FOSBAIT™ contains lanthanum carbonate (2:3) hydrate with molecular formula La₂(CO₃)₃·xH₂O (on average x=4-5 moles of water) and molecular weight 457.8 (anhydrous mass). Lanthanum (La) is a naturally occurring rare earth element. Lanthanum carbonate is practically insoluble in water.

DESCRIPTION AND COMPOSITION

FOSBAIT- 500

Each uncoated chewable tablet contains:

Lanthanum Carbonate equivalent to
Elemental Lanthanum...................................... 500 mg

Colour: Lanthanum Carbonate 500 mg and 250 mg tablets are white to off white uncoated rectangular shaped tablets plain on both sides.

FOSBAIT- 250

Each uncoated chewable tablet contains:

Lanthanum Carbonate equivalent to
Elemental Lanthanum...................................... 250 mg

Colour: Lanthanum Carbonate 500 mg and 250 mg tablets are white to off white uncoated rectangular shaped tablets plain on both sides.

MECHANISM OF ACTION

Lanthanum carbonate acts by dissociating in the acid environment of the upper GI tract to release lanthanum ions that bind dietary phosphate released from food during digestion to form Lanthanum Phosphate-an insoluble compound that is poorly absorbed across the gut wall. FOSBAIT™ inhibits absorption of phosphate by forming highly insoluble lanthanum phosphate complexes, consequently reducing both serum phosphate and calcium phosphate product.

PHARMACOKINETICS

Absorption/Distribution:
The concentration of lanthanum in plasma is very low (bioavailability <0.002%) after single or multiple dose oral administration of Lanthanum Carbonate to healthy subjects. Following oral administration in ESRD patients, the mean lanthanum Cmax was 1.0 ng/mL. During long-term administration (52 weeks) in ESRD patients, the mean lanthanum concentration in plasma was approximately 0.6 ng/mL. There was minimal increase in plasma lanthanum concentrations with increasing doses within the therapeutic dose range.
The effect of food on the bioavailability of Lanthanum Carbonate has not been evaluated, but the timing of food intake relative to lanthanum administration (during and 30 minutes after food intake) has a negligible effect on the systemic level of lanthanum. In vitro, lanthanum is highly bound (>99%) to human plasma proteins, including human serum albumin, a1-acid glycoprotein, and transferrin. There is no evidence from animal studies that lanthanum crosses the blood-brain barrier.

**Metabolism/Elimination:**
Lanthanum is not metabolized and is not a substrate of CYP450. Lanthanum was cleared from plasma following discontinuation of therapy with an elimination half-life 53 hours. In vitro metabolic inhibition studies showed that lanthanum at concentrations of 10 and 40 µg/ml does not have relevant inhibitory effects on any of the CYP450 isoenzymes tested (1A2, 2C9/10, 2C19, 2D6, and 3A4/5). Quantifiable amounts of lanthanum have not been measured in the dialysate of treated ESRD patients.

**Clinical Pharmacology:**
A 16 week randomized, double blind, placebo-controlled, dose-titration, phase III study was conducted to assess the efficacy and tolerability of lanthanum carbonate—a new phosphate binder for the treatment of hyperphosphatemia. Hemodialysis patients > or =18 years old entered into a 1- to 3-week washout period during which serum phosphorus levels rose to >5.9 mg/dL (1.90 mmol/L). In total, 126 patients were titrated with lanthanum carbonate at doses containing 375, 750, 1,500, 2,250, or 3,000 mg/d elemental lanthanum, given in divided doses with meals over a 6-week period, to achieve serum levels ≤ 5.9 mg/dL. By the end of dose titration, 11/126 (9%) patients received < 750 mg/d of lanthanum, 25 (20%) received 1,500 mg/d, 37 (29%) received 2,250 mg/d, and 53 (42%) received 3,000 mg/d. Following titration, patients were randomized to receive either lanthanum carbonate or placebo during a 4-week, double-blind maintenance phase. At the study endpoint, the mean difference in serum phosphorus between the lanthanum carbonate and placebo treatment arms was 1.91 mg/dL (0.62 mmol/L) (P < 0.0001). Calcium x phosphorus product (P < 0.0001) and serum PTH levels (P < 0.01) was also significantly lower with lanthanum carbonate versus placebo. The incidence of drug-related adverse events was similar between placebo- and lanthanum carbonate-treated patients. It was concluded that Lanthanum carbonate is an effective and well-tolerated agent for the treatment of hyperphosphatemia in patients with ESRD.2-3

A long-term, open-label extension study was conducted on the safety of treatment with Lanthanum carbonate, in patients receiving hemodialysis. A total of 77 patients (N = 77; 11 from Study 1, 66 from Study 2) were enrolled in this extension. All patients received lanthanum carbonate at the optimal dose for phosphorus control, determined in their previous study. Safety and tolerability were assessed by monitoring adverse events, laboratory parameters, and vital signs. The number of patients who maintained serum phosphorus levels at < or = 5.9 mg/dL (1.9 mmol/L) was recorded, along with serum calcium, calcium x phosphorus product, and parathyroid hormone levels. RESULTS: Lanthanum carbonate was well tolerated and was associated with few treatment-related adverse events. The most commonly reported adverse events were nausea (26.0%), peripheral edema (23.4%), and myalgia (20.8%). No treatment-related serious adverse events occurred. By Week 4, the mean serum phosphorus level had decreased by approximately 1 mg/dL to 5.7 +/- 2.0 mg/dL (1.84 +/- 0.7 mmol/L). At the end of the study, the mean pre-dialysis serum phosphorus level was 5.7 +/- 1.4 mg/dL (1.84 +/- 0.5 mmol/L); 53% of patients had controlled phosphorus levels. Calcium x phosphorus product decreased during Week 1 and remained within a clinically acceptable range thereafter. There were no clinically significant changes in serum calcium, or parathyroid hormone levels. Lanthanum carbonate is well tolerated and is effective for the long-term maintenance of serum phosphorus control in patients with end-stage renal disease.2-3

**Special Populations**

**Geriatric**
No differences have been observed in safety or effectiveness between patients ≥65 years of age and younger patients.

**Pediatric**
The use of Lanthanum Carbonate in pediatric population is not recommended.

**INDICATIONS**
FOSBAIT™ is indicated to reduce serum phosphate in patients with end-stage renal disease.

**CONTRAINDICATIONS**
None Known

**WARNING AND PRECAUTIONS**

**General**
Caution should be used in patients with the conditions of acute peptic ulcer, ulcerative colitis, Crohn's disease or bowel obstruction.

**Pregnancy**
Pregnancy Category C. FOSBAIT™ is not recommended for use during pregnancy.

**Labor and Delivery**
No lanthanum carbonate treatment-related effects on labor and delivery were seen in animal studies. The effects of lanthanum carbonate on labor and delivery in humans is unknown.

**Nursing Mothers**
It is not known whether lanthanum carbonate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when FOSBAIT™ is administered to a nursing woman.

**Information for the Patient**
FOSBAIT™ tablets should be taken with or immediately after meals. Tablets should be chewed completely before swallowing. The tablets should not be swallowed whole.

**ADVERSE REACTIONS**
The most common adverse reactions associated with Lanthanum Carbonate include gastrointestinal events, such as nausea and vomiting and they are generally abated over time with continued dosing.

**DRUG INTERACTIONS**
Lanthanum Carbonate is not metabolized.
Lanthanum Carbonate does not adversely affect the pharmacokinetics of warfarin, digoxin or metoprolol.
The absorption and pharmacokinetics of Lanthanum Carbonate are unaffected by co-administration with citrate containing compounds
It is recommended that compounds known to interact with antacids should not be taken within 2 hours of dosing with FOSBAIT™.

**OVERDOSAGE AND TREATMENT**
There is no experience with Lanthanum Carbonate over dosage. No acute toxicity occurred in animals by the oral route. No deaths and no adverse effects occurred in mice, rats or dogs after single oral doses of 2000 mg/kg. In clinical trials, daily doses up to 4718 mg/day of lanthanum were well tolerated in healthy adults when administered with food, with the exception of GI symptoms. Given the topical activity of lanthanum in the gut, and the excretion in feces of the majority of the dose, supportive therapy is recommended for over dosage.

**DOSAGE AND ADMINISTRATION**
The total daily dose of FOSBAIT™ should be divided and taken with meals. The recommended initial total daily dose of FOSBAIT™ is 750-1500 mg in two to three divided doses. The dose should be titrated 2 - 3 weeks until an acceptable serum phosphate level is reached. Serum
phosphate levels should be monitored as needed during dose titration and on a regular basis thereafter.

In clinical studies of ESRD patients\(^1\), Lanthanum Carbonate doses up to 3750 mg have been evaluated.

Most patients require a total daily dose between 1500mg and 3000mg to reduce plasma phosphate level to less than 60mg/dL.

**The tablet should be chewed completely before swallowing. Intact tablets should not be swallowed.**

KEEP THE MEDICINE OUT OF REACH OF CHILDREN

**STORAGE INSTRUCTIONS**

Store at a temperature below 30\(^\circ\)C, protect from light and moisture.

Keep the bottle tightly closed after opening

**REFERENCES**


