

JUXTAPID[®] (lomitapide)

Risk Evaluation and Mitigation Strategy (REMS) Program

PRESCRIBER TRAINING MODULE and KNOWLEDGE ASSESSMENT

This interactive tool:

- Provides an overview of the JUXTAPID REMS Program
- Discusses the risk of hepatotoxicity with JUXTAPID and the recommended hepatic monitoring requirements and dose adjustments, and
- Provides an overview of the prescriber, patient and pharmacy requirements for the JUXTAPID REMS program

User Guide

To become certified to prescribe JUXTAPID all prescribers must:

- **Successfully** complete this **Prescriber Training Module & Knowledge Assessment**
- **Submit** the signed **Juxtapid REMS Program Prescriber Enrollment Form** to the JUXTAPID REMS Coordinating Center
either by fax: 1-855-898-2498 or email: REMS@amrytpharma.com

At the end of the training module there is a Knowledge Assessment with interactive questions that you must pass. If your answer is incorrect you will be directed back to the relevant page in the materials and will be required to re-answer the question.

This prescriber training module and knowledge assessment is intended to be read in conjunction with the JUXTAPID REMS Factsheet and the JUXTAPID Prescribing Information (PI).

This program is expected to take **15-20** minutes.

Click here to begin



REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Contents

- Overview of the JUXTAPID REMS Program
- Key JUXTAPID Product Information
- JUXTAPID REMS Program Information
- Knowledge Assessment



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Overview

As there is a risk of hepatotoxicity with the use of JUXTAPID it is only available through a restricted program called the “JUXTAPID Risk Evaluation and Mitigation Strategy (REMS) Program”

The purpose of this training module is to educate health care professionals about the JUXTAPID REMS Program.



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



JUXTAPID REMS Program Goals

The aim of the JUXTAPID REMS Program is **to mitigate the risk of hepatotoxicity associated with the use of JUXTAPID** by ensuring that:

① Prescribers are educated about:

- the approved indication for JUXTAPID;
- the risk of hepatotoxicity associated with the use of JUXTAPID; and
- the need to monitor patients during treatment with JUXTAPID as per the product labeling.

② JUXTAPID is dispensed only to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)

and

③ Patients are informed about the risk of hepatotoxicity associated with the use of JUXTAPID and the need for baseline and periodic monitoring



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Indication

JUXTAPID is only 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 Related to the REMS:

- The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH).

Please see JUXTAPID full Prescribing Information for the limitations to use, and the **BOXED WARNING** on hepatotoxicity as included on www.juxtapidREMSprogram.com



Appropriate Patient Selection

JUXTAPID is indicated only for use in patients with HoFH.

- Patients must have a clinical or laboratory diagnosis consistent with HoFH.

Contraindications Related to the REMS:

- **Moderate or severe hepatic impairment or active liver disease** including unexplained persistent abnormal liver function tests.



Please see JUXTAPID full Prescribing Information as included on www.juxtapidREMSprogram.com for the full contraindications



Boxed Warning – Hepatic Information

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% 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 dose of Juxtapid if the ALT or AST are $\geq 3x$ ULN. Discontinue JUXTAPID for clinical significant liver toxicity.



Please see JUXTAPID full Prescribing Information including the full **BOXED WARNING** as included on www.juxtapidREMSprogram.com



REMS PROGRAM

Prescriber Training Module a

Risk of Hepatotoxicity: JUXTAPID can Cause Elevations in Transaminases

Elevations in transaminases (alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]) are associated with JUXTAPID. In the clinical trial, 10 (34%) of the 29 patients with HoFH had at least one elevation in ALT or AST $\geq 3x$ ULN, and 4 (14%) of the patients had at least one elevation in ALT or AST $\geq 5x$ ULN. There were no concomitant or subsequent clinically meaningful elevations in bilirubin, INR, or alkaline phosphatase.

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.

Continued next slide



REMS PROGRAM

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Risk of Hepatotoxicity

JUXTAPID Increases Hepatic Fat

Continued from previous slide

JUXTAPID 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% 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.

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

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Dosage & Administration

The recommended starting dose of JUXTAPID is 5 mg taken once daily (QD).

The dose should be escalated gradually based on acceptable safety and tolerability.

- After two weeks, increase the dose based on acceptable safety and tolerability to 10 mg, taken once daily.
- Then, at a minimum of four week intervals, increase dose to 20 mg, 40 mg, or 60 mg daily.

QD Dose	Duration of Administration Before Considering Dose Increase
5 mg	At least two weeks
10 mg	At least four weeks
20 mg	
40 mg	
60 mg	Maximum recommended dose



Monitoring of transaminases

Timing

Liver monitoring recommendations

Prior to initiating JUXTAPID

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin

If abnormal, consider initiating JUXTAPID only after an appropriate workup and the baseline abnormalities have been explained or resolved.

During the first year of treatment

ALT and AST (at a minimum) prior to each increase in dose or monthly, whichever occurs first

After the first year of treatment

ALT and AST (at a minimum) at least every 3 months and before any increase in dose

At any time during treatment

If transaminases are abnormal, reduce or withhold dosing of JUXTAPID and monitor as recommended in the Prescribing Information. 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 $\geq 2x$ ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause.



Hepatic Monitoring Recommendations

Continued from previous slide

ALT or AST	Treatment and Monitoring Recommendations*
≥3x and <5x ULN	<ul style="list-style-type: none">• 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.
≥5x ULN	<ul style="list-style-type: none">• Withhold dosing, obtain additional liver-related tests 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 tests more frequently.

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 investigate to identify the probable cause



*Recommendations based on an ULN of approximately 30-40 international units/L

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JUXTAPID REMS Program Goals

The aim of the JUXTAPID REMS Program is **to mitigate the risk of hepatotoxicity associated with the use of JUXTAPID** by ensuring that:

① Prescribers are educated about:

- the approved indication for JUXTAPID;
- the risk of hepatotoxicity associated with the use of JUXTAPID; and
- the need to monitor patients during treatment with JUXTAPID as per the product labeling.

② JUXTAPID is dispensed only to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)

and

③ Patients are informed about the risk of hepatotoxicity associated with the use of JUXTAPID and the need for baseline and periodic monitoring.



JUXTAPID REMS Key Elements

Prescriber

Prescribers
must be certified
to prescribe
JUXTAPID

Patient

Patients must undergo education about the approved indication for use (HoFH) and the risk of hepatotoxicity with JUXTAPID and the need for regular monitoring as part of the REMS Program.

Pharmacy

Pharmacies
must be certified
to distribute and
dispense
JUXTAPID



REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Prescriber Certification Process

① REVIEW the JUXTAPID

- JUXTAPID Prescribing Information
- JUXTAPID REMS Program **Fact Sheet**

② COMPLETE the JUXTAPID REMS Program

- **Prescriber Training Module** and Knowledge Assessment

③ AGREE to:

- Counsel patients using the JUXTAPID REMS Program **Patient Guide**
- Complete, sign and submit the JUXTAPID REMS Program **Patient-Prescriber Acknowledgement Form** with the patient
- Submit a JUXTAPID REMS Program **Prescription Authorization Form** for each prescription

④ SUBMIT to the REMS Coordinating Center the:

- Completed JUXTAPID REMS Program **Prescriber Enrollment Form**



JUXTAPID Prescription Process

1

- **Certify** as a Prescriber in the JUXTAPID REMS Program*

2

- **Review** Patient Guide with Patient
- Complete & Sign Patient Prescriber Acknowledgement Form (PPAF), give copy of Patient Guide PPAF to Patient
- Submit the PPAF to JUXTAPID REMS Program

3

- **Complete & Sign the Prescription Authorization Form (PAF)**
- Fax the PAF to the JUXTAPID REMS Program



*prescribers are only required to certify one time

JUXTAPID REMS Program:

Email: REMS@amrytpharma.com

☎ 1-855-898-2743 fax: 1-855-898-2498

REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Where do I find the REMS Program Materials?

All JUXTAPID REMS Program materials can be found on the JUXTAPID REMS Program website:

www.juxtapidREMSprogram.com

REMS Materials can also be requested by contacting the JUXTAPID REMS Coordinating Center at:

 1- 855-898-2743



Knowledge Assessment



REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Question 1

The goals of the JUXTAPID REMS program are:

(check the answer that is the most inclusive)

- To educate prescribers about the risk of hepatotoxicity with the use of JUXTAPID.
- To restrict the use of JUXTAPID to only those patients with a clinical and laboratory diagnosis of HoFH.
- To ensure both prescribers and patients understand the risk of hepatotoxicity with JUXTAPID and the need for monitoring of liver function.
- All of the above.



Question 1

The goals of the JUXTAPID REMS program are:

(check the answer that is the most inclusive)

- To educate prescribers about the risk of hepatotoxicity with the use of JUXTAPID.
- To restrict the use of JUXTAPID to only those patients with a diagnosis of HoFH.
- To ensure both prescribers and patients understand the risks of JUXTAPID and the need for monitoring of liver function.
- All of the above.



Partly correct

The education of prescribers about the risk of hepatotoxicity with the use of JUXTAPID is a key part of the JUXTAPID REMS Program. However there are other goals. Review the [REMS Program goals](#) and try again

Question 1

The goals of the JUXTAPID REMS program are:

(check the answer that is the most inclusive)

- To educate prescribers about the risk of hepatotoxicity with the use of JUXTAPID.
- To restrict the use of JUXTAPID to only those patients with a clinical or laboratory diagnosis of HoFH.**
- To ensure both prescribers and patients understand the risks of JUXTAPID and the need for monitoring of liver function.
- All of the above.

 **Partly correct**

The restriction of the use of JUXTAPID to patients with a clinical or laboratory diagnosis of HoFH is a key part of the JUXTAPID REMS Program. However there are other goals. [Review the REMS Program goals and try again](#)

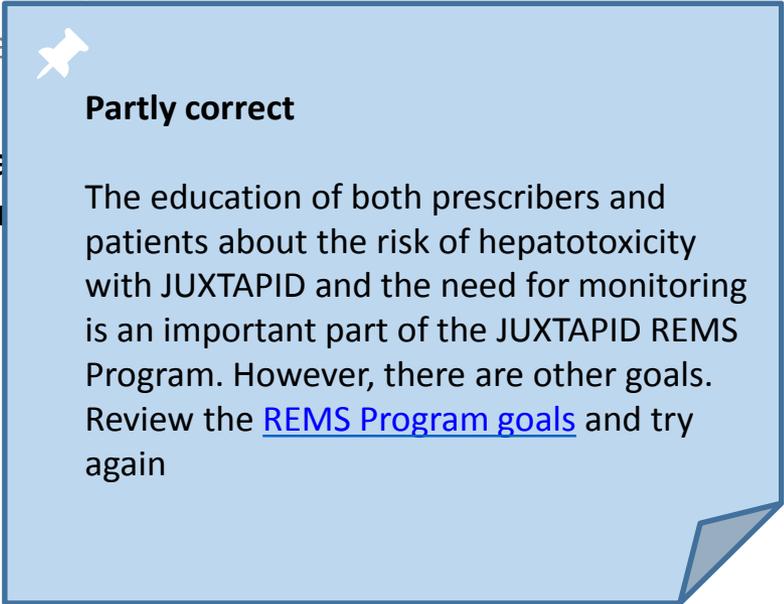


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- To restrict the use of JUXTAPID to only those patients with a diagnosis of HoFH.
- To ensure both prescribers and patients understand JUXTAPID and the need for monitoring of liver function tests.**
- All of the above.



Partly correct

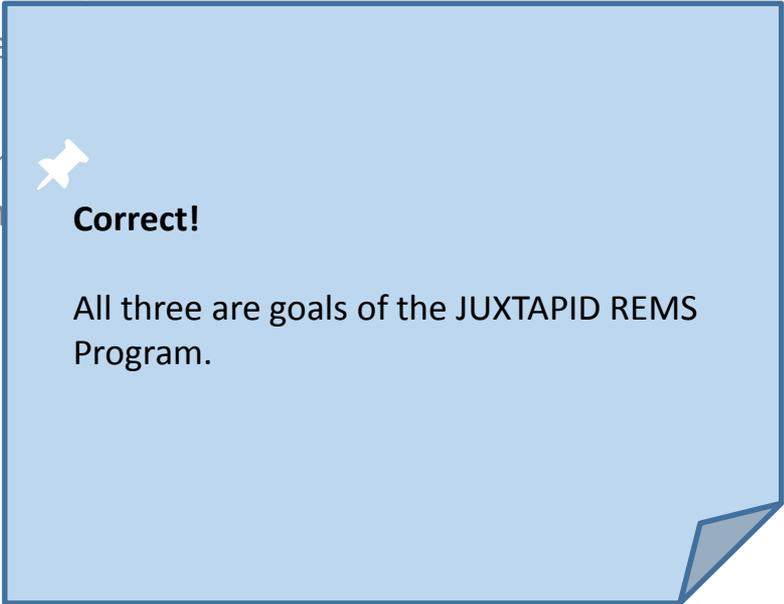
The education of both prescribers and patients about the risk of hepatotoxicity with JUXTAPID and the need for monitoring is an important part of the JUXTAPID REMS Program. However, there are other goals. Review the [REMS Program goals](#) and try again

Question 1

The goals of the JUXTAPID REMS program are:

(check the answer that is the most inclusive)

- To educate prescribers about the risk of hepatotoxicity with the use of JUXTAPID.
- To restrict the use of JUXTAPID to only those patients with a diagnosis of HoFH.
- To ensure both prescribers and patients understand the risks of JUXTAPID and the need for monitoring of liver function.
- All of the above.**



Correct!

All three are goals of the JUXTAPID REMS Program.



Click here to advance



Question 2

Which conditions are appropriate for the use of JUXTAPID?

- a. Mixed dyslipidemia.
- b. Homozygous familial hypercholesterolemia (HoFH).
- c. Heterozygous familial hypercholesterolemia (HeFH).
- d. All of the above.



Question 2

Which conditions are appropriate for the use of JUXTAPID?

- a. Mixed dyslipidemia.**
- b. Homozygous familial hypercholesterolemia (HoFH).
- c. Heterozygous familial hypercholesterolemia (HeFH).
- d. All of the above.



Incorrect

JUXTAPID is indicated for use in patients with homozygous familial hypercholesterolemia (HoFH).

Review the [Indication](#) for JUXTAPID and try again

Question 2

Which conditions are appropriate for the use of JUXTAPID?

- a. Mixed dyslipidemia.
- b. Homozygous familial hypercholesterolemia (HoFH).**
- c. Heterozygous familial hypercholesterolemia (HeFH).
- d. All of the above.

 **Correct!**

JUXTAPID is indicated for use 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).



[Click here to advance](#)



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Which conditions are appropriate for the use of JUXTAPID?

- a. Mixed dyslipidemia.
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- c. Heterozygous familial hypercholesterolemia (HeFH).**
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Incorrect

JUXTAPID is indicated for use in patients with homozygous familial hypercholesterolemia (HoFH).

Review the [Indication](#) for JUXTAPID and try again

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Which conditions are appropriate for the use of JUXTAPID?

- a. Mixed dyslipidemia.
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- c. Heterozygous familial hypercholesterolemia (HeFH).
- d. All of the above.**



Incorrect

JUXTAPID is indicated for use in patients with homozygous familial hypercholesterolemia (HoFH).

Review the [Indication](#) for JUXTAPID and try again

Question 3

What are the hepatic monitoring recommendations during the first year of treatment with JUXTAPID?

- a. Check transaminases only if the patient experiences signs and symptoms of liver injury.
- b. Monitor transaminase levels every 3 months.
- c. Monitor ALT and AST (at a minimum) prior to each increase of dose or monthly, what ever occurs first.



Question 3

What are the hepatic monitoring recommendations during the first year of treatment with JUXTAPID?

- a. Check transaminases only if the patient experiences signs and symptoms of liver injury.
- b. Monitor transaminase levels every 3 months
- c. Monitor ALT and AST (at a minimum) prior to what ever occurs first.



Incorrect

During the first year of therapy transaminases should be monitored every 30 days or prior to each increase in dose.

At a minimum ALT and AST should be checked every 30 days.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 3

What are the hepatic monitoring recommendations during the first year of treatment with JUXTAPID?

- a. Check transaminases only if the patient experiences signs and symptoms of liver injury.
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Question 3

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- a. Check transaminases only if the patient experiences signs and symptoms of liver injury.
- b. Monitor transaminase levels every 3 months.
- c. **Monitor ALT and AST (at a minimum) prior to each increase in dose, or what ever occurs first.**



Correct!

During the first year of therapy transaminases should be monitored every 30 days or prior to each increase in dose.

At a minimum ALT and AST should be checked every 30 days.

[Click here to advance](#)



Question 4

Jane Smith is 24 years old and has a clinical and laboratory diagnosis of HoFH. She has been on JUXTAPID for 13 months, appears to be compliant with her medication. You want to increase the dose, what should you do before you increase the dose?

- a. Measure AST, ALT, alkaline phosphatase and total bilirubin after the increase in dose.
- b. Increase her dose, see her back in a month.
- c. Measure AST, ALT, alkaline phosphatase and total bilirubin if not performed in the last 30 days and only adjust the dose if normal.



Question 4

Jane Smith is 24 years old and has a clinical and laboratory diagnosis of HoFH. She has been on JUXTAPID for 13 months, appears to be compliant with her medication. You want to increase the dose, what should you do before you increase the dose?

- a. Measure AST, ALT, alkaline phosphatase and t
- b. Increase her dose, see her back in a month.
- c. Measure AST, ALT, alkaline phosphatase and t days and only adjust the dose if normal.



Incorrect

Before you increase Ms. Smith's dose minimally AST and ALT should be measured and confirmed to be within acceptable ranges. Review the options and consider another approach.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again

Question 4

Jane Smith is 24 years old and has a clinical and laboratory diagnosis of HoFH. She has been on JUXTAPID for 13 months, appears to be compliant with her medication. You want to increase the dose, what should you do before you increase the dose?

- a. Measure AST, ALT, alkaline phosphatase and total
- b. Increase her dose, see her back in a month.**
- c. Measure AST, ALT, alkaline phosphatase and total days and only adjust the dose if normal within the



Incorrect

Before you increase Ms. Smith's dose minimally AST and ALT should be measured and confirmed to be within acceptable ranges. Review the options and consider another approach.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again

Question 4

Jane Smith is 24 years old and has a clinical and laboratory diagnosis of HoFH. She has been on JUXTAPID for 13 months, appears to be compliant with her medication. You want to increase the dose, what should you do before you increase the dose?

- a. Measure AST, ALT, alkaline phosphatase and total cholesterol
- b. Increase her dose, see her back in a month.
- c. **Measure AST, ALT, alkaline phosphatase and total cholesterol 30 days and only adjust the dose if normal within 30 days**

 Correct!

Before you increase Ms. Smith's dose minimally AST and ALT should be measured and confirmed to be within acceptable ranges.



[Click here to advance](#)



Question 5

Your patient Thomas Jones, who has a clinical and laboratory diagnosis of HoFH presents to your clinic after being on JUXTAPID for 6 months. His ALT is $\geq 5x$ the ULN.

Your next step should be:

- a. Withhold dosing, obtain additional liver related labs and investigate the potential cause.
- b. Repeat the ALT in one week, if still elevated reduce the dose, repeat ALT tests weekly until it is less than 3x ULN.
- c. Decrease the dose of JUXTAPID.
- d. Continue the JUXTAPID for another month and re-measure the ALT.



Question 5

Your patient Thomas Jones, who has a clinical and laboratory diagnosis of HoFH presents to your clinic after being on JUXTAPID for 6 months. His ALT is $\geq 5x$ the ULN.

Your next step should be:

- a. **Withhold dosing, obtain additional liver related laboratories to investigate the potential cause.**
- b. Repeat the ALT in one week, if still elevated weekly until it is less than 3x ULN.
- c. Decrease the dose of JUXTAPID.
- d. Continue the JUXTAPID for another month and recheck ALT.



Correct!

If AST and/or ALT is $\geq 5x$ ULN the dose of JUXTAPID should be withheld, obtain additional liver related laboratories if not already obtained and investigate the potential cause. Withhold dosing until transaminase levels drop below 3X ULN.



[Click here to advance](#)



Question 5

Your patient Thomas Jones, who has a clinical and laboratory diagnosis of HoFH presents to your clinic after being on JUXTAPID for 6 months. His ALT is $\geq 5x$ the ULN.

Your next step should be:

- a. Withhold dosing, obtain additional liver related labs to rule out potential cause.
- b. Repeat the ALT in one week, if still elevated repeat weekly until it is less than 3x ULN.**
- c. Decrease the dose of JUXTAPID.
- d. Continue the JUXTAPID for another month and recheck ALT.

 **Incorrect**

If AST and/or ALT is $\geq 5x$ ULN the dose of JUXTAPID should be withheld, obtain additional liver related laboratories if not already obtained and investigate the potential cause. Withhold dosing until transaminase levels drop below 3X ULN.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 5

Your patient Thomas Jones, who has a clinical and laboratory diagnosis of HoFH presents to your clinic after being on JUXTAPID for 6 months. His ALT is $\geq 5x$ the ULN.

Your next step should be:

- a. Withhold dosing, obtain additional liver related labs to identify potential cause.
- b. Repeat the ALT in one week, if still elevated repeat weekly until it is less than 3x ULN.
- c. **Decrease the dose of JUXTAPID.**
- d. Continue the JUXTAPID for another month and recheck ALT.



Incorrect

If AST and/or ALT is $\geq 5x$ ULN the dose of JUXTAPID should be withheld, obtain additional liver related laboratories if not already obtained and investigate the potential cause. Withhold dosing until transaminase levels drop below 3X ULN.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 5

Your patient Thomas Jones, who has a clinical and laboratory diagnosis of HoFH presents to your clinic after being on JUXTAPID for 6 months. His ALT is $\geq 5x$ the ULN.

Your next step should be:

- a. Withhold dosing, obtain additional liver related labs to identify potential cause.
- b. Repeat the ALT in one week, if still elevated repeat weekly until it is less than 3x ULN.
- c. Decrease the dose of JUXTAPID.
- d. **Continue the JUXTAPID for another month and recheck ALT.**

Incorrect

If AST and/or ALT is $\geq 5x$ ULN the dose of JUXTAPID should be withheld, obtain additional liver related laboratories if not already obtained and investigate the potential cause. Withhold dosing until transaminase levels drop below 3X ULN.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 6

Sandra Brown has been on JUXTAPID for 4 months. She presents to your clinic with nausea, vomiting, abdominal pain, jaundice and is feeling “achy all over”.

You check transaminases and the AST is 3x ULN, the ALT is 2 x ULN.

What should you do next?

- a. Discontinue JUXTAPID treatment.
- b. Identify the probable cause.
- c. Follow AST, ALT, total bilirubin and alkaline phosphatase until normal.
- d. All of the above



Question 6

Sandra Brown has been on JUXTAPID for 4 months. She presents to your clinic with nausea, vomiting, abdominal pain, jaundice and is feeling “achy all over”.

You check transaminases and the AST is 3x ULN, the ALT is 2x ULN.

What should you do next?

- a. **Discontinue JUXTAPID treatment.**
- b. Identify the probable cause.
- c. Follow AST, ALT, total bilirubin and alkaline
- d. All of the above.

Partly correct.

Although it is recommended that JUXTAPID treatment is discontinued in patients who experience symptoms of liver injury accompanied by elevations in transaminases. However, there are other actions that should be considered.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 6

Sandra Brown has been on JUXTAPID for 4 months. She presents to your clinic with nausea, vomiting, abdominal pain, jaundice and is feeling “achy all over”.

You check transaminases and the AST is 3x ULN, the ALT is 2x ULN.

What should you do next?

- a. Discontinue JUXTAPID treatment.
- b. Identify the probable cause.**
- c. Follow AST, ALT, total bilirubin and alkaline phosphatase.
- d. All of the above.

Partly correct.

Although the identification of the possible cause of the elevations in AST and ALT and the symptoms of liver injury is important, there are other actions that should be considered.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 6

Sandra Brown has been on JUXTAPID for 4 months. She presents to your clinic with nausea, vomiting, abdominal pain, jaundice and is feeling “achy all over”.

You check transaminases and the AST is 3x ULN, the ALT is 2x ULN.

What should you do next?

- a. Discontinue JUXTAPID treatment.
- b. Identify the probable cause.
- c. **Follow AST, ALT, total bilirubin and alkaline**
- d. All of the above.

Partly correct.

Although the AST and ALT are not higher than 3x ULN, the patient is experiencing symptoms accompanied with transaminase elevations. It is also important to follow liver functions until they resolve, however there may be other actions you should take.

Review the [Hepatic Monitoring Recommendations](#) for JUXTAPID and try again.

Question 6

Sandra Brown has been on JUXTAPID for 4 months. She presents to your clinic with nausea, vomiting, abdominal pain, jaundice and is feeling “achy all over”.

You check transaminases and the AST is 3x ULN, the ALT is 2x ULN.

What should you do next?

- a. Discontinue JUXTAPID treatment.
- b. Identify the probable cause.
- c. Follow AST, ALT, total bilirubin and alkaline phosphatase.
- d. **All of the above.**

Correct!

It is recommended that patients who experience elevations in transaminases accompanied by symptoms of liver injury accompanied by, discontinue treatment with JUXTAPID, LFTs should continue to be followed until they resolve, and further investigation should be instituted to identify the probable cause.



[Click here to advance](#)



Question 7

One of the key points in the REMS program is patient education on the risks of hepatotoxicity with JUXTAPID.

- a. True.
- b. False.



Question 7

One of the key points in the REMS program is patient education on the risks of hepatotoxicity with JUXTAPID.

- a. **True.**
- b. False.

Correct!

JUXTAPID is associated with a risk of hepatotoxicity and as a result there is a REMS Program in place to ensure that its benefits outweigh its risks. The REMS Program requires patients to participate in the treatment decision process. This requires the prescriber to review the Guide for Patients with the patient. Knowledge of the appropriate indication for use and the risk of hepatotoxicity is expected to allow them to participate effectively in that process.



Click here to advance



Question 7

One of the key points in the REMS program is patient education on the risks of hepatotoxicity with JUXTAPID.

- a. True.
- b. False.



Incorrect

Review the [goals of the JUXTAPID REMS program](#) and retry this question.

Question 8

How does a prescriber become certified in the JUXTAPID REMS Program?

- a. Complete and submit the JUXTAPID REMS Program Prescriber Enrollment Form
- b. Successfully complete the JUXTAPID REMS Program Prescriber Training Module and Knowledge Assessment
- c. Review the JUXTAPID PI and the JUXTAPID REMS Program Fact Sheet.
- d. All of the above.



Question 8

How does a prescriber become certified in the JUXTAPID REMS program?

- a. **Complete and submit the JUXTAPID REMS Program Prescriber Enrollment Form**
- b. Successfully complete the JUXTAPID REMS Program Prescriber Training Module and Knowledge Assessment
- c. Review the JUXTAPID PI and the JUXTAPID
- d. All of the above.

Almost.

To become a certified prescriber in the JUXTAPID REMS Program you must successfully complete the Prescriber Enrollment Form, Training Module and Knowledge Assessment, and review the PI and REMS Fact Sheet.

Review the [Prescriber Certification Process](#) and try again.

Question 8

How does a prescriber become certified in the JUXTAPID REMS Program?

- a. Complete and submit the JUXTAPID REMS Program Prescriber Enrollment Form
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- d. All of the above.



Almost.

To become a certified prescriber in the JUXTAPID REMS Program you must successfully complete the Prescriber Enrollment Form, Training Module and Knowledge Assessment, and review the PI and REMS Fact Sheet.

Review the [Prescriber Certification Process](#) and try again.

Question 8

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- a. Complete and submit the JUXTAPID REMS Program Prescriber Enrollment Form
- b. Successfully complete the JUXTAPID REMS Program Prescriber Training Module and Knowledge Assessment
- c. **Review the JUXTAPID PI and the JUXTAPID REMS Fact Sheet**
- d. All of the above.

 Almost.

To become a certified prescriber in the JUXTAPID REMS Program you must successfully complete the Prescriber Enrollment Form, Training Module and Knowledge Assessment, and review the PI and REMS Fact Sheet.

Review the [Prescriber Certification Process](#) and try again.

Question 8

How does a prescriber become certified in the JUXTAPID REMS program?

- a. Complete and submit the JUXTAPID REMS Program Prescriber Enrollment Form
- b. Successfully complete the JUXTAPID REMS Program Prescriber Training Module and Knowledge Assessment
- c. Review the JUXTAPID PI and the JUXTAPID
- d. **All of the above.**



Correct!

To become a certified prescriber in the JUXTAPID REMS Program you must successfully complete the prescriber enrollment form, training module and knowledge assessment, and review the PI and REMS Fact Sheet.



Click here to advance



CONGRATULATIONS!

You have successfully completed the **Prescriber Training Module and Knowledge Assessment**.

Click [here](#) for a copy of your Certificate of Completion

NEXT STEPS

- Complete and sign the **Prescriber Enrollment Form**, and
- Submit the Prescriber Enrollment Form to the JUXTAPID REMS Coordinating Center either by fax: 1-855-898-2498 or email: REMS@amrytpharma.com

If all the certification requirements are met, the JUXTAPID REMS Coordinating center will confirm you are certified as a prescriber in the JUXTAPID REMS Program. Once you are certified in the JUXTAPID REMS Program you can counsel patients on the REMS program requirements and prescribe JUXTAPID.



REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Note to Reviewer:

The following slides are the “refresher” slides that you are directed to after answering a question incorrectly. These slide are duplicates of the original slide with the exception of the hyperlink back to the question. These slide will not be visible in the training program, unless the participant answers the questions incorrectly.

JUXTAPID REMS Program Goals

The aim of the JUXTAPID REMS Program is **to mitigate the risk of hepatotoxicity associated with the use of JUXTAPID** by ensuring that:

❶ Prescribers are educated about:

- the approved indication for JUXTAPID;
- the risk of hepatotoxicity associated with the use of JUXTAPID; and
- the need to monitor patients during treatment with JUXTAPID as per the product labeling.

❷ JUXTAPID is dispensed only to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)

and

❸ Patients are informed about the risk of hepatotoxicity associated with the use of JUXTAPID and the need for baseline and periodic monitoring



To retry Question 1 click here



Redirect from Question 2

Indication

JUXTAPID is only 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.



To retry Question 2 click here



REMS PROGRAM

Prescriber Training Module and Knowledge Assessment

Monitoring of transaminases

Timing	Liver monitoring recommendations
Prior to initiating JUXTAPID	Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin
If abnormal, consider initiating JUXTAPID only after an appropriate workup and the baseline abnormalities have been explained or resolved.	
During the first year of treatment	ALT and AST (at a minimum) prior to each increase in dose or monthly, whichever occurs first
After the first year of treatment	ALT and AST (at a minimum) at least every 3 months and before any increase in dose

At any time during treatment

If transaminases are abnormal, reduce or withhold dosing of JUXTAPID and monitor as recommended in the Prescribing Information. 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 $\geq 2x$ ULN, or active liver disease, discontinue treatment with JUXTAPID and identify the probable cause.



Hepatic Monitoring Recommendations

ALT or AST	Treatment and Monitoring Recommendations*
≥3x and <5x ULN	<ul style="list-style-type: none"> • 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.
≥5x ULN	<ul style="list-style-type: none"> • Withhold dosing, obtain additional liver-related tests 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 tests more frequently.

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 investigate to identify the probable cause.

*Recommendations based on an ULN of approximately 30-40 international units/L

[To retry Question 4, click here](#)



Hepatic Monitoring Recommendations Continued from previous slide

ALT or AST	Treatment and Monitoring Recommendations*
≥3x and <5x ULN	<ul style="list-style-type: none"> • 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.
≥5x ULN	<ul style="list-style-type: none"> • Withhold dosing, obtain additional liver-related tests 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 tests more frequently.

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 investigate to identify the probable cause.

*Recommendations based on an ULN of approximately 30-40 international units/L

[To retry Question 5, click here](#)



Hepatic Monitoring Recommendations Continued from previous slide

ALT or AST	Treatment and Monitoring Recommendations*
≥3x and <5x ULN	<ul style="list-style-type: none">• 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.
≥5x ULN	<ul style="list-style-type: none">• Withhold dosing, obtain additional liver-related tests 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 tests more frequently.

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 investigate to identify the probable cause.

*Recommendations based on an ULN of approximately 30-40 international units/L

To retry Question 6 click here



JUXTAPID REMS Program Goals

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and

❸ Patients are informed about the risk of hepatotoxicity associated with the use of JUXTAPID and the need for baseline and periodic monitoring.



To retry Question 7 click here



Prescriber Certification Process

① REVIEW the JUXTAPID

- JUXTAPID Prescribing Information
- JUXTAPID REMS Program **Fact Sheet**

② COMPLETE the JUXTAPID REMS Program

- **Prescriber Training Module** and Knowledge Assessment

③ AGREE to:

- Counsel patients using the JUXTAPID REMS Program **Patient Guide**
- Complete, sign and submit the JUXTAPID REMS Program **Patient-Prescriber Acknowledgement Form** with the patient
- Submit a JUXTAPID REMS Program **Prescription Authorization Form** for each prescription

④ SUBMIT to the REMS Coordinating Center the:

- Completed JUXTAPID REMS Program **Prescriber Enrollment Form**



To retry Question 8, click here

