Cholestyramine for Oral Suspension USP contains the following inactive ingredients: acacia, FD&C Yellow No. 10, FD&C Yellow No. 6, flavor (natural and artificial Orange), polysorbate 80, propylene glycol alinate and sucrose. Cholestyramine for Oral Suspension USP, Light contains the following inactive ingredients: aspartame, citric acid, FD&C Yellow No. 10, FD&C Red No. 40 (natural and artificial Orange), maltodextrin, propylene glycol alinate and xanthan gum.

**Actions**

Cholestyramine is probably the sole precursor of bile acids. During normal digestion, bile acids are secreted into the intestine. A major portion of the bile acids is absorbed from the intestine and returned to the liver via the enterohepatic circulation. Only very small amounts of bile acids are found in normal serum.

Cholestyramine resin adsorbs and combines with the bile acids in the intestine to form an insoluble complex which is excreted in the feces. This results in a partial removal of bile acids from the enterohepatic circulation by preventing their absorption. The increased fecal loss of bile acids due to Cholestyramine administration leads to an increased oxidation of cholesterol to bile acids, a decrease in beta lipoprotein or low density lipoprotein plasma levels and a decrease in serum cholesterol levels. Although in man, Cholestyramine reduces an increase in hepatic synthesis of cholesterol plasma cholesterol levels fall.

In patients with partial biliary obstruction, the reduction of serum bile acid levels by Cholestyramine reduces excess bile acids deposited in the dermal tissue with resultant decrease in pruritus.

**Clinical Studies**

In a large, placebo-controlled, multi-center study, LRC-CPTP1, hypercholesterolemic subjects treated with Cholestyramine had mean reductions in total and low-density lipoprotein cholesterol (LDL-C) which exceeded those for diet and placebo treatment by 7.2% and 10.4%, respectively. Over the seven-year study period the Cholestyramine-treated subjects showed a 16% reduction in the relative risk of coronary heart disease death or non-fatal myocardial infarction (cumulative incidences of 7% Cholestyramine and 8.6% placebo). The subjects included in the study were men aged 35 to 59 with serum cholesterol levels above 250 mg/dL and no previous history of the relative risk factors for cardiovascular disease. It is not clear to what extent these findings can be extrapolated to females and other segments of the hypercholesterolemic population. (See also *PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility*.)

Two controlled clinical trials have examined the effects of Cholestyramine monotherapy upon coronary atherosclerotic lesions using coronary arteriography. In the NHLBI Type II Coronary Intervention TrialII, 116 patients (80% male) with coronary artery disease (CAD) documented by arteriography were randomized to Cholestyramine or placebo for five years of treatment. Final study arteriography revealed progression of coronary artery disease in 49% of placebo patients compared to 32% of the Cholestyramine group.

In the St. Thomas Atherosclerosis Regression Study (STARS)II, 90 hypercholesterolemic men with CAD were randomized to three blinded treatments: usual care, lipid-lowering diet, and lipid-lowering diet plus Cholestyramine. After 36 months, follow up angiography revealed a smaller rate of progression of disease in 45% of usual care patients, 15% of patients on lipid-lowering diet and 12% of those receiving diet plus Cholestyramine (p<0.02). The mean absolute width of coronary segments decreased in the usual care group, increased slightly (0.003 mm) in the diet group and increased by 0.103 mm in the diet plus Cholestyramine group (p<0.05). Thus in these randomized controlled clinical trials using coronary arteriography, Cholestyramine monotherapy had a statistically significant slowing progression of coronary atherosclerosis in the coronary arteries of patients with coronary artery disease.

The effect of intense lipid-lowering therapy on coronary atherosclerosis has been assessed by arteriography in hyperlipidemic patients. In these randomized, controlled clinical trials, significant slowing of the progression of coronary atherosclerosis has been demonstrated. In a 2-year study, patients randomized to diet plus placebo showed significant progression of atherosclerosis in the coronary arteries.

In patients with partial biliary obstruction, the reduction of serum bile acid levels by Cholestyramine reduces excess bile acids deposited in the dermal tissue with resultant decrease in pruritus.

**INDICATIONS AND USAGE**

1) Cholestyramine for Oral Suspension USP is indicated as adjunctive therapy to diet for the reduction of serum cholesterol levels in patients with primary hypercholesterolemia (elevated low density lipoprotein [LDL] cholesterol) who do not respond adequately to diet. Cholestyramine may be useful to lower LDL cholesterol in patients with symptomatic coronary artery disease, but it is not indicated where hyperglycieridemia is the abnormality of most concern.

Therapy with lipid-altering agents should be a component of multiple risk factor treatment guidelines are summarized below.

For TG levels >400 mg/dL, this equation is less accurate and LDL-C concentrations may be excluded, and a lipid profile performed to assess Total cholesterol, HDL-C, and triglycerides (TG). For individuals with TG less than 400 mg/dL (<4.5 mmol/L), LDL-C can be estimated using the following equation:

\[
LDL-C = \text{Total cholesterol} - \left[ (\text{Triglycerides} < 4000 \text{mg/dL}) / 5 \right] - \text{HDL-C}
\]

For TG levels >400 mg/dL, this equation is less accurate and LDL-C concentrations may be indicated to 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 NCEP guidelines should show an increase in treatment from triglycerides of 10% to 17% 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.

**PHENYLKETONURICS: CHOLESTYRAMINE for ORAL SUSPENSION USP, LIGHT CONTAINS 14.0 mg PHENYLALANINE PER 5 G DOSE.**

**PRECAUTIONS**

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Cholestyramine for oral suspension is contraindicated in patients with symptomatic coronary artery disease. Constipation associated with this drug may be severe and may require discontinuation of therapy.

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 increased. On the other hand, this effect may not be life-threatening in older or larger patients.

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 increased. On the other hand, this effect may not be life-threatening in older or larger patients.

**Drug Interactions**

Cholestyramine for Oral Suspension USP in at least 2 to 6 ounces of fluid. Mix each 9 gram dose of Cholestyramine for Oral Suspension USP in at least 2 to 6 ounces of fluid. Drink plenty of fluids and mix each 9 gram dose of Cholestyramine for Oral Suspension USP in at least 2 to 6 ounces of fluid. Mix each 9 gram dose of Cholestyramine for Oral Suspension USP in at least 2 to 6 ounces of fluid.
Drug Interactions

Cholestyramine for Oral Suspension USP may delay or reduce the absorption of concomitant oral medication such as phenytoin, warfarin, thiazolediuretics (acids), or pranorol (basic), as well as tacrycycline, penicillin G, phenobarbital, thyroid and throxine preparations, estrogens and progestins, and digoxins. Interference with the absorption of vitamin D and its metabolites has also been observed with another positively-charged bile acid sequestrant. Cholestyramine may interfere with the pharmacokinetics of drugs that undergo entero-hepatic circulation. The discontinuance of Cholestyramine could pose an increased risk of digoxin-related digitalis. If Cholestyramine is given for long periods of time, concomitant supplementation with malscific or (parenteral) forms of fat-soluble vitamins should be considered.

SIMPLEST—PROLONGED MAY BIND OTHER DRUGS GENERALLY, IT IS RECOMMENDED THAT PATIENTS TAKE OTHER DRUGS AT LEAST ONE HOUR BEFORE OR 4 TO 6 HOURS AFTER CHOLESTYRAMINE (OR AT AS GREAT AN INTERVAL AS POSSIBLE) TO AVOID IMPEDING THEIR ABSORPTION.

OAD REACTIONS

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 year old). Most instances of constipation are mild, transient, and controlled with conventional therapy. Some patients require a temporary decrease in dose or discontinuation of the therapy.

Less Frequent Adverse Reactions: Abdominal discomfort and/or pain, flatulence, nausea, vomiting, diarrhea, enteritis, anorexia, and 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 periurnal area. Rare reports of intestinal occlusion, including deaths, have been reported in pediatrics. Occasional patients have been observed in the biliary tree including calcification of the gallbladder, in patients to whom cholestyramine 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 cholestyramine resin. One patient diagnosed with abdominal syndrome complex was found to have a "pasty mass" in the transverse colon on x-ray.

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

Musculoskeletal—Backache, muscle and joint pains, arthritis.

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

Respiratory—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 with Cholestyramine has been reported in a patient taking 150% of the maximal recommended daily dosage for a period of several weeks with no effects were reported. Should an overdose occur, the chief potential harm would be obstruction of the gastro-intestinal tract. The location of such potential obstruction, the degree of obstruct-