BlueCross BlueShield Federal Employee Program

JUXTAPID
(lomitapide)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Juxtapid is a microsomal triglyceride transfer protein inhibitor used to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol, apolipoprotein B (apo-B), and non-high-density lipoprotein cholesterol in patients with homozygous familial hypercholesterolemia. Juxtapid is intended for use in combination with a low fat diet, supplying <20% of energy from fat, and other lipid-lowering treatments. Juxtapid directly binds and inhibits microsomal triglyceride transfer protein (MTP), which resides in the lumen of the endoplasmic reticulum, thereby preventing the assembly of apo B-containing lipoproteins in enterocytes and hepatocytes. This inhibits the synthesis of chylomicrons and VLDL. The inhibition of the synthesis of VLDL leads to reduced levels of plasma LDL-C (1).

Regulatory Status

FDA-approved indication: Juxtapid is a microsomal triglyceride transfer protein inhibitor indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH) (1).

Limitations of Use: (1)

1. The safety and effectiveness of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH.
2. The effect of Juxtapid on cardiovascular morbidity and mortality has not been determined.

Juxtapid carries a boxed warning regarding a serious risk of hepatotoxicity and accumulation of fat in the liver. Juxtapid can cause elevations in transaminases. Juxtapid also increases hepatic fat (hepatic steatosis) with or without concomitant increases in transaminases. Hepatic steatosis associated with Juxtapid treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis (1).

Juxtapid is contraindicated in patients with moderate or severe hepatic impairment (based on Child-Pugh category B or C), or active liver disease, including unexplained persistent elevations of serum transaminases. Before beginning treatment with Juxtapid, measure alanine

aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin. During the first year, measure liver-related tests (ALT and AST, at a minimum) prior to each increase in dose or monthly, whichever occurs first. After the first year, do these tests at least every 3 months and before any increase in dose. Modify the dose of Juxtapid if elevations of transaminases are ≥3x ULN are observed. Discontinue treatment with Juxtapid if persistent or clinically significant elevations of transaminase occur or if the elevations are accompanied by clinical symptoms of liver injury or toxicity, increases in bilirubin ≥2x ULN, or active liver disease (1).

CYP3A4 inhibitors increase the exposure of Juxtapid, with strong inhibitors increasing exposure approximately 27-fold. Concomitant use of moderate or strong CYP3A4 inhibitors with Juxtapid is contraindicated (1).

Based on findings from animal studies, Juxtapid is contraindicated in pregnant women since it may cause fetal harm. Females of reproductive potential should have a negative pregnancy test before starting Juxtapid and should be advised to use effective contraception during therapy with Juxtapid and for two weeks after the final dose. If pregnancy is detected, discontinue Juxtapid (1).

Because of the risk of hepatotoxicity, Juxtapid is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Juxtapid REMS Program. Under the Juxtapid REMS, only certified healthcare providers and pharmacies may prescribe and distribute Juxtapid (1).

Safety and effectiveness of Juxtapid in patients less than 18 years of age have not been established (1).

Summary

Juxtapid is a microsomal triglyceride transfer protein inhibitor indicated as an adjunct to a low-fat diet and other lipid lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). Juxtapid carries a boxed warning of hepatic steatosis and hepatotoxicity which requires frequent liver function monitoring. Juxtapid is contraindicated in

pregnancy. Concomitant administration of Juxtapid with moderate or strong CYP3A4 inhibitors or in patients with moderate or severe hepatic impairment or active liver disease is contraindicated (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Juxtapid while maintaining optimal therapeutic outcomes.

References

1. Juxtapid [package insert]. Dublin, Ireland; Amryt Pharma Group; September 2020.