For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

Foseal™-400 / 800

Sevelamer Hydrochloride Tablets

Therapeutic Category : Antihyperphosphatemic

Composition :

Foseal - 400		**Foseal - 800**	
Each film coated tablet contains :		Each film coated tablet contains :	
Sevelamer Hydrochloride	400 mg	Sevelamer Hydrochloride	800 mg
Excipients	q.s.	Excipients	q.s.
Starch (Maize Starch)		Starch (Maize Starch)	
Povidone		Povidone	
Colloidal Silicon Dioxide		Colloidal Silicon Dioxide	
Stearic Acid		Stearic Acid	
Isopropyl Alcohol		Isopropyl Alcohol	
Hypromellose		Hypromellose	
Macrogols		Macrogols	
Talc		Talc	
Methylene Chloride		Methylene Chloride	

Description :
Sevelamer hydrochloride is a polymeric phosphate binder intended for oral administration. Sevelamer hydrochloride is poly (allylamine hydrochloride) crosslinked with epichlorohydrin in which forty percent of the amines are protonated. It is known chemically as poly (allylamine-co-N,N, diallyl-1,3-diamino-2-hydroxypropane) hydrochloride. Sevelamer hydrochloride is hydrophilic, but insoluble in water.

Clinical Pharmacology :
Patients with end-stage renal disease (ESRD) retain phosphorus and can develop hyperphosphatemia. High serum phosphorus can precipitate serum calcium resulting in ectopic calcification. When the product of serum calcium & phosphorus concentrations (Ca x P) exceeds 55 mg^2/dl^2, there is an increased risk that ectopic calcification will occur. Hyperphosphatemia plays a role in the development of secondary hyperparathyroidism in renal insufficiency. An increase in parathyroid hormone (PTH) levels is characteristic of patients with chronic renal failure. Increased levels of PTH can lead to osteitis fibrosa, a bone disease. A decrease in serum phosphorus may decrease serum PTH levels. Treatment of hyperphosphotemia includes reduction in dietary intake of phosphate, inhibition of intestinal phosphate absorption with phosphate binders, and removal of phosphate with dialysis. Sevelamer hydrochloride taken with meals has been shown to decrease serum phosphorus concentrations in patients with ESRD who are on hemodialysis. Sevelamer hydrochloride does not contain aluminum or other metals and does not cause aluminum intoxication. Sevelamer hydrochloride treatment also results in a lowing of low-density lipoprotein (LDL) and total serum cholesterol levels.

Pharmacokinetics :
Sevelamer hydrochloride is not systemically absorbed. No absorption studies have been performed in patients with renal disease.

Indications :
Sevelamer Hydrochloride is indicated for the control of serum phosphorus in patients with Chronic Kidney Disease (CKD) on hemodialysis.

Dosage and Administration :
Patients Not Taking a Phosphate Binder : The recommended starting dose of Sevelamer hydrochloride is 800 to 1600 mg. which can be administered as one to two 800 mg Tablets or two to four 400 mg Tablets with each meal based on serum phosphorus level. Tablet 1 provides recommended starting doses of Sevelamer hydrochloride for patients not taking a phosphate binder.

Table 1 : Starting Dose for Patients Not Taking a Phosphate Binder

Serum Phosphorus	Sevelamer HCl 800 mg Tab	Sevelamer HCl 400 mg Tab
> 5.5 and < 7.5 mg/dl	1 tablet three times Daily with meals	2 tablets three times Daily with meals
≥ 7.5 and < 9 mg/dl	2 tablets three times Daily with meals	3 tablets three times Daily with meals
≥ 9 mg/dl	2 tablets three times Daily with meals	4 tablets three times Daily with meals

Patients Switching From Calcium Acetate : Table 2 gives recommended starting doses of sevelamer based on a patients current calcium acetate dose.

Table 2 : Starting Dose for Patients Switching From calcium Acetate to sevelamer Hydrochloride

Calcium acetate 667 mg (Tablets per meal)	Sevelamer HCl 800 mg (Tablets per meal)	Sevelamer HCl 400 mg (Tablets per meal)
1 Tablet	1 Tablet	2 Tablet
2 Tablets	2 Tablets	3 Tablets
3 Tablets	3 Tablets	5 Tablets

Dose Titration for All Patients Taking Sevelamer hydrochloride : Dosage should be adjusted based on the serum phosphorus concentration with a goal of lowering serum phosphorus to 5.5 mg/dL or less. The dose may be increased or decreased by one tablet per meal at two-week intervals as necessary. Table 3 gives a dose titration guideline.

Table 3 : Dose Titration Guideline

Serum Phosphorus	Sevelamer hydrochloride dose
> 5.5 mg/dl	Increase 1 tablet per at 2 week intervals
3.5 - 5.5 mg/dl	Maintain current dose
< 3.5 mg/dl	Decrease 1 tablet per meal

Contraindications :
Sevelamer hydrochloride is contraindicated in patients with hypophosphatemia or bowel obstruction. Sevelamer hydrochloride is contraindicated in patients known to be hypersensitive to sevelamer hydrochloride or any of the constituents of the formulation.

Precautions :
General : The safety and efficacy of sevelamer hydrochloride in patients with dysphagia, swallowing disorders, severe gastrointestinal (GI) motility disorders, or major GI tract surgery have not been established. Consequently, caution should be exercised when sevelamer hydrochloride is used in patients with these GI disorders. Sevelamer hydrochloride dose not contain calcium or alkali supplementation; serum calcium, bicarbonate, and chloride levels should be monitored.

The prescriber should inform patients to take sevelamer with meals and adhere to their prescribed diets. Instructions should be given on concomitant medications that should be dosed apart from sevelamer. Because the contents of sevelamer hydrochloride expand in water, tablets should be swallowed intact and should not be crushed, chewed, broken into pieces, or taken apart prior to administration.

Drug interactions : Sevelamer hydrochloride dose not alter the pharmacokinetics of digoxin, warfarin, enalapril, metoprolol and iron. However, when administering any other oral medication where a reduction in the bioavailability of that medication would have a clinically significant effect on safety or efficacy, the drug should be administered at least one hour before or three hours after sevelamer hydrochloride, or the physician should consider monitoring blood levels of the drug. Special precautions should be taken when prescribing sevelamer hydrochloride to patients also taking anti-arrhythmic and anti-seizure medications.

Pregnancy : Sevelamer hydrochloride belongs to Pregnancy Category C. In animal studies (rats), sevelamer hydrochloride caused reduced or irregular ossification of fetal bones, probably due to reduced absorption of fat-soluble vitamin. Requirements for vitamins and other nutrients are increased in pregnancy. The effect of sevelamer hydrochloride on the absorption of vitamins and other nutrients has not been studied in pregnant women.

Geriatric use : There is no evidence for special considerations when sevelamer hydrochloride is administered to elderly patients.

Pediatric use : The safety and efficiency of sevelamer hydrochloride has not been established in pediatric patients.

Adverse Reactions :
For treatment duration of two weeks, the adverse events reported for sevelamer hydrochloride are similar to those reported for placebo. The adverse events reported for long-term sevelamer hydrochloride treatment are : headache, infection, pain hypertension, hypotension, thrombosis, diarrhea, flatulence, dyspepsia, nausea, vomiting, constipation and cough. Other adverse events reported for sevelamer hydrochloride are : pruritus, rash and abdominal pain.

Overdosage :
Sevelamer hydrochloride has been given to normal healthy volunteers in doses of up to 14 grams per day for eight days with no adverse effects. Sevelamer hydrochloride has been given in average doses up to 13 grams per day to hemodialysis patients. There are no reported overdosages of sevelamer hydrochloride in patients. Since sevelamer hydrochloride is not absorbed, the risk of systemic toxicity is low.

Storage :
Store at 25°C (77°F); excursions permitted to 15 - 30°C (59 - 86°F).
Protect from moisture.
Keep away from the reach of children.

Presentation :
Blister of 10 tablets.

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