Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Questran 4g/sachet, Powder for oral suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 4 g of colestyramine.

Excipient(s) with known effect:
Each sachet contains 3.79 g sucrose (421 mg of sucrose per gram of powder), and 97.5 mg propylene glycol (as alginate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral suspension.

A fine, homogeneous, cream to buff-coloured powder for oral suspension. On reconstitution with 150 ml of water or fruit juice a uniform suspension is formed.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. A basic anion exchange resin to complex bile acids and reduce plasma levels of cholesterol.
2. Reduction of plasma cholesterol in hypercholesterolaemia, particularly in those patients who have been diagnosed as Fredrickson's Type II (high plasma cholesterol with normal or slightly elevated triglycerides).
3. Relief of pruritus associated with partial biliary obstruction and primary biliary cirrhosis.
4. Relief of diarrhoea associated with ileal reaction, Crohn's disease, vagotomy and diabetic vagal neuropathy.
5. Management of radiation-induced diarrhoea.

4.2 Posology and method of administration

Posology

Adults (including the elderly):

1. Hypercholesterolaemia
The usual total daily dose is 12 to 24 g (the contents of 3 to 6 sachets) in single or up to 4 divided doses. The maximum daily intake should not exceed 36 g (contents of 9 sachets).

2. Management of diarrhoea
The usual daily dose is 12 to 24 g (the contents of 3 to 6 sachets) in single or up to 4 divided doses. The maximum daily intake should not exceed 36 g (contents of 9 sachets). In all patients presenting with diarrhoea induced by bile acid malabsorption, if a response is not seen within 3 days, then alternative therapy should be initiated.

3. Pruritus
The usual daily dose is 4 to 8 g (contents of 1 to 2 sachets).

Doses of more than 24 g a day of colestyramine resin may interfere with normal fat absorption.

Paediatric population

Children 6 - 12 years:

The usual total daily dose is:

$$\frac{\text{Child's Weight in Kg} \times \text{Adult Dose}}{70}$$

To minimize potential gastrointestinal side effects, it is desirable to begin all therapy in children with one dose of Questran daily. The dosage is then increased gradually to the desired level for effective control.

Children under 6 years:
The dose has not been established in infants and children under 6 years of age.

Method of administration

Questran should not be taken in its dry form.

Questran should be administered mixed with water or a suitable liquid, such as fruit juice, and stirred to a uniform consistency.

Questran may also be mixed with skimmed milk, thin soups, pulpy fruits with high moisture content, e.g. apple sauce, etc.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Use in patients with complete biliary obstruction, since Questran cannot be effective where bile is not secreted into the intestine.

4.4 Special warnings and precautions for use

Before instituting therapy with Questran, diseases contributing to increased blood cholesterol such as hypothyroidism, diabetes mellitus, nephrotic syndrome, dysproteinaemia and obstructive liver disease should be investigated and specifically treated. In addition, prior to instituting therapy with Questran, 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 therapeutic response is usually seen within 4 weeks. Serum triglyceride levels should be measured periodically to detect whether significant changes have occurred.

Colestyramine may produce or aggravate pre-existing constipation or related conditions, such as haemorrhoids. In patients with constipation, the dosage of colestyramine 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 should be titrated to avert constipation.

Reduction of serum folate concentrations has been reported in children with familial hypercholesterolaemia. Supplementation with folic acid should be considered in these cases.

Colestyramine interferes with the absorption of fat-soluble vitamins, A, D and K. If it is to be administered over prolonged periods, supplementation of vitamin intake with water-miscible forms or by the parenteral route should be undertaken.

Chronic use of Questran 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.

There is a possibility that prolonged use of colestyramine resin in high doses may produce hyperchloremic 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 should be used with caution in patients with exudative or bloody diarrhoea, as it may increase the bleeding tendency due to hypoprothrombinaemia (Vitamin K deficiency) during chronic use.

This medicine contains 3.79 g sucrose in each sachet. The sucrose in Questran may be harmful to the teeth when used for a period of greater than 14 days.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine contains 97.5 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 medicinal products and other forms of interaction

Questran may delay or reduce the absorption of certain drugs (such as digitalis and its alkaloids, tetracycline, chlorothiazide, warfarin and thyroxine). The response to concomitant medication should be closely monitored and appropriate adjustments made if necessary.

Patients should take other drugs at least one hour before or 4-6 hours after Questran to minimise possible interference with their absorption.

Questran may interfere with the pharmacokinetics of drugs that undergo enterohepatic recirculation.

Table 1- Tabulated list of examples for colestyramine drug-drug interactions
The table provided below may not be complete.

Drug Class	**Drug(s)**
Antiarrhythmics	Amiodarone
Anticonvulsants	Valproate
Antiepileptics	Phenobarbital
Anti-infectives	Benzylpenicillin, Tetracycline
Antimetabolites	Methotrexate
Bile acids	Ursodeoxycholic acid
Cholesterol lowering drugs	Bezafibrate, Ezetimibe
Combined hormonal contraceptive	Ethinylestradiol
Coumarins	Phenprocoumon, warfarin
Digitalis glycosides	Digitoxin, digoxin
Immunosuppressants	Leflunomide, mycophenolate
Loop Diuretics	Furosemide
Nicotinic acid derivatives	Nicotinic acid
Nonsteroidal anti-inflammatory drugs	Diclofenac, meloxicam, piroxicam, sulindac, tenoxicam
Oestrogen modulators	Raloxifene
Statins	Fluvastatin, pravastatin
Thiazide diuretics	Hydrochlorothiazide
Thyroid hormones	Levothyroxine, liothyronine, thyroid extract

4.6 Fertility, pregnancy and lactation

Pregnancy
There is limited clinical experience of pregnant women. The data from experiments on animals is incomplete.

Breastfeeding
Cholestyramine is not excreted in breast milk. The reduced absorption of fat-soluble vitamins should be noted.

Fertility
No human data on the effect of colestyramine on fertility are available.

4.7 Effects on ability to drive and use machines

Questran has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Gastrointestinal side effects are those most frequently reported. The most common adverse reaction is constipation. Predisposing factors for most of these complaints when Questran is used as a cholesterol lowering agent 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 events:
Abdominal discomfort, flatulence, nausea, vomiting, diarrheoa, heartburn, anorexia, dyspepsia and steatorrhea, bleeding tendencies due to hypoprothrombinaemia (Vitamin K deficiency) as well as Vitamin A (night blindness has been reported rarely) and D deficiencies, hyperchloremic acidosis in children and patients with renal impairment, and osteoporosis. Rash and irritation of skin, tongue and perianal area. Rare reports of intestinal obstruction have been received post marketing, including two deaths in pediatric patients.

Other events (not necessarily drug-related) reported in patients taking Questran include:

Gastrointestinal - GI-rectal bleeding, hemorrhoidal bleeding, dysphagia, taste disturbance, rectal pain, eructation.

Laboratory test changes - Liver function abnormalities.

Hypersensitivity - Urticaria, shortness of breath.

Musculoskeletal - muscle and joint pains.

Neurologic - Headache, dizziness, fatigue, drowsiness, paresthesia.

Miscellaneous - Weight loss, weight gain, dental caries.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance Website: www.hpra.ie

4.9 Overdose

One case of medication error experienced heartburn and nausea after taking colestyramine 27 g three times a day for a week. The potential problem in overdosage would be obstruction of the gastrointestinal tract.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bile acid sequestrants, ATC code: C10AC01.

Colestyramine resin absorbs and combines with the bile acids in the intestine to form an insoluble complex which is excreted in the faeces. This results in a continuous, though partial, removal of bile acids from the enterohepatic circulation by preventing their reabsorption. 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 serum levels. Colestyramine is hydrophilic but it is not soluble in water, nor is it hydrolysed by digestive enzymes.

5.2 Pharmacokinetic properties

Colestyramine is not absorbed from the digestive tract.

5.3 Preclinical safety data

No further significant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acacia
Citric acid anhydrous
Orange juice flavour
Polysorbate 80
Propylene glycol alginate
Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30ºC.
Store in the original package.

6.5 Nature and contents of container

Original packs containing 50 or 60 low density polyetheylene laminated sachets per carton.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Cheplapharm Arzneimittel GmbH
Ziegelhof 24
17489
Greifswald
Germany

8 MARKETING AUTHORISATION NUMBER

PA2239/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 1 April 2009

10 DATE OF REVISION OF THE TEXT

March 2023