Redupho® 800

Sevelamer HCl

The active pharmaceutical ingredient in Redupho is sevelamer hydrochloride, a polymeric phosphate binder intended for oral administration.

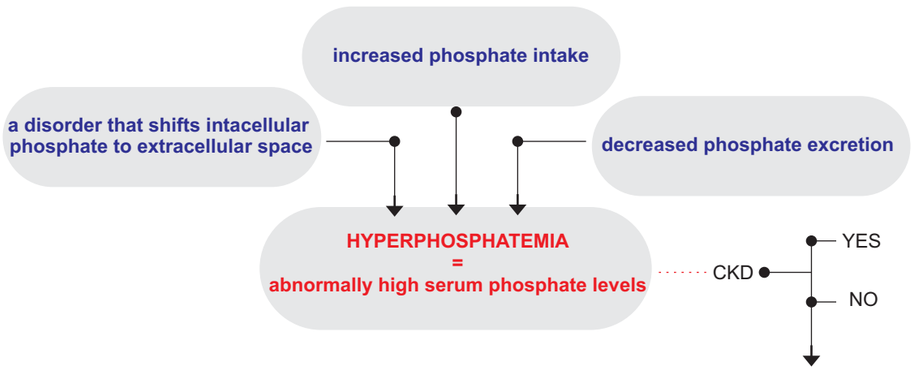
Renofa® 800

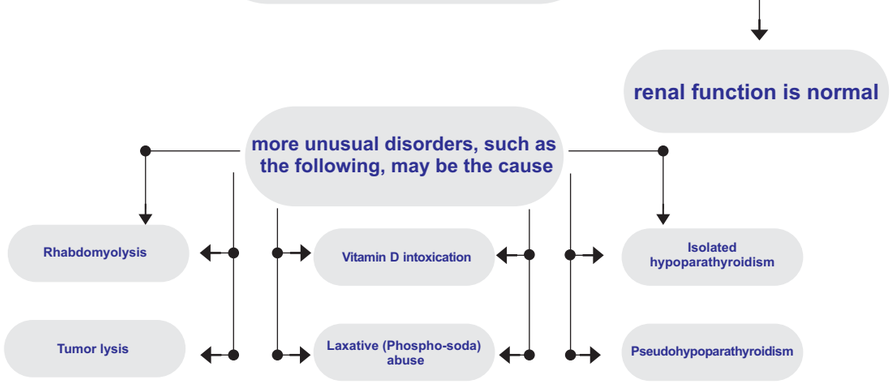
Sevelamer Carbonate

The active pharmaceutical ingredient in Renofa is sevelamer carbonate, a phosphate binder indicated for the control of serum phosphorus in adults and children 6 years of age and older with chronic kidney disease on dialysis.

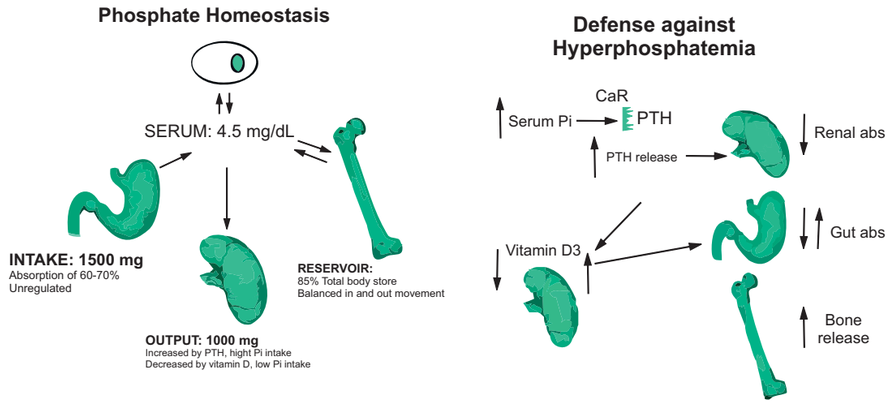
Indication:

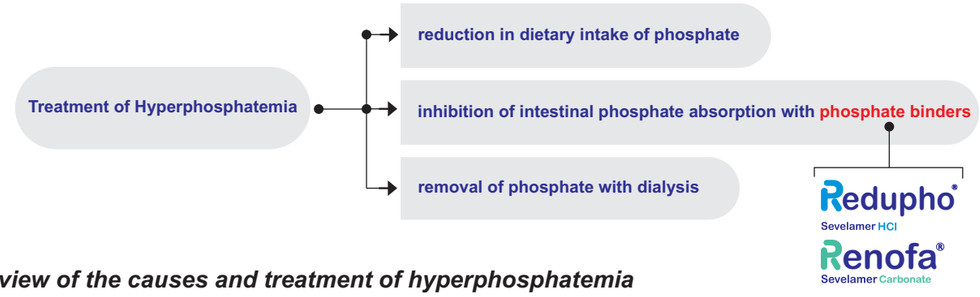
Sevelamer is indicated for treatment of hyperphosphatemia. It is given orally as either the carbonate or the hydrochloride. The initial dose is 0.8 to 1.6 g of sevelamer carbonate or sevelamer hydrochloride three times daily with each meal, depending on the severity of hyperphosphatemia. Doses should then be adjusted according to plasma-phosphate concentrations; the usual maintenance dose is from 0.8 to 4 g with each meal.



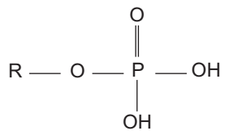


However, even severe hyperphosphatemia is for the most part clinically asymptomatic. Morbidity In patients with this condition is more commonly associated with an underlying disease than with increased phosphate values.





Overview of the causes and treatment of hyperphosphatemia



In the steady state, the serum phosphate concentration is primarily determined by the ability of the kidneys to excrete dietary phosphate.

Renal excretion is so efficient in normal subjects that balance can be maintained with only a minimal rise in serum phosphate concentration even if phosphorus intake is increased to as much as 4000 mg/day (130 mmol/day). Phosphorus intake above 4000 mg/day (130 mmol/day) causes only small elevations in serum phosphate concentrations as long as the intake is distributed over the course of the day. 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. High serum phosphorus can precipitate serum calcium resulting in ectopic calcification. When the product of serum calcium and phosphorus concentrations (Ca x P) exceeds 66, there is an increased risk that ectopic calcification will occur.

Redupho treatment also results in a lowering of low-density lipoprotein (LDL) and total serum cholesterol levels. Redupho taken with meals has been shown to decrease serum phosphorus concentrations in patients with ESRD who are on hemodialysis.

The main difference between sevelamer carbonate and sevelamer hydrochloride is that the chloride in the sevelamer resin was replaced by bicarbonate. That's the only difference. With sevelamer hydrochloride some patients develop metabolic acidosis because in the intestine chloride is exchanged for bicarbonate.

CONTRAINDICATIONS

Redupho is contraindicated in patients with hypophosphatemia or bowel obstruction. Redupho is contraindicated in patients known to be hypersensitive to sevelamer hydrochloride or any of its constituents.

Renofa is contraindicated in patients with bowel obstruction.

Sevelamer is contraindicated in patients with known hypersensitivity to sevelamer carbonate, sevelamer hydrochloride, or to any of the excipients.

Pharmacokinetics:

A study showed that sevelamer hydrochloride is not systemically absorbed. No absorption studies have been performed in patients with renal disease.
Geriatric use: There is no evidence for special considerations when Redupho is administered to elderly patients.
Pediatric use: The safety and efficacy of Redupho has not been established in pediatric patients.

WARNINGS AND PRECAUTIONS

- Gastrointestinal Adverse Events

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. Cases of bowel obstruction and perforation have also been reported with sevelamer use.

- Reductions in 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 6-10 times the recommended human dose.

ADVERSE REACTIONS

Most frequently occurring adverse reactions for Renofa in a short term (8-week crossover) study were: nausea (3%) and vomiting (3%). In long-term studies with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, the most common adverse events included: vomiting (22%), nausea (20%), diarrhea (19%), dyspepsia (16%), abdominal pain (9%), flatulence (8%) and constipation (8%).

- Cases of fecal impaction and, less commonly, ileus, bowel obstruction and bowel perforation have been reported.

DRUG INTERACTIONS

- In a normal volunteer study, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, decreased the bioavailability of ciprofloxacin by approximately 50%.
- In normal volunteer studies, sevelamer hydrochloride did not alter the pharmacokinetics of a single dose of digoxin, warfarin, enalapril, metoprolol, and iron.
- 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 Renofa, or the physician should consider monitoring blood levels of the drug.

Ref: FDA prescribing information, Drug Fact and Comparisons, Martindale

Renofa®
Sevelamer Carbonate

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

Redupho Dose	Renofa
> 5.5 and < 7.5 mg/dL	0.8 g three times daily with meals
≥ 7.5 mg/dL	1.6 g three times daily with meals

Table 2: Recommended Starting Dosage and Titration Increment based on Pediatric Patient's Body Surface Area (m^2)

BSA (m^2)	Starting dose per meal/snack	Titration increases/decreases per dose
≥ 0.75 to < 1.2	0.8 g	Titrate by 0.4 g
≥ 1.2	1.6 g	Titrate by 0.8 g

Table 3: Starting Dose for Dialysis Patients Switching From Calcium Acetate to Renofa 800·

Calcium Acetate 667 mg (Tablets per meal)	Renofa 800
1 tablet	0.8 g
2 tablets	1.6 g
3 tablets	2.4 g

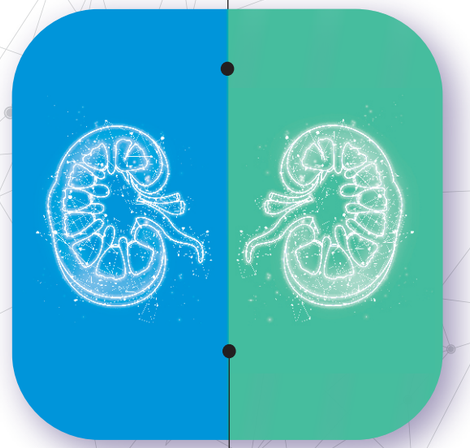


Table 1: Starting Dose for Dialysis Patients Not Taking a Phosphate Binder

Serum Phosphorus	Redupho ® 800 mg
> 6 and < 7.5 mg/dL1	tablet three times daily with meals
≥ 7.5 and < 9.0 mg/dL2	tablets three times daily with meals
> 9.0 mg/dL2	tablets three times daily with meals

Table 2: Starting Dose for Dialysis Patients Switching From Calcium Acetate to Redupho

Calcium Acetate 667 mg (Tablets per meal)	Redupho® 800 mg (Tablets per meal)
1 tablet	1 tablet
2 tablet	2 tablet
3 tablet	3 tablet

Table 3: Dose Titration Guideline

Serum Phosphorus	Redupho Dose
> 6 mg/dL	Increase 1 tablet per meal at 2 week intervals
3.5 -6 mg/dL	Maintain current dose
< 3.5 mg/dL	Decrease 1 tablet per meal

Redupho®
Sevelamer HCl

Ref: FDA prescribing information, Drug Fact and Comparisons, Martindale

Faran Shimi
Pharmaceutical Co.

+98 (21) 57941000
www.faranshimi.com
faranshimi

Redupho® 800

Sevelamer HCl

Renofa® 800

Sevelamer Carbonate

Faran shimi Pharmaceutical Co.

Every step of our research, trial and production, is a way to approach to a healthy society, reduce suffering, share knowledge and help people to have a better life
It's our ultimate responsibility.

Faran Shimi
Pharmaceutical Co.