Biocon

Sevelamer Carbonate Tablets 400 mg / 800 mg

BIOSEV® C-400/800 बायोसेव सी-४००/८००

Composition:
BIOSEV®C - 400
Each film coated tablet contains
Sevelamer Carbonate 400 mg
Excipients q.s.
Colours: Tartrazine yellow lake, Brilliant blue lake & Titanium dioxide IP

BIOSEV®C - 800
Each film coated tablet contains
Sevelamer Carbonate 800 mg
Excipients q.s.
Colours: Ponceau 4R and Titanium Dioxide IP

PHARMACEUTICAL FORM
Film-coated tablets

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Pharmacotherapeutic group: Treatment of hyperphosphatemia
ATC code: V03AE02

Mechanism of Action
Sevelamer is a polymeric compound which acts by binding to phosphate molecules in the gut, limiting phosphate absorption and thus lowering serum phosphate levels without altering calcium, aluminum, or bicarbonate concentrations.

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.

Preclinical Safety Data
Standard lifetime carcinogenicity bioassays were conducted in mice (at 9 g/kg per day, human equivalent dose 3 times the maximum clinical trial dose) and rats (at 0.3, 1, or 3 g/kg per day) with sevelamer hydrochloride. 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) and 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 per day (human equivalent dose 3 times the maximum clinical trial dose).

CLINICAL PARTICULARS
Therapeutic Indications
Sevelamer carbonate is indicated for control of hyperphosphatemia in patients with chronic kidney disease (CKD) on hemodialysis or peritoneal dialysis and patients with CKD not on dialysis, with serum phosphate levels greater than 5.5 mg/kg.

Posology and Method of Administration
Sevelamer carbonate should be taken 3 times a day with meals. The initial recommended dose of sevelamer based on the serum phosphate level is given in Table 1.

Serum Phosphorus Level in Patients (mg/dL)	Total Daily Dose of Sevelamer Carbonate to be Taken Over 3 Meals per Day (g*)
5.5 to ≤7.5	2.4
7.5 to ≥9	3.6 to 4.8
≥9	4.8

* Plus subsequent titration as per instructions.

Titration and Maintenance
Serum phosphorus levels must be monitored and the dose of sevelamer carbonate titrated every 2 to 4 weeks until an acceptable serum phosphorus level is reached; with regular monitoring thereafter.
For patients previously on phosphate binders (sevelamer hydrochloride), sevelamer should be given on a gram-for-gram basis, with the monitoring of serum phosphorus levels, to ensure optimal daily doses. For patients switching from calcium acetate based on current dosage: 667 mg calcium acetate is equivalent to 800 mg of sevelamer.

Special Populations
The safety and efficacy of sevelamer has not been established in children below the age of 18 years; and so use is not recommended in children.
The safety and efficacy of sevelamer have not been established in adult patients with CKD who are not on dialysis, with serum phosphorus less than 1.78 mmol/L. Therefore sevelamer is currently not recommended for use in these patients.

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

Contraindications
Sevelamer is contraindicated in patients with bowel obstruction and hypophosphatemia.

Special Warnings and Precautions for Use
The safety and efficacy of sevelamer have not been established in patients with the following disorders: dysphagia; swallowing disorders; severe gastrointestinal motility disorders including untreated or severe gastroparesis, retention of gastric contents and abnormal or irregular bowel motion; active inflammatory bowel disease and major gastrointestinal tract surgery. Therefore caution should be exercised when sevelamer is used in these patients.

Intestinal Obstruction and Ileus/Subileus
In very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate. Constipation may be a preceding symptom. Patients who are constipated should be monitored carefully while being treated with sevelamer. Treatment with sevelamer should be re-evaluated in patients who develop severe constipation or other severe gastrointestinal symptoms.

Fat-soluble Vitamins
Patients with CKD may develop low levels of fat-soluble vitamins A, D, E and K, depending on dietary intake and the severity of their disease. It cannot be excluded that sevelamer can bind fat-soluble vitamins contained in ingested food. In patients not taking supplemental vitamins but on sevelamer, serum vitamin A, D, E and K status should be assessed regularly. It is recommended that vitamin supplements be given, if necessary. It is recommended that CKD patients not on dialysis are given vitamin D supplements (approximately 400 IU of native vitamin D daily) which can be part of a multivitamin preparation to be taken apart from their dose of sevelamer. In patients undergoing peritoneal dialysis additional monitoring of fat-soluble vitamins and folic acid is recommended, since vitamin A, D, E and K levels were not measured in a clinical study in such patients.

Folate Deficiency
There is a possibility of folate deficiency during long-term sevelamer treatment.

Hypocalcemia/Hypercalcemia
Patients with CKD may develop hypocalcemia or hypercalcemia. Sevelamer does not contain any calcium. Serum calcium levels should therefore be monitored at regular intervals and elemental calcium should be given as a supplement if required.

Monitor Serum Chemistries
Patients with CKD are pre-disposed to developing metabolic acidosis. Therefore, monitoring serum levels of calcium, bicarbonate and chloride are recommended.

Peritonitis
Peritonitis is a known complication in patients receiving peritoneal dialysis; and also occurred in a clinical study with sevelamer hydrochloride. Patients on peritoneal dialysis should be closely monitored to ensure the correct use of appropriate aseptic technique with the prompt recognition and management of any signs and symptoms associated with peritonitis.

Swallowing and Choking Difficulties
Uncommon reports of difficulty in swallowing the sevelamer tablet have been reported. Many of these cases involved patients with co-morbid conditions including swallowing disorders or oesophageal abnormalities. Caution should be exercised when sevelamer is used in patients who have difficulty in swallowing. Consider using sevelamer powder for oral suspension in patients with a history of swallowing difficulty.

Anti-arrhythmic and Anti-seizure Medicinal Products
Caution should be exercised when prescribing sevelamer to patients also taking anti-arrhythmias and anti-seizure medicinal products (see **'Drug Interactions'** section).

Hypothyroidism
Closer monitoring of patients with hypothyroidism, co-administered with sevelamer and levothyroxine, is recommended (see **'Drug Interactions'** section).

Hyperparathyroidism
In patients with secondary hyperparathyroidism, sevelamer should be used within the context of a multiple therapeutic approach, which could include calcium or 1,25-dihydroxy vitamin D3 or one of its analogues as supplements, to lower the intact parathyroid hormone (iPTH) levels.

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

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Drug Interactions
Interaction studies have not been conducted in patients on dialysis.
In the interaction studies conducted in healthy volunteers, sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, decreased the bioavailability of ciprofloxacin by approximately 50% when co-administered with sevelamer hydrochloride in a single dose study. Consequently, sevelamer carbonate should not be taken simultaneously with ciprofloxacin.
Reduced levels of ciclosporin, mycophenolate mofetil and tacrolimus have been reported in transplant patients when co-administered with sevelamer hydrochloride without any clinical consequences (i.e., 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 a combination and after its withdrawal.
Very rare cases of hypothyroidism have been reported in patients co-administered with sevelamer hydrochloride and levothyroxine. Closer monitoring of thyroid stimulating hormone (TSH) levels is therefore recommended in patients receiving sevelamer carbonate and levothyroxine.
Patients taking anti-arrhythmic medicinal products for the control of arrhythmias and anti seizure medicinal products for the control of seizure disorders were excluded from clinical trials. Caution should be exercised when prescribing sevelamer to patients also taking these medicinal products.
In interaction studies in healthy volunteers, sevelamer hydrochloride had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol.
Sevelamer is not absorbed and may affect the bioavailability of other medicinal products. When administering any medicinal product where a reduction in the bioavailability could have a clinically significant effect on safety or efficacy, the medicinal product should be administered at least one hour before or three hours after sevelamer, or the physician should consider monitoring blood levels.

Pregnancy and Lactation
Pregnancy category C: There are no adequate and well-controlled studies in pregnant women. The potential risk to humans is unknown. Studies in animals showed some reproductive toxicity when sevelamer was administered to rats in high doses (see **Preclinical Safety Data** section). Sevelamer has also been shown to reduce the absorption of several vitamins including folic acid (see **Special Warnings and Precautions for Use** section). Sevelamer should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is unknown whether sevelamer is excreted in human breast milk. The non absorbing nature of sevelamer indicates that the excretion of sevelamer in breast milk is unlikely. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with sevelamer should be made taking into account the benefit of breast-feeding to the child and the benefit of sevelamer therapy to the woman.

Effects on Ability to Drive and Use Machines
No studies on the effects on ability to drive and use machines have been performed.

Adverse Effects
The most frequently occurring (⩾5% of patients) adverse effects possibly or probably related to sevelamer in clinical studies were all in the gastrointestinal disorders system organ class. Most of these adverse reactions were mild to moderate in intensity. Data possibly or probably related to sevelamer from these studies are listed by frequency below.
The reporting rate is classified as very common (⩾1/10), common (⩾1/100, <1/10), uncommon (⩾1/1000, <1/100), rare (⩾1/10,000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Gastrointestinal Disorders
Very common: nausea, vomiting, upper abdominal pain, constipation
Common: diarrhoea, dyspepsia, flatulence, abdominal pain

Others
Headache, infection, hypertension, hypotension, thrombosis, and cough.

Post-marketing Experience
During post-approval use, cases of pruritus, rash, intestinal obstruction, ileus/subileus, and intestinal perforation have been reported in patients during treatment with sevelamer.

Overdose
There are no reports of over dosage with sevelamer carbonate. The maximum dose of sevelamer carbonate studied in CKD patients on dialysis was 14 g. Since sevelamer is not absorbed, the risk of systemic toxicity is low.

PHARMACEUTICAL PARTICULARS
Shelf Life : Please refer carton/blister.

Storage and Precautions: Store below 30°C. Protect from moisture.
Keep out of reach of children

Special Precautions for Disposal and Other Handling
Any unused medicinal product or waste material should be disposed off in accordance with local requirements.

Nature and Contents of Container
BIOSEV®C- 400: Each carton contains 5 blister pack of 10 tablets each
BIOSEV®C- 800: Each carton contains 5 blister pack of 10 tablets each

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

® - Registered trademark

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free No: **1800 102 9465** or e-mail us at **drugsafety@biocon.com.**

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