Savatril
Tablet

DRUG INTERNATIONAL LTD.

Composition : **Savatril-50 :** Each film coated tablet contains Sacubitril INN 24 mg & Valsartan USP 26 mg.

Pharmacology : Sacubitril, a neprilysin inhibitor inhibits neprilysin (neutral endopeptidase; NEP) via LBQ657, the active metabolite of the prodrug sacubitril. Valsartan, an angiotensin II receptor blocker blocks the angiotensin II type-1 (AT_1) receptor. The cardiovascular and renal effects of sacubitril/valsartan in heart failure patients are attributed to the increased levels of peptides that are degraded by neprilysin, such as natriuretic peptides, by LBQ657, and the simultaneous inhibition of the effects of angiotensin II by valsartan. Valsartan inhibits the effects of angiotensin II by selectively blocking the AT_1 receptor, and also inhibits angiotensin II-dependent aldosterone release.

Indications : Sacubitril / Valsartan combination is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure and reduced left ventricular ejection fraction. For the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. It reduces NT-proBNP and is expected to improve cardiovascular outcome.

Dosage and administration :

Indication	Titration Step Dose (Twice Daily)		
	Starting	second	Final
Adult Heart Failure	100 mg	200 mg	
Pediatric Heart Failure Patient at least 40 kg, less than 50kg	50 mg	100 mg	150 mg (Three 50mg Tablet)
Pediatric Heart Failure Patient at least 50kg	100 mg	150 mg (Three 50mg Tablet)	200 mg

Adjust adult dose every 2 to 4 weeks and pediatric doses every 2 weeks to the target maintainance dose, as tolerated by the patient. Oral suspension Sacubitril/valsartan is recommended for children of less than 40 kg. **Reduce the starting dose to 50 mg twice-daily for:** patients not currently taking an angiotensin-converting enzyme inhibitor (ACE) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents, patients with severe renal impairment and with moderate hepatic impairment. Or, as directed by the registered physician.

Contraindication : It is contraindicated in patients have hypersensitivity to any component and history of angioedema related to previous ACE inhibitor or ARB therapy. Concomitant use with ACE inhibitors and concomitant use with aliskiren in patients with diabetes is also contraindicated.

Precautions : Signs and symptoms of angioedema and hypotension should be observed, Renal function and potassium should be monitored in susceptible patients.

Side effects : Most common adverse reactions include angioedema, hypotension, hyperkalemia, cough, dizziness, and renal failure.

Use in Pregnancy & Lactation : Sacubitril / Valsartan can cause fetal harm when administered to a pregnant woman. Because of the potential for serious adverse reactions in breastfed infants, breastfeeding is not recommended during treatment with sacubitril / valsartan.

Use in Child : Please see dosage and administration option.

Drug Interactions : **Dual blockade of the renin-angiotensin system:** Do not use with an ACEi and with aliskiren in patients with diabetes, avoid use with an ARB. **Potassium-sparing diuretics:** May lead to increased serum potassium. **NSAIDs:** May lead to increased risk of renal impairment. **Lithium:** Increased risk of lithium toxicity.

Overdose : Hypotension is the most likely result of overdosage due to the blood pressure lowering effects of sacubitril/ valsartan. Symptomatic treatment should be provided. It is unlikely to be removed by hemodialysis because of high protein binding.

Storage : Store bellow 30°C in a cool and dry place. Protect from light and moisture. Keep out of the reach of children.

Packing : **Savatril-50 :** Each box contains 1 x 10's tablets in a blister pack.