

## **APPENDIX 6**

### **REMS WEB PAGES**

## 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

### 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](#)

## Steps to Prescriber Certification

1

### Review the Prescriber Education Materials

- JUXTAPID [Prescribing Information](#)
- Prescriber Training Module
  - [Online](#)
  - or
  - For [Download \(PDF\)](#)

REVIEW

2

### 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](mailto:REMS@aegerion.com)

COMPLETE  
and SUBMIT

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.

Reference ID: 3356876 **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**

## **JUXTAPID REMS Program – Contact Us**

Phone: 1-85-JUXTAPID (1-855-898-2743)

Fax: 1-855-898-2498

E-mail: [REMS@aegerion.com](mailto: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](http://www.fda.gov/medwatch).

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## 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)  $\geq 3x$  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  $\geq 3$ x 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  $\geq 2$ x 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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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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AMY G EGAN  
08/13/2013