165mm

155mm

Proton pump inhibitors
During post-marketing experience, very rare cases of increased phosphate levels have been reported in patients taking proton pump inhibitors co-administered with sevelamer carbonate. Caution should be exercised when prescribing PPI to patients concomitantly treated with Sevemer. The phosphate serum level should be monitored and the Sevemer dosage adjusted consequently.

Bioavailability
Sevelamer carbonate 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 carbonate, or the physician should consider monitoring blood levels.

Digoxin, warfarin, enalapril or metoprolol
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.

PRESENTATION
Sevemer Sachet 1.6 g available in pack of 30's, 60's & 90's
Sevemer Sachet 2.4 g available in pack of 30's , 60's & 90's

Dosage :
As directed by the physician

INSTRUCTIONS:
Store below 30°C in a dry place, protect from light.
To be dispensed on the prescription of a registered medical practitioner only.
Keep out of the reach of children.

خوراک:
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات:
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

Sevemer

(Sevelamer Carbonate)

1.6g & 2.4g Sachet

سیویمر

(سیویلامر کاربونیٹ)

۱.۶ گرام اور ۲.۴ گرام ساشے

COMPOSITION:
Each sachet contains:
Sevelamer Carbonate.....1.6g

Each sachet contains:
Sevelamer Carbonate.....2.4g

CLINICAL PHARMACOLOGY
PHARMACODYNAMICS
Pharmacotherapeutic group: All other therapeutic products, drugs for treatment of hyperkalemia and hyperphosphataemia. ATC code: V03A E02.

Mechanism of action
Sevemer contains sevelamer, a non-absorbed 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.

PHARMACOKINETICS
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.
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.

SPECIAL POPULATION
Elderly population
No dosage adjustment is necessary in the elderly population.

Hepatic impairment
No studies have been performed in patients with hepatic impairment.

Paediatric population
The safety and efficacy of Sevemer in children below the age of 6 years or in children with a BSA below 0.75 m² have not been established. Not data are available.

The safety and efficacy of Sevemer in children over 6 year of age and a BSA >0.75 m² have been established.

For paediatric patients the oral suspension should be administered, as tablet formulations are not appropriate for this population.

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 carbonate 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 carbonate should be made taking into account the benefit of breast-feeding to the child and the benefit of sevelamer carbonate 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 BSA.

THERAPEUTIC INDICATIONS
Sevemer is indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis.

Sevemer is also indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease (CKD) not on dialysis with serum phosphorus ≥ 1.78 mmol/l.

Sevemer is indicated for the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m²) with chronic kidney disease.

Sevemer should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease.

DOSAGE & ADMINISTRATION
Posology
Starting dose Adults
The recommended starting dose of sevelamer carbonate for adults is 2.4 g or 4.8 g per day based on clinical needs and serum phosphorus level. Sevemer 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, see section "Titration and maintenance"

Children/adolescents (>6 years of age and a BSA of >0.75m²)
The recommended starting dose of sevelamer carbonate for children is between 2.4 g and 4.8 g per day based on the patient's BSA category. Sevemer must be taken three times per day with meals or snacks.

BSA (m^2)	Total daily dose of sevelamer carbonate to be taken over 3 meals/snacks per day
>0.75 to <1.2	2.4 g**
≥1.2	4.8 g**

**Plus subsequent titrating, see section "Titration and maintenance"

For patients previously on phosphate binders (sevelamer hydrochloride or calcium based), Sevemer should be given on a gram for gram basis with monitoring of serum phosphorus levels to ensure optimal daily doses.

Titration and maintenance
*Adults
For adult patients, 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.
In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the daily adult dose is expected to be an average of approximately 6 g per day.

**Children and adolescents (>6 years of age and a BSA of >0.75m²)
For paediatric patients, serum phosphorus levels must be monitored and the dose of sevelamer carbonate titrated in increments based on patient's BSA, three times per day every 2-4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter.

Paediatric dose based on BSA (m²)

BSA (m^2)	Starting dose	Titration increases/decreases
>0.75 to <1.2	0.8 g three times daily	Titrate up/down by 0.4 g three times daily
≥1.2	1.6 g three times daily	Titrate up/down by 0.8 g three times daily

Patients taking sevelamer carbonate should adhere to their prescribed diets.

METHOD OF ADMINISTRATION
Oral use.
Each sachet of 1.6 g of powder is to be dispersed in 40 mL of water prior to administration .The suspension should be ingested within 30 minutes after being prepared. Sevemer should be taken with food and not on an empty stomach.

As an alternative to water, the powder may be pre-mixed with a small amount of beverage or food (e.g. 100grams/120 ml) and consumed within 30 minutes. Do not heat Sevemer powder (e.g. microwave) or add to heated foods or liquids.

ADVERSE REACTIONS

Immune system disorders
Very rare : Hypersensitivity

Gastrointestinal disorders
Very common : Nausea, vomiting, upper abdominal pain, constipation
Common : Diarrhoea, dyspepsia, flatulence, abdominal pain
Not known : Intestinal obstruction, ileus/subileus, intestinal perforation, gastrointestinal hemorrhage, intestinal ulceration, gastrointestinal necrosis, colitis, intestinal mass

Skin and subcutaneous tissue disorders
Not known: Pruritus, rash

Investigations
Not known : Crystal deposit intestine

CONTRAINDICATIONS
- Hypersensitivity to the active substance or to any of the excipients.
- Hypophosphataemia
- Bowel obstruction.

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

The safety and efficacy of sevelamer carbonate 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 Sevemer should only be initiated after careful benefit/risk assessment. If the therapy is initiated, patients suffering from these disorders should be monitored. Sevemer treatment should be reevaluated 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 (capsules/tablets), 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 Sevemer. The treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Fat-soluble vitamins and folate deficiency
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 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. 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.

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 carbonate 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 CKD 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 trial 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.

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

Hyperparathyroidism
Sevelamer carbonate is not indicated for the control of hyperparathyroidism. In patients with secondary hyperparathyroidism sevelamer carbonate 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.

Inflammatory gastrointestinal disorders
Cases of serious inflammatory disorders of different parts of the gastrointestinal tract (including serious complications such as haemorrhage, perforation, ulceration, necrosis, colitis and colonic/caecal mass) associated with the presence of sevelamer crystals have been reported. Inflammatory disorders may resolve upon sevelamer discontinuation. Sevelamer carbonate treatment should be re-evaluated in patients who develop severe gastrointestinal symptoms.

DRUG INTERACTIONS
Dialysis
Interaction studies have not been conducted in patients on dialysis.

Ciprofloxacin
In interaction studies in healthy volunteers, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, decreased the bioavailability of ciprofloxacin by approximately 50% when co-administered with sevelamer hydrochloride in a single dose study. Consequently, sevelamer carbonate should not be taken simultaneously with ciprofloxacin.

Ciclosporin, mycophenolate mofetil and tacrolimus in transplant patients
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 a close monitoring of blood concentrations of ciclosporin, mycophenolate mofetil and tacrolimus should be considered during the use of combination and after its withdrawal.

Levothyroxine
Very rare cases of hypothyroidism have been reported in patients co-administered with 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.

Anti-arrhythmics and anti-seizure medicinal products
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. Therefore, possible reduction in absorption cannot be excluded. The anti-arrhythmic medicinal product should be taken at least one hour before or three hours after Sevemer and blood monitoring can be considered.