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5.40.01

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Cardiovascular Agents	**Original Policy Date:**	April 15, 2013
Subject:	Juxtapid	**Page:**	1 of 6

Last Review Date: June 16, 2022

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.

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).

Related policies
Evkeeka, Nexletol Nexlizet, Praluent, Repatha

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 may be 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. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Juxtapid and for 2 weeks after the final dose
8. Physician is enrolled in the Juxtapid REMS program
9. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Evkeeza, or Nexletol/Nexlizet

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. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Juxtapid and for 2 weeks after the final dose
6. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Evkeeza, or Nexletol/Nexlizet

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

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 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.

Policy History

Date	Action
April 2013	Addition to PA
June 2013	Annual review
June 2014	Annual review and reference update.
September 2015	Annual review and reference update
April 2016	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 Policy number change from 5.16.01 to 5.40.01
June 2016	Annual review
December 2016	Annual review and reference update

September 2017	Annual editorial review Addition of no dual therapy with a proprotein convertase subtilisin/kexin type 9 inhibitor or Kynamro (mipomersen)
September 2018	Annual review and reference update
September 2019	Annual editorial review. Removal of Kynamro from dual therapy questions
June 2020	Annual review
September 2020	Annual review and reference update
March 2021	Addition of requirement: no dual therapy with Nexletol/Nexlizet Revised pregnancy requirement removing males with partners of reproductive potential
June 2021	Annual editorial review. Revised dual therapy requirement to include not dual therapy with Evkeeza.
June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.