

Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic Class:

Bile Acid Sequestrants

Overview:

The bile acid sequestrants comprise one of four subclasses of antilipemic agents. The three products available in the United States are cholestyramine, colesevelam and colestipol. Cholestyramine was the first lipid-lowering agent approved by the FDA (1964). Since then, the FDA has approved several agents for the treatment of hyperlipidemia.

Bile acid sequestrants act mainly within the lumen of the gastrointestinal (GI) tract. These agents combine with bile acids in the intestine as they undergo enterohepatic circulation to form insoluble, non-absorbable chemical complexes that are excreted in the feces. Since cholesterol is the precursor of bile acids, interference with reuptake of bile acids stimulates cholesterol synthesis via an increase in the activity of HMG-CoA reductase. Newly formed cholesterol is shunted into the bile acid-synthesis pathway. In addition, the hepatocytes respond to this change in plasma cholesterol by intensifying uptake of low-density lipoprotein cholesterol (LDL-C), thereby decreasing plasma cholesterol. Plasma cholesterol and LDL-C concentrations fall in patients with primary type II hyperlipoproteinemia.

Clinically, all of the bile acid sequestrants lower LDL and total cholesterol and are approved for the treatment of primary hypercholesterolemia. Cholestyramine is also indicated to treat pruritus secondary to cholestasis. Colesevelam also reduces apolipoprotein B (apoB) and increases HDL cholesterol. Colesevelam recently received approval as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Triglycerides increase with colestipol therapy. Thus, colestipol is appropriate for type II hyperlipoproteinemia without hypertriglyceridemia.

Because bile acid sequestrants are not systemically absorbed, they are often preferred for the treatment of hyperlipidemia during pregnancy. However, GI-related adverse events occur very frequently. The most common adverse event is constipation that is usually mild and transient but can produce fecal impaction. Additionally, these agents tend to be unpalatable (mainly the powders and granules) and have a higher discontinuation rate compared to other antilipemics.

Cholestyramine is available as a powder packaged in bulk canisters and packets; there are regular and sugar-free varieties. The sugar-free products contain aspartame and should not be given to patients with phenylketonuria. Colestipol offers granules (canisters and packets), flavored granules (canisters and packets), and tablets. Colestipol flavored granules have been reported by patients to be more palatable than the regular granules; the tablet provides a more convenient dosage form and eliminates the need to consume a gritty slurry. Colesevelam is available in tablet form only. To date, there are no published clinical trials to support the claim that any one agent has a lower incidence of side effects than the other agents in the class.

Generic Name	Brand Name	Manufacturer	Generic Available
Cholestyramine	Questran [®] , Questran [®] Light, Prevalite [®]	Various	Yes
Colesevelam	WelChol [®]	Sankyo	No
Colestipol	Colestid [®]	Pfizer, various	Yes

Summary:

The bile acid sequestrants appear to be equally efficacious in the treatment of hyperlipidemia. Currently, these agents are primarily used in combination with HMG-CoA reductase inhibitors when additional LDL-C or total cholesterol lowering is required. Colestipol and colesevelam offer a tablet, which is a more convenient and, perhaps, more palatable dosage form. There are no head-to-head studies between colesevelam and cholestyramine or colestipol to support a lower incidence of gastrointestinal side effects with colesevelam. Cholestyramine and colestipol are available generically. Selection of an agent for the preferred drug list should be based upon the total cost impact to the program.