165mm

82.5mm

82.5mm

155mm

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.

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 Sevelamer carbonate Winthrop. The phosphate serum level should be monitored and the Sevelamer carbonate 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.

OVERDOSAGE
The symptoms observed in case of overdose are similar to adverse reactions, including mainly constipation and other known gastrointestinal disorders.
Appropriate symptomatic treatment should be provided.

PRESENTATION
Sevemer 800mg Tablet available in blister pack of 1x10's

Dosage:
As directed by the physician.

INSTRUCTIONS:
Store below 30°C.
Protect from sunlight & moisture.
Keep out of the reach of children.
To be dispensed on the prescription of a registered medical practitioner only.

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.

ART No: 1619

Sevemer

(Sevelamer Carbonate)

سیویمر

(سیویلامر کاربونیٹ)

800mg Tablets

۸۰۰ ملی گرام گولیاں

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

CLINICAL PHARMACOLOGY
Pharmacodynamic properties
Mechanism of action
Sevemer contains sevelamer, a non-absorbed phosphate binding crosslinked polymer. 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.

Pharmacodynamic effects
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

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. No data are available.

THERAPEUTIC INDICATIONS
Sevelamer carbonate 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 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
The recommended starting dose of sevelamer carbonate is 2.4 g or 4.8 g per day based on

165mm

82.5mm

82.5mm

155mm

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"

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
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 Sevemer should adhere to their prescribed diets.

METHOD OF ADMINISTRATION
Oral use.
Tablets should be swallowed intact and should not be crushed, chewed, or broken into pieces prior to administration.
Sevemer should be taken with food and not on an empty stomach.

ADVERSE REACTIONS

System Organ Class	Very common	Common	Very rare	Not known
Immune system disorders			Hypersensitivity	
Gastrointestinal disorders	Nausea, Vomiting, Upper abdominal pain, Constipation	Diarrhoea, Dyspepsia, Flatulence, Abdominal pain		Intestinal obstruction, Ileus/subileus, Intestinal perforation[1], Gastrointestinal hemorrhage[1] Intestinal ulceration[1], Gastrointestinal necrosis[1], Colitis[1], Intestinal mass[1]
Skin and subcutaneous tissue disorders				Pruritus, Rash
Investigations				Crystal deposit intestine[1]

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. Sevelamer carbonate treatment should be reevaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Intestinal obstruction and ileus/subileus
In rare cases, sevelamer carbonate may cause bowel blockage or reduced bowel movement. Constipation can be an early warning sign, so patients with constipation should be monitored closely. Treatment should be reconsidered if severe constipation or serious stomach/bowel symptoms occur.

Fat-soluble vitamins and folate deficiency
Patients with CKD may have low levels of vitamins A, D, E, K, and folic acid. Sevelamer carbonate may reduce absorption of these vitamins from food. Vitamin levels should be checked regularly, and supplements should be given if needed. CKD patients not on dialysis are usually advised to take vitamin D supplements. Patients on peritoneal dialysis may need extra monitoring for vitamin and folate levels.

Hypocalcemia/ hypercalcaemia
CKD patients can develop low or high calcium levels. Regular blood calcium monitoring is recommended, and calcium supplements may be needed.

Metabolic acidosis
CKD patients are at risk of metabolic acidosis, so serum bicarbonate levels should be checked regularly.

Peritonitis
Patients on peritoneal dialysis have a risk of infection called peritonitis. Proper dialysis hygiene and early recognition of symptoms are important. Patients should be monitored closely.

Hypothyroidism
Patients taking both sevelamer carbonate and levothyroxine should have closer thyroid monitoring.

Hyperparathyroidism
Sevelamer carbonate alone is not used to control hyperparathyroidism. It should be used along with other treatments such as calcium and vitamin D to reduce parathyroid hormone levels.

Inflammatory gastrointestinal disorders
Serious inflammation and complications in the digestive tract have been reported with sevelamer use. Symptoms may improve after stopping the medicine. Treatment should be reviewed if severe gastrointestinal symptoms develop.

Sodium content
This medicine contains very little sodium and is considered essentially sodium-free.

Fertility, pregnancy and lactation
Pregnancy
There are no or limited amount of data from the use of sevelamer in pregnant women.

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.

Fertility
There are no data from the effect of sevelamer on fertility in humans.

Interaction with other medicinal products and other forms of interaction
Dialysis
Interaction studies have not been conducted in patients on dialysis.