SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

QUESTRAN® LITE 4g/sachet Powder for Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of QUESTRAN LITE powder contains 4 g of anhydrous colestyramine, the active ingredient.

Excipients with known effect:

Each 4 g sachet contains 30 mg aspartame, from which are 16,8 mg phenylalanine, as sweetener. This medicine contains 32,5 mg propylene glycol in each sachet.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension.

Off-white fine powder with a faint orange odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For reduction of serum cholesterol and low-density cholesterol, lipoprotein levels in primary hypercholesterolaemia in conjunction with an appropriate diet. QUESTRAN LITE is indicated as adjunctive therapy to diet for the reduction of elevated serum cholesterol in patients with primary hypercholesterolaemia (elevated low-density lipoproteins) who do not respond adequately to diet.

QUESTRAN LITE may be useful to lower elevated cholesterol that occurs in patients with combined

hypercholesterolaemia and hypertriglyceridaemia, but it is not indicated where hypertriglyceridaemia is the abnormality of most concern.

For the reduction of pruritus associated with partial biliary obstruction e.g. as in cholestatic jaundice.

For the treatment of diarrhoea due to bile acid malabsorption. (See section 4.4: Oral rehydration therapy).

4.2 Posology and method of administration

Posology

Hypercholesterolaemia and hyperlipoproteinaemia may be manifestations of altered metabolism resulting from either dietary excesses or diseases such as hypothyroidism, diabetes, nephrosis, pancreatitis or biliary cirrhosis. The primary objective of therapy should be to control any underlying disease. Proper diet and weight control in these patients is also essential.

Adults:

To reduce cholesterol:

Begin with one 4 g sachet (see section 6.6 once or twice daily). The dose can be increased to 8 g (two sachets) in the morning and in the evening. If necessary, medication may be increased to the maximum of 24 g of colestyramine per day. It is recommended that increases in dose be gradual. If dose increases are necessary, they should be done gradually, and with periodic assessment of lipid/lipoprotein levels at intervals of not less than 4 weeks.

The suggested time of administration is mealtime, but this may be modified to avoid interference with the absorption of other medicines. Although the recommended dosing schedule is twice daily, QUESTRAN LITE may be administered in 1 – 4 doses per day. No more than 24 g (6 sachets) of the active ingredient a day, should be administered as larger doses of QUESTRAN LITE may interfere with normal fat absorption.

To relieve pruritus due to partial biliary obstruction:

4 g (one sachet) or 8 g (two sachets) daily.

To relieve diarrhoea induced by bile acid malabsorption:

The initial dosage of QUESTRAN LITE should be 4 g (one sachet) three times a day, with subsequent adjustment as needed.

NOTE

IN ALL PATIENTS PRESENTING WITH DIARRHOEA INDUCED BY BILE ACID MALABSORPTION, A RESPONSE SHOULD BE SEEN WITHIN 3 DAYS. IF THIS IS NOT THE CASE, ALTERNATE THERAPY SHOULD BE INITIATED.

To familiarise the patient with QUESTRAN LITE and to minimise gastrointestinal side effects, it is desirable to begin all therapy with one dose of QUESTRAN LITE daily. The dosage is then increased within a day or two to the starting dose for effective control.

NOTE

QUESTRAN LITE SHOULD NOT BE TAKEN IN ITS DRY FORM. ALWAYS MIX QUESTRAN LITE WITH WATER OR OTHER FLUIDS BEFORE INGESTING.

One 4 g sachet = 4.68 g QUESTRAN LITE powder

= 4 g anhydrous colestyramine

Patients with renal impairment

There are no special dose recommendations for this patient group.

Patients with hepatic impairment

There are no special dose recommendations for this patient group.

Paediatric population

The precise dosage for children has not yet been established.

Method of administration

To be taken orally.

Place the contents of a 4 g sachet QUESTRAN LITE on the surface of 115 - 170 mL of water or beverage, such as milk, fruit juice or broth. Use more water or beverage for the two sachets (200 - 300 mL). Stir to a uniform suspension. QUESTRAN LITE may also be used with pulpy fruits, such as apple sauce or crushed pineapple.

4.3 Contraindications

QUESTRAN LITE is contraindicated in patients who have shown hypersensitivity to colestyramine or to any of the other ingredients in the formulation (see section 6.1).

QUESTRAN LITE is contraindicated in patients with complete biliary obstruction.

4.4 Special warnings and precautions for use

QUESTRAN LITE should not be used in patients with exudative or bloody diarrhoea.

As a precautionary measure, since QUESTRAN LITE may bind to other medicine given concurrently, patients should take other medicine at least one hour before or 4 - 6 hours after QUESTRAN LITE to avoid impeding their absorption, or at as great an interval as possible.

General

Before instituting therapy with QUESTRAN LITE, diseases contributing to increased blood cholesterol such as hypothyroidism, diabetes mellitus, nephrotic syndrome, dysproteinaemias and obstructive liver disease should be investigated 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 hypercholesterolaemia. 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.

IF ADEQUATE CHOLESTEROL REDUCTION IS NOT ATTAINED, THERAPY WITH QUESTRAN LITE SHOULD BE DISCONTINUED.

There is a possibility that prolonged use of QUESTRAN LITE in high doses may produce hyperchloraemic acidosis since it is the chloride form of an anion exchange resin. This is especially true in younger and smaller patients where the relative dosage may be higher as well as in patients with renal impairment.

QUESTRAN LITE may produce or aggravate pre-existing constipation or related conditions such as haemorrhoids. In patients with constipation, the dosage of QUESTRAN LITE should be decreased since it may produce impaction. In patients presenting with clinically symptomatic coronary artery disease, where straining of the stool is to be avoided, the dosage of QUESTRAN LITE should be titrated to avert constipation.

Chronic use of QUESTRAN LITE may be associated with increased bleeding tendency due to hypoprothrombinaemia associated with vitamin K deficiency. This will usually respond promptly to parenteral vitamin K administration; recurrences can be prevented by oral administration of vitamin K. Reduction of serum or red cell folate has been reported and treatment with folic acid should be considered in these cases.

QUESTRAN LITE should be used with caution in patients with peptic ulcers or with a history of peptic ulcer disease as it might aggravate or activate this condition.

Oral rehydration therapy

In patients with diarrhoea, fluid and electrolyte depletion may occur. Administration of appropriate fluid and electrolyte replacement is the most important measure.

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.

Phenylketonurics:

QUESTRAN LITE contains aspartame, which provides the equivalent of 3,6 mg of phenylalanine per gram of powder.

This medicine contains 32,5 mg propylene glycol per sachet.

Propylene glycol at doses exceeding 1 mg / kg / day in neonates and 50 mg / kg / day in children younger than 5 years should be avoided. Concomitant use of other substrates for the enzyme alcohol dehydrogenase such as ethanol can induce serious side effects. For propylene glycol at doses exceeding 50 mg / kg / day, medical monitoring is required in patients with impaired renal or hepatic function.

4.5 Interaction with other medicines and other forms of interaction

SINCE QUESTRAN LITE MAY BIND OTHER MEDICINES GIVEN CONCURRENTLY, PATIENTS SHOULD TAKE OTHER MEDICINE AT LEAST ONE HOUR BEFORE OR 4 - 6 HOURS AFTER QUESTRAN LITE TO AVOID IMPEDING THEIR ABSORPTION, OR AT AS GREAT AN INTERVAL AS POSSIBLE.

Since colestyramine is an anion-exchange resin, QUESTRAN LITE has a strong affinity for acidic materials.

QUESTRAN LITE may delay or reduce the absorption of concomitant oral medicine such as amiodarone,

phenobarbitone, valproate, penicillin G, tetracycline, vancomycin, methotrexate, propranolol, ursodeoxycholic acid, ezetimibe, ethinylestradiol, phenprocoumon, warfarin, digoxin, leflunomide, mycophenolate, furosemide, acetylsalicylic acid, diclofenac, meloxicam, piroxicam, sulindac, tenoxicam, spironolactone, chlorothiazide, hydrochlorothiazide, levothyroxine, liothyronine, thyroid extract.

The discontinuance of QUESTRAN LITE (colestyramine) could pose a hazard to health if a potentially toxic medicine such as digoxin has been titrated to a maintenance level while the patient was taking QUESTRAN LITE.

QUESTRAN LITE in combination with spironolactone may increase the potential for the development of hyperchloraemic acidosis.

Also, QUESTRAN LITE may interfere with the pharmacokinetics of medicines (e.g., oestrogens) that undergo enterohepatic recirculation.

Absorption of fat-soluble vitamins:

Because it sequesters bile acids, QUESTRAN LITE may interfere with normal fat absorption. QUESTRAN LITE may prevent absorption of fat-soluble vitamins, such as vitamins A, D and K. Therefore, when QUESTRAN LITE is to be given for long periods, daily water miscible or parenteral supplements of vitamins A, D and K should be considered.

4.6 Fertility, pregnancy and lactation

The safety of QUESTRAN LITE in pregnancy and lactation has not been established and the possibility of interference with absorption of fat-soluble vitamins should be considered (see section 4.3).

4.7 Effects on ability to drive and use machines

QUESTRAN LITE is not expected to have an effect on the ability to drive and use machines.

4.8 Undesirable effects

a) Summary of safety profile

The most common adverse reaction is constipation. Predisposing factors for most of these complaints when QUESTRAN LITE is used as cholesterol lowering medicine 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.

Frequency categories are defined according to the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).

b) Tabulated list of adverse reactions

System Organ Class	**Frequency**	**Adverse Reaction(s)**
Blood and lymphatic system disorders	Uncommon	Bleeding tendencies due to hypoprothrombinaemia (Vitamin K deficiency)
Metabolism and nutrition disorders	Uncommon	Vitamin A deficiency, vitamin D deficiency, hyperchloremic acidosis in children and patients with renal impairment (see section 4.4)
Eye disorders	Uncommon	Night blindness (Vitamin A deficiency)
Gastrointestinal disorders	Very common	Constipation
	Uncommon	Abdominal discomfort, flatulence, nausea, vomiting, diarrhoea, heartburn, anorexia, dyspepsia, steatorrhea, tongue irritation, perianal irritation
	Rare	Intestinal obstruction
Hepatobiliary disorders	Not known	Biliary colic
Skin and subcutaneous tissue disorders	Uncommon	Rash, irritation of skin
Musculoskeletal and connective	Uncommon	Osteoporosis

tissue disorders		
Renal and urinary disorders	Not known	Calcified material has occasionally been observed in the biliary tree (including calcification of the gallbladder)

Reports of intestinal obstruction have been received post-marketing, including two deaths in paediatric patients. Calcified material has occasionally been observed in the biliary tree, including calcification of the gallbladder, in patients to whom colestyramine has been given. However, this may be a manifestation of the liver disease and not medicine related.

One patient experienced biliary colic on each of three occasions on which he took colestyramine. 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 medicine related) reported in patients taking QUESTRAN LITE include:

System Organ Class	**Adverse Reaction(s)**
Blood and lymphatic system disorders	Decreased or increased prothrombin time, ecchymoses, anaemia, swollen glands
Nervous system disorders	Headache, anxiety, vertigo, dizziness, syncope, drowsiness, femoral nerve pain, paraesthesia
Eye disorders	Uveitis
Ear and labyrinth disorders	Tinnitus
Respiratory, thoracic and mediastinal disorders	Asthma, wheezing, shortness of breath
Gastrointestinal disorders	GI-rectal bleeding, black stools, haemorrhoidal bleeding, bleeding from known duodenal ulcer, dysphagia, hiccups, ulcer attack, sour taste, pancreatitis, rectal pain, diverticulitis, eructation
Skin and subcutaneous tissue disorders	Urticaria, oedema
Musculoskeletal, connective tissue and bone disorders	Backache, muscle and joint pains, arthritis

Renal and urinary disorders	Haematuria, dysuria, burnt odour to urine, diuresis
Reproductive system and breast disorders	Increased libido
General disorders and administration site reactions	Weight loss, weight gain, dental bleeding, dental caries, fatigue
Investigations	Liver function abnormalities

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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

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. Other possible side effects of overdosage may include constipation, abdominal discomfort, flatulence, nausea, vomiting, diarrhoea, heartburn, dyspepsia and steatorrhoea, biliary colic, rash and irritation of skin, tongue and perianal area.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A7.5 - Serum-cholesterol reducers

ATC code: C10AC01.

Colestyramine adsorbs and combines with the bile acids in the intestine to form an insoluble complex which is excreted in the faeces. The increased faecal loss of bile acids leads to an increased oxidation of cholesterol to bile

acids and a decrease in serum cholesterol levels and low-density lipoprotein cholesterol serum levels.

When administered properly, colestyramine usually leads to a significant reduction (15 % or more) in serum cholesterol levels.

In patients with pruritus associated with partial biliary obstruction, the reduction of serum bile acid levels by colestyramine is thought to reduce excess bile acids deposited in the dermal tissues and promote their excretion with the faeces. The relief from itching afforded to most of these patients by colestyramine is attributed to this mobilisation. It is postulated that in "bile-salt" diarrhoea, colestyramine binds conjugated dihydroxy bile salts which are known to have a cathartic effect.

5.2 Pharmacokinetic properties

Colestyramine is a basic anion exchange resin. Colestyramine is very hydrophilic, but it is not soluble in water, nor is it hydrolysed by digestive enzymes. Thus, colestyramine is not absorbed from the intestinal tract.

5.3 Preclinical safety data

In studies conducted in rats in which colestyramine 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 tumours induced by potent carcinogens, the incidence of such tumours was observed to be greater in colestyramine-treated rats than in control rats. The relevance of laboratory observation from studies in rats to the clinical use of QUESTRAN LITE is not known. A long-term study in humans does not reveal any significant difference between patients treated with colestyramine and those treated with placebo with respect to the incidence of cancer.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aspartame

Citric acid

Colloidal anhydrous silica

Orange juice flavour

Propylene glycol alginate

Xanthum gum

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

QUESTRAN LITE should be stored at or below 25 ˚C.

6.5 Nature and contents of container

QUESTRAN LITE is available in 4 g sachets, each sachet providing 4 g of anhydrous colestyramine. Sachets are in cartons of 50's.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Equity Pharmaceuticals (Pty) Ltd

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene

Pretoria, 0157

8. REGISTRATION NUMBER

D/7.5/39

9. DATE OF FIRST AUTHORIZATION

25 November 1971

10. DATE OF REVISION OF THE TEXT

05 April 2024