

## **VI.2 Elements for a public summary**

### ***VI.2.1 Overview of disease epidemiology***

#### ***High levels of cholesterol in the blood (Hypercholesterolemia)***

Elevated blood cholesterol is not in itself a disease, but it may contribute to the development of atherosclerosis (building up of deposits in the blood vessels). The ratio between harmful LDLcholesterol (low density lipoprotein) in the blood and the beneficial HDL-cholesterol (high density lipoprotein) that has a protective effect, is important for the formation of atherosclerosis. LDL cholesterol can be lowered by diet and medication. HDL cholesterol can be raised by exercise and diet changes.

#### ***Itching due to inhibited drainage of bile.***

The liver has a variety of different functions. One of these is to cleanse the blood of unwanted substances. These substances are excreted with the bile, which leaks into the intestine. For various reasons, the drainage of bile can be inhibited, so that the unwanted substances cannot be excreted. This may result in itching. This type of itching is often called "hepatic itching".

#### ***Diarrhea caused by bile acids***

Bile acid is important for the absorption of fat from food and released from the gallbladder by consuming fatty meals. 98-99% of the bile acid is absorbed in the lower part of the small intestine and returned back to the liver. If for any reason this absorption does not occur in the lower part of the small intestine, an increased amount of bile acid ends up in the large intestine, the regular

suction of liquid does not take place, and a watery diarrhea results.

### VI.2.2 *Summary of treatment benefits*

Cholestyramine is used in treatment of high levels of cholesterol in the blood, to reduce itching caused by bile salts and to treat diarrhea caused by excess levels of bile acids in the intestine. Cholesterol that is ingested or manufactured in the body is eliminated primarily by conversion to bile acids in the liver and excretion into the intestine with bile. The bile enters the intestine, and most of the bile acids are reabsorbed from the intestine. These reabsorbed bile acids are removed from the blood by the liver and excreted again into bile. Thus, bile acids re-circulate in the body. Cholestyramine binds to bile acids in the intestine. This prevents their absorption, and the cholestyramine/bile acid complexes are eliminated in the stool. As a result, the body loses bile acids. To compensate for this loss, the liver increases the conversion of cholesterol to bile acids. The conversion of cholesterol to bile acids reduces the cholesterol in the body, and the levels of cholesterol drop in the blood.

One of the most troubling symptoms in patients with liver and biliary disease is itching. The itching is believed in some cases to be the result of accumulation of bile acids in the skin due to the inability of the liver or bile ducts to eliminate bile acids normally. By binding bile acids in the intestines and preventing their absorption, cholestyramine hastens the elimination of bile acids from the body and skin, and the itching improves.

In diarrhea caused by excess bile acids in the intestine the binding of bile to cholestyramine relieves the diarrhea.

### VI.2.3 *Unknowns relating to treatment benefits*

No studies have been conducted in the elderly. Therefore no recommendations regarding dosage can be given *and treatment benefits has not been* systematically collected

### VI.2.4 *Summary of safety concerns*

Risk	What is known	Preventability
<b>Reduction or delay in absorption of other medicines taken at the same time.</b>	Colestyramine may bind other medicinal products taken at the same time and thereby delay or prevent these other medicines to work.	It is recommended to take other medicines either at least 1 hour before or 4-6 hours after cholestyramine.
<b>Vitamin A, D, E, K and folate deficiency</b>	Colestyramine can affect the normal absorption of fat when given in high dose (24 mg daily). Then it can inhibit the absorption of fat soluble vitamins, vitamin A, D, E, K and folate.	Supplement with vitamins may be recommended

Risk	What is known	Preventability
	Therefore supplement with vitamins may be recommended	
<b>You have too much acidity in your blood (hyperchloremic acidosis)</b>	Due to the chemical properties of cholestyramine (a chloride salt of a basic anion exchanger) longer use of high doses can cause acidification of the blood. This happens more frequent in younger and smaller patients in whom the relative dosage may be higher	The patient and doctor is informed about this and can take precautions if symptoms occur.
<b>Constipation (including intestinal obstruction)</b>	Cholestyramine may cause or aggravate constipation	The doctor should be cautious about this when the titration of dose is done. Treatment with medicine to avoid constipation may be necessary.
<b>Use in the elderly</b>	Information about the use of cholestyramine in the elderly is missing	Recommendations about dose in the elderly cannot be given.

#### **VI.2.5 Summary of additional risk minimisation measures by safety concern**

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Colestyramin BBS Consult can be found on the homepage of the Danish Medicines Agency after the product has been approved.

#### **VI.2.6 Planned post authorisation development plan (if applicable)**

Not Applicable.

#### **VI.2.7 Summary of changes to the risk management plan over time**

Not Applicable.