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# JUXTAPID

## Risk Evaluation and Mitigation Strategy (REMS) Program

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### PRESCRIBER TRAINING MODULE

# Contents

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Introduction

JUXTAPID Product Information

JUXTAPID REMS Program Information

Knowledge Assessment

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## INTRODUCTION

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## Introduction

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**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

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## Indication

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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.



## 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.

## 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)  $\geq 3x$  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  $\geq 3x$  ULN. Discontinue JUXTAPID for clinically significant liver toxicity.



## **Risk of Hepatotoxicity**

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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  $\geq 2x$  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  $\geq 3$  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.



## **Dosing and Administration**

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- 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

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- 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



## 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.



## 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
$\geq 3x$ and $< 5x$ ULN	<ul style="list-style-type: none"><li>• Confirm elevation with a repeat measurement within one week.</li><li>• If confirmed, reduce the dose and obtain additional liver-related tests if not already measured (such as alkaline phosphatase, total bilirubin, and INR).</li><li>• 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.</li><li>• If resuming JUXTAPID after transaminases resolve to <math>&lt; 3x</math> ULN, consider reducing the dose and monitor liver-related tests more frequently.</li></ul>

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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	<ul style="list-style-type: none"><li>• 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.</li><li>• If resuming JUXTAPID after transaminases resolve to &lt;3x ULN, reduce the dose and monitor liver-related laboratories more frequently.</li></ul>

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  $\geq 2 \times$  ULN, or active liver disease, then stop treatment with JUXTAPID and investigate to identify the probable cause.



## **Adverse Reaction Reporting**

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**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](http://www.fda.gov/medwatch).**





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## JUXTAPID REMS PROGRAM INFORMATION

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## **JUXTAPID REMS Program**

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### **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.



## **JUXTAPID REMS Program**

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**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.



## 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 downloaded from the JUXTAPID REMS Program website at:

**[www.JUXTAPIDREMSProgram.com](http://www.JUXTAPIDREMSProgram.com)**

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



## 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.



**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 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

### To enroll in JUXTAPID REMS Program:

- Download the JUXTAPID REMS Program Prescriber Enrollment Form at [www.JUXTAPIDREMSProgram.com](http://www.JUXTAPIDREMSProgram.com) or request a copy by calling 1-85-JUXTAPID (1-855-898-2743)
- Complete the Enrollment Form
- Sign and submit the Enrollment Form:
  - Fax to 1-855-898-2498 or
  - Scan and email to [REMS@aegeion.com](mailto:REMS@aegeion.com)





## 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](http://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](mailto: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)



## 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

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## Knowledge Assessment

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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.



# 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

## 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.



## 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



## 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



## 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.



## 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

## 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.



## 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

## 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.



## 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



## 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

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Question

7

**JUXTAPID is available only through certified pharmacies**

- True
- False



## 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)



# Completion of JUXTAPID REMS Program Training

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## You Have Completed the JUXTAPID REMS Program Training

To enroll in JUXTAPID REMS program, complete the Enrollment Form and return the form via fax or email.

- Fax to 1-855-898-2498 or
- Scan and email to [REMS@aegerion.com](mailto: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](http://www.JUXTAPIDREMSProgam.com)**

