Valsartan at half the usually recommended starting dose. After initiation, increase the dose every 2 to 4 weeks.

- In patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2), start Sacubitril / Valsartan at half the usually recommended starting dose. After initiation, increase the dose to follow the recommended dose escalation thereafter.
- In patients with moderate hepatic impairment (Child-Pugh B classification), start Sacubitril/Valsartan at half the usually recommended starting dose. After initiation, increase the dose to follow the recommended dose escalation thereafter.
- Sacubitril/Valsartan is contraindicated with concomitant use of an angiotensin-converting enzyme (ACE) inhibitor or Angiotensin Receptor Blocker (ARB). If switching from an ACE inhibitor or ARB to Sacubitril/Valsartan allow a washout period of 36 hours between administration of the two drugs.

Missed Dose:

If a dose is missed, patients should be advised to take it as soon as they remember and then take the next tablet at the usual time. Doses should not be doubled to make up for the missed dose.

Pharmacokinetics:

Absorption: Following oral administration, SacuAct dissociates into sacubitril, which is then further metabolised to LBQ657, and valsartan, which reach peak plasma concentrations in 0.5 hours, 3 hours, and 1.5 hours, respectively. The oral absolute bioavailability of sacubitril and valsartan is estimated to be ≥60% and 23%, respectively.

Distribution: Sacubitril, LBQ657, and valsartan are highly bound to plasma proteins (94% - 97%). Based on the comparison of plasma and CSF exposures, LBQ657 does cross the blood brain barrier to a very limited extent, i.e., 0.3%.

Metabolism: Sacubitril is readily converted to LBQ657 by esterases, with LBQ657 not further metabolised to a significant extent. Valsartan is minimally metabolised, as only about 20% of the dose is recovered as metabolites. A hydroxyl metabolite has been identified in plasma at low concentrations (<10%).

Elimination: Following oral administration, 52% to 68% of sacubitril (primarily as LBQ657) and ~13% of valsartan and its metabolites are excreted in urine; 37% to 48% of sacubitril (primarily as LBQ657), and 86% of valsartan and its metabolites are excreted in feces. Sacubitril, LBQ657, and valsartan are eliminated from plasma with a mean elimination half-life (t1/2) of approximately 1.4 hours, 11.5 hours, and 9.9 hours, respectively.

Storage: Do not store above 30°C and protect from moisture.