LoCHOLEST advertisement.

[s.l.]: [s.n.], 1997

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BILE ACID SEQUESTRANTS* NEVER TASTED THIS GOOD

- Fresh strawberry taste to enhance compliance
- Uniquely smooth, non-gritty texture
- In the treatment of pruritus associated with cholestasis

LoCholest™
CHOLESTYRAMINE FOR ORAL SUSPENSION, USP

POWDER 4 GRAMS
CHOLESTYRAMINE RESIN, USP, PER PACKET OR SCOOPFUL

THE TRULY PALATABLE TREATMENT FOR CHOLESTASIS-RELATED PRURITUS.

LoCholest is indicated for the relief of pruritus associated with partial biliary obstruction. It is contraindicated in patients with complete biliary obstruction where bile is not secreted into the intestines and in patients who have shown hypersensitivity to any of its components. The most common adverse reaction to cholestyramine is constipation.

*LoCholest was compared to Questran® (cholestyramine for oral suspension, USP) and Prevalite® (cholestyramine for oral suspension, USP). Questran is a registered trademark of Bristol-Myers Squibb Co. Prevalite is a registered trademark of Upsher-Smith Laboratories, Inc. Comparison data on file at Warner Chilcott, Inc.

Please see brief summary of prescribing information on the next page.

P2015 12/97

WARNER CHILCOTT LABORATORIES

LoCHOLEST™ Powder
LoCHOLEST™ Light Powder

(CHOLESTYRAMINE FOR ORAL SUSPENSION, USP; REGULAR AND LIGHT)

The following is a brief summary of the prescribing information. For full prescribing information, see package insert.

INDICATIONS:

1. LoCHOLEST™ Powder is indicated as adjunctive therapy to diet for the reduction of elevated serum cholesterol in patients with primary hypercholesterolemia (elevated low density lipoprotein [LDL] cholesterol) who do not respond adequately to diet. LoCHOLEST™ Powder may be useful to lower LDL cholesterol in patients who also have hypertriglyceridemia, but it is not indicated where hypertriglyceridemia is the abnormality of most concern.
2. LoCHOLEST™ Powder is indicated for the relief of pruritus associated with partial biliary obstruction. Cholestyramine resin has been shown to have a variable effect on serum cholesterol in these patients. Patients with primary biliary cirrhosis may exhibit an elevated cholesterol as part of their disease.

CONTRAINDICATIONS:

LoCHOLEST™ Powder is contraindicated in patients with complete biliary obstruction where bile is not secreted into the intestine and in those individuals who have shown hypersensitivity to any of its components.

WARNINGS:

PHENYLKETONURICS: LoCHOLEST™ LIGHT POWDER CONTAINS 22.4 MG PHENYLALANINE PER 5.7 GRAM DOSE.

PRECAUTIONS:

General: Chronic use of cholestyramine resin may be associated with increased bleeding tendency due to hypoprothrombinemia associated with Vitamin K deficiency. This will usually respond promptly to parenteral Vitamin K_1 and recurrences can be prevented by oral administration of Vitamin K_1. Reduction of serum or red cell folate has been reported over long term administration of cholestyramine resin. Supplementation with folic acid should be considered in these cases.

There is a possibility that prolonged use of cholestyramine resin, since it is a chloride form of anion exchange resin, may produce hyperchloremic acidosis. This would especially be true in younger and smaller patients where the relative dosage may be higher. Caution should also be exercised in patients with renal insufficiency or volume depletion, and in patients receiving concomitant spironolactone.

Cholestyramine resin may produce or worsen preexisting constipation. The dosage should be increased gradually in patients to minimize the risk of developing fecal impaction. In patients with preexisting constipation, the starting dose should be 1 pouch or 1 scoop once daily for 5 to 7 days, increasing to twice daily with monitoring of constipation and of serum lipoproteins, at least twice, 4 to 6 weeks apart. Increased fluid intake and fiber intake should be encouraged to alleviate constipation and a stool softener may occasionally be indicated. If the initial dose is well tolerated, the dose may be increased as needed by one dose/day (at monthly intervals) with periodic monitoring of serum lipoproteins. If constipation worsens or the desired therapeutic response is not achieved at one to six doses/day, combination therapy or alternate therapy should be considered. Particular effort should be made to avoid constipation in patients with symptomatic coronary artery disease. Constipation associated with cholestyramine resin may aggravate hemorrhoids.

Information for Patients: Inform your physician if you are pregnant or plan to become pregnant or are breast-feeding. Drink plenty of fluids and mix each 9 gram dose of LoCHOLEST™ Powder (Cholestyramine for Oral Suspension, USP) in at least 2 to 6 ounces of fluid or each 5.7 gram dose of LoCHOLEST™ Light Powder in at least 2 to 3 ounces of fluid before taking. Sipping or holding the resin suspension in the mouth for prolonged periods may lead to changes in the surface of the teeth resulting in discoloration, erosion of enamel or decay; good oral hygiene should be maintained.

Laboratory Tests: Serum cholesterol levels should be determined frequently during the first few months of therapy and periodically thereafter. Serum triglyceride levels should be measured periodically to detect whether significant changes have occurred.

The LRC-CPPT showed a dose-related increase in serum triglycerides of 10.7% to 17.1% in the cholestyramine-treated group, compared with an increase of 7.9% to 11.7% in the placebo group. Based on the mean values and adjusting for the placebo group, the cholestyramine-treated group showed an increase of 5% over pre-entry levels the first year of the study and an increase of 4.3% the seventh year.

Drug Interactions: Cholestyramine resin may delay or reduce the absorption of concomitant oral medication such as phenylbutazone, warfarin, thiazide diuretics (acidic) or propranolol (basic), as well as tetracycline, penicillin G, phenobarbital, thyroid and thyroxine preparations, estrogens and progestins, and digitalis. Interference with the absorption of oral phosphate supplements has been observed with another positively-charged bile acid sequestrant. Cholestyramine resin may interfere with the pharmacokinetics of drugs that undergo enterohepatic circulation. The discontinuance of cholestyramine resin could pose a hazard to health if a potentially toxic drug such as digitalis has been titrated to a maintenance level while the patient was taking cholestyramine resin.

Because cholestyramine binds bile acids, cholestyramine resin may interfere with normal fat digestion and absorption and thus may prevent absorption of fat soluble vitamins such as A, D, E, and K. When cholestyramine resin is given for long periods of time, concomitant supplementation with water-miscible (or parenteral) forms of fat-soluble vitamins should be considered.

SINCE CHOLESTYRAMINE RESIN MAY BIND OTHER DRUGS GIVEN CONCURRENTLY, IT IS RECOMMENDED THAT PATIENTS SHOULD TAKE OTHER DRUGS AT LEAST 1 HOUR BEFORE OR 4 TO 6 HOURS AFTER CHOLESTYRAMINE RESIN (OR AT AS GREAT AN INTERVAL AS POSSIBLE) TO AVOID IMPEDING THEIR ABSORPTION.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In studies conducted in rats in which cholestyramine resin was used as a tool to investigate the role of various intestinal factors, such as fat, bile salts and microbial flora, in the development of intestinal tumors induced by potent carcinogens, the incidence of such tumors was observed to be greater in cholestyramine resin-treated rats than in control rats.

The relevance of this laboratory observation from studies in rats to the clinical use of cholestyramine resin is not known. In the LRC-CPPT study referred to above, the total incidence of fatal and nonfatal neoplasms was similar in both treatment groups. When the many different categories of tumors are examined, various alimentary system cancers were somewhat more prevalent in the cholestyramine group. The small numbers and the multiple categories prevent conclusions from being drawn. However, in view of the fact that cholestyramine resin is confined to the GI tract and not absorbed, and in light of the animal experiments referred to above, a six-year post-trial follow-up analysis of the LRC-CPPT patient population has been completed (a total of 13.4 years of in-trial plus post-trial follow-up) and revealed no significant difference in the incidence of cause-specific mortality or cancer morbidity between cholestyramine and placebo treated patients.

Pregnancy: Teratogenic Effects, Pregnancy Category C: Since cholestyramine resin is not absorbed systemically, it is not expected to cause fetal harm when administered during pregnancy in recommended dosages. There are, however, no adequate and well-controlled studies in pregnant women, and the known interference with absorption of fat-soluble vitamins may be detrimental even in the presence of supplementation.

Nursing Mothers: Caution should be exercised when cholestyramine resin is administered to a nursing mother. The possible lack of proper vitamin absorption described in the "Pregnancy" section may have an effect on nursing infants.

Pediatric Use: As experience in the pediatric population is limited, a practical dosage schedule has not been established.

In calculating pediatric dosages, 44.4 mg of anhydrous cholestyramine resin are contained in 100 mg of LoCHOLEST™ Powder and 70.2 mg of anhydrous cholestyramine resin are contained in 100 mg of LoCHOLEST™ Light Powder.

The effect of long-term drug administration, as well as its effect in maintaining lowered cholesterol levels in pediatric patients, are unknown.

ADVERSE REACTIONS:

The most common adverse reaction is constipation. When used as a cholesterol-lowering agent predisposing factors for most complaints of constipation are high dose and increased age (more than 60 years old). Most instances of constipation are mild, transient, and controlled with conventional therapy. Some patients require a temporary decrease in dosage or discontinuation of therapy.

Less Frequent Adverse Reactions—Abdominal discomfort and/or pain, flatulence, nausea, vomiting, diarrhea, eructation, anorexia, steatorrhea, bleeding tendencies due to hypoprothrombinemia (Vitamin K deficiency) as well as Vitamin A (one case of night blindness reported) and D deficiencies, hyperchloremic acidosis in children, osteoporosis, rash and irritation of the skin, tongue and perianal area. One 10 month-old baby with biliary atresia had an impaction presumed to be due to cholestyramine resin after 3 days of administration of 9 grams daily. She developed acute intestinal sepsis and died.

Occasional calcified material has been observed in the biliary tree, including calcification of the gallbladder, in patients to whom cholestyramine resin has been given. However, this may be a manifestation of the liver disease and not drug related.

One patient experienced biliary colic on each of three occasions on which he took a cholestyramine for oral suspension product. One patient diagnosed as acute abdominal symptom complex was found to have a "pasty mass" in the transverse colon on x-ray.

Other events (not necessarily drug related) reported in patients taking cholestyramine resin include:

Gastrointestinal—GI-rectal bleeding, black stools, hemorrhoidal bleeding, bleeding from known duodenal ulcer, dysphagia, hiccups, ulcer attack, sour taste, pancreatitis, rectal pain, diverticulitis.

Laboratory test changes—Liver function abnormalities.

Hematologic—Prolonged prothrombin time, ecchymosis, anemia.

Hypersensitivity—Urticaria, asthma, wheezing, shortness of breath.

Musculoskeletal—Backache, muscle and joint pains, arthritis.

Neurologic—Headache, anxiety, vertigo, dizziness, fatigue, tinnitus, syncope, drowsiness, femoral nerve pain, paresthesia.

Eye—Uveitis.

Renal—Hematuria, dysuria, burnt odor to urine, diuresis.

Miscellaneous—Weight loss, weight gain, increased libido, swollen glands, edema, dental bleeding, dental caries, erosion of tooth enamel, tooth discoloration.

OVERDOSAGE: Overdosage of cholestyramine resin has been reported in a patient taking 150% of the maximum recommended daily dosage for a period of several weeks. No ill effects were reported. Should an overdosage occur, the chief potential harm would be obstruction of the gastrointestinal tract. The location of such potential obstruction, the degree of obstruction, and the presence or absence of normal gut motility would determine treatment.

STORAGE: Store at controlled room temperature 15°-30°C (59°-86°F).

Caution: Federal law prohibits dispensing without prescription.

Manufactured for:
Warner Chilcott Laboratories
100 Enterprise Dr.
Rockaway, NJ 07866
Manufactured by:
Eon Labs Manufacturing, Inc.

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