SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT:

SEVLAREN 800mg Tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film-coated tablet contains:

Sevelamer carbonate 800mg

For the full list of excipients, *see section 6.1.*

3. PHARMACEUTICAL FORM: Tablet

White to off White circular shaped biconvex film-coated tablets plain on both sides.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Sevelamer carbonate 400 / 800 mg film-coated tablets are indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis. Sevelamer carbonate 400 / 800 mg film-coated tablets are also indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease not on dialysis with serum phosphorus ≥ 1.78 mmol/l. Sevelamer carbonate 400 / 800 mg film-coated tablets should be used within the context of a multiple therapeutic approach, which would include calcium supplement, 1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease.

4.2 Posology and method of administration:

Starting dose

The recommended starting dose of sevelamer carbonate is 2.4 g or 4.8 g per day based on clinical needs and serum phosphorus level. Sevelamer carbonate 400 / 800 mg filmcoated tablets must be taken three times per day with meals.

Serum phosphorus level in patients	Total daily dose of sevelamer carbonate to be taken over 3 meals per day

1.78 – 2.42 mmol/l (5.5 – 7.5 mg/dl)	2.4 g*
> 2.42 mmol/l (> 7.5 mg/dl)	4.8 g*

*Plus, subsequent titrating as per instructions

For patients previously on phosphate binders (sevelamer hydrochloride or calcium based), Sevelamer carbonate 400 / 800 mg film-coated tablets should be given on a gram for gram basis with monitoring of serum phosphorus levels to ensure optimal daily doses.

Titration and Maintenance

Serum phosphorus levels must be monitored and the dose of Sevelamer carbonate titrated every 2-4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter. Patients taking Sevelamer carbonate 400 / 800 mg film-coated tablets should adhere to their prescribed diets. In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the daily dose is expected to be an average of approximately 6 g per day.

Paediatric population

The safety and efficacy of Sevelamer carbonate 400 / 800 mg film-coated tablets has not been established in children below the age of 18 years. Sevelamer carbonate 400 / 800 mg film-coated tablets are not recommended in children below the age of 18 years.

Method of administration

Tablets should be swallowed intact and should not be crushed, chewed, or broken into pieces prior to administration.

4.3 Contraindications:

- Hypersensitivity to the active substance or to any of the excipients.

- Hypophosphataemia

- Bowel obstruction

4.4 Special warnings and precautions for use:

Efficacy and safety of Sevelamer carbonate 400 / 800 mg film-coated tablets have not been studied in children below the age of 18 years.

The safety and efficacy of Sevelamer carbonate 400 / 800 mg film-coated tablets have not been established in adult patients with chronic kidney disease not on dialysis with serum phosphorus < 1.78 mmol/l. Therefore, Sevelamer carbonate 400 / 800 mg filmcoated tablets are currently not recommended for use in these patients.

The safety and efficacy of Sevelamer carbonate 400 / 800 mg film-coated tablets have not been established in patients with the following disorders:

- Dysphagia

- Swallowing disorders

- Severe gastrointestinal motility disorders including untreated or severe gastroparesis, retention of gastric contents and abnormal or irregular bowel motion

- Active inflammatory bowel disease

- Major gastrointestinal tract surgery

Therefore, caution should be exercised when Sevelamer carbonate 400 / 800 mg filmcoated tablets are used in these patients.

Intestinal obstruction and ileus/subileus

In very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate. Constipation may be a preceding symptom. Patients who are constipated should be monitored carefully while being treated with Sevelamer carbonate 400 / 800 mg film-coated tablets. Sevelamer carbonate 400 / 800 mg filmcoated tablets treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Fat-soluble vitamins

Patients with CKD may develop low levels of fat-soluble vitamins A, D, E and K, depending on dietary intake and the severity of their disease. It cannot be excluded that Sevelamer carbonate 400 / 800 mg film-coated tablets can bind fat-soluble vitamins contained in ingested food. In patients not taking supplemental vitamins but on sevelamer, serum vitamin A, D, E and K status should be assessed regularly. It is

recommended that vitamin supplements be given if necessary. It is recommended that CKD patients not on dialysis are given vitamin D supplements (approximately 400 IU of native vitamin D daily) which can be part of a multivitamin preparation to be taken apart from their dose of Sevelamer carbonate 400 / 800 mg film-coated tablets. In patients undergoing peritoneal dialysis additional monitoring of fat soluble vitamins and folic acid is recommended, since vitamin A, D, E and K levels were not measured in a clinical study in these patients.

Folate deficiency

There is at present insufficient data to exclude the possibility of folate deficiency during long term Sevelamer carbonate 400 / 800 mg film-coated tablets treatment.

Hypocalcaemia/hypercalcaemia

Patients with CKD may develop hypocalcaemia or hypercalcaemia. Sevelamer carbonate 400 / 800 mg filmcoated tablets do not contain any calcium. Serum calcium levels should therefore be monitored at regular intervals and elemental calcium should be given as a supplement if required.

Metabolic acidosis

Patients with chronic kidney disease are predisposed to developing metabolic acidosis. As part of good clinical practice, monitoring of serum bicarbonate levels is therefore recommended.

Peritonitis

Patients receiving dialysis are subject to certain risks for infection specific to dialysis modality. Peritonitis is a known complication in patients receiving peritoneal dialysis and in a clinical study with sevelamer hydrochloride, a greater number of peritonitis cases were reported in the sevelamer group than in the control group. Patients on peritoneal dialysis should be closely monitored to ensure the correct use of appropriate aseptic technique with the prompt recognition and management of any signs and symptoms associated with peritonitis.

Swallowing and choking difficulties

Uncommon reports of difficulty swallowing the Sevelamer carbonate 400 / 800 mg film-coated tablet have been reported. Many of these cases

involved patients with comorbid conditions including swallowing disorders or oesophageal abnormalities. Caution should be exercised when Sevelamer carbonate 400 / 800 mg film-coated tablets are used in patients with difficulty swallowing. For patients with swallowing difficulties, sevelamer carbonate is also available as a powder for oral suspension.

Anti-arrhythmic and anti-seizure medicinal products

Caution should be exercised when prescribing Sevelamer carbonate 400 / 800 mg filmcoated tablets to patients also taking anti-arrhythmias and anti-seizure medicinal products.

Hypothyroidism

Closer monitoring of patients with hypothyroidism co-administered with sevelamer carbonate and levothyroxine is recommended.

Long-term chronic treatment

In a clinical trial of one year, no evidence of accumulation of sevelamer was seen. However, the potential absorption and accumulation of sevelamer during long-term chronic treatment (> one year) cannot be totally excluded.

Hyperparathyroidism

Sevelamer carbonate 400 / 800 mg film-coated tablets are not indicated for the control of hyperparathyroidism. In patients with secondary hyperparathyroidism Sevelamer carbonate 400 / 800 mg film-coated tablets should be used within the context of a multiple therapeutic approach, which could include calcium as supplements, 1,25 - dihydroxy Vitamin D3 or one of its analogues to lower the intact parathyroid hormone (iPTH) levels.

Lactose intolerance

Sevelamer carbonate 400 / 800 mg film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Fertility

There are no data from the effect of sevelamer on fertility in humans. Studies in animals have shown that sevelamer did not impair fertility in male or female rats at exposures at a human equivalent dose 2 times the maximum clinical trial dose of 13 g/day, based on a comparison of relative body surface area.

4.5 Interaction with other medicinal products and other forms of interaction:

Interaction studies have not been conducted in patients on dialysis.

In interaction studies in healthy volunteers, sevelamer hydrochloride, which contains the same active moiety as in Sevelamer carbonate 400 / 800 mg film-coated tablets, decreased the bioavailability of ciprofloxacin by approximately 50% when coadministered with sevelamer hydrochloride in a single dose study. Consequently, Sevelamer carbonate 400 / 800 mg film-coated tablets should not be taken simultaneously with ciprofloxacin. Reduced levels of ciclosporin, mycophenolate mofetil and tacrolimus have been reported in transplant patients when co-administered with sevelamer hydrochloride without any clinical consequences (i.e. graft rejection). The possibility of an interaction cannot be excluded and a close monitoring of blood concentrations of ciclosporin, mycophenolate mofetil and tacrolimus should be considered during the use of combination and after its withdrawal.

Very rare cases of hypothyroidism have been reported in patients co-administered sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, and levothyroxine. Closer monitoring of thyroid stimulating hormone (TSH) levels is therefore recommended in patients receiving sevelamer carbonate and levothyroxine.

Patients taking anti-arrhythmic medicinal products for the control of arrhythmias and anti-seizure medicinal products for the control of seizure disorders were excluded from clinical trials. Caution should be exercised when prescribing Sevelamer carbonate 400 / 800 mg film-coated tablets to patients also taking these medicinal products.

In interaction studies in healthy volunteers, sevelamer hydrochloride, which contains the same active moiety as Sevelamer carbonate 400 / 800 mg film-coated tablets, had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol. Sevelamer carbonate 400 / 800 mg film-coated tablets are not absorbed and may affect the bioavailability of

other medicinal products. When administering any medicinal product where a reduction in the bioavailability could have a clinically significant effect on safety or efficacy, the medicinal product should be administered at least one hour before or three hours after Sevelamer carbonate 400 / 800 mg film-coated tablets, or the physician should consider monitoring blood levels.

4.6 Fertility, pregnancy, and lactation:

Pregnancy

There are no data from the use of sevelamer in pregnant women. Studies in animals have shown some reproductive toxicity when sevelamer was administered to rats at high doses. Sevelamer has also been shown to reduce the absorption of several vitamins including folic acid. The potential risk to humans is unknown. Sevelamer carbonate 400 / 800 mg film-coated tablets should only be given to pregnant women if clearly needed and after a careful risk/benefit analysis has been conducted for both the mother and the foetus.

Breast-feeding

It is unknown whether sevelamer is excreted in human breast milk. The non-absorbed nature of sevelamer indicates that excretion of sevelamer in breast milk is unlikely. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Sevelamer carbonate 400 / 800 mg film-coated tablets should be made taking into account the benefit of breast-feeding to the child and the benefit of Sevelamer carbonate 400 / 800 mg film-coated tablets therapy to the woman.

Fertility

There are no data from the effect of sevelamer on fertility in humans. Studies in animals have shown that sevelamer did not impair fertility in male or female rats at exposures at a human equivalent dose 2 times the maximum clinical trial dose of 13 g/day, based on a comparison of relative body surface area.

4.7 Effects on ability to drive and use machines:

There is no information available for effect of Sevelamer Carbonate on ability to drive and use machine.

4.8 Undesirable effects

The following adverse reactions have been reported with sevelamer:
Gastrointestinal disorders

Very common: Nausea, vomiting, upper abdominal pain, constipation
Common: Diarrhoea, dyspepsia, flatulence, abdominal pain

Apart from these cases of pruritus, rash, intestinal obstruction, ileus/subileus, and intestinal perforation have been reported in patients during treatment with sevelamer.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacy and Poisons Board- Pharmacovigilance Electronic Reporting System (PvERS); *https://pv.pharmacyboardkenya.org* .

4.9 Overdose

No cases of overdose have been reported. Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been given to normal healthy volunteers in doses of up to 14 grams per day for eight days with no undesirable effects. In CKD patients, the maximum average daily dose studied was 14.4 grams of sevelamer carbonate in a single daily dose.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Drugs for treatment of hyperkalemia and hyperphosphatemia

ATC code: V03AE02

5.1 Pharmacodynamic properties

Sevelamer carbonate 400 / 800 mg film-coated tablets contain sevelamer, a nonabsorbed phosphate binding crosslinked polymer, free of metal and calcium. Sevelamer contains multiple amines separated by one carbon from the polymer backbone which become protonated in the stomach. These protonated amines bind negatively charged ions such as dietary phosphate in the intestine. By binding phosphate in the gastrointestinal tract and decreasing absorption, sevelamer lowers the phosphorus concentration in the serum. Regular monitoring of serum

phosphorus levels is always necessary during phosphate binder administration.

Sevelamer has been shown to bind bile acids in vitro and in vivo in experimental animal models. Bile acid binding by ion exchange resins is a well-established method of lowering blood cholesterol. In clinical trials of sevelamer, both the mean totalcholesterol and LDL-cholesterol declined by 15-39%. The decrease in cholesterol has been observed after 2 weeks of treatment and is maintained with long-term treatment. Triglycerides, HDL-cholesterol and albumin levels did not change following sevelamer treatment. Because sevelamer binds bile acids, it may interfere with the absorption of fat soluble vitamins such as A, D, E and K. Sevelamer does not contain calcium and decreases the incidence of hypercalcaemic episodes as compared to patients using calcium based phosphate binders alone. The effects of Sevelamer on phosphorus and calcium were proven to be maintained throughout a study with one year follow-up. This information was obtained from studies in which Sevelamer hydrochloride was used.

5.2 Pharmacokinetic properties

Pharmacokinetic studies have not been carried out with Sevelamer carbonate. Sevelamer hydrochloride, which contains the same active moiety as Sevelamer carbonate, is not absorbed from the gastrointestinal tract, as confirmed by an absorption study in healthy volunteers.

5.3 Preclinical safety data

Non-clinical data with sevelamer reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity or genotoxicity. Carcinogenicity studies with oral sevelamer hydrochloride were conducted in mice (doses of up to 9 g/kg/day) and rats (0.3, 1, or 3 g/kg/day). There was an increased incidence of urinary bladder transitional cell papilloma in male rats of the high dose group (human equivalent dose twice the maximum clinical trial dose of 14.4 g). There was no increased incidence of tumors observed in mice (human equivalent dose 3 times the maximum clinical trial dose).

In an in vitro mammalian cytogenetic test with metabolic activation, sevelamer hydrochloride caused a statistically significant increase in the number of structural chromosome aberrations. Sevelamer hydrochloride was not mutagenic in the Ames bacterial mutation assay.

In rats and dogs, sevelamer reduced absorption of fat-soluble vitamins D, E and K (coagulation factors), and folic acid.

Deficits in skeletal ossification were observed in several locations in foetuses of female rats dosed with sevelamer at intermediate and high doses (human equivalent dose less than the maximum clinical trial dose of 14.4 g). The effects may be secondary to vitamin D depletion.

In pregnant rabbits given oral doses of sevelamer hydrochloride by gavage during organogenesis, an increase of early resorptions occurred in the high-dose group (human equivalent dose twice the maximum clinical trial dose).

Sevelamer hydrochloride did not impair the fertility of male or female rats in a dietary administration study in which the females were treated from 14 days prior to mating through gestation and the males were treated for 28 days prior to mating. The highest dose in this study was 4.5 g/kg/day (human equivalent dose 2 times the maximum clinical trial dose of 13 g/day, based on a comparison of relative body surface area).

6. **PHARMACEUTICAL PARTICULARS**

6.1 List of excipients

1. Microcrystalline Cellulose PH 102
2. Polyvinyl Pyrrolidone K 30 (Povidone)
3. Purified Water
4. Colloidal Silicon Dioxide
5. Magnesium Stearate
6. Film Coating Material (ICMS 2398)
7. Titanium Dioxide
8. Purified Talc
9. Triethyl Citrate
10. Isopropyl Alcohol
11. Methylene Chloride (Dichloromethane)

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

24 months

6.4 Special precautions for storage:

Store at a temperature not exceeding 30°C. Protect from light and moisture.

6.5 Nature and contents of the container:

1) 10 tablets in Alu-Alu blister, 10 such blisters are packed in a primary carton along with the package insert.

2) 10 tablets in Alu-Alu blister, 3 such blisters are packed in a primary carton along with the package insert.

3) 10 tablets in Alu-Alu blister, 1 such blister is packed in a primary carton along with the package insert.

4) 10 tablets in Alu-Alu blister, 1 such blister is packed in a monocarton along with package insert. Such 10 monocartons are packed in an outer carton.

6.6 Special precautions for disposal:

Not applicable

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

MARKETING AUTHORIZATION HOLDER

La Renon Healthcare Pvt. Ltd.
207-208, ISCON Elegance, Circle-P,
Prahlad Nagar Cross Roads, S.G. Highway,
Ahmedabad-380015, Gujarat, India.

Manufactured By:

Stanford Laboratories Pvt. Ltd.
(A subsidiary company of La Renon Healthcare Pvt. Ltd.)
8, Industrial Area, Mehatpur, Dist. Una, (H.P.) 174315,
India.

8. MARKETING AUTHORIZATION NUMBER:

H2019/CTD6179/921ER

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION

09 August 2018

10. DATE OF REVISION OF THE TEXT:

27.03.2026