AUSTRALIAN PRODUCT INFORMATION

QUESTRAN® LITE

colestyramine powder for oral solution

1 NAME OF THE MEDICINE

Colestyramine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

QUESTRAN LITE is a powder for oral solution containing 850 mg per gram of colestyramine as the active ingredient. The 4.7 g sachet contains 4 g of colestyramine and the 9.4 g sachet contains 8 g of colestyramine.

Excipients of known effect: aspartame

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

QUESTRAN LITE is a cream coloured, fine, dispersible powder.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

1. Reduction of serum cholesterol levels and prevention of coronary heart disease. QUESTRAN LITE is indicated as adjunctive therapy to diet for the reduction of elevated serum cholesterol in patients with primary hypercholesterolemia (elevated low-density lipoproteins). QUESTRAN LITE may be useful to lower elevated cholesterol that occurs in patients with combined hypercholesterolemia and hypertriglyceridemia, but it is not indicated where hypertriglyceridemia is the abnormality of most concern

2. Relief of pruritus associated with partial biliary obstruction. Patients with primary biliary cirrhosis may exhibit elevated serum cholesterol as part of their disease. When colestyramine is used to treat the pruritus of partial biliary obstruction, it may lower serum cholesterol levels, produce no change, or cause rapid escape from a temporary lowering to pre-treatment levels or rebound

3. Relief of diarrhoea following ileal resection or ileal disease (cholerrhoeic enteropathy)

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults

Usual maintenance therapy: 12 to 16 g of colestyramine equivalent to 14.1 to 18.8 g QUESTRAN LITE per day (without regard to meals), is usually effective.

Children

Dosage in infants and children has not been established. Begin therapy with small doses. Subsequent adjustment should be made according to clinical response or laboratory results and the benefit/risk ratio.

Use for Cholesterol Lowering

Define the type of hyperlipoproteinaemia.

A trial of diet, weight reduction etc., should be undertaken before therapy with QUESTRAN LITE. Baseline cholesterol levels should be established, and the patient should be monitored both clinically and with serum cholesterol levels. Failure of cholesterol to fall or a significant rise in triglyceride level are indications to discontinue the medication.

Begin with 4 g colestyramine in the morning or evening, increasing to the required maintenance dose over 2 to 4 weeks. If the patient takes more than 24 g colestyramine daily, they should be observed for increased side effects.

Preparation

QUESTRAN LITE should be taken mixed with water, juice or highly fluid foods.

When mixing individual sachets for immediate use, place the contents of a 4g sachet of QUESTRAN LITE on the surface of 100 to 150 mL water or fruit juice (200 to 300mL for an 8 g sachet of QUESTRAN LITE). Mix immediately by stirring vigorously. Continue stirring or shaking until mixture is even. After dosing, rinse the container to ensure full dose.

Alternatively, QUESTRAN LITE may be mixed with highly fluid soups, pulpy fruits with a high moisture content (e.g. apple puree or crushed pineapple), or if care is taken to avoid excessive foaming, a carbonated beverage.

In all patients presenting with a diarrhoea induced by bile acid malabsorption, a response should be seen within 3 days. If this is not the case, alternative therapy should be initiated.

Instructions to the Patient

Patients should be advised as to the method of administration (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Patients should be advised to take other drugs at least one hour before or four to six hours after taking QUESTRAN LITE.

4.3 CONTRAINDICATIONS

Hypersensitivity to any of the components of QUESTRAN LITE.

Complete biliary obstruction where no bile is secreted into the intestine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

General

Colestyramine should not be taken in its dry form. It must always be mixed with water or other fluids before ingesting.

Experience in infants and children is limited and a practical dosage schedule has not been established. The effects of long-term drug administration as well as its effects in maintaining lowered cholesterol levels in paediatric patients are unknown.

QUESTRAN LITE SHOULD BE USED WITH CAUTION IN PATIENTS WITH PHENYLKETONURIA. QUESTRAN LITE POWDER CONTAINS 16.8 mg PHENYLALANINE PER 4 g DOSE OF COLESTYRAMINE.

Before instituting therapy with QUESTRAN LITE, diseases contributing to increased blood cholesterol such as hypothyroidism, diabetes mellitus, nephrotic syndrome, dysproteinemias and obstructive liver disease should be looked for and specifically treated.

In addition, prior to instituting therapy with QUESTRAN LITE, an attempt should be made to control serum cholesterol by appropriate dietary regimen, weight reduction and the treatment of any underlying disorder which might be the cause of the hypercholesterolemia. Serum cholesterol levels should be determined frequently during the first few months of therapy and periodically thereafter. A favourable trend in cholesterol reduction should occur during the first month of QUESTRAN LITE therapy. The therapy should be continued to sustain cholesterol reduction. Serum triglyceride levels should be measured periodically to detect whether significant changes have occurred.

Vitamin Supplements

Because it sequesters bile acids, colestyramine may interfere with normal fat absorption and may prevent absorption of fat-soluble vitamins such as A, D and K. If colestyramine is to be given for a long time, supplementary vitamins A and D should be given daily in a water miscible form or parenterally.

Bleeding Tendencies

Chronic use of colestyramine resin may be associated with increased bleeding tendency due to hypoprothrombinaemia associated with a vitamin K deficiency. This will usually respond to parenteral vitamin K, and recurrences can be prevented by oral dosage of vitamin K. Increased prothrombin time may be a hazard with anticoagulants which depress prothrombin. Reduction of serum or red cell folate has been reported, and treatment with folic acid should be considered in these cases.

Concomitant Medication

Since colestyramine may bind other drugs given concurrently, the interval between administration of colestyramine and other medicaments should be as great as feasible. Other drugs should be taken at least one hour before or four to six hours after colestyramine to avoid impeding their absorption.

Fat Digestion

QUESTRAN LITE in large doses may (24 g/day) interfere with normal fat digestion.

Serum Triglyceride Levels Should be Checked Periodically

Hyperchloraemic Acidosis

There is a possibility that prolonged use of colestyramine, because it is the chloride form of a resin, may lead to hyperchloraemic acidosis, especially in younger children and smaller patients where the relative dosage may be higher.

Hyperchloraemic acidosis has been reported in two elderly female patients who had received colestyramine in conjunction with spironolactone. Caution is advised if the simultaneous administration of colestyramine and aldosterone antagonists is intended.

Constipation

Colestyramine may produce or severely worsen pre-existing constipation. In patients with constipation, dosage of colestyramine should be reduced to avoid the possibility of impaction. In patients for whom QUESTRAN LITE is to be used as a cholesterol lowering agent, gastrointestinal dysfunction should be evaluated before using this preparation. In these patients, efforts should be made to avert severe constipation and its inherent problems, especially in those with clinically symptomatic coronary artery disease.

Use in the Elderly

No data available.

Paediatric Use

See Section 4.2 DOSE AND METHOD OF ADMINISTRATION.

Effects on 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.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Since colestyramine is an anion exchange resin, QUESTRAN LITE may have a strong affinity for acidic materials; it may also absorb neutral or basic materials to some extent. Therefore, colestyramine resin may delay or reduce the absorption of concomitantly dosed medicaments such as phenylbutazone, warfarin, chlorothiazide (acidic), as well as tetracycline, phenobarbital (phenobarbitone), thyroid and levothyroxine preparations, digitalis and inorganic iron.

Discontinuation of colestyramine could be hazardous to health if a potentially toxic drug such as digitalis had been titrated to a maintenance level while the patient was taking colestyramine resin.

QUESTRAN LITE may interfere with the pharmacokinetics of drugs (e.g. estrogens) that undergo enterohepatic recirculation.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy

Pregnancy category: B2

The physiological hyperlipidaemia of pregnancy does not require treatment.

Use of colestyramine in pregnancy, lactation or by women of childbearing age requires that potential benefits of therapy be weighed against possible hazards to mother and child. The known interference with absorption of fat-soluble vitamins may be detrimental even in the presence of supplementation. Safety of use of colestyramine resin by pregnant women has not been established.

Use in Lactation

See Section 4.6 FERTILITY, PREGNANCY AND LACTATION – Use in Pregnancy.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

More Common

Constipation is the major single complaint and may be severe and occasionally accompanied by faecal impaction and/or haemorrhoids with or without bleeding.

Predisposing factors for most of these complaints in patients treated to lower cholesterol levels, are high dose (more than 24 g colestyramine daily) and old age (more than 60 years). Most instances of constipation are mild, transient and controlled with standard treatment. Some patients require a temporary decrease in dosage or discontinuation of therapy.

Less Common

<u>Gastrointestinal</u>

Abdominal discomfort (pain and distension), flatulence, nausea, vomiting, heartburn, diarrhoea, anorexia, dyspepsia and steatorrhoea.

<u>Haematological</u>

Bleeding tendencies (hypoprothrombinaemia) due to vitamin K deficiency, as well as vitamin A (one case of night blindness reported) and D deficiencies.

Skin and Mucosa

Rash and irritation of the skin, tongue and perianal area.

Other

Hyperchloraemic acidosis, osteoporosis. Occasional calcified material has been observed in the biliary duct including calcification of the gall bladder in patients to whom colestyramine has been given. However, this may be a manifestation of the patient's liver disease and not drug related.

One patient experienced biliary colic on each of three occasions which he took QUESTRAN LITE. One patient diagnosed as acute abdominal symptom complex was found to have a "pasty mass" in the transverse colon on X-ray.

Rare reports of intestinal obstruction have been received post marketing, including two deaths in paediatric patients.

Other Events Not Necessarily Drug Related

Gastrointestinal

Rectal bleeding, black stools, haemorrhoidal bleeding, bleeding from known duodenal ulcer, dysphagia, hiccoughs, ulcer attack, sour taste, pancreatitis, rectal pain, diverticulitis, eructation.

Laboratory Test Changes

Liver function abnormalities.

Haematological

Increased or decreased prothrombin time, ecchymosis, anaemia.

Cardiovascular

Claudication, xanthomas of hands and fingers, angina, arteritis, thrombophlebitis, myocardial infarction, myocardial ischaemia, increased postprandial angina.

Hypersensitivity

Urticaria, asthma, wheezing, shortness of breath.

Musculoskeletal

Backache, muscle and joint pains, arthritis.

Neurological

Headache, anxiety, vertigo, dizziness, fatigue, tinnitus, syncope, drowsiness, femoral nerve pain, paraesthesia.

Eye

Arcus juvenilis, uveitis.

Renal

Haematuria, dysuria, burnt odour to urine, diuresis.

Miscellaneous

Weight loss, weight gain, increased libido, swollen glands, oedema, dental bleeding, dental caries, chest pain.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

One case of overdosage with QUESTRAN LITE has been reported in a patient taking 150% of the maximum recommended daily dosage for several weeks. No ill effects were observed.

Should 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.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Cholesterol is the major, and probably the sole, precursor of bile acids. A major portion of the bile acids secreted into the intestine with the bile is reabsorbed and returned to the liver via the portal circulation in an enterohepatic cycle. Only very small amounts of bile acids are found in normal serum.

Colestyramine combines with bile acids in the intestine to form an insoluble complex which is excreted in the faeces. This process results in a continuous, though partial, removal of bile acids from enterohepatic circulation by preventing their reabsorption. Besides bile acids, some other anions are strongly bound to the resin, but cations or neutral compounds are usually less firmly bound.

The increased loss of bile acids due to colestyramine administration leads to increased oxidation of cholesterol to bile acids, a decrease in beta lipoprotein or low-density lipoprotein in plasma and a decrease in serum cholesterol levels. Although in man colestyramine produces an increase in hepatic synthesis of cholesterol, plasma cholesterol levels fall. Apparently, this fall is secondary to an increased clearance of cholesterol rich lipoproteins from plasma. Serum triglyceride levels may increase or remain unchanged in patients treated with colestyramine.

Colestyramine is insoluble in water and is not absorbed from the gastrointestinal tract. It is not affected by digestive enzymes.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

QUESTRAN LITE contains the following excipients: aspartame, citric acid, colloidal anhydrous silica, Orange Juice 059107 AGEP0551 (ARTG PI No: 1291), propylene glycol alginate and xanthan gum.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30ºC.

6.5 NATURE AND CONTENTS OF CONTAINER

Container type: sachet (Al laminated with PE/paper)

Pack size: 4 g x 50 sachets and 8 g x 50 sachets

Some strengths, pack sizes and/or pack types may not be marketed.

Australian Register of Therapeutic Goods (ARTG)

AUST R 11971 – QUESTRAN LITE colestyramine 850mg/g powder sachet

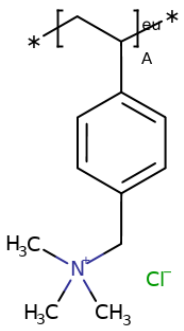
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure

Colestyramine is the chloride salt of a basic anion exchange resin.



Chemical name: [4-[3-(4-ethylphenyl)butyl]phenyl]-trimethylazanium

Molecular formula: $C_{21}H_{30}ClN$

Molecular weight: 341.92

CAS Number

11041-12-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

13/08/1991

10 DATE OF REVISION

03/05/2022

Summary Table of Changes

Section Changed	Summary of New Information
6.1	Minor editorial changes
6.5	Insert AUST R numbers
8	Update sponsor's details

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