SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SELAGLOB 800
Sevelamer Hydrochloride Tablets 800 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Film Coated tablet contains:
Sevelamer Hydrochloride ……..800 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film Coated tablet
A white coloured Caplet shaped film coated tablet having a break line on one side, other side plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sevelamer Hydrochloride is indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis. Sevelamer Hydrochloride should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 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

Posology

Starting dose

The recommended starting dose of sevelamer hydrochloride is 2.4 g or 4.8 g per day based on clinical needs and serum phosphorus level. Sevelamer Hydrochloride must be taken three times per day with meals.

Serum phosphorus level in patients not on phosphate binders	Starting dose of Sevelamer hydrochloride 800 mg tablets
1.76 - 2.42 mmol/l (5.5 - 7.5 mg/dl)	1 tablet, 3 times per day
> 2.42 mmol/l (> 7.5 mg/dl)	2 tablets, 3 times per day

*Plus subsequent titrating as per instructions

For patients previously on phosphate binders, Sevelamer Hydrochloride should be given on a gram for gram basis with monitoring of serum phosphorus levels to ensure optimal daily doses.

Titration and maintenance

Serum phosphate levels should be closely monitored and the dose of Sevelamer Hydrochloride adjusted accordingly with the goal of lowering serum phosphate to 1.76 mmol/l (5.5 mg/dl) or less. Serum phosphate should be tested every two to three weeks until a stable serum phosphate level is reached and on a regular basis thereafter.

The dose range may vary between 1 and 5 tablets of 800 mg per meal. The average actual daily dose used in the chronic phase of a one year clinical study was 7 grams of sevelamer.

Paediatric population

The safety and efficacy of this product has not been established in patients below the age of 18 years. Sevelamer Hydrochloride is not recommended in children below the age of 18 years.

Renal impairment

The safety and efficacy of this product has not been established in predialysis patients. Sevelamer Hydrochloride is not recommended in these patients.

Method of administration

For oral use

Patients should take Sevelamer Hydrochloride with meals and adhere to their prescribed diets. The tablets must be swallowed whole. Do not chew.

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 Hydrochloride has not been studied in patients with:

•Swallowing disorders

•Active inflammatory bowel disease

•Gastrointestinal motility disorders including untreated or severe gastroparesis, diverticulosis, retention of gastric contents and abnormal or irregular bowel motion

•Patients with a history of major gastrointestinal surgery

Therefore caution should be exercised when Sevelamer Hydrochloride is used in patients with these disorders.

Intestinal obstruction and ileus/subileus

In very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment with Sevelamer Hydrochloride. Constipation may be a preceding symptom. Patients who are constipated should be monitored carefully while being treated with Sevelamer Hydrochloride. Sevelamer Hydrochloride treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Fat-soluble vitamins

Depending on diet intake and the nature of end stage renal failure, dialysis patients may develop low vitamin A, D, E and K levels. It cannot be excluded that Sevelamer Hydrochloride can bind fat-soluble vitamins contained in ingested food. Therefore, in patients not taking these vitamins, monitoring vitamin A, D and E levels and assessing vitamin K status through the measurement of thromboplastin time should be considered and the vitamins should be supplemented if necessary. Additional monitoring of vitamins and folic acid is recommended in patients receiving peritoneal dialysis, since in the clinical study, vitamin A, D, E and K levels were not measured in these patients.

Folate deficiency

There is at present insufficient data to exclude the possibility of folate deficiency during long term Sevelamer Hydrochloride treatment.

Hypocalcaemia/hypercalcaemia

Patients with renal insufficiency may develop hypocalcaemia or hypercalcaemia. Sevelamer Hydrochloride does not contain calcium. Serum calcium levels should be monitored as is done in normal follow-up of a dialysis patient. Elemental calcium should be given as a supplement in case of hypocalcaemia.

Metabolic acidosis

Patients with chronic renal failure are predisposed to developing metabolic acidosis. Worsening of acidosis has been reported upon switching from other phosphate binders to sevelamer in a number of studies where lower bicarbonate levels in the sevelamer-treated patients compared to patients treated with calcium-based binders were observed. Closer monitoring of serum bicarbonate levels is therefore recommended.

Peritonitis

Patients receiving dialysis are subject to certain risks for infection specific to the dialysis modality. Peritonitis is a known complication in patients receiving peritoneal dialysis (PD) and in a clinical study with Sevelamer Hydrochloride, a number of peritonitis cases were reported. Therefore, patients on PD should be

closely monitored to ensure the reliable 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 Hydrochloride tablet have been reported. Many of these cases involved patients with co-morbid conditions including swallowing disorders or oroesophageal abnormalities. Caution should be exercised when Sevelamer Hydrochloride is used in patients with difficulty swallowing.

Anti-arrhythmic and anti-seizure medicinal products

Caution should be exercised when prescribing Sevelamer Hydrochloride to patients also taking anti-arrhythmias and anti-seizure medicinal products.

Hypothyroidism

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

Long term chronic treatment

As data on the chronic use of sevelamer for over one year are not yet available, potential absorption and accumulation of sevelamer during long-term chronic treatment cannot be totally excluded.

Hyperparathyroidism

Sevelamer Hydrochloride alone is not indicated for the control of hyperparathyroidism. In patients with secondary hyperparathyroidism Sevelamer Hydrochloride should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25-dihydroxy Vitamin D3 or one of its analogues to lower the intact parathyroid hormone (iPTH) levels.

Serum chloride

Serum chloride may increase during Sevelamer Hydrochloride treatment as chloride may be exchanged for phosphorus in the intestinal lumen. Although no clinically significant serum chloride increase has been observed in the clinical studies, serum chloride should be monitored as is done in the routine follow-up of a dialysis patient. One gram of Sevelamer Hydrochloride contains approximately 180 mg (5.1mEq) chloride.

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 decreased the bioavailability of ciprofloxacin by approximately 50% when co-administered with Sevelamer Hydrochloride in a single dose study.

Consequently, Sevelamer Hydrochloride should not be taken simultaneously with ciprofloxacin.
Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from clinical trials. Caution should be exercised when prescribing Sevelamer Hydrochloride to patients also taking these medications.
During post marketing experience, very rare cases of increased TSH levels have been reported in patients co-administered Sevelamer Hydrochloride and levothyroxine. Closer monitoring of TSH levels is therefore recommended in patients receiving both medications.
Reduced levels of ciclosporin, mycophenolate mofetil and tacrolimus have been reported in transplant patients when coadministered 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 mycophenolate mofetil, ciclosporin and tacrolimus should be considered during the use of combination and after its withdrawal.
In interaction studies in healthy volunteers, Sevelamer Hydrochloride had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol. Sevelamer Hydrochloride is 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 Hydrochloride, or the physician should consider monitoring blood levels.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of Sevelamer Hydrochloride has not been established in pregnant women. In animal studies there was no evidence that sevelamer induced embryo-foetal toxicity. Sevelamer Hydrochloride 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

The safety of Sevelamer Hydrochloride has not been established in lactating women. Sevelamer Hydrochloride should only be given to lactating women if clearly needed and after a careful risk/benefit analysis has been conducted for both the mother and the infant.

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.

4.7 Effects on ability to drive and use machines

No studies on the effects on ability to drive and use machines have been performed.

4.8 Undesirable effects

In parallel design studies involving 244 haemodialysis patients with treatment duration of up to 54 weeks and 97 peritoneal dialysis patients with treatment duration of 12 weeks, the most frequently occurring (≥5% of patients) adverse reactions possibly or probably related to Sevelamer Hydrochloride were all in the gastrointestinal disorders system organ class.

Adverse reactions from these studies (299 patients) and from uncontrolled clinical trials (384 patients) are listed by frequency in the table below. The reporting rate is classified as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Gastrointestinal disorders
Very common (≥1/10): Nausea, vomiting Common (≥1/100 to <1/10): Diarrhoea, dyspepsia, flatulence, upper abdominal pain, constipation

Post-marketing experience: During post-approval use of Sevelamer Hydrochloride, cases of pruritus, rash, abdominal pain, intestinal obstruction, ileus/subileus, diverticulitis and intestinal perforation have been reported.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via the pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org

4.9 Overdose

No case of overdose has been reported.

Sevelamer Hydrochloride has been given to normal healthy volunteers in doses up to 14 grams, the equivalent of seventeen 800 mg tablets, per day for eight days with no undesirable effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Treatment of hyperphosphatemia. ATC code: V03AE02.

Sevelamer Hydrochloride contains sevelamer, a non-absorbed phosphate binding poly(allylamine hydrochloride) polymer, free of metal and calcium. It contains multiple amines separated by one carbon from the polymer backbone. These amines become partially protonated in the intestine and interact with phosphate molecules through ionic and hydrogen bonding. By binding phosphate in the gastrointestinal tract, sevelamer lowers the phosphate concentration in the serum.

In clinical trials, sevelamer has been shown to be effective in reducing serum phosphorus in patients receiving haemodialysis or peritoneal dialysis. Sevelamer decreases the incidence of hypercalcaemic episodes as compared to patients using calcium based phosphate binders alone, probably because the product itself does not contain calcium. The effects on phosphate and calcium were proven to be maintained throughout a study with one year follow-up.

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 mean total and LDL cholesterol declined by 15-31%. This effect is observed after 2 weeks is maintained with long-term treatment. Triglycerides, HDL cholesterol and albumin did not change.

In the clinical studies in haemodialysis patients, sevelamer alone did not have a consistent and clinically significant effect on serum intact parathyroid hormone (iPTH). In the 12 week study involving peritoneal dialysis patients however, similar iPTH reductions were seen compared with patients receiving calcium acetate. In patients with secondary hyperparathyroidism Sevelamer Hydrochloride should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25-dihydroxy Vitamin D3 or one of its analogues to lower the intact parathyroid hormone (iPTH) levels.

In a clinical trial of one-year duration, Sevelamer Hydrochloride had no adverse effect on bone turnover or mineralisation compared to calcium carbonate.

5.2 Pharmacokinetic properties

Sevelamer Hydrochloride is not absorbed from the gastrointestinal tract according to a single dose pharmacokinetic study in healthy volunteers. Pharmacokinetic studies have not been carried out in renal failure patients.

5.3 Preclinical safety data
Preclinical data reveal no special hazard based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.
In reproductive toxicity studies, no teratogenic effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
•Maize Starch
•Dibasic Calcium Phosphate
•Lactose
•Methyl Paraben
•Propyl Paraben
•Purified Water
•Sodium Starch Glycolate
•Colloidal Anhydrous Silica (Aerosil)
•Magnesium Stearate
•Purified Talc

6.2 Incompatibilities
None reported.

6.3 Shelf life
36 months from the date of manufacture.

6.4 Special precautions for storage
Do not store above 25°C. Protect from moisture.

6.5 Nature and contents of container
10 Tablets are packed in 1 Alu-Alu blister. Such 3 Blisters are packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

6.6 Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)
H2025/CTD7105/13739

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
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10. DATE OF REVISION OF THE TEXT
20-08-2026