Juxtapid

Description

Juxtapid (lomitapide)

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.

The Juxtapid label includes a boxed warning of the risk of hepatotoxicity. 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, 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).

Juxtapid has a pregnancy category X; therefore, it is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Based on animal data, Juxtapid may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should have a negative pregnancy test before starting Juxtapid and should use effective contraception during therapy with Juxtapid (1).

Because of the risk of hepatotoxicity associated with Juxtapid therapy, Juxtapid is available through a restricted program under the REMS. Under the Juxtapid REMS, only certified healthcare providers and pharmacies may prescribe and distribute Juxtapid (1).

Safety and effectiveness have not been established in pediatric patients (1).
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**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Juxtapid may be considered **medically necessary** in patients 18 years of age and older with a diagnosis of homozygous familial hypercholesterolemia and if the conditions indicated below are met.

Juxtapid is considered **investigational** in patients who are less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**

18 years of age or older

**Diagnosis**

Patient must have the following:

Homozygous familial hypercholesterolemia

**AND ALL** of the following:

1. Documented confirmation of diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
2. Genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus
3. Recent ALT, AST, alkaline phosphatase, and total bilirubin levels
   a. Agreement to monitor levels after a dose increase or at least monthly for the first year
4. Used in conjunction with a low fat diet
5. Used in combination with other lipid-lowering treatments
6. **NO** moderate or severe hepatic impairment (Child-Pugh B or C) or active liver disease
7. If patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and after treatment
8. Physician is enrolled in the Juxtapid REMS program
9. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 inhibitor

**Prior – Approval Renewal Requirements**

**Age**
18 years of age or older

**Diagnosis**
Patient must have the following:

- **Homozygous familial hypercholesterolemia**

  **AND ALL** of the following:
  1. Agreement to monitor ALT, AST, alkaline phosphatase, and total bilirubin levels every 3 months.
  2. Used in conjunction with a low fat diet
  3. Used in combination with other lipid-lowering treatments
  4. **NO** moderate or severe hepatic impairment (Child-Pugh B or C) or active liver disease
  5. If patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and after treatment
  6. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 inhibitor

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

**Duration**
12 months

**Prior – Approval Renewal Limits**

**Duration**
12 months

**Rationale**
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 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

Policy History

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<td>April 2013</td>
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<td>June 2013</td>
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<td>September 2015</td>
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<tr>
<td>April 2016</td>
<td>Addition of documented confirmation of diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis; genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus. Change of not pregnant to if patient or their partner are of child bearing age, the patient has been or will be instructed to practice effective contraception during therapy and after treatment</td>
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<td>September 2019</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.