Selcarb Tablets
(Sevelamer Carbonate)

سیلکارب گولیاں
سیویلامر کاربونیٹ

Composition:
Selcarb-800 mg
Each film coated tablet contains:
Sevelamer carbonate..... 800mg
(Innovator's Spec.)

Description:
The active ingredient in Selcarb is sevelamer carbonate, a polymeric amine that binds phosphate and is meant for oral administration. It was developed as a pharmaceutical alternative to sevelamer hydrochloride (Renavel). Sevelamer carbonate is an anion exchange resin, with the same polymeric structure as sevelamer hydrochloride, in which carbonate replaces chloride as the counterion. While the counterions differ for the two salts, the polymer itself, the active moiety involved in phosphate-binding, is the same.Selcarb (sevelamer carbonate) is known chemically as poly(allylamine-co-N,N'-diallyl-1,3-diamino-2-hydroxypropane) carbonate salt. Sevelamer carbonate is hygroscopic, but insoluble in water.

Clinical pharmacology

Mechanism of action:
Selcarb 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).

Pharmacodynamics:
In addition to effects on serum phosphorus levels, sevelamer hydrochloride has been shown to bind bile acids in vitro and in vivo in experimental animal models. Because sevelamer binds bile acids, it may interfere with normal fat absorption and thus may reduce absorption of fat soluble vitamins such as A, D and K. In clinical trials of sevelamer hydrochloride, both the mean total and LDL cholesterol declined by 15%–31%; the clinical significance of this finding, which was observed after 2 weeks, is unclear. Triglycerides, HDL cholesterol, and albumin did not change.

Pharmacokinetics:
Studies using 14C- Sevelamer carbonate in 16 healthy male and female volunteers showed that sevelamer carbonate is not systemically absorbed. No absorption studies have been performed in patients with renal disease.

Indications:
Selcarb is indicated for the control of hyperphosphataemia in patients with chronic kidney disease on dialysis.

Contraindications:
Selcarb is contraindicated in patients with hypophosphataemia or bowel obstruction. Selcarb is also contraindicated in patients known to be hypersensitive to sevelamer carbonate or any of the other components of the tablet.

WARNINGS AND PRECAUTIONS:
Selcarb tablets should be swallowed whole and should not be crushed, chewed, or broken into pieces. BEFORE you use Selcarb talk to your doctor or pharmacist if you: have difficulty swallowing (swallowing disorders or problems with your esophagus) have an intestinal disorder such as, conditions that slow down the passage of food through the intestine and lead to blockage. have had surgery on your intestines. have severe or worsening constipation have low phosphorus levels in your blood. have low calcium levels in your blood. are pregnant, plan to become pregnant or are nursing have any allergies to this drug or its ingredients or components of the container.

INTERACTIONS WITH THIS MEDICATION:
Selcarb may affect the way other medicines work. Please tell your doctor or pharmacist what medicine you have recently taken, are taking or intend to take including those available without prescription and herbal remedies. These medicines may need to be taken one hour before or three hours after SELCARB. Remember, Selcarb must always be

taken with food. If you see another doctor or a dentist while you are using Selcarb, you should tell them that you are using Selcarb. Drugs that may interact with Selcarb include: ciprofloxacin and levothyroxine. Your doctor may order blood tests to more closely monitor the thyroid hormones in your blood if you are taking levothyroxine and Selcarb.

Selcarb may also interact with drugs that are used to prevent the rejection of a transplanted organ, such as cyclosporin, mycophenolate and tacrolimus.

Selcarb may interact with drugs that are used to treat stomach ulcer known as proton pump inhibitors (e.g. pantoprazole, omeprazole).

PROPER USE OF THIS MEDICATION:

Tablets should be swallowed intact and should not be crushed, chewed, or broken into pieces prior to administration.

Usual starting dose: Dosage is individualized. Your doctor will determine your dosage.

Selcarb should be taken immediately prior to or with meals.

The total daily dose should be divided according to meal portions during the day.

Average maintenance dose is approximately 7-8 tablets of 800 mg each day. Always follow your physician's dosage instructions.

Nonclinical toxicology:

Carcinogenesis, Mutagenesis, Impairment of fertility Standard lifetime carcinogenicity bioassays were conducted in mice and rats. Rats were given sevelamer hydrochloride by diet at 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 13 g). Mice received dietary administration of sevelamer hydrochloride at doses of up to 9 g/kg/day (human equivalent dose 3 times the maximum clinical trial dose). There was no increased incidence of tumors observed in mice.

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.

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 3 times the maximum clinical trial dose of 13 g).

Use in specific populations

Pregnancy

Risk Summary

Sevelamer carbonate is not absorbed systemically following oral administration and maternal use is not expected to result in fetal exposure to the drug.

Clinical Considerations:

Sevelamer carbonate may decrease serum levels of fat soluble vitamins and folic acid in pregnant women.

Consider supplementation.

Lactation Risk Summary:

Selcarb is not absorbed systemically by the mother following oral administration, and breast feeding is not expected to result in exposure of the child to Selcarb.

Clinical Considerations:

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 Selcarb in lowering serum phosphorus levels was studied in patients 6 years of age and older with CKD. In this study, Selcarb 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, Selcarb 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.

Selcarb has not been studied in pediatric patients below 6 years of age.

Geriatric use:

Clinical studies of Selcarb 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.

Instructions to Patients:

The contents of sevelamer carbonate expand in water thus tablets should be swallowed intact and should not be crushed, chewed or broken into pieces prior to administration.

Interactions:

Drug-Drug Interactions Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been studied in human drug-drug interaction studies. In interaction studies in healthy volunteers, sevelamer hydrochloride had no effect on the bioavailability of a single-dose of digoxin, warfarin, enalapril, metoprolol or iron However, the bioavailability of ciprofloxacin was decreased by approximately 50% when co-administered with sevelamer hydrochloride in a single dose study.

Consequently, sevelamer hydrochloride (and thus sevelamer carbonate) should not be taken simultaneously with ciprofloxacin. During postmarketing experience, reduced concentrations of cyclosporin, mycophenolatemofetil and tacrolimus have been reported in transplant patients when co-administered with sevelamer hydrochloride. The possibility of an interaction cannot be excluded and close monitoring of blood concentrations of cyclosporin, mycophenolatemofetil and tacrolimus or dosing these medicines apart from Selcarb to prevent GI binding (at least one hour before or three hours after Selcarb) should be considered during the use of any of these agents in combination with Selcarb and after its withdrawal. During postmarketing experience, very rare cases of increased thyroid stimulating hormone (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. During postmarketing experience, very rare cases of increased phosphate levels have been reported in patients taking proton pump inhibitors co-administered with sevelamer carbonate. When administering an oral medication where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, the drug should be administered at least one hour before or three hours after sevelamer carbonate, or the physician should consider monitoring blood levels of the drug. Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from the clinical trials. Special precautions should be taken when prescribing sevelamer carbonate to patients also taking these medications.

Drug-Food Interactions:

There have been no adequate, well-controlled studies regarding the effect of a variety of foods on the intestinal phosphorus binding of sevelamer. In all clinical studies patients were instructed to take sevelamer with meals.

Drug-Herb Interactions:

There have been no adequate, well-controlled studies regarding drug-herb interactions.

Drug-Laboratory Interactions:

There have been no adequate, well-controlled studies regarding drug-laboratory interactions.

Drug-Lifestyle Interactions:

There have been no adequate, well-controlled studies regarding drug-lifestyle interactions.

Nervous system disorders: Headache

Vascular disorders: Hypotension, hypertension

General disorders: Pain

Skin and subcutaneous site conditions: Pruritis, Rash

Infections and infestations: Pharyngitis

Most of these events are commonly observed in patients Stage 5 Chronic Kidney Disease and are not necessarily attributable to sevelamer carbonate.

DOSAGE AND ADMINISTRATION:

Dosing Considerations:

Selcarb (sevelamer carbonate) tablets should not be bitten, chewed or broken apart prior to dosing.

Selcarb should be taken immediately prior to or with meals, since its action is to bind ingested phosphate.

When administering any other medication where a reduction in the bioavailability of that medication

would have a clinically significant effect on safety or efficacy, the physician should consider monitoring blood levels or dosing that medicine apart from Selcarb to prevent GI binding (at least one hour before or three hours after Selcarb).

Recommended Dose and Dosage Adjustment:

The recommended dosing to be used when initiating Selcarb in patients not using another phosphate binder are outlined below in **Table:**

Selcarb Dosing

SERUM PHOSPHORUS	SELCARB 800 mg
> 5.5 and < 7.5mg/dL	(0.8g)1 tablet three times daily with food
≥ 7.5 mg/dL	(1.6g)2 tablets three times daily with food

For patients previously on sevelamer hydrochloride, Selcarb should be given on a gram for gram basis with monitoring of serum phosphorus levels to ensure optimal daily doses.

In a study in 84 chronic kidney disease (CKD) patients on hemodialysis, a similar reduction in serum phosphorus was seen with equivalent doses (approximately mg for mg) of sevelamer hydrochloride and calcium acetate.

Selcarb (sevelamer carbonate)

Table . Starting Dose for Dialysis Patients Switching From Calcium Acetate to Selcarb

Calcium Acetate 667 mg (Tablets per meal) Selcarb 800 mg Tablet (Tablets per meal)

1 tablet	0.8g	1 tablet
2 tablets	1.6g	2 tablets
3 tablets	2.4g	3 tablets

Dose adjustments, when necessary should be done every 1 to 3 weeks by increasing one tablet per meal (3 tablets per day) until the desired serum levels are met.

The total dose should be divided according to the meal portion during the day.

Maintenance:

Serum phosphorus should be monitored on a regular basis with the goal of maintaining serum phosphorus levels consistent with current medical standards (see Dosing Considerations).

In clinical trials, the average actual daily dose of sevelamer carbonate was approximately 6 g per day. The highest studied daily dose of sevelamer carbonate taken was 14.4 g per day in CKD patients.

Missed Dose:

If a dose is forgotten, it should be skipped. Double dosing is not advisable.

OVERDOSAGE:

In CKD patients on dialysis, the maximum dose studied was 14.4 grams of sevelamer carbonate and 13 grams of sevelamer hydrochloride. Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, has been given to normal healthy volunteers in doses of up to 14.4 grams per day for eight days with no adverse effects. 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.

Storage:

Store below 30°C.

Protect from heat light & moisture.

Keep all medicines out of the reach of children.

Presentation:

Selcarb 800mg is available in Aluminum blister pack of 3x 10 tablets.

خوراک: دوا ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

احتیاط: دوا کو ٹھنڈی اور خشک جگہ پر دھوپ سے بچا کر رکھیں۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

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