HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use JUXTAPID safely and effectively. See full prescribing information for JUXTAPID.

JUXTAPID™ (lomitapide) capsules, for oral use
Initial U.S. Approval: 2012

WARNING: RISK OF HEPATOTOXICITY
See full prescribing information for complete boxed warning.

JUXTAPID can cause elevations in transaminases (5.1).

- **Measure alanine and aspartate aminotransferases (ALT, AST), alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended (2.4, 5.1).**
- **During treatment, adjust the dose of JUXTAPID if the ALT or AST is ≥3 times the upper limit of normal (ULN) (2.4, 5.1).**
- **Discontinue JUXTAPID for clinically significant liver toxicity (2.4, 5.1).**

JUXTAPID increases hepatic fat (hepatic steatosis) with or without concomitant increases in transaminases (5.1).

- **Hepatic steatosis associated with JUXTAPID may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis (5.1).**

Because of the risk of hepatotoxicity, JUXTAPID is available only through a restricted program called the JUXTAPID REMS PROGRAM (5.2).

---------- INDICATIONS AND USAGE----------

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

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

----------DOSAGE AND ADMINISTRATION----------

- Before treatment, measure ALT, AST, alkaline phosphatase, and total bilirubin; obtain a negative pregnancy test in females of reproductive potential; and initiate a low-fat diet supplying <20% of energy from fat (2.1).
- Initiate treatment at 5 mg once daily. Titrate dose based on acceptable safety/tolerability: increase to 10 mg daily after at least 2 weeks; and then, at a minimum of 4-week intervals, to 20 mg, 40 mg, and up to the maximum recommended dose of 60 mg daily (2.1).
- Due to reduced absorption of fat-soluble vitamins/fatty acids: Take daily vitamin E, linoleic acid, alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) supplements (2.1, 5.4)
- Take once daily, whole, with water and without food, at least 2 hours after evening meal (2.2).
- Patients with end-stage renal disease on dialysis or with baseline mild hepatic impairment should not exceed 40 mg daily (2.5, 2.6).

---------- DOSAGE FORMS AND STRENGTHS----------

Capsules: 5 mg, 10 mg, and 20 mg (3).

---------- CONTRAINDICATIONS ----------

- Pregnancy (4)
- Concomitant use with strong or moderate CYP3A4 inhibitors (4).
- Moderate or severe hepatic impairment or active liver disease including unexplained persistent abnormal liver function tests (4).

---------- WARNINGS AND PRECAUTIONS ----------

- Embryo-Fetal Toxicity: Females of Reproductive Potential should have a negative pregnancy test before starting JUXTAPID and use contraception during treatment (5.3)
- Gastrointestinal adverse reactions occur in 93% of patients and could affect absorption of concomitant oral medications (5.5).

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (incidence ≥28%) are diarrhea, nausea, vomiting, dyspepsia, and abdominal pain (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Aegerion Pharmaceuticals at 1-855-303-2347 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS----------

- CYP3A4 inhibitors increase exposure to lomitapide. Strong and moderate CYP3A4 inhibitors are contraindicated with JUXTAPID. Patients must avoid grapefruit juice. Do not exceed 30 mg daily of JUXTAPID when used concomitantly with weak CYP3A4 inhibitors, including atorvastatin and oral contraceptives (2.3, 4, 5.6, 7.1, 7.2).
- Warfarin: Lomitapide increases plasma concentrations of warfarin. Monitor international normalized ratio (INR) regularly, especially with JUXTAPID dose adjustment (5.8, 7.3).
- Simvastatin and lovastatin exposure increase with JUXTAPID. Limit dose when co-administered with JUXTAPID due to myopathy risk (5.7, 7.4).
- P-glycoprotein (P-gp) Substrates: Consider dose reduction of P-gp substrate because of possible increased absorption with JUXTAPID (7.5).
- Bile Acid Sequestrants: Separate JUXTAPID dosing by at least 4 hours (7.6).

---------- USE IN SPECIFIC POPULATIONS ----------

- Nursing mothers: Discontinue drug or nursing (8.3).
- Pediatric Patients: Safety and effectiveness not established (8.4).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised:

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF HEPATOTOXICITY

JUXTAPID can cause elevations in transaminases. In the JUXTAPID clinical trial, 10 (34%) of the 29 patients treated with JUXTAPID had at least one elevation in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), or alkaline phosphatase *[see Warnings and Precautions (5.1)]*.

JUXTAPID also increases hepatic fat, with or without concomitant increases in transaminases. The median absolute increase in hepatic fat was 6% after both 26 and 78 weeks of treatment, from 1% at baseline, measured by magnetic resonance spectroscopy. Hepatic steatosis associated with JUXTAPID treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis *[see Warnings and Precautions (5.1)]*.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended. During treatment, adjust the dose of JUXTAPID if the ALT or AST are ≥3x ULN. Discontinue JUXTAPID for clinically significant liver toxicity [*see Dosage and Administration (2.4)* and *Warnings and Precautions (5.1)*].

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 *[see Warnings and Precautions (5.2)]*.

1 INDICATIONS AND USAGE

1.1 Homozygous Familial Hypercholesterolemia

JUXTAPID is 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).

Limitations of Use

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

2 DOSAGE AND ADMINISTRATION

2.1 Initiation and Maintenance of Therapy

Before beginning treatment with JUXTAPID:

- Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin *[see Warnings and Precautions (5.1)]*;
- Obtain a negative pregnancy test in females of reproductive potential *[see Warnings and Precautions (5.3)]*; and,
- Initiate a low-fat diet supplying <20% of energy from fat *[see Warnings and Precautions (5.5)]*.

The recommended starting dosage of JUXTAPID is 5 mg once daily, and the dose should be escalated gradually based on acceptable safety and tolerability. Transaminases should be measured prior to any increase in dose *[see Warnings and Precautions (5.1)]*. The maintenance dosage of JUXTAPID should be individualized, taking into account patient characteristics such as goal of therapy and response to treatment, to a maximum of 60 mg daily as described in Table 1. Modify dosing for patients taking concomitant CYP3A4 inhibitors, renal impairment, or baseline hepatic impairment *[see Dosing and Administration (2.3), (2.5), and (2.6)]*. Dose adjustments are also required for patients who develop transaminase values ≥3x the upper limit of normal (ULN) during treatment with JUXTAPID *[see Dosage and Administration (2.4)]*.

Table 1: Recommended Regimen for Titrating Dosage

DOSAGE	DURATION OF ADMINISTRATION BEFORE CONSIDERING INCREASE TO NEXT DOSAGE
5 mg daily	At least 2 weeks
10 mg daily	At least 4 weeks
20 mg daily	At least 4 weeks
40 mg daily	At least 4 weeks
60 mg daily	Maximum recommended dosage

To reduce the risk of developing a fat-soluble nutrient deficiency due to JUXTAPID's mechanism of action in the small intestine, patients treated with JUXTAPID should take daily supplements that contain 400 international units vitamin E and at least 200 mg linoleic acid, 210 mg alpha-linolenic acid (ALA), 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA) *[see Warnings and Precautions (5.4)]*.

2.2 Administration

JUXTAPID should be taken once daily with a glass of water, without food, at least 2 hours after the evening meal because administration with food may increase the risk of gastrointestinal adverse reactions *[see Warnings and Precautions (5.5)]*. Patients should swallow JUXTAPID capsules whole. Capsules should not be opened, crushed, dissolved, or chewed.

2.3 Dosing with Cytochrome P450 3A4 Inhibitors

JUXTAPID is contraindicated with concomitant use of moderate and strong cytochrome P450 3A4 (CYP3A4) inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*.

The recommended maximum dosage of JUXTAPID is 30 mg daily with concomitant use of weak CYP3A4 inhibitors (such as alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide, cilostazol, cimetidine, cyclosporine, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, lapatinib, nilotinib, oral contraceptives, pazopanib, ranitidine, ranolazine, tipranavir/ritonavir, ticagrelor, zileuton) *[see Drug Interactions (7.2)]*.

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