Initial REMS Approval: 12/2012
Most Recent Modification: 8/2013

NDA 203858

JUXTAPID (lomitapide) capsules

Drug Class: Microsomal Triglyceride Transfer Protein Inhibitor (MTP-I)

Aegerion Pharmaceuticals, Inc. (Aegerion)
101 Main Street Suite 1850
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - the risk of hepatotoxicity associated with the use of JUXTAPID; and
  - the need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH).

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare Providers (HCP) who prescribe JUXTAPID are specially certified.

a. Aegerion will ensure HCPs who prescribe JUXTAPID are specially certified.

To become specially certified to prescribe JUXTAPID, prescribers must enroll in JUXTAPID REMS program. Prescribers must complete the following requirements:

i. Review the Prescribing Information (PI)

ii. Complete the *Prescriber Training Module*

iii. Complete and sign the *Prescriber Enrollment Form* and submit it to the JUXTAPID REMS Program.

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b. Aegerion will:

i. Ensure that the *Prescriber Training Module* and the *Prescriber Enrollment Form* are available on the JUXTAPID REMS Program website (www.JUXTAPIDREMSProgram.com), or can be obtained by contacting the JUXTAPID REMS Program by phone at 1-85-JUXTAPID (1-855-898-2743).Ensure that prescribers complete the *Prescriber Training Module* and *Prescriber Enrollment Form* before activating prescribers' certification in the JUXTAPID REMS Program.

ii. Ensure that prescribers are notified when they have been successfully certified by the JUXTAPID REMS Program.

iii. Inform certified prescribers following substantial changes to the JUXTAPID REMS or JUXTAPID REMS Program. Substantial changes include: significant changes to the operation of the JUXTAPID REMS Program or changes to the Prescribing Information that affect the risk-benefit profile of JUXTAPID.

iv. To facilitate prescriber certification, Aegerion will communicate information to prescribers and professional societies through JUXTAPID REMS Program website and *Dear Healthcare Provider* and *Dear Professional Society* letters.

1) *Dear Healthcare Provider* letter - Aegerion will distribute a *Dear Healthcare Provider* letter within 60 days of JUXTAPID REMS approval to inform potential prescribers about the REMS and the REMS requirements. The *Dear Healthcare Provider* letter will be distributed by mass mailing to healthcare providers certified by the American Board of Clinical Lipidology, directors of apheresis centers, and to healthcare providers known to be experienced in treating patients with HoFH. The letter will be accompanied by the PI and will be available from the JUXTAPID REMS Program website (www.JUXTAPIDREMSProgram.com) at the time of the mailing and will remain on the website for 12 months after the mailing, or can be requested from the JUXTAPID REMS Program by phone at 1-85-JUXTAPID (1-855-898-2743).

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2) *Dear Professional Society* letter - Aegerion will send a *Dear Professional Society* letter within 60 days of JUXTAPID REMS approval to the leadership of the following professional societies and will request that these societies disseminate the content of the letter to their professional membership:

   a) National Lipid Association

   b) The Endocrine Society

   c) The American Association of Clinical Endocrinologists

   d) American Heart Association

   e) American College of Cardiology

   f) American Society of Preventive Cardiology

   g) Preventive Cardiology Nurses Association

   h) American Society for Apheresis

   The letter will be provided to MedWatch at the same time it is provided to the professional organizations.

3) JUXTAPID REMS Program Website - A JUXTAPID REMS Program website (www.JUXTAPIDREMSProgram.com) will be available at the time of approval.

The *Prescriber Training Module- downloadable PDF and online versions, Prescriber Enrollment Form- downloadable PDF and online versions, Dear Healthcare Provider* and *Dear Professional Society* letters, and JUXTAPID REMS Program website are part of the JUXTAPID REMS and are appended.

2. JUXTAPID will be dispensed only by specially certified pharmacies.

a. Aegerion will ensure that JUXTAPID will only be dispensed by certified pharmacies.

b. To become certified to dispense JUXTAPID, each pharmacy representative must agree to the following:

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i. To educate all pharmacy staff involved in the dispensing of JUXTAPID on the JUXTAPID REMS Program requirements.

ii. Put processes and procedures in place to verify, prior to dispensing JUXTAPID, that:

1) the prescriber is certified in the JUXTAPID REMS Program.
2) the JUXTAPID REMS *Prescription Authorization Form* is received for each new prescription.

iii. To be audited to ensure that all processes and procedures are in place and are being followed for the JUXTAPID REMS Program.

iv. To provide prescription data to the JUXTAPID REMS Program.

The JUXTAPID REMS *Prescription Authorization Form* is part of the REMS and is appended.

3. JUXTAPID will be dispensed only to patients with evidence or other documentation of safe-use conditions.

a. JUXTAPID will only be dispensed to patients whose prescribers are specially certified in the JUXTAPID REMS Program and attest on the JUXTAPID REMS *Prescription Authorization Form* that:

i. they understand that 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);

ii. they affirm that their patient has a clinical or laboratory diagnosis consistent with HoFH;

iii. they understand that JUXTAPID has not been studied in patients less than 18 years of age; and

iv. liver-related laboratory tests have been obtained as directed in the PI.

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B. Implementation System

1. Aegerion will ensure that JUXTAPID is distributed to and dispensed only by certified pharmacies.
2. Aegerion will maintain, monitor, and evaluate the implementation of the JUXTAPID REMS program.
    a. Aegerion will develop and follow written procedures and scripts to implement the REMS.
    b. Aegerion will maintain a secure, validated database of all certified prescribers and pharmacies that is in compliance with 21 CFR Part 11 regulations.
    c. Aegerion will send confirmation of certification to each certified pharmacy.
    d. Aegerion will maintain a JUXTAPID REMS Program Coordinating Center with a Call Center to support patients, prescribers, and pharmacies in interfacing with the JUXTAPID REMS.
    e. Aegerion will ensure that all materials listed in or appended to the JUXTAPID REMS Program will be available through the JUXTAPID REMS Program website (www.JUXTAPIDREMSProgram.com) or by calling the JUXTAPID REMS Program Call Center at 1-85-JUXTAPID (1-855-898-2743).
    f. If there are substantive changes to the JUXTAPID REMS or JUXTAPID REMS Program, Aegerion will update all affected materials, and notify enrolled prescribers and certified pharmacies, as applicable. Substantive changes are defined as: significant changes to the operation of the JUXTAPID REMS Program or changes to the PI that affect the risk-benefit profile of JUXTAPID.
    g. Aegerion will monitor and audit the certified pharmacies to ensure that all processes and procedures are in place and functioning to support the requirements of the JUXTAPID REMS Program. Corrective action will be instituted by Aegerion if noncompliance is found.
    h. Based on monitoring and evaluation of the JUXTAPID REMS elements to assure safe use, Aegerion will take reasonable steps to improve implementation of these elements

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and to maintain compliance with the JUXTAPID REMS Program requirements, as applicable.

C. Timetable for Submission of Assessments

Aegerion will submit REMS Assessments to the FDA 6 months, 12 months, and annually thereafter from the date of initial approval of this REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Aegerion will submit each assessment so that it will be received by the FDA on or before the due date.

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APPENDIX 1

PRESCRIBER TRAINING MODULE

- Online Version
- Downloadable Version

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Important Safety Information | Prescribing Information | Medication Guide | Contact REMS

Create Profile

Please complete the following information in order to register for and access the REMS program training module.

* Required Fields

*First Name :

*Last Name :

*Email :

Zip Code :

Submit

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Indication and Important Safety Information

EXPAND SAFETY INFORMATION

INDICATION

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COLLAPSE SAFETY INFORMATION

INDICATION

JUXTAPID is a microsomal triglyceride transfer protein (MTP) 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).

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.

IMPORTANT SAFETY 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.

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.

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.

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.

CONTRAINDICATIONS

- Pregnancy
- Concomitant administration of moderate or strong CYP3A4 inhibitors
- Moderate or severe hepatic impairment or active liver disease including unexplained persistent elevations of serum transaminases

WARNINGS AND PRECAUTIONS

JUXTAPID can cause elevations in transaminases and hepatic steatosis. Although cases of hepatic failure have not been reported, there is concern that JUXTAPID could induce steatohepatitis, which can progress to cirrhosis over several years. Modify the dose of JUXTAPID if elevations of transaminases are observed and discontinue JUXTAPID for persistent or clinically significant elevations. If transaminase elevations are accompanied by clinical symptoms of liver injury, such as nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like-symptoms, increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause. Use JUXTAPID with caution when co-administered with agents known to be hepatotoxic. Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment. 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.

Females of reproductive potential should have a negative pregnancy test before starting JUXTAPID and should use effective contraception during therapy with JUXTAPID.

Given its mechanism of action in the small intestine, JUXTAPID may reduce the absorption of fat-soluble nutrients. 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).

Gastrointestinal adverse reactions are common and may lead to treatment discontinuation. To reduce the risk of gastrointestinal adverse reactions, patients should adhere to a low-fat diet supplying less than 20% of energy from fat and the dosage of JUXTAPID should be increased gradually.

Combination with CYP3A4 inhibitors increases exposure to lomitapide. Strong and moderate CYP3A4 inhibitors should not be used with JUXTAPID. JUXTAPID dosage should not exceed 30 mg daily when used concomitantly with weak CYP3A4 inhibitors.

Due to risk of myopathy associated with simvastatin or lovastatin, doses of these agents should be limited when co-administered with JUXTAPID.

JUXTAPID increases the plasma concentrations of warfarin. Increases or decreases in the dose of JUXTAPID may lead to supra- or subtherapeutic anticoagulation, respectively. Patients taking warfarin should undergo regular monitoring of the INR, especially after any changes in JUXTAPID dosage.

Avoid use of JUXTAPID in patients with rare hereditary disorders of galactose intolerance.

ADVERSE REACTIONS

The most common adverse reactions were gastrointestinal, reported by 27 (93%) of 29 patients. Adverse reactions reported by 8 (28%) or more patients in the HoFH clinical trial included diarrhea, nausea, vomiting, dyspepsia and abdominal pain. Other common adverse reactions, reported by 5 to 7 (17-24%) patients, included weight loss, abdominal discomfort, abdominal distension, constipation, flatulence, increased ALT, chest pain, influenza, nasopharyngitis, and fatigue.

Reporting of Adverse Reactions

All healthcare professionals should report all suspected adverse reactions. Please contact Aegerion Pharmaceuticals, Inc. at 1-855-303-2347 or the FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.

Please see Prescribing Information including BOXED WARNING.

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JUXTAPID
Risk Evaluation and Mitigation Strategy (REMS) Program

PRESCRIBER TRAINING MODULE

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Introduction

JUXTAPID is available only through a restricted program called the JUXTAPID REMS Program.

- Prescribers must complete this training module and enroll in the JUXTAPID REMS Program prior to prescribing JUXTAPID.

The purpose of this training module is to educate prescribers about the JUXTAPID REMS Program.

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - The risk of hepatotoxicity associated with the use of JUXTAPID;
  - The need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH).

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Indication

JUXTAPID (lomitapide) 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.

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Appropriate Patient Selection

Key considerations for appropriate patient selection:

- JUXTAPID is indicated for use in patients with HoFH.
- Patient must have a clinical or laboratory diagnosis consistent with HoFH.
- JUXTAPID has not been studied in pediatric patients less than 18 years.

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Boxed Warning

WARNING: RISK OF HEPATOTOXICITY

- JUXTAPID (lomitapide) 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.
- 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.
- 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.

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Risk of Hepatotoxicity

JUXTAPID can cause elevations in transaminases and hepatic steatosis. Although cases of hepatic failure have not been reported, there is concern that JUXTAPID could induce steatohepatitis, which can progress to cirrhosis over several years. If transaminase elevations are accompanied by clinical symptoms of liver injury, such as nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like-symptoms, increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause.

Clinical data suggest that hepatic fat accumulation is reversible after stopping treatment with JUXTAPID, but whether histological sequelae remain is unknown.

Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury.

- Patients taking JUXTAPID should not consume more than 1 alcoholic drink per day.

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Risk of Hepatotoxicity

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Caution should be exercised when JUXTAPID is used with other medications known to have potential for hepatotoxicity, including:

- isotretinoin,
- amiodarone,
- acetaminophen (greater than >4 g/day for ≥3 days/week),
- methotrexate,
- tetracyclines, and
- tamoxifen.

The effect of concomitant administration of JUXTAPID with other hepatotoxic medications is unknown. More frequent monitoring of liver-related laboratories may be warranted.

JUXTAPID has not been studied concomitantly with other LDL-lowering agents that can also increase hepatic fat. Therefore, the combined use of such agents is not recommended.

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Dosing and Administration

- JUXTAPID is a once-daily oral therapy.
- JUXTAPID should be taken in the evening, with a glass of water, without food, and at least 2 hours after dinner.
- 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.
- Prior to initiating JUXTAPID treatment, patients should follow a low-fat diet supplying less than 20% of energy from fat and should continue this diet during treatment.
- To reduce the risk of gastrointestinal adverse events, patients should adhere to a low-fat diet supplying less than 20% of energy from fat and the dosage of JUXTAPID should be increased gradually.

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Dosing and Administration

CONTINUED FROM PREVIOUS SLIDE

- The recommended starting daily dose of JUXTAPID is 5 mg.
- The dose should be escalated gradually based on acceptable safety and tolerability.
  - After 2 weeks, increase the dose, based on acceptable safety and tolerability, to 10 mg daily.
  - Then, at a minimum of 4-week intervals, to daily 20 mg, 40 mg, and the maximum recommended dose of 60 mg.

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

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Patient Monitoring of Transaminases

Timing	Recommendations
Prior to initiating JUXTAPID	Screen for ALT, AST, alkaline phosphatase and total bilirubin elevations.
During dose escalation of JUXTAPID	Check ALT and AST (at a minimum) prior to each dose escalation.
During maintenance therapy, once patient has been stabilized on an individualized dose	During the first year check ALT and AST (at a minimum) monthly. After the first year do these tests at least every 3 months and before any increase in dose.

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Patient Monitoring of Transaminases

In the event that ALT/AST elevations occur during therapy with JUXTAPID, the recommendations below should be followed:

ALT OR AST	Treatment and Monitoring Recommendations
≥3x and <5x ULN	• Confirm elevation with a repeat measurement within one week. • If confirmed, reduce the dose and obtain additional liver-related tests if not already measured (such as alkaline phosphatase, total bilirubin, and INR). • Repeat tests weekly and withhold dosing if there are signs of abnormal liver function (increase in bilirubin or INR), if transaminase levels rise above 5x ULN, or if transaminase levels do not fall below 3x ULN within approximately 4 weeks. In these cases of persistent or worsening abnormalities, also investigate to identify the probable cause. • If resuming JUXTAPID after transaminases resolve to <3x ULN, consider reducing the dose and monitor liver-related tests more frequently.

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Patient Monitoring of Transaminases

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In the event that ALT/AST elevations occur during therapy with JUXTAPID, the recommendations below should be followed:

ALT OR AST	Treatment and Monitoring Recommendations
≥5x ULN	• Withhold dosing, obtain additional liver-related laboratories if not already measured (such as alkaline phosphatase, total bilirubin, and INR), and investigate to identify the probable cause. • If resuming JUXTAPID after transaminases resolve to <3x ULN, reduce the dose and monitor liver-related laboratories more frequently.
	Stopping Treatment: If liver aminotransferase elevations are accompanied by clinical symptoms of liver injury (e.g., nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like symptoms) or increases in bilirubin ≥ 2 X ULN, or active liver disease, then stop treatment with JUXTAPID and investigate to identify the probable cause.

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Adverse Reaction Reporting

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.

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JUXTAPID REMS Program

Key program elements:

- Prescriber training on the risk of hepatotoxicity associated with the use of JUXTAPID, appropriate patient selection and the need to monitor patients during treatment.
- Prescribers of JUXTAPID must be certified.
  - Certification consists of reviewing training and enrolling into JUXTAPID REMS program.
- Documentation of safe use conditions required for dispensing JUXTAPID:
  - Prescribers must use a Prescription Authorization Form for each new prescription to ensure safe use of JUXTAPID.
- Controlled distribution of JUXTAPID through certified pharmacies.

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JUXTAPID REMS Program

Before prescribing JUXTAPID, prescribers must complete the following steps:

1. Review the Prescribing Information and this Prescriber Training Module.
2. Complete, sign and submit the one-time JUXTAPID REMS Program Prescriber Enrollment Form.
3. Complete, sign and submit the JUXTAPID REMS Program Prescription Authorization Form for each patient.

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Review Prescriber Education Materials

1 Review

Review the following Prescriber Education Materials:

a. JUXTAPID Prescribing Information
b. This Prescriber Training Module

Note

Materials can be accessed from the JUXTAPID REMS Program website at:
www.JUXTAPIDREMSProgram.com
Or request these materials by calling 1-85-JUXTAPID (1-855-898-2743).

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Enroll in JUXTAPID REMS Program

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I understand that JUXTAPID is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce LDL-C, TC, apo B and non HDL-C in patients with HoFH.
- I understand that JUXTAPID is only available through the JUXTAPID REMS Program and that I must comply with the program requirements in order to prescribe JUXTAPID.
- I have completed the JUXTAPID REMS Prescriber Training Module.
- I understand that there is a risk of hepatotoxicity associated with JUXTAPID.

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Reference ID: 3356376

Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I understand that serum ALT, AST, alkaline phosphatase, and total bilirubin levels must be measured before initiating therapy with JUXTAPID.
- I understand that during the first year of treatment with JUXTAPID liver-related laboratory tests (ALT and AST at a minimum) must be measured prior to each increase in dose or monthly, whichever comes first.
- I understand that after the first year, these parameters must be measured at least every 3 months and before any increase in dose.
- I understand that JUXTAPID has not been studied in patients less than 18 years of age.

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Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I agree that personnel from the JUXTAPID REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to JUXTAPID or the JUXTAPID REMS Program.
- I will complete and submit a JUXTAPID REMS Program *Prescription Authorization Form* for each new prescription.
- I agree that Aegerion, its agents and contractors such as the pharmacy providers may contact me via phone, mail, or email to survey me on the effectiveness of the program requirements for the JUXTAPID REMS Program.

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Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

You can enroll in the JUXTAPID REMS program in two ways:

1. Online at **enrollment.JUXTAPIDREMSProgram.com or**
2. Download the JUXTAPID REMS Program Prescriber Enrollment Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
   - Complete the Enrollment Form and return via fax or email
     - Fax to 1-855-898-2498 or
     - Scan and email to REMS@aegerion.com

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Submit Prescription Authorization Form

3 Submit

When prescribing JUXTAPID, a prescriber must complete a Prescription Authorization Form for each new prescription.

By completing the Prescription Authorization Form, the prescriber attests:

Prescriber Attestation

- I understand that 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 HoFH.
- I affirm that my patient has a clinical or laboratory diagnosis consistent with HoFH.
- I understand that JUXTAPID has not been studied in pediatric patients less than 18 years.
- I attest that I have obtained the liver-related laboratory tests for this patient as directed in the JUXTAPID prescribing information.

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Submit Prescription Authorization Form

CONTINUED FROM PREVIOUS SLIDE

3 Submit

Prescribers must complete a Prescription Authorization Form and submit to a certified pharmacy:

- Download the Prescription Authorization Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
- Complete the Prescription Authorization Form
- Sign and submit the Prescription Authorization Form:
  - Fax to 1-855-898-2498 or
  - Scan and email to REMS@aegerion.com

  (Either will route directly to the certified pharmacy)

Note

For a list of certified pharmacies call: 1-85-JUXTAPID (1-855-898-2743)

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Recommended Patient Counseling Information

Patients should be informed of the risk of hepatotoxicity and the need for regular blood tests.

When counseling a patient on initiating JUXTAPID:

- Advise the patient of the risk of hepatotoxicity and the need to have regular blood tests performed to monitor for evidence of liver injury or dysfunction
- Inform the patient about the existence and purpose of a JUXTAPID REMS Program including dispensing only through certified pharmacies.
- For Females of Reproductive Potential: Confirm the absence of pregnancy and counsel the patient about the potential for fetal harm. Instruct her to use reliable methods of contraception and confirm use. Instruct patients to contact their prescriber immediately and stop taking JUXTAPID if pregnancy should occur.

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Knowledge Assessment

The following questions about JUXTAPID are provided to reinforce learning.

Provide the correct answer to the following questions.

If you have difficulty answering these questions, please review the previous slides and refer to the Prescribing Information.

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Knowledge Assessment

Question 1

Which of the following statements is TRUE?

- JUXTAPID is contraindicated in patients with moderate and severe hepatic impairment
- JUXTAPID can cause elevations in transaminases (ALT and AST)
- JUXTAPID increases hepatic fat with or without concomitant increases in transaminases
- All of the above

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Knowledge Assessment

Question 1

Which of the following statements is TRUE?

- JUXTAPID is contraindicated in patients with moderate and severe hepatic impairment
- JUXTAPID can cause elevations in transaminases (ALT and AST)
- JUXTAPID increases hepatic fat with or without concomitant increases in transaminases
- **All of the above**

Correct answer

Answer

JUXTAPID is associated with a risk of hepatotoxicity.

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Knowledge Assessment

Question 1

Which of the following statements is TRUE?

- JUXTAPID is contraindicated in patients with moderate and severe hepatic impairment
- JUXTAPID can cause elevations in transaminases (ALT and AST)
- JUXTAPID increases hepatic fat with or without concomitant increases in transaminases
- **All of the above**

Incorrect answer. Correct answer is **All of the above**

Answer

JUXTAPID is associated with a risk of hepatotoxicity.

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Knowledge Assessment

Question 2

In the first year of treatment, liver-related tests (ALT and AST at minimum) should be evaluated:

- A. Prior to an increase in dose
- B. Monthly
- C. Every three months
- Answers A and B
- Answers A and C

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Knowledge Assessment

Question 2

In the first year of treatment, liver-related tests (ALT and AST at minimum) should be evaluated:

- A. Prior to an increase in dose
- B. Monthly
- C. Every three months
- **Answers A and B**
- Answers A and C

Correct answer

Answer

ALT, AST, alkaline phosphatase, and total bilirubin should be measured before initiation of treatment with JUXTAPID. During the first year, measure liver-related tests (ALT and AST at 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.

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Knowledge Assessment

Question 2

In the first year of treatment, liver-related tests (ALT and AST at minimum) should be evaluated:

- A. Prior to an increase in dose
- B. Monthly
- C. Every three months
- **Answers A and B**
- Answers A and C

Incorrect answer. Correct answer is **Answers A and B**

Answer

ALT, AST, alkaline phosphatase, and total bilirubin should be measured before initiation of treatment with JUXTAPID. During the first year, measure liver-related tests (ALT and AST at 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.

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Knowledge Assessment

Question 3

The goal(s) of the JUXTAPID REMS Program are:

- To educate prescribers about the risk of hepatotoxicity associated with the use of JUXTAPID.
- To educate prescribers about the need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.
- All of the above
- None of the above

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Knowledge Assessment

Question 3

The goal(s) of the JUXTAPID REMS Program are:

- To educate prescribers about the risk of hepatotoxicity associated with the use of JUXTAPID.
- To educate prescribers about the need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.
- **All of the above**
- None of the above

Correct answer

Answer

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - the risk of hepatotoxicity associated with the use of JUXTAPID; and
  - the need to monitor patients during treatment with JUXTAPID as per product labeling
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.

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Knowledge Assessment

Question 3

The goal(s) of the JUXTAPID REMS Program are:

- To educate prescribers about the risk of hepatotoxicity associated with the use of JUXTAPID.
- To educate prescribers about the need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.
- **All of the above**
- None of the above

Incorrect answer. Correct answer is **All of the above**

Answer

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - the risk of hepatotoxicity associated with the use of JUXTAPID; and
  - the need to monitor patients during treatment with JUXTAPID as per product labeling
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.

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Knowledge Assessment

Question 4

At initiation of treatment, which of the following liver-related laboratories should be measured:

- ALT and AST
- Alkaline phosphatase
- Total bilirubin
- All of the above

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Knowledge Assessment

Question 4

At initiation of treatment, which of the following liver-related laboratories should be measured:

- ALT and AST
- Alkaline phosphatase
- Total bilirubin
- **All of the above**

Correct answer

Answer

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiation of treatment with JUXTAPID.

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Knowledge Assessment

Question 4

At initiation of treatment, which of the following liver-related laboratories should be measured:

- ALT and AST
- Alkaline phosphatase
- Total bilirubin
- **All of the above**

Incorrect answer. Correct answer is **All of the above**

Answer

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiation of treatment with JUXTAPID.

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Knowledge Assessment

Question 5

How often should the Prescription Authorization Form be completed:

- Each new prescription
- Only on the first prescription
- Every refill
- Once a year

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Knowledge Assessment

Question 5

How often should the Prescription Authorization Form be completed:

- Each new prescription
- Only on the first prescription
- Every refill
- Once a year

Correct answer

Answer

For each new prescription, the prescriber must complete a Prescription Authorization Form.

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Knowledge Assessment

Question 5

How often should the Prescription Authorization Form be completed:

- Each new prescription
- Only on the first prescription
- Every refill
- Once a year

Incorrect answer. Correct answer is **Each new prescription**

Answer

For each new prescription, the prescriber must complete a Prescription Authorization Form.

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Knowledge Assessment

Question 6

A patient has an ALT value 4x ULN on treatment with JUXTAPID. The appropriate action is:

- Withhold treatment until ALT <3x ULN
- Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN
- Permanently discontinue treatment and investigate to identify probable cause
- Continue with the same dose of JUXTAPID and repeat ALT measurement monthly

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Knowledge Assessment

Question 6

A patient has an ALT value 4x ULN on treatment with JUXTAPID. The appropriate action is:

- Withhold treatment until ALT <3x ULN
- **Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN**
- Permanently discontinue treatment and investigate to identify probable cause
- Continue with the same dose of JUXTAPID and repeat ALT measurement monthly

Correct answer

Answer

Confirm elevation with a repeat measurement within one week. If confirmed, reduce the dose and obtain additional liver-related laboratories if not already measured (such as alkaline phosphatase, total bilirubin, and INR). Repeat transaminase measurements weekly, withhold dosing if transaminase levels do not fall below 3x ULN within 4 weeks, or if levels rise above 5x ULN , and investigate to identify the probable cause.

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Knowledge Assessment

Question 6

A patient has an ALT value 4x ULN on treatment with JUXTAPID. The appropriate action is:

- Withhold treatment until ALT <3x ULN
- **Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN**
- Permanently discontinue treatment and investigate to identify probable cause
- Continue with the same dose of JUXTAPID and repeat ALT measurement monthly

Incorrect answer. Correct answer is **Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN**

Answer

Confirm elevation with a repeat measurement within one week. If confirmed, reduce the dose and obtain additional liver-related laboratories if not already measured (such as alkaline phosphatase, total bilirubin, and INR). Repeat transaminase measurements weekly, withhold dosing if transaminase levels do not fall below 3x ULN within 4 weeks, or if levels rise above 5x ULN , and investigate to identify the probable cause.

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Knowledge Assessment

Question 7

JUXTAPID is available only through certified pharmacies

- True
- False

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Knowledge Assessment

Question 7

JUXTAPID is available only through certified pharmacies

- True
- False

Correct answer

Answer

JUXTAPID is available only through pharmacies that are specially certified and agree to follow the REMS requirements.

NOTE: For a list of certified pharmacies call: 1-85-JUXTAPID (1-855-898-2743)

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Knowledge Assessment

Question 7

JUXTAPID is available only through certified pharmacies

- True
- False

Incorrect answer. Correct answer is True

Answer

JUXTAPID is available only through pharmacies that are specially certified and agree to follow the REMS requirements.

NOTE: For a list of certified pharmacies call: 1-85-JUXTAPID (1-855-898-2743)

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Indication and Important Safety Information

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INDICATION

Completion of JUXTAPID REMS Program Training

You Have Completed the JUXTAPID REMS Program Training

You can enroll in the JUXTAPID REMS program in two ways:

1. Online at **enrollment.JUXTAPIDREMSProgram.com** or
2. Download the JUXTAPID REMS Program Prescriber Enrollment Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
   - Complete the Enrollment Form and return via fax or email
     - Fax to 1-855-898-2498 or
     - Scan and email to REMS@aegerion.com

For more information on the JUXTAPID REMS Program, please call 1-85-JUXTAPID (1-855-898-2743) or visit www.JUXTAPIDREMSProgam.com

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JUXTAPID

Risk Evaluation and Mitigation Strategy (REMS) Program

PRESCRIBER TRAINING MODULE

Reference ID: 3356376

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INTRODUCTION

Introduction

JUXTAPID is available only through a restricted program called the JUXTAPID REMS Program.

- Prescribers must complete this training module and enroll in the JUXTAPID REMS Program prior to prescribing JUXTAPID.

The purpose of this training module is to educate prescribers about the JUXTAPID REMS Program.

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - The risk of hepatotoxicity associated with the use of JUXTAPID;
  - The need to monitor patients during treatment with JUXTAPID as per product labeling.
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH).

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JUXTAPID PRODUCT INFORMATION

Indication

JUXTAPID (lomitapide) 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.

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Appropriate Patient Selection

Key considerations for appropriate patient selection:

- JUXTAPID is indicated for use in patients with HoFH.
- Patient must have a clinical or laboratory diagnosis consistent with HoFH.
- JUXTAPID has not been studied in pediatric patients less than 18 years.

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Boxed Warning

WARNING: RISK OF HEPATOTOXICITY

- JUXTAPID (lomitapide) 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.
- 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.
- 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.

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Risk of Hepatotoxicity

JUXTAPID can cause elevations in transaminases and hepatic steatosis. Although cases of hepatic failure have not been reported, there is concern that JUXTAPID could induce steatohepatitis, which can progress to cirrhosis over several years. If transaminase elevations are accompanied by clinical symptoms of liver injury, such as nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like-symptoms, increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause.

Clinical data suggest that hepatic fat accumulation is reversible after stopping treatment with JUXTAPID, but whether histological sequelae remain is unknown.

Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury.

- Patients taking JUXTAPID should not consume more than 1 alcoholic drink per day.

CONTINUED ON NEXT SLIDE

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Risk of Hepatotoxicity

CONTINUED FROM PREVIOUS SLIDE

Caution should be exercised when JUXTAPID is used with other medications known to have potential for hepatotoxicity, including:

- isotretinoin,
- amiodarone,
- acetaminophen (greater than >4 g/day for ≥3 days/week),
- methotrexate,
- tetracyclines, and
- tamoxifen.

The effect of concomitant administration of JUXTAPID with other hepatotoxic medications is unknown. More frequent monitoring of liver-related laboratories may be warranted.

JUXTAPID has not been studied concomitantly with other LDL-lowering agents that can also increase hepatic fat. Therefore, the combined use of such agents is not recommended.

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Dosing and Administration

- JUXTAPID is a once-daily oral therapy.
- JUXTAPID should be taken in the evening, with a glass of water, without food, and at least 2 hours after dinner.
- 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.
- Prior to initiating JUXTAPID treatment, patients should follow a low-fat diet supplying less than 20% of energy from fat and should continue this diet during treatment.
- To reduce the risk of gastrointestinal adverse events, patients should adhere to a low-fat diet supplying less than 20% of energy from fat and the dosage of JUXTAPID should be increased gradually.

CONTINUED ON NEXT SLIDE

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Dosing and Administration

CONTINUED FROM PREVIOUS SLIDE

- The recommended starting daily dose of JUXTAPID is 5 mg.
- The dose should be escalated gradually based on acceptable safety and tolerability.
  - After 2 weeks, increase the dose, based on acceptable safety and tolerability, to 10 mg daily.
  - Then, at a minimum of 4-week intervals, to daily 20 mg, 40 mg, and the maximum recommended dose of 60 mg.

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

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Reference ID: 3356376

Patient Monitoring of Transaminases

Timing	Recommendations
Prior to initiating JUXTAPID	Screen for ALT, AST, alkaline phosphatase and total bilirubin elevations.
During dose escalation of JUXTAPID	Check ALT and AST (at a minimum) prior to each dose escalation.
During maintenance therapy, once patient has been stabilized on an individualized dose	During the first year check ALT and AST (at a minimum) monthly. After the first year do these tests at least every 3 months and before any increase in dose.

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Reference ID: 3356376

Patient Monitoring of Transaminases

In the event that ALT/AST elevations occur during therapy with JUXTAPID, the recommendations below should be followed:

ALT OR AST	Treatment and Monitoring Recommendations
≥3x and <5x ULN	• Confirm elevation with a repeat measurement within one week. • If confirmed, reduce the dose and obtain additional liver-related tests if not already measured (such as alkaline phosphatase, total bilirubin, and INR). • Repeat tests weekly and withhold dosing if there are signs of abnormal liver function (increase in bilirubin or INR), if transaminase levels rise above 5x ULN, or if transaminase levels do not fall below 3x ULN within approximately 4 weeks. In these cases of persistent or worsening abnormalities, also investigate to identify the probable cause. • If resuming JUXTAPID after transaminases resolve to <3x ULN, consider reducing the dose and monitor liver-related tests more frequently.

CONTINUED ON NEXT SLIDE

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Patient Monitoring of Transaminases

CONTINUED FROM PREVIOUS SLIDE

In the event that ALT/AST elevations occur during therapy with JUXTAPID, the recommendations below should be followed:

ALT OR AST	Treatment and Monitoring Recommendations
≥5x ULN	• Withhold dosing, obtain additional liver-related laboratories if not already measured (such as alkaline phosphatase, total bilirubin, and INR), and investigate to identify the probable cause. • If resuming JUXTAPID after transaminases resolve to <3x ULN, reduce the dose and monitor liver-related laboratories more frequently.
	Stopping Treatment: If liver aminotransferase elevations are accompanied by clinical symptoms of liver injury (e.g., nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like symptoms) or increases in bilirubin ≥ 2 X ULN, or active liver disease, then stop treatment with JUXTAPID and investigate to identify the probable cause.

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Adverse Reaction Reporting

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.

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JUXTAPID REMS PROGRAM INFORMATION

JUXTAPID REMS Program

Key program elements:

- Prescriber training on the risk of hepatotoxicity associated with the use of JUXTAPID, appropriate patient selection and the need to monitor patients during treatment.
- Prescribers of JUXTAPID must be certified.
  - Certification consists of reviewing training and enrolling into JUXTAPID REMS program.
- Documentation of safe use conditions required for dispensing JUXTAPID:
  - Prescribers must use a Prescription Authorization Form for each new prescription to ensure safe use of JUXTAPID.
- Controlled distribution of JUXTAPID through certified pharmacies.

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JUXTAPID REMS Program

Before prescribing JUXTAPID, prescribers must complete the following steps:

1. Review the Prescribing Information and this Prescriber Training Module.
2. Complete, sign and submit the one-time JUXTAPID REMS Program Prescriber Enrollment Form.
3. Complete, sign and submit the JUXTAPID REMS Program Prescription Authorization Form for each patient.

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Review Prescriber Education Materials

1 Review

Review the following Prescriber Education Materials:

a. JUXTAPID Prescribing Information

b. This Prescriber Training Module

Note

Materials can be accessed from the JUXTAPID REMS Program website at:
www.JUXTAPIDREMSProgram.com

Or request these materials by calling 1-85-JUXTAPID (1-855-898-2743).

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Reference ID: 3356376

Enroll in JUXTAPID REMS Program

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I understand that JUXTAPID is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce LDL-C, TC, apo B and non HDL-C in patients with HoFH.
- I understand that JUXTAPID is only available through the JUXTAPID REMS Program and that I must comply with the program requirements in order to prescribe JUXTAPID.
- I have completed the JUXTAPID REMS Prescriber Training Module.
- I understand that there is a risk of hepatotoxicity associated with JUXTAPID.

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CONTINUED ON NEXT SLIDE

Reference ID: 3356376

Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I understand that serum ALT, AST, alkaline phosphatase, and total bilirubin levels must be measured before initiating therapy with JUXTAPID.
- I understand that during the first year of treatment with JUXTAPID liver-related laboratory tests (ALT and AST at a minimum) must be measured prior to each increase in dose or monthly, whichever comes first.
- I understand that after the first year, these parameters must be measured at least every 3 months and before any increase in dose.
- I understand that JUXTAPID has not been studied in patients less than 18 years of age.

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CONTINUED ON NEXT SLIDE

Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

In completing the one-time JUXTAPID REMS Program Prescriber Enrollment Form, prescribers will be required to attest to the following:

Prescriber Attestation

- I agree that personnel from the JUXTAPID REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to JUXTAPID or the JUXTAPID REMS Program.
- I will complete and submit a JUXTAPID REMS Program *Prescription Authorization Form* for each new prescription.
- I agree that Aegerion, its agents and contractors such as the pharmacy providers may contact me via phone, mail, or email to survey me on the effectiveness of the program requirements for the JUXTAPID REMS Program.

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CONTINUED ON NEXT SLIDE

Enroll in JUXTAPID REMS Program

CONTINUED FROM PREVIOUS SLIDE

2 Enroll

You can enroll in the JUXTAPID REMS program in two ways:

1. Online at **enrollment.JUXTAPIDREMSProgram.com or**
2. Download the JUXTAPID REMS Program Prescriber Enrollment Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
   - Complete the Enrollment Form and return via fax or email
     - Fax to 1-855-898-2498 or
     - Scan and email to REMS@aegerion.com

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Reference ID: 3356376

Submit Prescription Authorization Form

3 Submit

When prescribing JUXTAPID, a prescriber must complete a Prescription Authorization Form for each new prescription.

By completing the Prescription Authorization Form, the prescriber attests:

Prescriber Attestation

- I understand that 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 HoFH.
- I affirm that my patient has a clinical or laboratory diagnosis consistent with HoFH.
- I understand that JUXTAPID has not been studied in pediatric patients less than 18 years.
- I attest that I have obtained the liver-related laboratory tests for this patient as directed in the JUXTAPID prescribing information.

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CONTINUED ON NEXT SLIDE

Reference ID: 3356376

Submit Prescription Authorization Form

CONTINUED FROM PREVIOUS SLIDE

3 Submit

Prescribers must complete a Prescription Authorization Form and submit to a certified pharmacy:

- Download the Prescription Authorization Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
- Complete the Prescription Authorization Form
- Sign and submit the Prescription Authorization Form:
  - Fax to 1-855-898-2498 or
  - Scan and email to REMS@aegerion.com

  (Either will route directly to the certified pharmacy)

Note

For a list of certified pharmacies call: 1-85-JUXTAPID (1-855-898-2743)

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Recommended Patient Counseling Information

Patients should be informed of the risk of hepatotoxicity and the need for regular blood tests.

When counseling a patient on initiating JUXTAPID:

- Advise the patient of the risk of hepatotoxicity and the need to have regular blood tests performed to monitor for evidence of liver injury or dysfunction
- Inform the patient about the existence and purpose of a JUXTAPID REMS Program including dispensing only through certified pharmacies.
- For Females of Reproductive Potential: Confirm the absence of pregnancy and counsel the patient about the potential for fetal harm. Instruct her to use reliable methods of contraception and confirm use. Instruct patients to contact their prescriber immediately and stop taking JUXTAPID if pregnancy should occur.

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KNOWLEDGE ASSESSMENT

Knowledge Assessment

The following questions about JUXTAPID are provided to reinforce learning.

Provide the correct answer to the following questions.

If you have difficulty answering these questions, please review the previous slides and refer to the Prescribing Information.

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Knowledge Assessment

Question 1

Which of the following statements is TRUE?

- ❑ JUXTAPID is contraindicated in patients with moderate and severe hepatic impairment
- ❑ JUXTAPID can cause elevations in transaminases (ALT and AST)
- ❑ JUXTAPID increases hepatic fat with or without concomitant increases in transaminases
- ❑ All of the above

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Reference ID: 3356376

Knowledge Assessment

Question 1

Which of the following statements is TRUE?

- ❑ JUXTAPID is contraindicated in patients with moderate and severe hepatic impairment
- ❑ JUXTAPID can cause elevations in transaminases (ALT and AST)
- ❑ JUXTAPID increases hepatic fat with or without concomitant increases in transaminases
- ☑ **All of the above**

Answer

JUXTAPID is associated with a risk of hepatotoxicity.

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Knowledge Assessment

Question 2

In the first year of treatment, liver-related tests (ALT and AST at minimum) should be evaluated:

- ❑ A. Prior to an increase in dose
- ❑ B. Monthly
- ❑ C. Every three months
- ❑ Answers A and B
- ❑ Answers A and C

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Knowledge Assessment

Question 2

In the first year of treatment, liver-related tests (ALT and AST at minimum) should be evaluated:

- ❑ A. Prior to an increase in dose
- ❑ B. Monthly
- ❑ C. Every three months
- ☑ **Answers A and B**
- ❑ Answers A and C

Answer

ALT, AST, alkaline phosphatase, and total bilirubin should be measured before initiation of treatment with JUXTAPID. During the first year, measure liver-related tests (ALT and AST at 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.

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Knowledge Assessment

Question 3

The goal(s) of the JUXTAPID REMS Program are:

- ❑ To educate prescribers about the risk of hepatotoxicity associated with the use of JUXTAPID.
- ❑ To educate prescribers about the need to monitor patients during treatment with JUXTAPID as per product labeling.
- ❑ To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.
- ❑ All of the above
- ❑ None of the above

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Knowledge Assessment

Question 3

The goal(s) of the JUXTAPID REMS Program are:

- ☐ To educate prescribers about the risk of hepatotoxicity associated with the use of JUXTAPID.
- ☐ To educate prescribers about the need to monitor patients during treatment with JUXTAPID as per product labeling.
- ☐ To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.
- ☑ **All of the above**
- ☐ None of the above

Answer

The goals of the JUXTAPID REMS Program are:

- To educate prescribers about:
  - the risk of hepatotoxicity associated with the use of JUXTAPID; and
  - the need to monitor patients during treatment with JUXTAPID as per product labeling
- To restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with HoFH.

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Knowledge Assessment

Question 4

At initiation of treatment, which of the following liver-related laboratories should be measured:

- ❑ ALT and AST
- ❑ Alkaline phosphatase
- ❑ Total bilirubin
- ❑ All of the above

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Knowledge Assessment

Question 4

At initiation of treatment, which of the following liver-related laboratories should be measured:

- ❑ ALT and AST
- ❑ Alkaline phosphatase
- ❑ Total bilirubin
- ☑ **All of the above**

Answer

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiation of treatment with JUXTAPID.

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Knowledge Assessment

Question 5

How often should the Prescription Authorization Form be completed:

- ❑ Each new prescription
- ❑ Only on the first prescription
- ❑ Every refill
- ❑ Once a year

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Knowledge Assessment

Question 5

How often should the Prescription Authorization Form be completed:

- ☑ **Each new prescription**
- ☐ Only on the first prescription
- ☐ Every refill
- ☐ Once a year

Answer

For each new prescription, the prescriber must complete a Prescription Authorization Form.

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Knowledge Assessment

Question 6

A patient has an ALT value 4x ULN on treatment with JUXTAPID. The appropriate action is:

- ❑ Withhold treatment until ALT <3x ULN
- ❑ Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN
- ❑ Permanently discontinue treatment and investigate to identify probable cause
- ❑ Continue with the same dose of JUXTAPID and repeat ALT measurement monthly

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Knowledge Assessment

Question 6

A patient has an ALT value 4x ULN on treatment with JUXTAPID. The appropriate action is:

- ❑ Withhold treatment until ALT <3x ULN
- ☑ **Reduce the dose and repeat ALT measurement weekly until ALT is <3x ULN**
- ❑ Permanently discontinue treatment and investigate to identify probable cause
- ❑ Continue with the same dose of JUXTAPID and repeat ALT measurement monthly

Answer

Confirm elevation with a repeat measurement within one week. If confirmed, reduce the dose and obtain additional liver-related laboratories if not already measured (such as alkaline phosphatase, total bilirubin, and INR). Repeat transaminase measurements weekly, withhold dosing if transaminase levels do not fall below 3x ULN within 4 weeks, or if levels rise above 5x ULN , and investigate to identify the probable cause.

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Knowledge Assessment

Question 7

JUXTAPID is available only through certified pharmacies

- ❑ True
- ❑ False

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Knowledge Assessment

Question 7

JUXTAPID is available only through certified pharmacies

- ☑ True
- ☐ False

Answer

JUXTAPID is available only through pharmacies that are specially certified and agree to follow the REMS requirements.

NOTE: For a list of certified pharmacies call: 1-85-JUXTAPID (1-855-898-2743)

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Reference ID: 3356376

Completion of JUXTAPID REMS Program Training

You Have Completed the JUXTAPID REMS Program Training

You can enroll in the JUXTAPID REMS program in two ways:

1. Online at **enrollment.JUXTAPIDREMSProgram.com** or
2. Download the JUXTAPID REMS Program Prescriber Enrollment Form at **www.JUXTAPIDREMSProgram.com** or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
   - Complete the Enrollment Form and return via fax or email
     - Fax to 1-855-898-2498 or
     - Scan and email to REMS@aegerion.com

For more information on the JUXTAPID REMS Program, please call 1-85-JUXTAPID (1-855-898-2743) or visit www.JUXTAPIDREMSProgam.com

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APPENDIX 2

PRESCRIBER ENROLLMENT FORM

- Online Version
- Downloadable Version

Online JUXTAPID REMS Program Prescriber Enrollment Form

JUXTAPID will only be available through the JUXTAPID REMS Program. In order to prescribe JUXTAPID, a prescriber must:

1. Review the Prescribing Information (PI) and complete the Prescriber Training Module;
2. Complete this one-time JUXTAPID REMS Program Prescriber Enrollment Form; and
3. Complete and submit a JUXTAPID REMS Prescription Authorization Form for each new prescription

Complete this enrollment form, sign the document per the instructions below, and click submit

Note: * indicates required fields

PRESCRIBER INFORMATION

First Name*: Middle Initial: Last Name*:

Credentials*: ☐ MD ☐ DO ☐ NP ☐ PA Other:

Physician Specialty: ☐ Cardiology ☐ Endocrinology ☐ Internal Medicine ☐ Other (specify)

Practice/Facility Name:

Address 1*:

Address 2:

City*: State*: Zip Code*: Phone Number*: Fax Number*:

Email*: abergi@access-medical.com NPI #:

OFFICE CONTACT

First Name: Last Name:

Phone Number (if different from above): Fax Number (if different from above):

Email* (if office contact is provided):

PRESCRIBER ATTESTATION

By completing this form, I attest that:

- I understand that 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).
- I understand that JUXTAPID is only available through the JUXTAPID REMS Program and that I must comply with the program requirements in order to prescribe JUXTAPID.
- I have completed the JUXTAPID REMS *Prescriber Training Module*.
- I understand that there is a risk of hepatotoxicity associated with JUXTAPID.
- I understand that serum ALT, AST, alkaline phosphatase and total bilirubin must be measured before initiating therapy with JUXTAPID.
- I understand that during the first year of treatment with JUXTAPID liver-related laboratory tests (ALT and AST at a minimum) must be measured prior to each increase in dose or monthly, whichever comes first.
- I understand that after the first year, these parameters should be measured at least every 3 months and before any increase in dose.
- I agree that personnel from the JUXTAPID REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to JUXTAPID or the JUXTAPID REMS Program.
- I will complete and submit a JUXTAPID REMS Program Prescription Authorization Form for each new prescription.
- I agree that Aegerion, its agents and contractors such as the pharmacy providers may contact me via phone, mail, or email to survey me on the effectiveness of the program requirements for the JUXTAPID REMS Program.

Please enter your First and Last Name in the Signature field below. Once you enter this information, the Enrollment Form will be considered signed

Signature*: Date*: 6/27/2013

Submit

If you have any questions, please contact the JUXTAPID REMS Program.

Phone: 1-85-JUXTAPID (1-855-898-2743) | Fax: 1-855-898-2498 | www.JUXTAPIDREMSProgram.com

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Reference ID: 3356376

Online JUXTAPID REMS Program Prescriber Enrollment Form

You have successfully submitted your online enrollment form. You will receive a confirmation email from Centric Health Resources who administers the JUXTAPID REMS Program on behalf of Aegerion Pharmaceuticals. Click here to view/print your Online Enrollment Form

If you have any questions, please contact the JUXTAPID REMS Program.

Phone: 1-85-JUXTAPID (1-855-898-2743) | Fax: 1-855-898-2498 | www.JUXTAPIDREMSProgram.com

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Reference ID: 3356376

JUXTAPID REMS PROGRAM PRESCRIBER ENROLLMENT FORM

(PLEASE PRINT) * INDICATES REQUIRED FIELDS

JUXTAPID will only be available through the JUXTAPID REMS Program. In order to prescribe JUXTAPID, a prescriber must:

1) Review the Prescribing Information (PI) and complete the Prescriber Training Module;
2) Complete this one-time JUXTAPID REMS Program Prescriber Enrollment Form; and
3) Complete and submit a JUXTAPID REMS Prescription Authorization Form for each new prescription.

Complete this enrollment form and fax it to the JUXTAPID REMS Program at 1-855-898-2498 or scan and email to REMS@aegerion.com.

PRESCRIBER INFORMATION

First Name*: _____ Middle Initial: _____ Last Name*: _____

Credentials*: ❑ MD ❑ DO ❑ NP ❑ PA Other: _____

Physician Specialty: ❑ Cardiology ❑ Endocrinology ❑ Internal Medicine ❑ Other (specify) _____

Practice/Facility Name: _____

Address 1*: _____

Address 2: _____

City*: _____ State*: _____ Zip code*: _____ Phone Number*: _____ Fax Number*: _____

Email*: _____ NPI #: _____

OFFICE CONTACT

First Name: _____ Last Name: _____

Phone Number (if different from above): _____ Fax Number (if different from above): _____

Email* (if office contact is provided): _____

PRESCRIBER ATTESTATION

By completing this form, I attest that:

- I understand that 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).
- I understand that JUXTAPID is only available through the JUXTAPID REMS Program and that I must comply with the program requirements in order to prescribe JUXTAPID.
- I have completed the JUXTAPID REMS *Prescriber Training Module*.
- I understand that there is a risk of hepatotoxicity associated with JUXTAPID.
- I understand that serum ALT, AST, alkaline phosphatase and total bilirubin must be measured before initiating therapy with JUXTAPID.
- I understand that during the first year of treatment with JUXTAPID liver-related laboratory tests (ALT and AST at a minimum) must be measured prior to each increase in dose or monthly, whichever comes first.
- I understand that after the first year, these parameters should be measured at least every 3 months and before any increase in dose.
- I agree that personnel from the JUXTAPID REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to JUXTAPID or the JUXTAPID REMS Program.
- I will complete and submit a JUXTAPID REMS Program Prescription Authorization Form for each new prescription.
- I agree that Aegerion, its agents and contractors such as the pharmacy providers may contact me via phone, mail, or email to survey me on the effectiveness of the program requirements for the JUXTAPID REMS Program.

Signature*: _____ Date*: _____

If you have any questions, please contact the JUXTAPID REMS Program.
Phone: 1-85-JUXTAPID (1-855-898-2743) | Fax: 1-855-898-2498 | www.JUXTAPIDREMSProgram.com

APPENDIX 3

DEAR HEALTHCARE PROVIDER (HCP) LETTER

Aegerion Pharmaceuticals

Important Drug Warning

Subject: Risk of hepatotoxicity with JUXTAPID™ (lomitapide) capsules
Appropriate patient selection and monitoring
Prescriber Action: Training and enrollment as part of JUXTAPID REMS Program

January 11, 2013

Dear Healthcare Provider:

Aegerion Pharmaceuticals, Inc. would like to inform you about the approval of JUXTAPID™ (lomitapide) capsules, a microsomal triglyceride transfer protein (MTP) 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).

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for JUXTAPID. The purpose of the REMS is to help ensure that the benefits of treatment with JUXTAPID outweigh the **risk of hepatotoxicity**.

JUXTAPID has a **Boxed Warning** in the 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.
- 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.
- 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.
- 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.

101 MAIN STREET | SUITE 1850 | CAMBRIDGE, MA 02142
WWW.AEGERION.COM

Aegerion Pharmaceuticals

Appropriate Patient Selection

- JUXTAPID is indicated for use in patients with HoFH.
- Patients must have a clinical or laboratory diagnosis consistent with HoFH.
- JUXTAPID has not been studied in pediatric patients less than 18 years.

Prescriber Action

JUXTAPID will only be available through the JUXTAPID REMS Program. In order to prescribe JUXTAPID, prescribers must:

- Review the JUXTAPID REMS Prescribing Information and Prescriber Training Module;
- Complete and submit the one-time JUXTAPID REMS Program Prescriber Enrollment Form;
- Complete and submit a JUXTAPID REMS Prescription Authorization Form for each new prescription; and
- Comply with the requirements of the JUXTAPID REMS Program.

Certified Pharmacies

- JUXTAPID is only dispensed through certified pharmacies.

More specific details about prescriber enrollment and the JUXTAPID REMS Program can be found at www.JUXTAPIDREMSProgram.com. For more information, you may also contact JUXTAPID REMS Program toll-free at 1-85-JUXTAPID (1-855-898-2743).

Reporting Adverse Events

HCPs should report all suspected adverse events associated with the use of JUXTAPID. Please contact Aegerion at 1-855-303-2347 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The information in this letter is not intended as a complete description of the benefits and risks associated with the use of JUXTAPID. Please see the accompanying Prescribing Information and Medication Guide.

Sincerely,

_____

Dr. Mark Sumeray
Chief Medical Officer

Aegerion Pharmaceuticals, Inc.

Reference ID: 3356376

APPENDIX 4

DEAR PROFESSIONAL SOCIETY LETTER

Aegerion Pharmaceuticals

Important Drug Warning

Subject: Risk of hepatotoxicity with JUXTAPID™ (lomitapide) capsules
Appropriate patient selection and monitoring
Prescriber Action: Training and enrollment as part of REMS Program

January 11, 2013

Dear Professional Association:

This letter highlights important safety information your members need to know when prescribing JUXTAPID. To ensure the safe and appropriate use of JUXTAPID, it is important that you share the information included in this letter with your members who may treat patients with homozygous familial hypercholesterolemia (HoFH).

JUXTAPID™ (lomitapide) capsules, a microsomal triglyceride transfer protein (MTP) inhibitor 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).

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for JUXTAPID. The purpose of the REMS is to help ensure that the benefits of treatment with JUXTAPID outweigh the **risk of hepatotoxicity**.

JUXTAPID has a **Boxed Warning** in the 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.
- 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.
- 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.
- 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.

101 MAIN STREET | SUITE 1850 | CAMBRIDGE, MA 02142
WWW.AEGERION.COM

Reference ID: 3356376

Aegerion Pharmaceuticals

Appropriate Patient Selection

- JUXTAPID is indicated for use in patients with HoFH.
- Patients must have a clinical or laboratory diagnosis consistent with HoFH.
- JUXTAPID has not been studied in pediatric patients less than 18 years.

Prescriber Action

In order to prescribe JUXTAPID, prescribers must review the Prescribing Information and Prescriber Training Module, and enroll in the JUXTAPID REMS program.

Certified Pharmacies

JUXTAPID is only dispensed through certified pharmacies.

More specific details about prescriber responsibilities, enrollment and educational materials for JUXTAPID REMS Program can be found at www.JUXTAPIDREMSProgram.com. For more information, you may also contact JUXTAPID REMS Program toll-free at 1-85-JUXTAPID (1-855-898-2743).

The information in this letter is not intended as a complete description of the benefits and risks associated with the use of JUXTAPID. Please see accompanying Prescribing Information and Medication Guide.

Please share the information on the JUXTAPID REMS Program and the materials referenced above with your membership in order to ensure the safe and appropriate use of JUXTAPID. Thank you for your consideration of this request.

Sincerely,

_____

Dr. Mark Sumeray
Chief Medical Officer

Aegerion Pharmaceuticals, Inc.

101 MAIN STREET | SUITE 1850 | CAMBRIDGE, MA 02142
WWW.AEGERION.COM

Reference ID: 3356376

APPENDIX 5

PRESCRIPTION AUTHORIZATION FORM

Juxtapid™ (lomitapide) capsules

JUXTAPID REMS PROGRAM PRESCRIPTION AUTHORIZATION FORM

Instructions: This form should be completed for each new prescription. Please print – all fields are required. This form consists of 3 parts: (1) Patient Information; (2) Prescription; and (3) Prescriber Information and Attestation of REMS Requirements.

Please FAX completed form to JUXTAPID REMS Program at 1-855-898-2498 or scan and email to REMS@aegerion.com; either will route directly to the certified pharmacy.

PATIENT INFORMATION

First Name: _____ Last Name: _____ Date of Birth: _____

Address: _____ City: _____ State: _____ Zip: _____

JUXTAPID PRESCRIPTION

Dose: _____ mg po q hs (recommended starting dosage is 5 mg daily). Quantity to dispense: _____ Refills: _____

Additional Instructions: _____

_____

PRESCRIBER INFORMATION and ATTESTATION OF REMS REQUIREMENTS

Prescriber Information:

First Name: _____ Last Name: _____

Practice/Group Name: _____ Office Contact Person: _____

Address 1: _____

Address 2: _____ Suite: _____

City: _____ State: _____ Zip: _____

Office Phone: _____ Office Fax: _____

License #: _____ NPI #: _____

Attestation of REMS Requirements:

- I understand that 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).
- I affirm that my patient has a clinical or laboratory diagnosis consistent with HoFH.
- I understand that JUXTAPID has not been studied in pediatric patients less than 18 years.
- I attest that I have obtained the liver-related laboratory tests for this patient as directed in JUXTAPID's prescribing information.

Prescriber Signature _____ _____ _____

Substitution Permitted | Dispense as Written | Date

JUXTAPID REMS Program information may be found at www.JUXTAPIDREMSProgram.com
or by calling 1-85-JUXTAPID (1-855-898-2743).

APPENDIX 6

REMS WEB PAGES

Juxtapid™
(lomitapide) capsules

JUXTAPID REMS Program

Program Requirements | Training & Enrollment | Initiating Treatment | Important Safety Information

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug and is required by the US Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

Aegerion Pharmaceuticals, Inc. (Aegerion) has worked with the FDA to develop the JUXTAPID REMS Program:

- to educate prescribers about:
  - the risk of hepatotoxicity associated with the use of JUXTAPID; and
  - the need to monitor patients during treatment with JUXTAPID as per product labeling.
- to restrict access to therapy with JUXTAPID to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH).

Program Requirements

JUXTAPID is only available through the JUXTAPID REMS Program. The JUXTAPID REMS Program requirements include:

- For Prescribers
  - **Training** on the risk of hepatotoxicity associated with the use of JUXTAPID; appropriate patient selection and monitoring; and the REMS requirements
  - **Certification** by completion of training, and enrollment in the JUXTAPID REMS Program
  - **Attestation** of patient safe use for each new prescription by completing a Prescription Authorization Form

Find out more about Training and Enrollment

- For Pharmacies
  - Certification and enrollment in the REMS Program in order to dispense JUXTAPID

Reference ID: 3356376

Materials for Healthcare Providers

- Prescribing Information
- Dear Healthcare Provider Letter
- Online JUXTAPID REMS Program Prescriber Training Module
- Online JUXTAPID REMS Program Prescriber Enrollment Form
- JUXTAPID REMS Program Prescriber Training Module
- JUXTAPID REMS Program Prescriber Enrollment Form
- JUXTAPID REMS Prescription Authorization Form
- Contact REMS

the JUXTAPID REMS Program.

Steps to Prescriber Certification

1 REVIEW

Review the Prescriber Education Materials

- JUXTAPID Prescribing Information
- Prescriber Training Module
  - Online
    or
  - For Download (PDF)

2 COMPLETE and SUBMIT

Complete and Submit the JUXTAPID REMS Program Prescriber Enrollment Form

You can do this in two ways:

1. Online or
2. Download the JUXTAPID REMS Program Prescriber Enrollment Form or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
   - Complete the Enrollment Form and return via fax or email:
     - Fax to 1-855-898-2498 or
     - Scan and email to REMS@aegerion.com

By completing the Prescriber Enrollment Form, the prescriber agrees to comply with the JUXTAPID REMS Program requirements. A confirmation of your certification in the JUXTAPID REMS Program will be sent to you so you can begin to prescribe JUXTAPID.

Initiating Treatment

Before starting a patient on JUXTAPID, enrolled prescribers must:

- Affirm that the patient has a clinical or laboratory diagnosis consistent with HoFH.
- Obtain liver-related laboratory tests as directed in the JUXTAPID prescribing information.
- Confirm the absence of pregnancy and counsel the patient about the potential for fetal harm, if the patient is a woman of reproductive potential. Instruct her to use reliable methods of contraception and confirm use. Instruct patients to contact their prescriber immediately and

Reference ID: 3356376

JUXTAPID REMS Program – Contact Us

Phone: 1-85-JUXTAPID (1-855-898-2743)
Fax: 1-855-898-2498
E-mail: REMS@aegerion.com
Hours of Operation: Monday-Friday: 8 AM-7 PM ET

To learn more about the risk of hepatotoxicity associated with the use of JUXTAPID, please refer to the Prescribing Information. Before initiating treatment with JUXTAPID, prescribers must discuss the risks of JUXTAPID with their patients.

Reporting of Adverse Reactions

All healthcare professionals should report all suspected adverse reactions. Please contact Aegerion Pharmaceuticals, Inc. at 1-855-303-2347 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This site is intended for U.S. residents only.

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Aegerion® Pharmaceuticals

Indication and Important Safety Information

COLLAPSE SAFETY INFORMATION

INDICATION

JUXTAPID is a microsomal triglyceride transfer protein (MTP) 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).

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.

IMPORTANT SAFETY 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.

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.

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.

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.

CONTRAINDICATIONS

- Pregnancy
- Concomitant administration of moderate or strong CYP3A4 inhibitors
- Moderate or severe hepatic impairment or active liver disease including unexplained persistent elevations of serum transaminases

WARNINGS AND PRECAUTIONS

JUXTAPID can cause elevations in transaminases and hepatic steatosis. Although cases of hepatic failure have not been reported, there is concern that JUXTAPID could induce steatohepatitis, which can progress to cirrhosis over several years. Modify the dose of JUXTAPID if elevations of transaminases are observed and discontinue JUXTAPID for persistent or clinically significant elevations. If transaminase elevations are accompanied by clinical symptoms of liver injury, such as nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like-symptoms, increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause. Use JUXTAPID with caution when co-administered with agents known to be hepatotoxic. Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment. 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.

Females of reproductive potential should have a negative pregnancy test before starting JUXTAPID and should use effective contraception during therapy with JUXTAPID.

Given its mechanism of action in the small intestine, JUXTAPID may reduce the absorption of fat-soluble nutrients. 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).

Gastrointestinal adverse reactions are common and may lead to treatment discontinuation. To reduce the risk of gastrointestinal adverse reactions, patients should adhere to a low-fat diet supplying less than 20% of energy from fat and the dosage of JUXTAPID should be increased gradually.

Combination with CYP3A4 inhibitors increases exposure to lomitapide. Strong and moderate CYP3A4 inhibitors should not be used with JUXTAPID. JUXTAPID dosage should not exceed 30 mg daily when used concomitantly with weak CYP3A4 inhibitors.

Due to risk of myopathy associated with simvastatin or lovastatin, doses of these agents should be limited when co-administered with JUXTAPID.

JUXTAPID increases the plasma concentrations of warfarin. Increases or decreases in the dose of JUXTAPID may lead to supra- or subtherapeutic anticoagulation, respectively. Patients taking warfarin should undergo regular monitoring of the INR, especially after any changes in JUXTAPID dosage.

Avoid use of JUXTAPID in patients with rare hereditary disorders of galactose intolerance.

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/s/

AMY G EGAN
08/13/2013