New Zealand Data Sheet

1. QUESTRAN LITE

Cholestyramine resin for Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aspartame Formulation.

QUESTRAN LITE is a sugar free formulation containing 4g of cholestyramine per 4.7g of QUESTRAN LITE powder.
Cholestyramine is the chloride salt of a basic anion exchange resin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of serum cholesterol levels and prevention of coronary heart disease. QUESTRAN 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.

Relief of pruritus associated with partial biliary obstruction. Patients with primary biliary cirrhosis may exhibit elevated serum cholesterol as part of their disease. When cholestyramine 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 pretreatment levels or rebound.

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

4.2 Dosage and method of administration

<u>Adults</u>:
Usual maintenance therapy: 12 to 16g of cholestyramine resin equivalent to 14.1 to 18.8g QUESTRAN LITE per day (without regard to meals), is usually effective.

<u>Children</u>:
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 in 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 4g cholestyramine (4.7 QUESTRAN LITE) in the morning or evening, increasing to the required maintenance dose over 2 to 4 weeks. If the patient takes more than 24g cholestyramine resin daily, he/she 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 100-150mL water or fruit juice (200-300mL for an 8g sachet of QUESTRAN LITE). Mix immediately by stirring vigorously or preferably by shaking in a Questran Lite shaker. 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 PATIENT
Patients should be advised as to the method of administration (see section 4.2, Dosage 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

Cholestyramine resin 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 16.8mg PHENYLALANINE PER 4g DOSE OF CHOLESTYRAMINE.

General:
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 favorable 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, cholestyramine resin may interfere with normal fat absorption and may prevent absorption of fat soluble vitamins such as A, D and K. If cholestyramine 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 cholestyramine 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 cholestyramine may bind other drugs given concurrently, the interval between administration of cholestyramine 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 cholestyramine to avoid impeding their absorption.

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

Serum triglycerides:
Serum triglyceride levels should be checked periodically.

Hyperchloraemic acidosis:
There is a possibility that prolonged use of cholestyramine, 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 cholestyramine in conjunction with spironolactone. Caution is advised if the simultaneous administration of cholestyramine and aldosterone antagonists is intended.

Constipation:
Cholestyramine may produce or severely worsen pre-existing constipation. In patients with constipation, dosage of cholestyramine 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.

4.5 Interaction with other medicines and other forms of interaction

Since cholestyramine 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, cholestyramine resin may delay or reduce the absorption of concomitantly dosed medicaments such as phenylbutazone, warfarin, chlorothiazide (acidic), as well as tetracycline, phenobarbitone, thyroid and thyroxine preparations, digitalis and inorganic iron.

Discontinuation of cholestyramine resin 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 cholestyramine resin.

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

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy (Category B2) **and lactation**

The physiological hyperlipidaemia of pregnancy does not require treatment.

Use of cholestyramine resin 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 cholestyramine resin by pregnant women has not been established.

4.7 Effects on ability to drive and use machines

No data available.

4.8 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 24g cholestyramine 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:

Gastrointestinal

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

Haematological

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 cholestyramine 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.

Hypensensitivity
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 of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

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 advice on the management of overdosage, please contact the Nationals Poisons Information Centre (telephone 13 11 26).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Cholestyramine resin 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 cholestyramine 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 cholestyramine 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 cholestyramine.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aspartame, citric acid, colloidal silicon dioxide, orange flavour 059107 AGEP0551, propylene glycol alginate, xanthan gum.

6.2 Incompatibilities

No data available.

6.3 Shelf life

36 months from date of manufacture stored at or below 30°C.

6.4 Special precautions for storage

Keep out of reach of children. Store below 30°C.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Questran Lite is available in boxes of 50 sachets.
Each sachet contains 4 g of anhydrous cholestyramine resin in 4.7 g of Questran Lite Powder with Aspartame.

6.6 Special precautions for disposal (and other handling).

Questran Lite should not be taken in its dry form.

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Pharmacy Retailing (NZ) Limited Trading as Healthcare Logistics 58 Richard Pearse Drive
Airport Oaks
Auckland, New Zealand

Telephone (09) 9185 100
Fax: (09) 9185 101

9. DATE OF FIRST APPROVAL

14 July 2010

10. DATE OF REVISION OF THE TEXT

May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections revised	Update to the SPC-style format