165mm

155mm

that medication would have a clinically significant effect on its safety or efficacy (e.g., cyclosporine, tacrolimus, levothyroxine), consider separation of the timing of the administration of the two drugs. The duration of separation depends upon the absorption characteristics of the medication concomitantly administered, such as the time to reach peak systemic levels and whether the drug is an immediate release or an extended-release product. Where possible consider monitoring clinical responses and/or blood levels of concomitant drugs that have a narrow therapeutic range.

OVERDOSAGE
In Chronic Kidney Disease patients on dialysis, the maximum dose studied was 14 grams of sevelamer carbonate and 13 grams of sevelamer hydrochloride. There are no reports of overdosage with sevelamer carbonate or sevelamer hydrochloride in patients. Since sevelamer is not absorbed, the risk of systemic toxicity is low.

PRESENTATION
Sevemer Sachet 2.4g available in pack of 3 x10's, 6x10's & 9x10'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)

2.4g Sachet

سیویمر

(سیویلامر کاربونیٹ)

۲.۴ گرام ساشے

COMPOSITION:
Sevemer Sachet 2.4g
Each sachet contains:
Sevelamer Carbonate..... 2.4g

CLINICAL PHARMACOLOGY
PHARMACODYNAMICS
Mechanism Of Action
Sevelamer carbonate for oral suspension contains sevelamer carbonate, a non-absorbed phosphate binding cross-linked polymer, free of metal and calcium. It contains multiple amines separated by one carbon from the polymer backbone. These amines exist in a protonated form in the intestine and interact with phosphate molecules through ionic and hydrogen bonding. By binding phosphate in the gastrointestinal tract and decreasing absorption, sevelamer carbonate lowers the phosphate concentration in the serum (serum phosphorus).

PHARMACOKINETICS
A mass balance study using C-sevelamer hydrochloride, in 16 healthy male and female volunteers showed that sevelamer hydrochloride is not systemically absorbed. No absorption studies have been performed in patients with renal disease.

In vivo:
Sevelamer carbonate has been studied in human drug-drug interaction studies (9.6 grams once daily with a meal) with warfarin and digoxin. Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been studied in human drug-drug interaction studies (2.4 to 2.8 grams single dose or three times daily with meals or two times daily without meals) with ciprofloxacin, digoxin, enalapril, iron, metoprolol, mycophenolate mofetil and warfarin. Coadministered single dose of 2.8 grams of sevelamer hydrochloride in fasted state decreased the bioavailability of ciprofloxacin by approximately 50% in healthy subjects. Concomitant administration of sevelamer and mycophenolate mofetil in adult and pediatric patients decreased the mean MPA C and AUC by 36% and 26% respectively.
Sevelamer carbonate or sevelamer hydrochloride did not alter the pharmacokinetics of enalapril, digoxin, iron, metoprolol and warfarin when coadministered.
During post marketing experience, cases of increased thyroid stimulating hormone (TSH) levels have been reported in patients coadministered sevelamer hydrochloride and levothyroxine. Reduction in concentrations of cyclosporine and tacrolimus leading to dose increases has also been reported in transplant patients when coadministered with sevelamer hydrochloride without any clinical consequences (for example, graft rejection). The possibility of an interaction cannot be excluded with these drugs.

SPECIAL POPULATION
Pregnancy:
Sevelamer carbonate is not absorbed systemically following oral administration and maternal use is not expected to result in fetal exposure to the drug. Sevelamer carbonate may decrease serum levels of fat-soluble vitamins and folic acid in pregnant women. Consider supplementation

Lactation:
Sevelamer carbonate is not absorbed systemically by the mother following oral administration, and breastfeeding is not expected to result in exposure of the child to sevelamer carbonate. Sevelamer carbonate may decrease serum levels of fat-soluble vitamins and folic acid in pregnant Women. Consider supplementation.

Pediatric Use:
The safety and efficacy of sevelamer carbonate in lowering serum phosphorus levels was studied in patients 6 years of age and older with CKD. In this study, sevelamer carbonate was apparently less effective in children with a low baseline serum phosphorus, which described children <13 years of age and children not on dialysis. Given its mechanism of action, sevelamer carbonate is expected to be effective in lowering serum phosphorus levels in pediatric patients with CKD. Most adverse events that were reported as related, or possibly related, to sevelamer carbonate were gastrointestinal in nature. No new risks or safety signals were identified with the use of sevelamer carbonate in the trial.

Geriatric Use:
Clinical studies of sevelamer carbonate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range

THERAPEUTIC INDICATIONS
Sevelamer carbonate for oral suspension is indicated for the control of serum phosphorus in adults and children 6 years of age and older with chronic kidney disease (CKD) on dialysis.

DOSAGE & ADMINISTRATION
Starting Dose for Adult Patients Not Taking a Phosphate Binder. The recommended starting dose of sevelamer carbonate is 0.8 to 1.6 grams taken orally with meals based on serum phosphorus level.

Posology
For a 2.4 g dose, the powder for oral suspension should be dispersed in 60 ml of water per sachet. Drink within 30 minutes of being prepared. It is important to drink all of the liquid and it may be necessary to rinse the glass with water and drink this as well to ensure that all of the powder is swallowed.
Instead of water, the powder may be premixed with a small amount of cold beverage (about 120 ml or half a glass) or food (about 100 g) and consumed within 30 minutes.
Do not heat Sevemer powder (e.g., Microwave) or add to hot foods or liquids.
The recommended starting dose of this medicine for adults and elderly is 2.4-4.8 g per day equally divided over three meals. The exact starting dose and regimen will be determined by your doctor. Check with your doctor, pharmacist or nurse if you are not sure.
Take Sevemer after your meal or with food. If a dose of 0.4 g is to be administered, please use the dedicated 0.8 g powder presentation with dosing spoon.

Use in children and adolescents:
The recommended starting dose of Sevemer for children is based on their height and weight (used to calculate body surface area by your physician). For children, the powder is preferred, as tablets are not appropriate in this population. This medicine should not be given on an empty stomach and should be taken with meals or snacks. The exact starting dose and regimen will be determined by your doctor. Initially, your doctor will check the levels of phosphorus in your blood every 2-4 weeks and they may adjust the dose of Sevemer when necessary to reach an adequate phosphate level.

METHOD OF ADMINISTRATION
For oral administration only.

ADVERSE REACTIONS
Like all medicines, this medicine can cause side effects, although not everybody gets them. Constipation is a very common side effect (may affect more than 1 in 10 people). It can be an early symptom of a blockage in your intestine. In case of constipation, please inform your doctor or pharmacist.
Some side effects could be serious.
If you get any of the following side effects, seek immediate medical attention: - Allergic reaction (signs including rash, hives, swelling, trouble breathing). This is a very rare side effect (may affect up to 1 in 10,000 people).
Blockage in the intestine (signs include: severe bloating, abdominal pain, swelling or cramps, severe constipation) has been reported. Frequency is not known (frequency cannot be estimated from the available data).
Rupture in the intestinal wall (signs include: severe stomach pain, chills, fever, nausea, vomiting, or a tender abdomen) has been reported. Frequency is not known.
Serious inflammation of the large bowel (symptoms include: severe abdominal pain, stomach or intestine disorders, or blood in the stool [gastrointestinal bleeding]) and crystal deposit in the intestine have been reported. Frequency is not known.

Other side effects have been reported in patients taking Sevemer:
Very common: (may affect more than 1 in 10 people): vomiting, upper abdominal pain, nausea
Common: (may affect up to 1 in 10 people): diarrhea, stomach ache, indigestion, flatulence
Not known: (frequency cannot be estimated from available data): cases of itching, rash, slow intestine motility (movement)

CONTRAINDICATIONS
Sevelamer carbonate for oral suspension is contraindicated in patients with bowel obstruction. Sevelamer carbonate for oral suspension is contraindicated in patients with known hypersensitivity to sevelamer carbonate, sevelamer hydrochloride, or to any of the excipients.

PRECAUTIONS
Gastrointestinal Adverse Events:
Patients with dysphagia, swallowing disorders, severe gastrointestinal (GI) motility disorders, including severe constipation, or major GI tract surgery were not included in the sevelamer carbonate clinical studies.
Cases of dysphagia and esophageal tablet retention have been reported in association with use of the tablet formulation of sevelamer, some requiring hospitalization and intervention. Consider using sevelamer suspension in patients with a history of swallowing disorders. Cases of bowel obstruction, bleeding gastrointestinal ulcers, colitis, ulceration, necrosis, and perforation have also been reported with sevelamer use. Inflammatory disorders may resolve upon sevelamer discontinuation. Treatment with sevelamer should be reevaluated in patients who develop severe gastrointestinal symptoms.

Monitor for Reduced Vitamins D, E, K (clotting factors) and Folic Acid Levels
In preclinical studies in rats and dogs, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, reduced vitamins D, E, and K (coagulation parameters) and folic acid levels at doses of 6 to 10 times the recommended human dose. In short-term clinical trials, there was no evidence of reduction in serum levels of vitamins. However, in a one-year clinical trial, 25-hydroxyvitamin D (Normal range 10 to 55 ng/mL) fell from 39 ± 22 ng/mL to 34 ± 22 ng/mL ($p<0.01$) with sevelamer hydrochloride treatment. Most (approximately 75%) patients in sevelamer hydrochloride clinical trials were receiving vitamin supplement.

DRUG INTERACTIONS
There are no empirical data on avoiding drug interactions between sevelamer carbonate and most concomitant oral drugs. For oral medication where a reduction in the bioavailability of