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

This package insert is continually updated. Please read carefully before using a new pack.

Sevelamer Carbonate Tablets and Powder for Oral Suspension

RENVELA TABLETS
Each film coated tablet contains 800 mg of sevelamer carbonate on an anhydrous basis.

RENVELA SACHETS
Each sachet contains 0.8 g of sevelamer carbonate for oral suspension on anhydrous basis

DESCRIPTION

Renvela contains sevelamer, a non-absorbed phosphate binding cross-linked polymer, free of metal and calcium. Renvela (sevelamer carbonate) was developed as a pharmaceutical alternative to sevelamer hydrochloride. 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 from the two salts the polymer itself, the active moiety involved in phosphate binding, is the same.

Therapeutic or Pharmacological Class
ATC (Anatomical Therapeutic Classification) for sevelamer carbonate is: V03AE02: Treatment of Hyperphosphatemia.

Pharmaceutical Form (s)

Tablets or powder for solution for oral
suspensionSterility statement: Non-sterile

- Tablets:

Renvela tablets: 800 mg white oval, film-coated tablets imprinted with “Renvela 800”
Renvela 800 mg tablets are supplied as white, oval, film-coated tablets imprinted with Renvela 800, containing 800 mg of sevelamer carbonate on an anhydrous basis, microcrystalline cellulose, sodium chloride, zinc stearate and coating components hypromellose and diacetylated monoglycerides.
1 Bottle of 30 count 800 mg Tablets

- Powder for solution for oral suspension:

Renvela powder: 0.8 g pale yellow powder.

Renvela sachets are supplied as powder for oral suspension containing 0.8 g of sevelamer carbonate on ananhydrous basis, natural and artificial citrus cream flavoring, propylene glycol alginate, sodium chloride, sucralose, and ferric oxide (yellow).

Each sachet is opaque, foil lined, and heart sealed.

Renvela 0.8 g sachets are packaged in boxes of 90 count sachets.

Composition

Active ingredient:

Each Renvela tablet contains 800 mg of sevelamer carbonate on an anhydrous basis.

Each Renvela sachet contains 0.8 g of sevelamer carbonate for oral suspension on anhydrous basis

Excipients:

Renvela tablets contain the following excipients: microcrystalline cellulose, sodium chloride and zinc stearate. The tablet coating contains hypromellose and diacetylated monoglycerides. The tablet printing ink also contains hypromellose in addition to iron oxide black ink, propylene glycol, isopropyl alcohol.
Each sachet of Renvela powder contains the following excipients: natural and artificial citrus cream flavor, propylene glycol alginate, sodium chloride, sucralose, and ferric oxide (yellow).
Renvela (sevelamer carbonate) is known chemically as poly (allylamine-co-N,N'-diallyl-1,3-diamino-2-hydroxypropane) carbonate salt.

Structural Formula

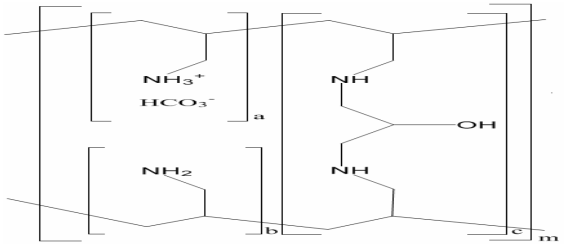

Figure 1.Chemical structure of Sevelamer Carbonate

a, b = number of primary amine groups a + b = 9

c = number of crosslinking groups c = 1

m = large number to indicate extended polymer network

NATURE AND CONTENTS OF CONTAINER

Renvela are packaged in white high-density polyethylene bottles (HDPE), with a child resistant polypropylene cap and an induction seal.

Renvela powder is packaged in opaque, foiled lined, heat sealed sachets.

INDICATIONS AND USAGE

Renvela is indicated for control of serum phosphorous in patients with chronic kidney disease on haemodialysis or peritoneal dialysis and patients with CKD not on dialysis with serum phosphorous ≥5.5 mg/dl

DOSAGE AND ADMINISTRATION

General

Starting dose:

The recommended starting dose is 2.4 to 4.8 g for adults per day based on clinical needs and phosphorus level. Renvela must be taken three times per day with meals.
For patients previously on phosphate binders (sevelamer hydrochloride or calcium base), Renvela 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 every 2-4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter.
Patients taking Renvela should adhere to their prescribed diets.
In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the adult daily dose is expected to be an average of approximately 6 g per day.

Special Populations
Children

The safety and efficacy of Renvela has not been established in children below the age of 18 years. Renvela is not recommended for use in children below the age of 18 years.
Elderly

There is no evidence for special considerations when Renvela is administered to elderly patients.

Administration
Route of administration is oral.
Renvela is available as tablets or powder for oral suspension.
Renvela 800 mg tablets can be taken three times per day with meals at a dosage based on individual patient requirements to control phosphate levels. Tablets should be swallowed intact and should not be crushed, chewed, or broken into pieces prior to administration.
Renvela 800 mg powder sachet can be taken three times per day with meals individually or in combination at a dosage based on individual patient requirements to control phosphate levels.
The powder should be dispersed in water (30 ml for 0.8 g powder sachet) prior to administration.
Multiple sachets may be mixed together, as long as the appropriate amount of water is used.
Patient should drink the preparation within 30 minutes.
As an alternative to water, the powder may be pre-mixed with a small amount of beverage or food (e.g. 4 ounces/120 ml) and consumed within 30 minutes. Do not heat Renvela (e.g., microwave) or add to hot foods or liquids

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

Food effect
In all clinical studies patients were instructed to take sevelamer with meals.

CONTRAINDICATIONS

Renvela is contraindicated in patients with hypophosphatemia or bowel obstruction.

Renvela is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients

WARNINGS

The safety and efficacy of Renvela in patients with dysphagia, swallowing disorders, severe gastrointestinal motility disorders including severe constipation or major gastrointestinal tract surgery have not been established. Consequently, caution should be exercised when Renvela is used in patients with these disorders. Renvela treatment should be reevaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.
Uncommon case reports of difficulty swallowing the tablet have been reported. Many of these cases involved patients with contributing co-morbid conditions affecting the ability to swallow including swallowing disorders or oroesophageal abnormalities. Caution should be exercised when the tablets are used in these patients. Consider using powder for oral suspension in patients with a history of difficulty swallowing.

Patients with CKD may develop low vitamin A, D, E and K levels, depending on dietary intake and the severity of their disease. Treatment with sevelamer in preclinical studies, approximately at the equivalent of 6-10 times the maximum clinical trial dose, has been shown to reduce the absorption of vitamins D, E and K, and folic acid. Therefore, in patients not taking supplemental vitamins but on sevelamer, serum vitamin A, D, and E levels and vitamin K status should be assessed regularly.

Cases of serious inflammatory disorders of the gastrointestinal tract (with complications including hemorrhage, perforation, ulceration, necrosis, colitis, and colonic/cecal mass) associated with the presence of sevelamer crystals have been reported (see Postmarketing section). Inflammatory disorders may resolve upon Renvela discontinuation. Treatment with Renvela should be reevaluated in patients who develop severe gastrointestinal symptoms.

INTERACTIONS

Sevelamer carbonate has been studied in two human drug-drug interaction studies. In interaction studies in healthy volunteers, sevelamer carbonate did not affect the bioavailability of either warfarin or digoxin.

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 post marketing experience, reduced concentrations of cyclosporin, mycophenolate mofetil and tacrolimus have been reported in transplant patients when co-administered with sevelamer hydrochloride without any clinical consequences (for example, graft rejection). The possibility of an interaction cannot be excluded and close monitoring of blood concentrations of cyclosporin, mycophenolate mofetil and tacrolimus should be considered during the use of any of these agents in combination with sevelamer and after its withdrawal.

During post-marketing 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.

Food
In all clinical studies patients were instructed to take sevelamer with meals.

PREGNANCY
Pregnancy Category C
The safety of Renvela has not been established in pregnant or lactating women. Renvela should only be given to pregnant or lactating women if clearly needed and after careful risk/benefit analysis has been conducted for both the mother and fetus or infant.
Studies in animals have shown minimal reproductive toxicity when sevelamer was administered to rats at high doses (see section "Impairment of Fertility" in section Reproduction toxicity).
There have been no adequate well controlled studies in women undergoing labor and delivery.

LACTATION
There have not been studies of the excretion of sevelamer in human milk, but since sevelamer is not absorbed, excretion in breast milk is not expected.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS
No effects on ability to drive and use machines have been observed.

ADVERSE REACTIONS

The most frequently occurring adverse reactions for the Renvela Tablets in a short term (8-week cross-over) study were: nausea (3%) and vomiting (3%). Most frequently occurring treatment related adverse events for Renvela powder in a short term (4-week cross-over) study were: nausea (7%), constipation (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%).

In a parallel study with a treatment duration of 12 weeks, the adverse events reported for sevelamer hydrochloride in peritoneal dialysis patients (N=97) were similar to adverse events observed in hemodialysis patients. Adverse events possibly related to sevelamer hydrochloride included dyspepsia (12.4%), diarrhea (5.2%), nausea (5.2%), constipation (4.1%), pruritus (4.1%), abdominal distension (3.1%), vomiting (3.1%), fatigue (3.1 %), and anorexia (3.1 %).

In a double-blind, placebo-controlled, dose titration study with a treatment duration of 8 weeks, the adverse events experienced by the patients in the sevelamer carbonate and placebo groups were similar. The most frequently reported treatment-related events were gastrointestinal disorders. Adverse reactions among those treated with sevelamer carbonate included: constipation (7.4%), abdominal distension (4.4 %), and abdominal discomfort (3.0%).

During post-marketing experience, the following adverse events have been reported in patients receiving Renvela although no direct relationship to Renvela could be established: hypersensitivity, pruritus, rash, abdominal pain and uncommon cases of ileus, intestinal obstruction and intestinal perforation.

Sevelamer carbonate has also been studied in patients with CKD not on dialysis

POSTMARKETING
Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

During post-marketing experience, the following adverse events have been reported in patients receiving Renvela: Hypersensitivity pruritus, rash, abdominal pain and uncommon cases of ileus, intestinal obstruction and intestinal perforation.

Cases of serious inflammatory disorders of the gastrointestinal tract (with complications including hemorrhage, perforation, ulceration, necrosis, colitis, and intestinal mass) associated with the presence of sevelamer crystals have been reported (see Warnings section).

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.

ABUSE AND DEPENDENCE
There have been no reports of abuse or dependence of sevelamer carbonate or sevelamer hydrochloride in patients. Since sevelamer is not absorbed, the risk of abuse or dependence is low.

INCOMPATIBILITIES / COMPATIBILITIES
There are no known pharmaceutical incompatibilities.

STORAGE CONDITIONS AND SHELF-LIFE
***Storage precautions*:**
Store Renvela tablets and Renvela powder below 25°C (77°F)
Protect from moisture.
Keep the bottle tightly closed

Shelf life:
See outer carton for expiry date.
Do not use Renvela after the expiration date.

Importer :
Sanofi Healthcare India Private Limited,

Gala No. 4, Ground Floor, Building No. B1,Citylink Warehousing Complex, S. No.121/10/A, 121/10/B & 69, NH3, Vadape, Tal : BHIWANDI-16 (THANE Z5) Pin : 421302

Manufactured by:
Genzyme Ireland Ltd.
IDA Industrial Park
Old Kimeadan Road
Waterford, Ireland

Renvela® is a Trademark of Genzyme Corporation

Source: CCDS Ver.No 8 dated 25-July 2019

Updated: Feb 2022