Professional Information

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

RENVELA® TABLETS (film coated tablets)

COMPOSITION:

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

Excipients:

RENVELA TABLETS: Microcrystalline cellulose, sodium chloride, zinc stearate, Opadry clear (diacetylated monoglycerides, hypromellose) and Opacode black ink (hypromellose, iron oxide black). Sugar free.

CATEGORY AND CLASS:

A 32.16 Others

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Sevelamer carbonate is 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 dietary tract and

decreasing absorption, sevelamer carbonate lowers the phosphate concentration in the serum.

In addition to effects on serum phosphate 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. Mean LDL cholesterol and mean total cholesterol declined significantly on sevelamer treatment (-39 % and -21 %, respectively). This effect is observed after 2 weeks. Triglycerides, HDL cholesterol and albumin did not change.

Pharmacokinetic properties:

Pharmacokinetic studies have not been carried out with sevelamer carbonate. Sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, is not absorbed from the gastrointestinal tract, as confirmed by an absorption study in healthy volunteers.

INDICATIONS:

RENVELA TABLETS are indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis and adult chronic kidney disease (CKD) patients not on dialysis with serum phosphorus > 1,78 mmol/l.

CONTRAINDICATIONS:

- Hypersensitivity to sevelamer carbonate or any other ingredients of RENVELA TABLETS (see COMPOSITION).
- Patients with hypophosphataemia or bowel obstruction.

WARNINGS AND SPECIAL PRECAUTIONS:

The safety and efficacy of RENVELA TABLETS 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 TABLETS is used in patients with these disorders. RENVELA TABLETS treatment should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Case reports of difficulty swallowing the RENVELA TABLETS tablet have been reported. Many of these cases involved patients with contributing co-morbid conditions affecting the ability to swallow, including swallowing disorders or oesophageal abnormalities. Caution should be exercised when RENVELA TABLETS are used in these patients.

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 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 RENVELA TABLETS, serum vitamin A, D, and E levels and vitamin K status should be assessed regularly.

Cases of serious inflammatory disorders of the gastrointestinal tract (including serious complications such as bleeding, perforation, ulceration, necrosis and colitis) associated with the presence of sevelamer crystals have been reported. However, the causality of the sevelamer crystals in initiating such disorders has not been demonstrated. Treatment with RENVELA TABLETS should be re-evaluated in patients who develop severe gastrointestinal symptoms.

Effects on driving and using machines:

No studies on the effects on the ability to drive and use machines have been performed.

INTERACTIONS:

RENVELA has been studied in two medicine 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 (RENVELA TABLETS), has been studied in medicine 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 RENVELA TABLETS (sevelamer carbonate), should not be taken simultaneously with ciprofloxacin.

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

During post-marketing experience, 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 RENVELA TABLETS.

During post-marketing experience, cases of increased phosphate levels have been reported in patients taking proton pump inhibitors co-administered with sevelamer hydrochloride which contains the same active moiety as RENVELA TABLETS (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 medicine should be administered at least one hour before or three hours after taking RENVELA TABLETS, or the medical practitioner should consider monitoring blood levels of the medicine. Patients taking antidysrhythmic medications for the control of dysrhythmias and anti-seizure medications for the control of seizure disorders were excluded from the clinical trials. Special precautions should be taken when prescribing RENVELA TABLETS to patients also taking these medications.

HUMAN REPRODUCTION:

The safety of RENVELA TABLETS has not been established in pregnant or lactating women.

DOSAGE AND DIRECTIONS FOR USE:

RENVELA tablets (800 mg) can be taken three times per day with meals at a dosage based on individual patient requirements to control phosphate levels. The tablets should

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

Initial dose:

The recommended starting dose is 2,4 to 4,8 g per day based on clinical needs and phosphorus level. RENVELA TABLETS must be taken three times per day with meals. For patients previously on phosphate binders, RENVELA TABLETS 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 RENVELA TABLETS titrated every 2 - 4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter.

Patients taking RENVELA TABLETS should adhere to their prescribed diets.

In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the daily dose is expected to be an average of approximately 6 g per day.

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

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

SIDE EFFECTS:

The safety of sevelamer (as either carbonate and hydrochloride salts) has been investigated in numerous clinical trials involving a total of 969 haemodialysis patients with treatment duration of 4 to 50 weeks (724 patients treated with sevelamer hydrochloride and 245 with sevelamer carbonate), 97 peritoneal dialysis patients with treatment duration of 12 weeks (all treated with sevelamer hydrochloride) and 128 patients with CKD not on dialysis with treatment duration of 8 to 12 weeks (79 patients treatment with sevelamer hydrochloride and 49 with sevelamer carbonate). The most frequently occurring (≥ 5 % of patients) undesirable effects possibly or probably related to sevelamer, including RENVELA TABLETS were in the gastrointestinal disorders system organ class. Most of these adverse reactions were mild to moderate in intensity.

The reporting rate is classified as very common (≥ 1/10), common (≥ 1/100, < 1/10).

Gastrointestinal disorders:

Very common: nausea, vomiting, upper abdominal pain, constipation

Common: diarrhoea**,** dyspepsia, flatulence, abdominal pain

Post-marketing experience:

Cases of hypersensitivity, pruritus, rash, abdominal pain, intestinal obstruction, ileus and intestinal perforation may occur during treatment with RENVELA TABLETS (see WARNINGS AND SPECIAL PRECAUTIONS).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

In CKD patients on dialysis, the maximum dose studied was 14,4 grams of sevelamer carbonate. There are no reports of overdosage with sevelamer carbonate in patients. Sevelamer is not systemically absorbed. Treatment is symptomatic and supportive.

IDENTIFICATION:

RENVELA TABLETS: White to off-white oval tablet, printed with “RENVELA 800” on crown, single side, in black ink.

PRESENTATION:

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

The bottle for the 30 tablets pack size is packaged in an outer carton.

Pack sizes: 30, 180, 270.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from moisture. Keep tablets in the bottle until required for use.

Keep bottle tightly closed.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBERS

RENVELA TABLETS: 45/32.16/0305

Professional Information

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

sanofi-aventis south africa (pty) ltd

2 Bond Street,

Midrand 1685

South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date of registration: 05 June 2014

Date revised: 09 September 2019

Signed: _____