Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

SEVELARED 800mg
(Sevelamer Carbonate 800 mg film-coated tablets)

2. Qualitative and quantitative composition

Each film-coated tablet contains:
Sevelamer carbonate ... 800 mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

White to off-white, oval, film-coated tablets, plain on one side and imprinted 'R789' on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Sevelamer carbonate 400 mg/800 mg film-coated tablets are indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis.

Sevelamer carbonate 400 mg/800 mg film-coated tablets are 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 mg/800 mg film-coated tablets should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25-dihydroxy Vitamin D_3 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 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 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 by 0.8 g three times per day (2.4 g/day) increments every 2–4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter.

Patients taking sevelamer 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.

Missed dose
If a dose is missed, the missed dose should be omitted and the next dose taken at the usual time with a meal. A double dose should not be taken to make up for a missed dose.

Discontinuation of treatment
Maintaining sevelamer treatment is important to control serum phosphate levels. Discontinuation of sevelamer treatment may lead to important consequences such as calcification of blood vessels. Any decision to stop treatment should be taken by the prescriber, with the patient counselled to seek advice from their doctor or pharmacist before stopping.

Paediatric population
The safety and efficacy of sevelamer have not been established in children below the age of 18 years.

Method of administration
For oral use. The 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 listed in section 6.1
- Hypophosphataemia
- Bowel obstruction

4.4 Special warnings and precautions for use

Efficacy and safety of sevelamer carbonate 400 mg/800 mg tablets have not been established in children below the age of 18 years.

The safety and efficacy of sevelamer have not been established in adult patients with chronic kidney disease not on dialysis with serum phosphorus < 1.78 mmol/l. Therefore sevelamer is currently not recommended for use in these patients.

The safety and efficacy of sevelamer 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

Treatment of these patients with sevelamer should only be initiated after careful benefit/risk assessment. If therapy is initiated, patients suffering from these disorders should be monitored. Sevelamer treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

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. Treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Fat-soluble vitamins: Patients with chronic kidney disease (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 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. Vitamin supplements are recommended if necessary. CKD patients not on dialysis are recommended to be given vitamin D supplements (approximately 400 IU of native vitamin D daily), which can be part of a multivitamin preparation taken apart from their dose of sevelamer. 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 treatment. In patients not taking supplemental folic acid but on sevelamer, folate level should be assessed regularly.

Hypocalcaemia/hypercalcaemia: Patients with CKD may develop hypocalcaemia or hypercalcaemia. Sevelamer does 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 prompt recognition and management of any signs and symptoms associated with peritonitis.

Swallowing and choking difficulties: Uncommon reports of difficulty swallowing the sevelamer tablet have been reported. Many of these cases involved patients with co-morbid conditions including swallowing disorders or oesophageal abnormalities. Caution should be exercised when sevelamer is used in patients with difficulty swallowing. The use of sevelamer powder for oral suspension should be considered in patients with a history of difficulty swallowing.

Antiarrhythmic and anti-seizure medicinal products: Caution should be exercised when prescribing sevelamer carbonate 400 mg/800 mg tablets to patients also taking antiarrhythmic and anti-seizure medicinal products.

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

Hyperparathyroidism: Sevelamer is not indicated for the control of hyperparathyroidism. In patients with secondary hyperparathyroidism, sevelamer should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25-dihydroxy Vitamin D_3 or one of its analogues, to lower intact parathyroid hormone (iPTH) levels.

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 sevelamer, decreased the bioavailability of ciprofloxacin by approximately 50% when co-administered with sevelamer hydrochloride in a single dose study. Consequently, sevelamer 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 (e.g. graft rejection). The possibility of an interaction cannot be excluded, and close monitoring of blood concentrations of ciclosporin, mycophenolate mofetil and tacrolimus should be considered during use of the 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 to patients also taking these medicinal products.

In interaction studies in healthy volunteers, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol. Sevelamer is not absorbed and may affect the bioavailability of other medicinal products. When administering any medicinal product where a reduction in 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, or the physician should consider monitoring blood levels.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of sevelamer in pregnant women. Animal studies 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 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/metabolites are excreted in human 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 should be made taking into account the benefit of breast-feeding to the child and the benefit of sevelamer therapy to the woman.

Fertility
There are no data on 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
Sevelamer has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
The following adverse reactions have been reported with sevelamer:

System Organ Class	Frequency	Adverse reaction
Gastrointestinal disorders	Very common	Nausea, vomiting, upper abdominal pain, constipation
	Common	Diarrhoea, dyspepsia, flatulence, abdominal pain
	Not known	Pruritus, rash, intestinal obstruction, ileus/subileus, intestinal perforation

Reporting of suspected adverse reactions: 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 chronic kidney disease patients, the maximum average daily dose studied was 14.4 grams of sevelamer carbonate in a single daily dose.

In the event of a possible overdose, the patient should be monitored closely and appropriate supportive treatment given; there is no specific antidote for sevelamer.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: All other therapeutic products, drugs for treatment of hyperkalaemia and hyperphosphataemia. ATC code: V03A E02.

Mechanism of action
Sevelamer carbonate 400 mg/800 mg film-coated tablets contain sevelamer, a non-absorbed phosphate-binding cross-linked 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 mean total cholesterol 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 shown 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 tumours 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

Mannitol, Crospovidone Type B (XL-10), Hydroxypropyl Cellulose (Klucel LF), Colloidal Silicon Dioxide, Zinc Stearate, Opadry AMB Translucent (OY-B-29000), Opacode Black S-1-17823.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

No special storage conditions.

6.5 Nature and contents of container

270's HDPE Bottle with child-resistant plastic cap with pulp liners and silica gel canisters 1 gm.
Container – 625cc HDPE Container.
Closure – Child-resistant plastic cap with pulp liner, 53mm.
Desiccant – 1 gram 2-in-1 desiccant canister.

180's HDPE Bottle with child-resistant plastic cap with pulp liners and silica gel canisters 1 gm.
Container – 400cc HDPE Container.
Closure – Child-resistant plastic cap with pulp liner, 53mm.
Desiccant – 1 gram 2-in-1 desiccant canister.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

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8. Marketing authorisation number

H2025/CTD12807/27401

9. Date of first authorisation/renewal of the authorisation

1st June, 2025

10. Date of revision of the text

25th August, 2026