For use in India only

Not to be sold by retail without the prescription of a Registered Medical Practitioner.

PRESCRIBING INFORMATION

Sacubitril and Valsartan Tablets (24+26) 50 mg, (49+51) 100 mg & (97+103) 200 mg

Sacutan™ 50/100/200

सेकूटन-५०/१००/२००

GENERIC NAME

Sacubitril and Valsartan Tablets (24mg/26mg) 50mg
Sacubitril and Valsartan Tablets (49mg/51mg) 100mg
Sacubitril and Valsartan Tablets (97mg/103mg) 200mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sacubitril and Valsartan Tablets (24mg/26mg) 50mg
Each Film Coated Tablet Contains
Sacubitril 24 mg and Valsartan 26 mg
Colours: Titanium Dioxide IP Ferric Oxide Red-USP-NF Ferric Oxide Black-USP-NF

Sacubitril and Valsartan Tablets (49mg/51mg) 100mg
Each Film coated Tablet Contains
Sacubitril 49 mg and Valsartan 51 mg
Colours: Titanium Dioxide IP Ferric Oxide Yellow-USP-NF Ferric Oxide Red-USP-NF

Sacubitril and Valsartan Tablets (97mg/103mg) 200mg
Each Film coated Tablet Contains
Sacubitril 97 mg and Valsartan 103 mg
Colours: Titanium Dioxide IP Ferric Oxide Red-USP-NF Ferric Oxide Black-USP-NF

3. DOSAGE FORM AND STRENGTH

Film coated tablets;
50mg (Sacubitril 24 mg and Valsartan 26 mg)
100mg (Sacubitril 49 mg and Valsartan 51 mg)
200mg (Sacubitril 97 mg and Valsartan 103 mg)

4. CLINICAL PARTICULARS

4.1. Indications

Sacubitril/Valsartan tablets are 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.
These tablets are usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other Angiotensin receptor blockers (ARB).

4.2. Posology and Method of Administration

General Considerations

Sacubitril and valsartan tablets are contraindicated with concomitant use of an angiotensin-converting enzyme (ACE) inhibitor. If switching from an ACE inhibitor to Sacubitril/Valsartan allow a washout period of 36 hours between administrations of the two drugs.
The recommended starting dose of Sacubitril/Valsartan tablets is 49mg/51mg orally twice-daily.
Double the dose of Sacubitril/Valsartan tablets after 2 to 4 weeks to the target maintenance dose of 97mg/103mg twice daily, as tolerated by the patient.

Dose Adjustment for Patients Not Taking an ACE inhibitor or ARB or Previously Taking Low Doses of These Agents

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 tablets at half the usually recommended starting dose. After initiation, increase the dose to follow the recommended dose escalation thereafter.

Dose Adjustment for Severe Renal Impairment

In adult patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2), start Sacubitril/Valsartan tablets at half the usually recommended starting dose. After initiation, increase the dose to follow the recommended dose escalation thereafter.
No starting dose adjustment is needed for mild or moderate renal impairment.

Dose Adjustment for Hepatic Impairment

In adults with moderate hepatic impairment (Child-Pugh B classification), start Sacubitril/valsartan tablets at half the usually recommended starting dose. After initiation, increase the dose to follow the recommended dose escalation thereafter.
No starting dose adjustment is needed for mild hepatic impairment.
Use in patients with severe hepatic impairment is not recommended.

4.3. Contraindications

Sacubitril/Valsartan tablets are contraindicated:

- In patients with hypersensitivity to any component.
- In patients with a history of angioedema related to previous ACE inhibitor or ARB therapy.
- With concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor.
- With concomitant use of aliskiren in patients with diabetes.
- Severe hepatic impairment, biliary cirrhosis and cholestasis.
- Second and third trimester of pregnancy.

4.4. Special Warnings and Precautions for Use

Fetal Toxicity

Sacubitril/Valsartan tablets can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. When pregnancy is detected, consider alternative drug treatment and discontinue Sacubitril/valsartan tablets. However, if there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system, and if the drug is considered lifesaving for the mother, advise a pregnant woman of the potential risk to the fetus.

Angioedema

Sacubitril/Valsartan tablets may cause angioedema. If angioedema occurs, discontinue Sacubitril/Valsartan tablets immediately, provide appropriate therapy, and monitor for airway compromise. Sacubitril/Valsartan tablets must not be re-administered. In cases of confirmed angioedema where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms.
Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, administer appropriate therapy, e.g., subcutaneous epinephrine/adrenaline solution 1:1000 (0.3 mL to 0.5 mL) and take measures necessary to ensure maintenance of a patent airway.
Sacubitril/Valsartan tablets have been associated with a higher rate of angioedema in Black than in non-Black patients.
Patients with a prior history of angioedema may be at increased risk of angioedema with Sacubitril/Valsartan tablets. Sacubitril/Valsartan tablets must not be used in patients with a known history of angioedema related to previous ACE inhibitor or ARB therapy. Sacubitril/Valsartan should not be used in patients with hereditary angioedema.

Hypotension

Sacubitril/Valsartan tablets lower 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 Sacubitril/Valsartan tablets or start at a lower dose. If hypotension occurs, consider dose adjustment of diuretics, concomitant antihypertensive drugs, and treatment of other causes of hypotension (e.g., hypovolemia). If hypotension persists despite such measures, reduce the dosage or temporarily discontinue Sacubitril/valsartan tablets. Permanent discontinuation of therapy is usually not required.

Impaired Renal Function

As a consequence of inhibiting the renin-angiotensin-aldosterone system (RAAS), decreases in renal function may be anticipated in susceptible individuals treated with Sacubitril/valsartan tablets. 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 Sacubitril/Valsartan tablets in patients who develop a clinically significant decrease in renal function.
As with all drugs that affect the RAAS, Sacubitril/Valsartan tablets 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.

Hyperkalemia

Through its actions on the RAAS, hyperkalemia may occur with Sacubitril/Valsartan tablets. 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 Sacubitril/Valsartan tablets may be required.

4.5. Drug Interactions

Dual Blockade of the Renin-Angiotensin-Aldosterone System

Concomitant use of Sacubitril/Valsartan tablets with an ACE inhibitor is contraindicated because of the increased risk of angioedema.
Avoid use of Sacubitril/Valsartan tablets with an ARB, because Sacubitril/Valsartan tablets contain the angiotensin II receptor blocker Valsartan.
The concomitant use of Sacubitril/Valsartan tablets with aliskiren is contraindicated in patients with diabetes. Avoid use with aliskiren in patients with renal impairment (eGFR < 60 mL/min/1.73 m^2).

Potassium-Sparing Diuretics

As with other drugs that block angiotensin II or its effects, 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.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors)

In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, concomitant use of NSAIDs, including COX-2 inhibitors, with Sacubitril/valsartan tablets may result in worsening of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically.

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 Sacubitril/valsartan tablets.

4.6. Use in Special Populations (such as pregnant women, **lactating women, paediatric patients, geriatric patients etc.)**
Pregnancy

Risk Summary

Sacubitril/valsartan tablets can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. In animal reproduction studies, Sacubitril/Valsartan tablets treatment during organogenesis resulted in increased embryo-fetal lethality in rats and rabbits and teratogenicity in rabbits. When pregnancy is detected, consider alternative drug treatment and discontinue Sacubitril/Valsartan tablets. However, if there is no appropriate alternative to therapy with drugs affecting the renin angiotensin system, and if the drug is considered life saving for the mother, advise a pregnant woman of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Oligohydramnios in pregnant women who use drugs affecting the renin-angiotensin system in the second and third trimesters of pregnancy can result in the following: reduced fetal renal function leading to anuria and renal failure, fetal lung hypoplasia, skeletal deformations, including skull hypoplasia, hypotension, and death.
Perform serial ultrasound examinations to assess the intra-amniotic environment. Fetal testing may be appropriate, based on the week of gestation. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. If oligohydramnios is observed, consider alternative drug treatment. Closely observe neonates with histories of in utero exposure to Sacubitril/Valsartan tablets for hypotension, oliguria, and hyperkalemia. In neonates with a history of in utero exposure to Sacubitril/Valsartan tablets, if oliguria or hypotension occurs, support blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and replacing renal function.

Data

Animal Data

Sacubitril/Valsartan tablets treatment during organogenesis resulted in increased embryo-fetal lethality in rats. Sacubitril and valsartan tablets are teratogenic based on a low incidence of fetal hydrocephaly, associated with maternally toxic doses, which was observed in rabbits. The adverse embryo-fetal effects of Sacubitril and valsartan tablets are attributed to the angiotensin receptor antagonist activity.
Pre-and postnatal development studies in rats at sacubitril and valsartan indicate that treatment with Sacubitril and valsartan tablets during organogenesis, gestation and lactation may affect pup development and survival *[Reference: ENTRESTO US FDA label. Dated: Oct.2019].*

Lactation

Risk Summary

There is no information regarding the presence of Sacubitril/Valsartan in human milk, the effects on the breastfed infant, or the effects on milk production. Sacubitril/Valsartan is present in rat milk. Because of the potential for serious adverse reactions in breastfed infants from exposure to sacubitril/valsartan, advise a nursing woman that breastfeeding is not recommended during treatment with Sacubitril/Valsartan tablets.

Data

Following an oral dose (15 mg sacubitril/15 mg valsartan/kg) of [^{14}C] Sacubitril/valsartan tablets to lactating rats, transfer of LBQ657 into milk was observed. After a single oral administration of 3 mg/kg [^{14}C] valsartan to lactating rats, transfer of valsartan into milk was observed *[Reference: ENTRESTO US FDA label. Dated: Oct.2019].*

Paediatric Use

Safety and effectiveness have not been established in pediatric patients less than 1 year of age.

Geriatric Use

No relevant pharmacokinetic differences have been observed in elderly (≥ 65 years) or very elderly (≥ 75 years) patients compared to the overall population.

Hepatic Impairment

No dose adjustment is required when administering Sacubitril/Valsartan tablets to patients with mild hepatic impairment (Child-Pugh A classification). The recommended starting dose in patients with moderate hepatic impairment (Child-Pugh B classification) is 24mg/26mg twice daily. The use of Sacubitril/Valsartan tablets in patients with severe hepatic impairment (Child-Pugh C classification) is not recommended, as no studies have been conducted in these patients.

Renal Impairment

No dose adjustment is required in patients with mild (eGFR 60 to 90 mL/min/1.73 m^2) to moderate (eGFR 30 to 60 mL/min/1.73 m^2) renal impairment. The recommended starting dose in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2) is 24mg/26 mg twice daily.

4.7. Effects on Ability to Drive and Use Machines

Sacubitril/Valsartan tablets have a minor influence on the ability to drive and use machines. When driving vehicles or operating machines it should be taken into account that occasionally dizziness or fatigue may occur.

4.8. Undesirable Effects

Clinically significant adverse reactions that appear include:

- Angioedema
- Hypotension
- Impaired Renal Function
- Hyperkalemia

Tabulated list of adverse reactions
Adverse reactions are ranked by System organ class and then by frequency with the most frequent first, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.

System Organ Class	Preferred term	Frequency category
Blood and lymphatic system disorders	Anaemia	Common
Immune system disorders	Hypersensitivity	Uncommon
Metabolism and nutrition disorders	Hyperkalaemia	Very common
	Hypokalaemia	Common
	Hypoglycaemia	Common
Nervous system disorders	Dizziness	Common
	Headache	Common
	Syncope	Common
	Dizziness postural	Uncommon
Ear and labyrinth disorders	Vertigo	Common
Vascular disorders	Hypotension	Very common
	Orthostatic hypotension	Common
Respiratory, thoracic and mediastinal disorders	Cough	Common
Gastrointestinal disorders	Diarrhoea	Common
	Nausea	Common
	Gastritis	Common
Skin and subcutaneous tissue disorders	Pruritus	Uncommon
	Rash	Uncommon
	Angioedema	Uncommon
Renal and urinary disorders	Renal impairment	Very common
	Renal failure (renal failure, acute renal failure)	Common
General disorders and administration site conditions	Fatigue	Common
	Asthenia	Common

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. To report Suspected Adverse Reactions, contact MSN Laboratories Private Limited at pharmacovigilance@msnlabs.com or through company website www.msnlabs.com->Contact us->Medical Enquiry/ to report a side effect.

4.9. Overdose

Limited data are available with regard to over dosage with Sacubitril/valsartan tablets. Hypotension is the most likely result of over dosage due to the blood pressure lowering effects of Sacubitril/valsartan tablets. Symptomatic treatment should be provided.
Sacubitril/valsartan tablets are unlikely to be removed by hemodialysis because of high protein binding.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

Sacubitril/Valsartan tablets contain a neprilysin inhibitor, sacubitril, and an angiotensin receptor blocker, valsartan. Sacubitril/Valsartan tablets inhibit neprilysin (neutral endopeptidase; NEP) via LBQ657, the active metabolite of the prodrug sacubitril, and blocks the angiotensin II type-1 (AT1) receptor via valsartan. The cardiovascular and renal effects of Sacubitril/Valsartan tablets 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 AT1 receptor, and also inhibits angiotensin II-dependent aldosterone release.

5.2 Pharmacodynamic Properties

The pharmacodynamic effects of Sacubitril/Valsartan tablets were evaluated after single and multiple dose administrations in healthy subjects and in patients with heart failure, and are consistent with simultaneous neprilysin inhibition and renin-angiotensin system blockade. In a 7-day valsartan-controlled study in patients with reduced ejection fraction (HFrEF), administration of Sacubitril/valsartan tablets resulted in a significant non-sustained increase in natriuresis, increased urine cGMP, and decreased plasma MR-proANP and NT-proBNP compared to valsartan.
In a 21-day study in HFrEF patients, Sacubitril/valsartan tablets significantly increased urine ANP and cGMP and plasma cGMP, and decreased plasma NT-proBNP, aldosterone and endothelin-1. Sacubitril/valsartan tablets also blocked the AT1-receptor as evidenced by increased plasma renin activity and plasma renin concentrations. In PARADIGM-HF, Sacubitril/valsartan tablets decreased plasma NTproBNP (not a neprilysin substrate) and increased plasma BNP (a neprilysin substrate) and urine cGMP compared with enalapril.
QT Prolongation: In a thorough QTc clinical study in healthy male subjects, single doses of 194 mg sacubitril/206 mg valsartan and 583 mg sacubitril/617 mg valsartan had no effect on cardiac repolarization.
Amyloid-β: Neprilysin is one of multiple enzymes involved in the clearance of amyloid-β (Aβ) from the brain and cerebrospinal fluid (CSF). Administration of 194 mg sacubitril/206 mg valsartan once-daily for 2 weeks to healthy subjects was associated with an increase in CSF Aβ1-38 compared to placebo; there were no changes in concentrations of CSF Aβ1-40 or CSF Aβ1-42. The clinical relevance of this finding is unknown.
Blood Pressure: Addition of a 50 mg single dose of sildenafil to Sacubitril/valsartan tablets at steady state (194 mg sacubitril/206 mg valsartan once daily for 5 days) in patients with hypertension was associated with additional blood pressure (BP) reduction (~ 5/4 mmHg, systolic/diastolic BP) compared to administration of Sacubitril/valsartan tablets alone *[Reference: ENTRESTO US FDA label. Dated: Oct.2019].*
Co-administration of Sacubitril/Valsartan tablets did not significantly alter the BP effect of intravenous nitroglycerin.

5.3 PHARMACOKINETIC PROPERTIES

Absorption

Following oral administration, Sacubitril/valsartan tablets dissociates into sacubitril and valsartan. Sacubitril is further metabolized to LBQ657. The peak plasma concentrations of sacubitril, LBQ657, and valsartan are reached in 0.5 hours, 2 hours, and 1.5 hours, respectively. The oral absolute bioavailability of sacubitril is estimated to be ≥ 60%. The valsartan in Sacubitril/valsartan tablets is more bioavailable than the valsartan in other marketed tablet formulations; 26 mg, 51 mg, and 103 mg of valsartan in Sacubitril/valsartan tablets is equivalent to 40 mg, 80 mg, and 160 mg of valsartan in other marketed tablet formulations, respectively.
Following twice-daily dosing of Sacubitril/valsartan tablets, steady state levels of sacubitril, LBQ657, and valsartan are reached in 3 days. At steady state, sacubitril and valsartan do not accumulate significantly, whereas LBQ657 accumulates by 1.6-fold. Sacubitril/valsartan tablets administration with food has no clinically significant effect on the systemic exposures of sacubitril, LBQ657, or valsartan. Although there is a decrease in exposure to valsartan when Sacubitril/valsartan tablets are administered with food, this decrease is not accompanied by a clinically significant reduction in the therapeutic effect. Sacubitril/valsartan tablets can therefore be administered with or without food.

Distribution

Sacubitril, LBQ657 and valsartan are highly bound to plasma proteins (94% to 97%). Based on the comparison of plasma and CSF exposures, LBQ657 crosses the blood brain barrier to a limited extent (0.28%). The average apparent volumes of distribution of valsartan and sacubitril are 75 and 103 L, respectively.

Metabolism

Sacubitril is readily converted to LBQ657 by esterases; LBQ657 is not further metabolized to a significant extent. Valsartan is minimally metabolized; 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.

Linearity/Nonlinearity

The pharmacokinetics of sacubitril, LBQ657, and valsartan were linear over an Sacubitril/valsartan tablets dose range of 24 mg sacubitril/26 mg valsartan to 194 mg sacubitril/206 mg valsartan.

Drug Interactions:

Effect of Co-administered Drugs on Sacubitril/Valsartan tablets:

Because CYP450 enzyme-mediated metabolism of sacubitril and valsartan is minimal, coadministration with drugs that impact CYP450 enzymes is not expected to affect the pharmacokinetics of Sacubitril/Valsartan tablets. Dedicated drug interaction studies demonstrated that coadministration of furosemide, warfarin, digoxin, carvedilol, a combination of levonorgestrel/ethinyl estradiol, amlodipine, omeprazole, hydrochlorothiazide (HCTZ), metformin, atorvastatin, and sildenafil, did not alter the systemic exposure to sacubitril, LBQ657 or valsartan.
Effect of Sacubitril/valsartan tablets *on Co-administered Drugs:*
In vitro data indicate that sacubitril inhibits OATP1B1 and OATP1B3 transporters.

6. NONCLINICAL PROPERTIES

6.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies conducted in mice and rats with sacubitril and valsartan did not identify any carcinogenic potential for Sacubitril/valsartan tablets. The LBQ657 C_{max} at the high dose (HD) of 1200 mg/kg/day in male and female mice was, respectively, 14 and 16 times that in humans at the MRHD. The LBQ657 C_{max} in male and female rats at the HD of 400 mg/kg/day was, respectively, 1.7 and 3.5 times that at the MRHD. The doses of valsartan studied (high dose of 160 and 200 mg/kg/day in mice and rats, respectively) were about 4 and 10 times, respectively, the MRHD on a mg/m^2 basis.
Mutagenicity and clastogenicity studies conducted with Sacubitril/valsartan tablets, sacubitril, and valsartan did not reveal any effects at either the gene or chromosome level.

Impairment of Fertility

Sacubitril/valsartan tablets did not show any effects on fertility in rats up to a dose of 73 mg sacubitril/77 mg valsartan/kg/day (≤ 1.0fold and ≤ 0.18-fold the MRHD on the basis of the AUCs of valsartan and LBQ657, respectively).

Animal Toxicology and/or Pharmacology

The effects of Sacubitril/valsartan tablets on amyloid-β concentrations in CSF and brain tissue were assessed in young (2 to 4 years old) cynomolgus monkeys treated with Sacubitril/valsartan tablets (24 mg sacubitril/26 mg valsartan/kg/day) for 2 weeks. In this study, Sacubitril/valsartan tablets affected CSF Aβ clearance, increasing CSF Aβ 1-40, 1-42, and 1-38 levels in CSF; there was no corresponding increase in Aβ levels in the brain. In addition, in a toxicology study in cynomolgus monkeys treated with Sacubitril/valsartan tablets at 146 mg sacubitril/154 mg valsartan/kg/day for 39-weeks, there was no amyloid-β accumulation in the brain *[Reference: ENTRESTO US FDA Label. Dated: Oct-2019]*

7. PHARMACEUTICAL PARTICULARS

7.1 Incompatibilities

None

7.2 Packing Information

7's & 14's Alu-Alu blister pack

8.3 Storage and Handling Instructions

Do not store above 30°C.
Store in the original package in order to protect from moisture.
Keep out of the sight and reach of children.

8. PATIENT COUNSELING INFORMATION

Pregnancy: Advise female patients of childbearing age about the consequences of exposure to Sacubitril/valsartan during pregnancy. Discuss treatment options with women planning to become pregnant. Ask patients to report pregnancies to their physicians as soon as possible.
Angioedema: Advise patients to discontinue use of their previous ACE inhibitor or ARB. Advise patients to allow a 36 hour washout period if switching from or to an ACE inhibitor.

9. DETAILS OF MANUFACTURER

MSN Laboratories Private Limited
(Formulations Division), Plot No. 42,
Anrich Industrial Estate, Bollaram,
Sangareddy District - 502 325,
Telangana, India.

10. DETAILS OF MANUFACTURING LICENCE NUMBER

Mfg. Lic. No.: 38/MD/AP/2007/F/CC

11. DATE OF REVISION

February 2023

TM- Trademark under registration

B33253-00

Version No. 01

Black