Initial REMS Approval: 01/2013

Most Recent Modification: 05/2014

NDA 203568

KYNAMRO® (mipomersen sodium)

Drug Class: Oligonucleotide Inhibitor of Apolipoprotein B-100 Synthesis

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
Telephone: 617-252-7500

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of the KYNAMRO REMS Program are:

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

II. REMS Elements

A. Elements to Assure Safe Use (ETASU)

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

a. Genzyme will ensure HCPs who prescribe KYNAMRO are specially certified.

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

    i. Review the Prescribing Information (PI).

    ii. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.

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

b. Genzyme will:

    i. Ensure that the KYNAMRO REMS Prescriber Education and Enrollment Kit is available through the REMS website at www.KynamroREMS.com or from the KYNAMRO REMS Program coordinating center at 877-596-2676. The KYNAMRO REMS Prescriber Education and Enrollment Kit consists of:

        - the PI,
        - *Prescriber Training* slide set,
        - *Summary of Monitoring Recommendations*,
        - *Prescriber Enrollment Form*, and
        - *Prescription Authorization Form*.

    ii. Ensure that prescriber enrollment can be completed by faxing the forms to the KYNAMRO REMS Program coordinating center at 877-778-9008.

    iii. Ensure that HCPs complete the *Prescriber Training* and the *Prescriber Enrollment Form* before activating prescribers' certification in the KYNAMRO REMS Program.

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

    v. Inform certified prescribers following substantive changes to the KYNAMRO REMS or KYNAMRO REMS Program. Substantive changes include: significant changes to the operation of the KYNAMRO REMS Program or changes to the PI that affect the risk-benefit profile of KYNAMRO.

The following materials are part of the KYNAMRO REMS and are appended:

- KYNAMRO REMS Prescriber Education and Enrollment Kit:

    - *Prescriber Training* slide set
    - *Summary of Monitoring Recommendations*
    - *Prescriber Enrollment Form*
    - *Prescription Authorization Form*
- KYNAMRO REMS website

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

a. Genzyme will ensure that KYNAMRO will be dispensed only by certified pharmacies.

b. To become certified to dispense KYNAMRO, the authorized pharmacy representative must agree to the following:

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

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

1) the prescriber is certified in the KYNAMRO REMS Program;

2) the KYNAMRO 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 KYNAMRO REMS Program.

iv. To provide prescription data to the KYNAMRO REMS program.

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

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

i. they understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and

non-high density lipoprotein-cholesterol (non-HDL-C) in patients with HoFH;

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

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

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

B. Implementation System

1. Genzyme will ensure that KYNAMRO is distributed to and dispensed only by certified pharmacies.

2. Genzyme will maintain, monitor, and evaluate the implementation of the KYNAMRO REMS Program.

a. Genzyme will develop and follow written procedures and scripts to implement the REMS.

b. Genzyme will maintain a secure, validated database of all certified prescribers and pharmacies that is in compliance with 21 CFR Part 11 regulations.

c. Genzyme will send confirmation of certification to each certified pharmacy.

d. Genzyme will maintain a KYNAMRO REMS Program coordinating center with a call center to support patients, prescribers, and pharmacies in interfacing with the KYNAMRO REMS Program.

e. Genzyme will ensure that all materials listed in or appended to the KYNAMRO REMS Program will be available through the KYNAMRO REMS website at www.KynamroREMS.com or from the KYNAMRO REMS Program coordinating center at 877-596-2676.

f. If there are substantive changes to the KYNAMRO REMS or KYNAMRO REMS Program, Genzyme will update all affected materials and notify enrolled prescribers and certified pharmacies, as applicable. Substantive changes include significant changes to the operation of the KYNAMRO REMS Program or changes to the PI that affect the risk-benefit profile of KYNAMRO.

g. Genzyme 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 KYNAMRO REMS Program. Corrective action will be instituted by Genzyme if noncompliance is found.

h. Based on monitoring and evaluation of the KYNAMRO REMS elements to assure safe use, Genzyme will take reasonable steps to improve implementation of these elements and to maintain compliance with the KYNAMRO REMS Program requirements, as applicable.

C. Timetable for Submission of Assessments

Genzyme will submit REMS Assessments to FDA at 6 months, 12 months, and annually thereafter from the date of initial approval of the KYNAMRO 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. Genzyme will submit each assessment so that it will be received by FDA on or before the due date.

APPENDICES

APPENDIX 1

WEBSITE SCREEN SHOT - TRAINING SLIDE SET

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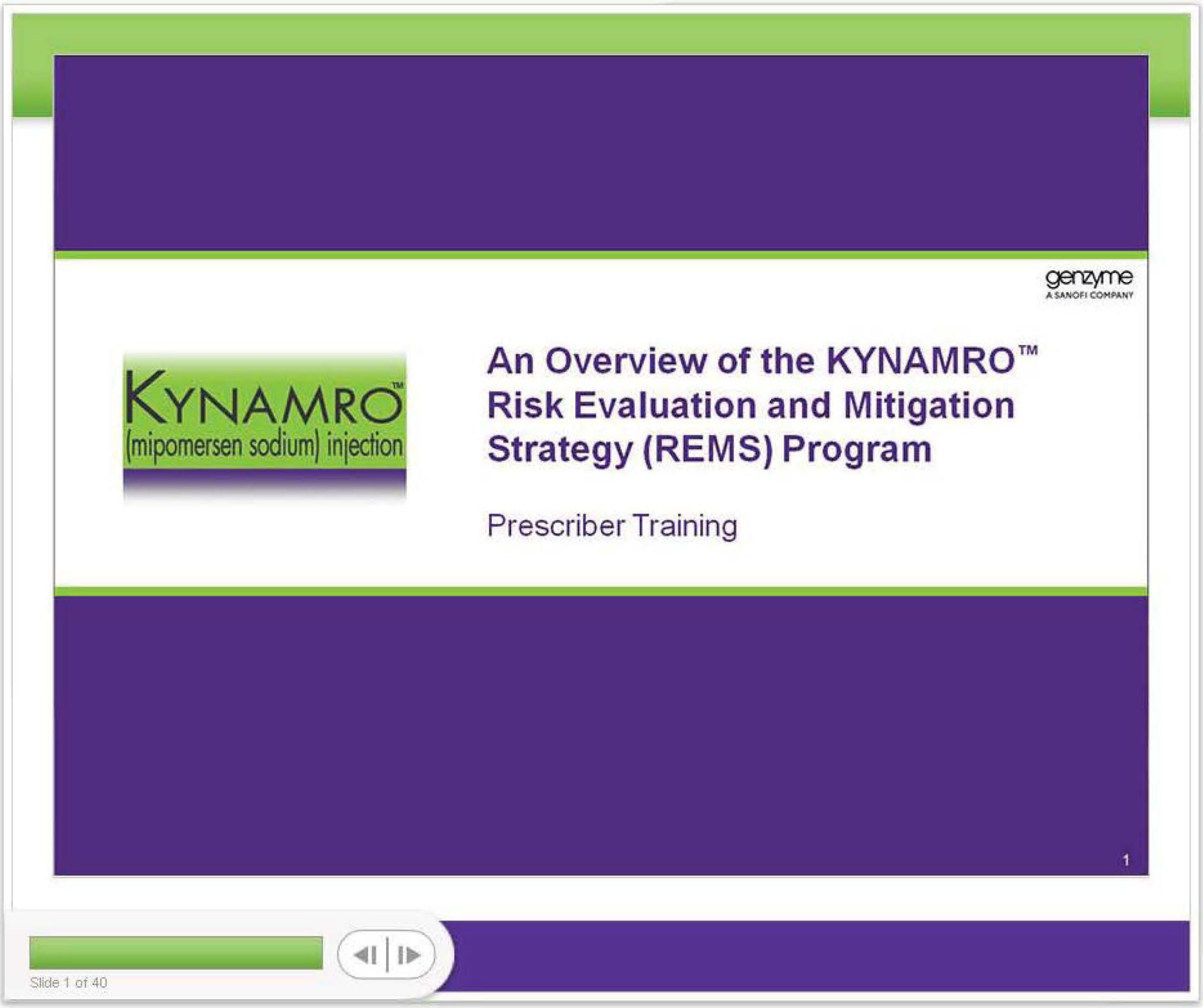
Prescribing Information Important Safety Information



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An Overview of the KYNAMRO™ Risk Evaluation and Mitigation Strategy (REMS) Program

Prescriber Training

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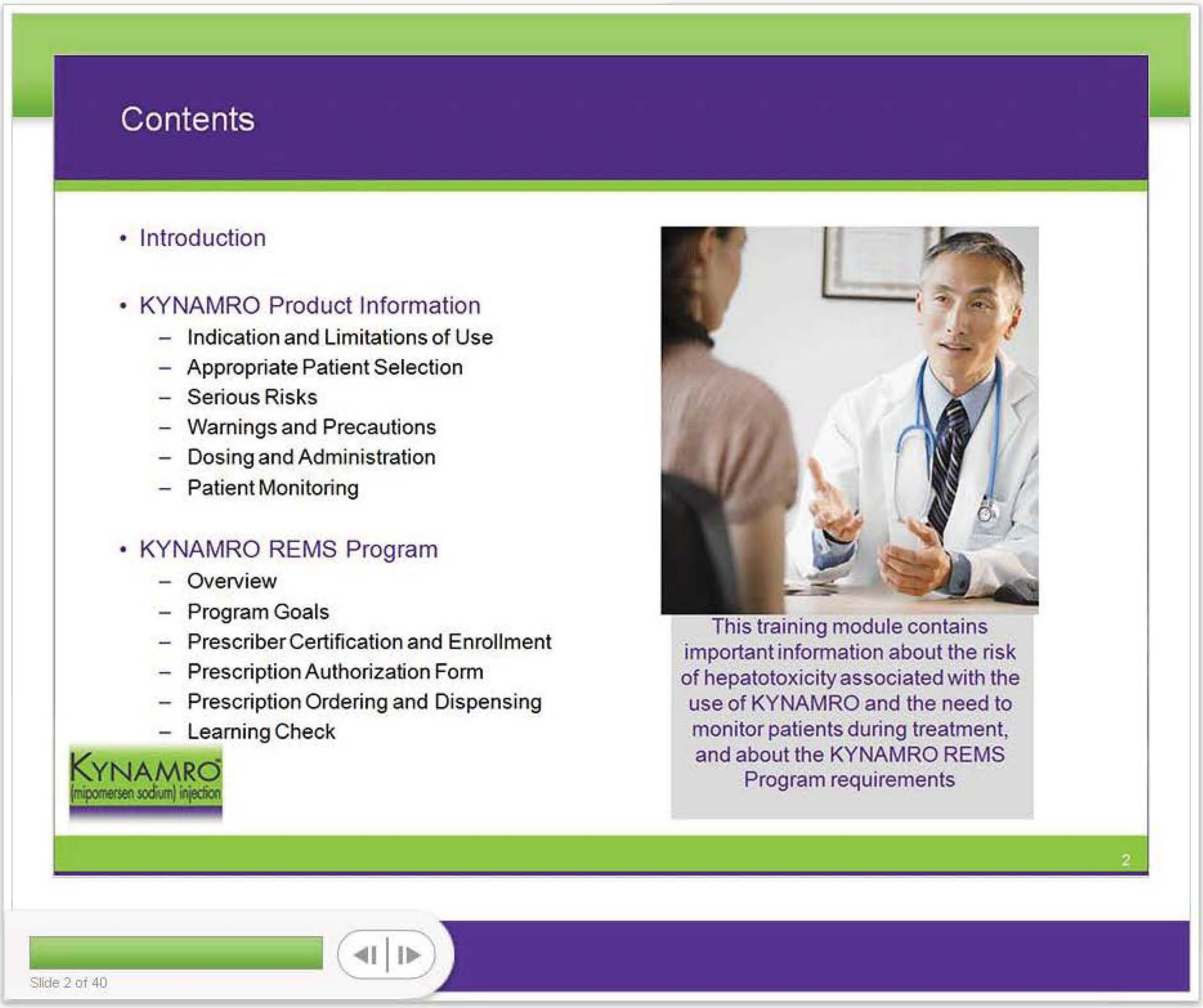

Contents

- Introduction
- KYNAMRO Product Information
  - Indication and Limitations of Use
  - Appropriate Patient Selection
  - Serious Risks
  - Warnings and Precautions
  - Dosing and Administration
  - Patient Monitoring
- KYNAMRO REMS Program
  - Overview
  - Program Goals
  - Prescriber Certification and Enrollment
  - Prescription Authorization Form
  - Prescription Ordering and Dispensing
  - Learning Check

This training module contains important information about the risk of hepatotoxicity associated with the use of KYNAMRO and the need to monitor patients during treatment, and about the KYNAMRO REMS Program requirements

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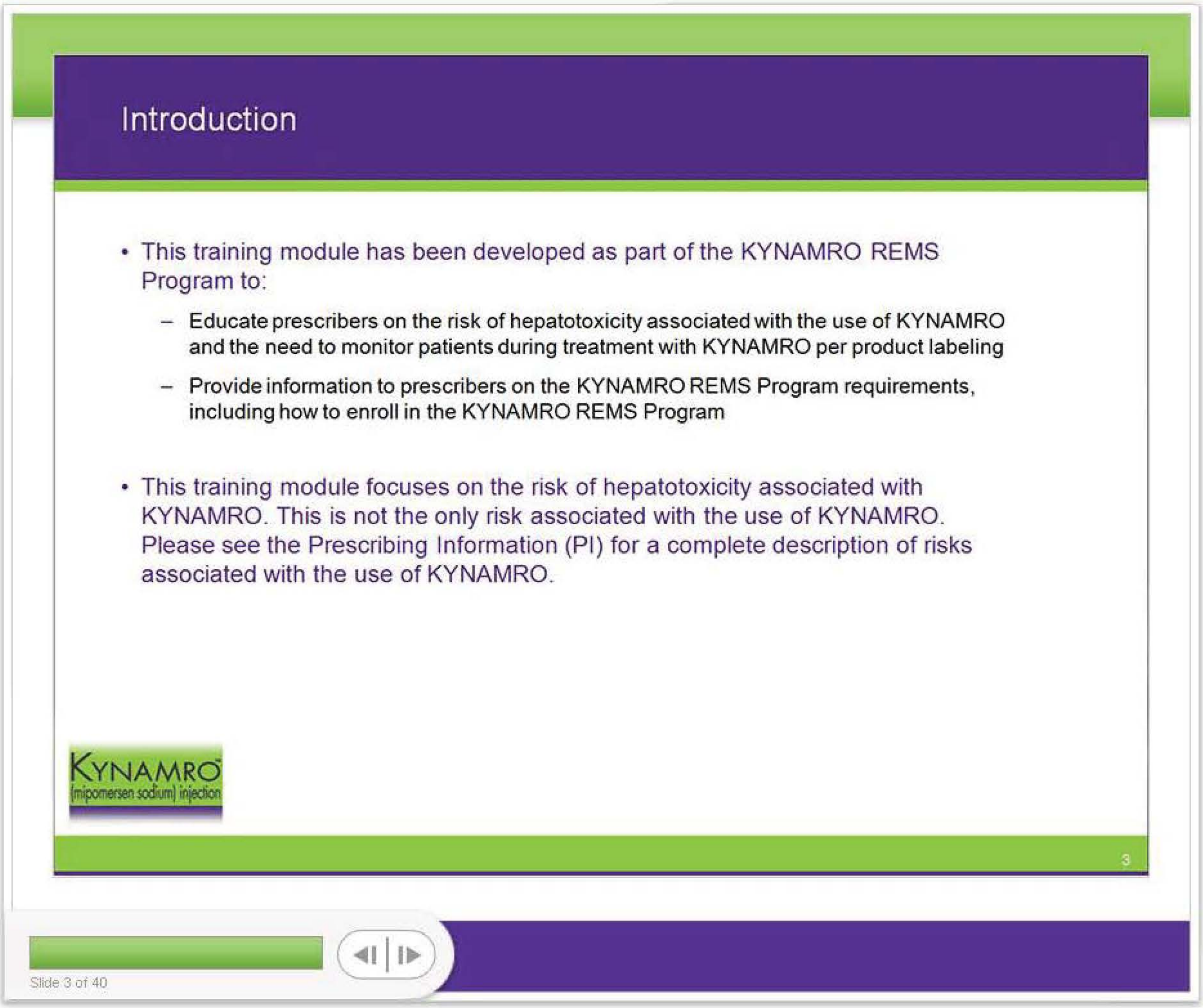

Introduction

- This training module has been developed as part of the KYNAMRO REMS Program to:
  - Educate prescribers on the risk of hepatotoxicity associated with the use of KYNAMRO and the need to monitor patients during treatment with KYNAMRO per product labeling
  - Provide information to prescribers on the KYNAMRO REMS Program requirements, including how to enroll in the KYNAMRO REMS Program
- This training module focuses on the risk of hepatotoxicity associated with KYNAMRO. This is not the only risk associated with the use of KYNAMRO. Please see the Prescribing Information (PI) for a complete description of risks associated with the use of KYNAMRO.

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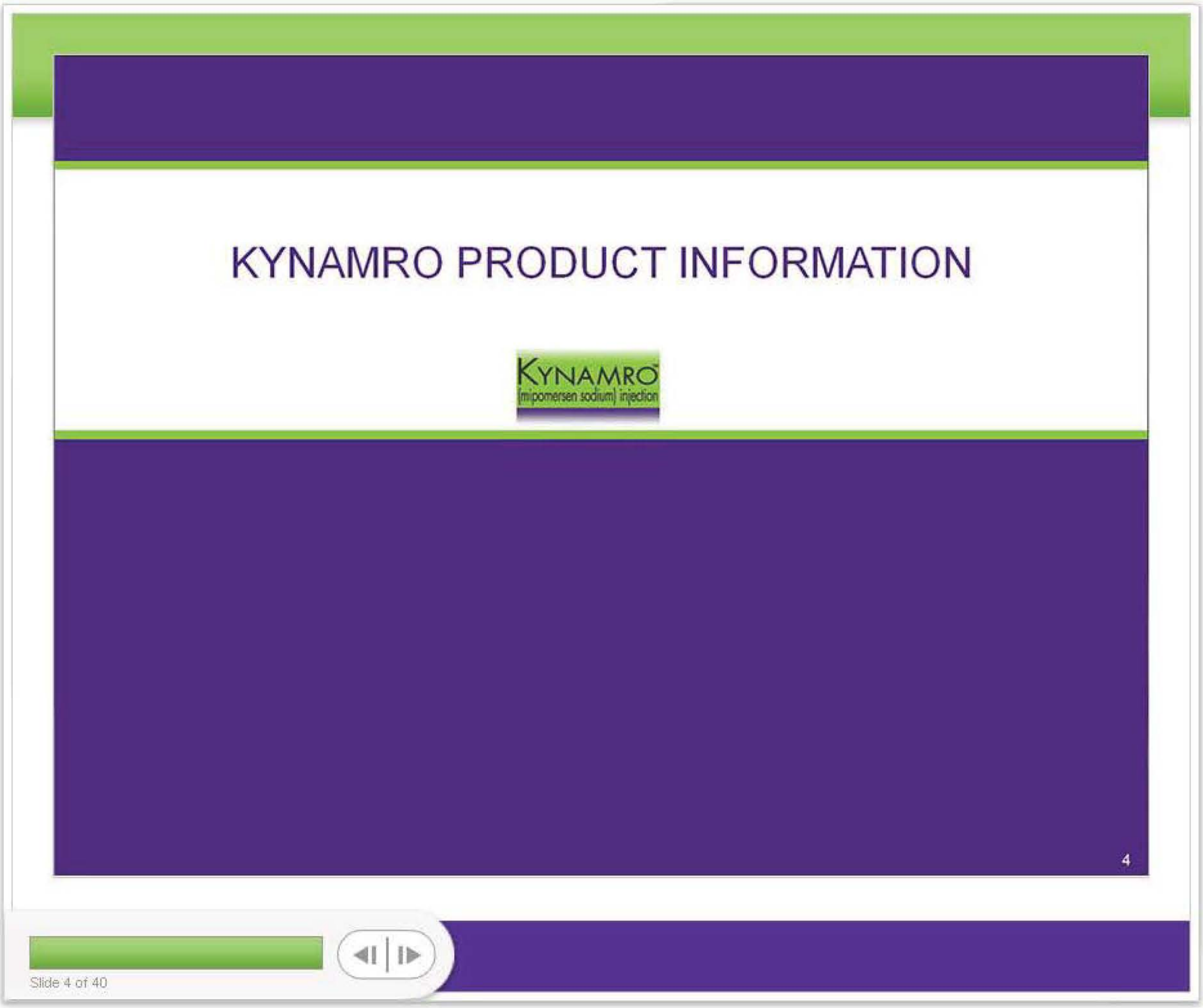
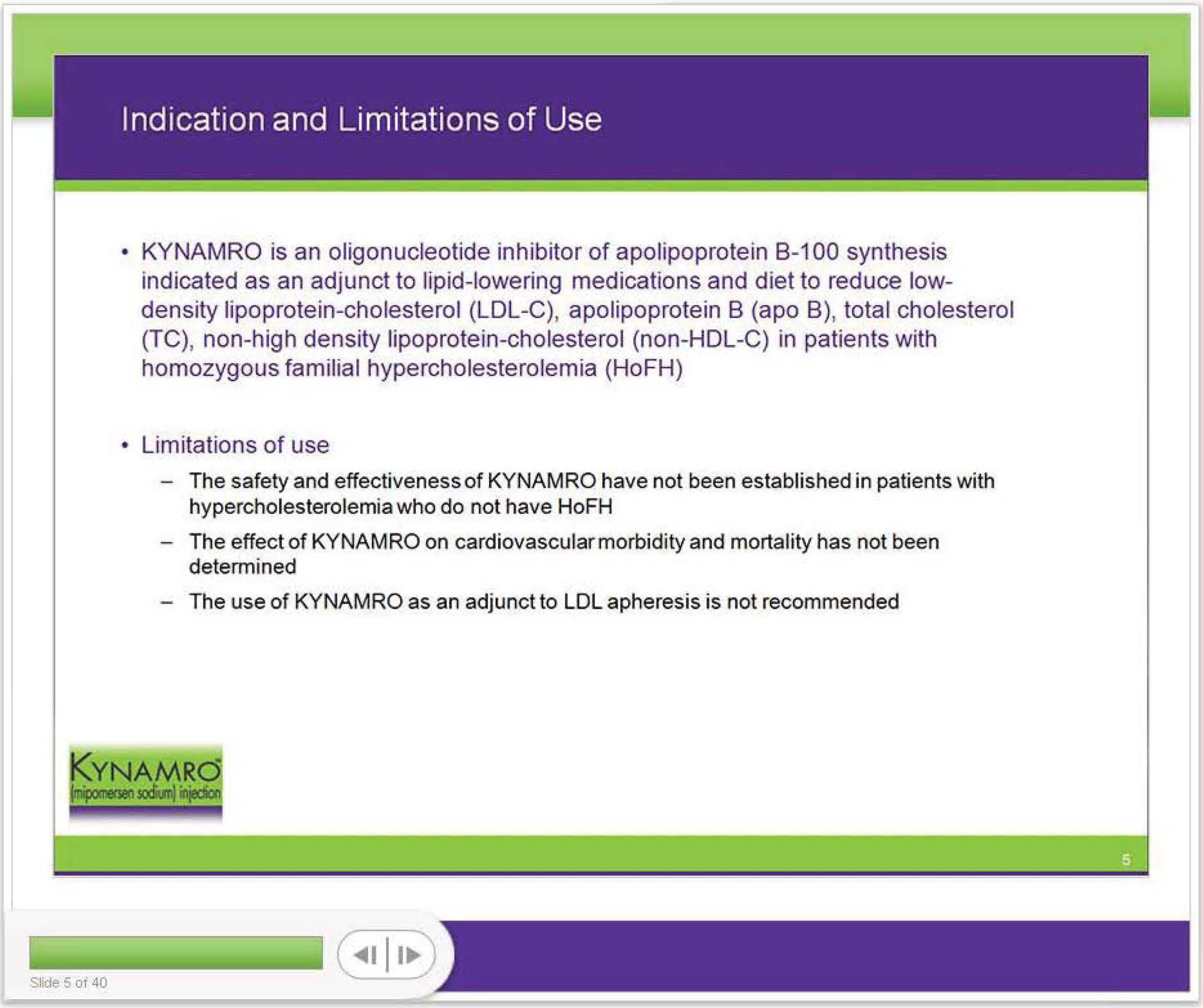


KYNAMRO PRODUCT INFORMATION



Indication and Limitations of Use

- KYNAMRO is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis indicated as an adjunct to lipid-lowering medications and diet to reduce low-density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)
- Limitations of use
  - The safety and effectiveness of KYNAMRO have not been established in patients with hypercholesterolemia who do not have HoFH
  - The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
  - The use of KYNAMRO as an adjunct to LDL apheresis is not recommended

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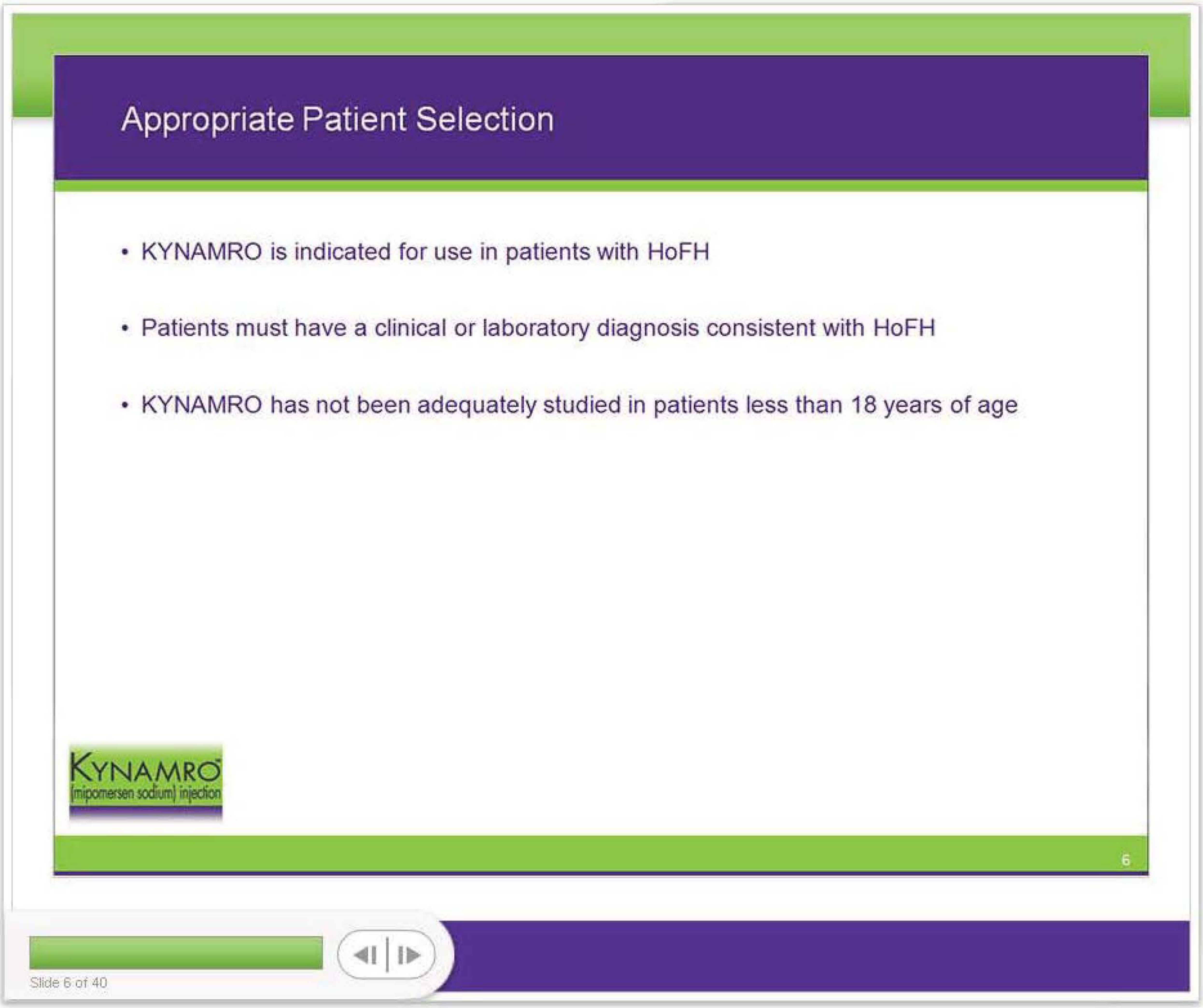
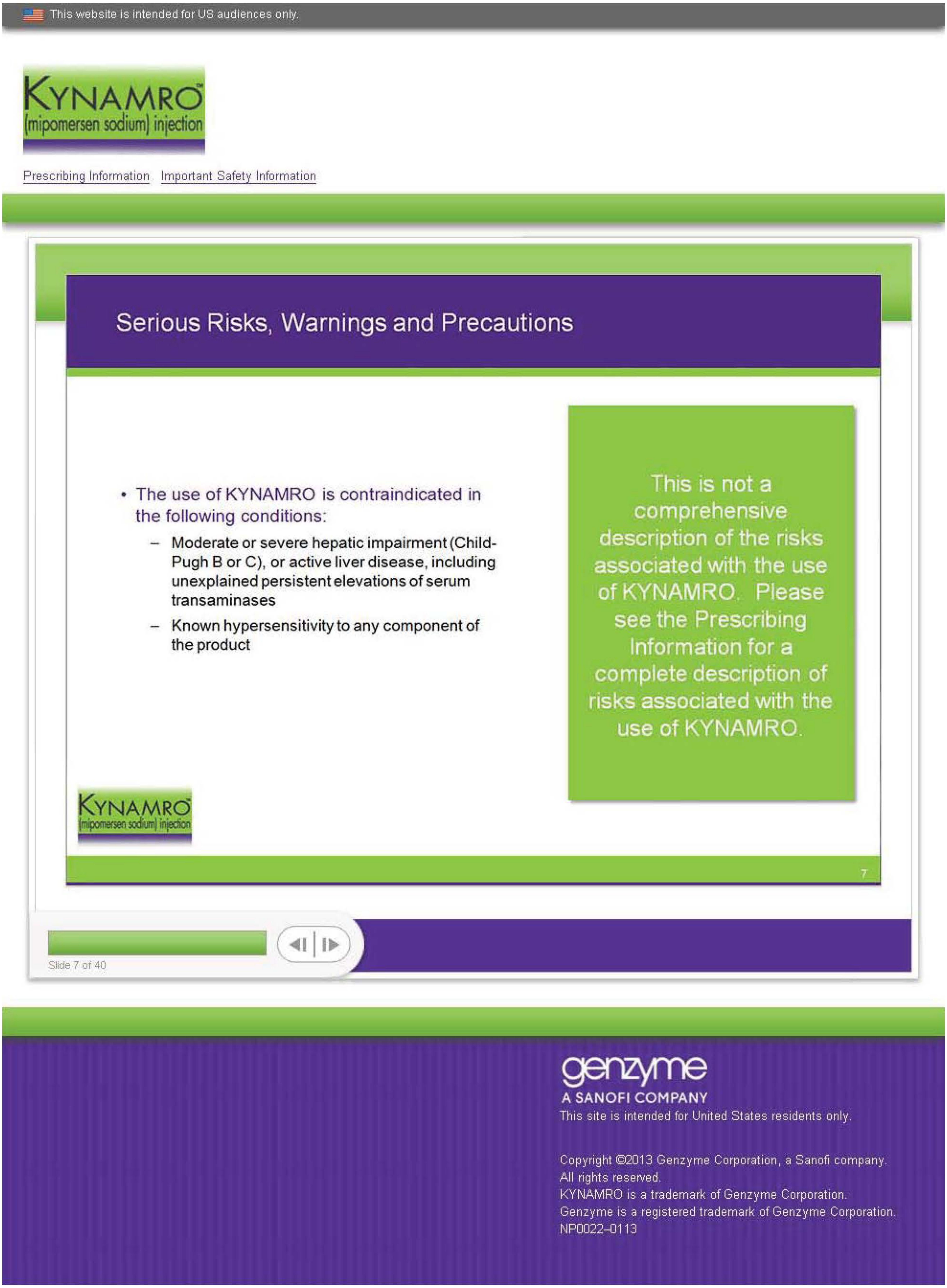


Appropriate Patient Selection

- KYNAMRO is indicated for use in patients with HoFH
- Patients must have a clinical or laboratory diagnosis consistent with HoFH
- KYNAMRO has not been adequately studied in patients less than 18 years of age



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Prescribing Information | Important Safety Information

Serious Risks, Warnings and Precautions

- The use of KYNAMRO is contraindicated in the following conditions:
    - Moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases
    - Known hypersensitivity to any component of the product

This is not a comprehensive description of the risks associated with the use of KYNAMRO. Please see the Prescribing Information for a complete description of risks associated with the use of KYNAMRO.

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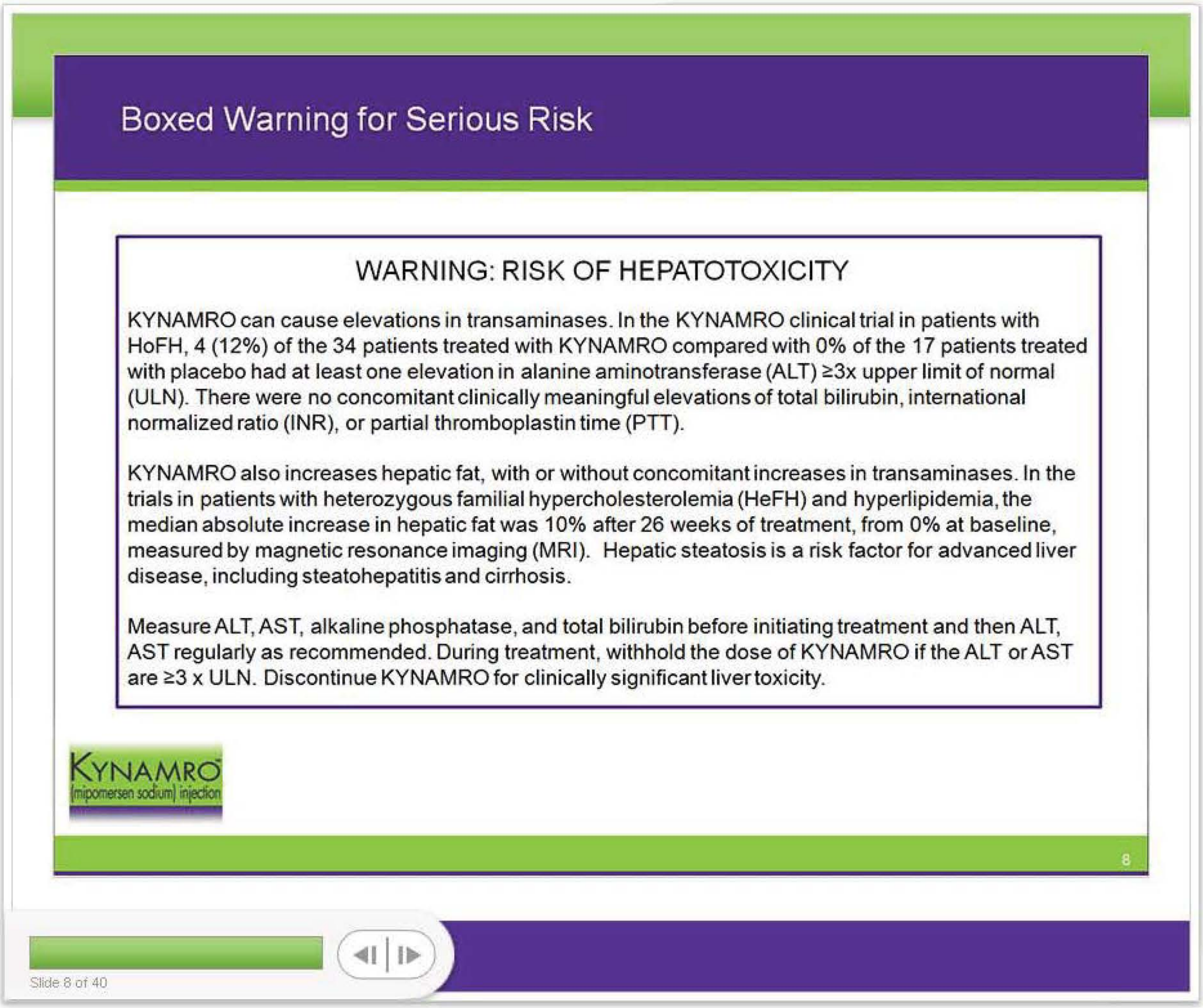

Boxed Warning for Serious Risk

WARNING: RISK OF HEPATOTOXICITY

KYNAMRO can cause elevations in transaminases. In the KYNAMRO clinical trial in patients with HoFH, 4 (12%) of the 34 patients treated with KYNAMRO compared with 0% of the 17 patients treated with placebo had at least one elevation in alanine aminotransferase (ALT) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), or partial thromboplastin time (PTT).

KYNAMRO also increases hepatic fat, with or without concomitant increases in transaminases. In the trials in patients with heterozygous familial hypercholesterolemia (HeFH) and hyperlipidemia, the median absolute increase in hepatic fat was 10% after 26 weeks of treatment, from 0% at baseline, measured by magnetic resonance imaging (MRI). Hepatic steatosis is a risk factor for advanced liver disease, including steatohepatitis and cirrhosis.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT, AST regularly as recommended. During treatment, withhold the dose of KYNAMRO if the ALT or AST are ≥3 x ULN. Discontinue KYNAMRO for clinically significant liver toxicity.

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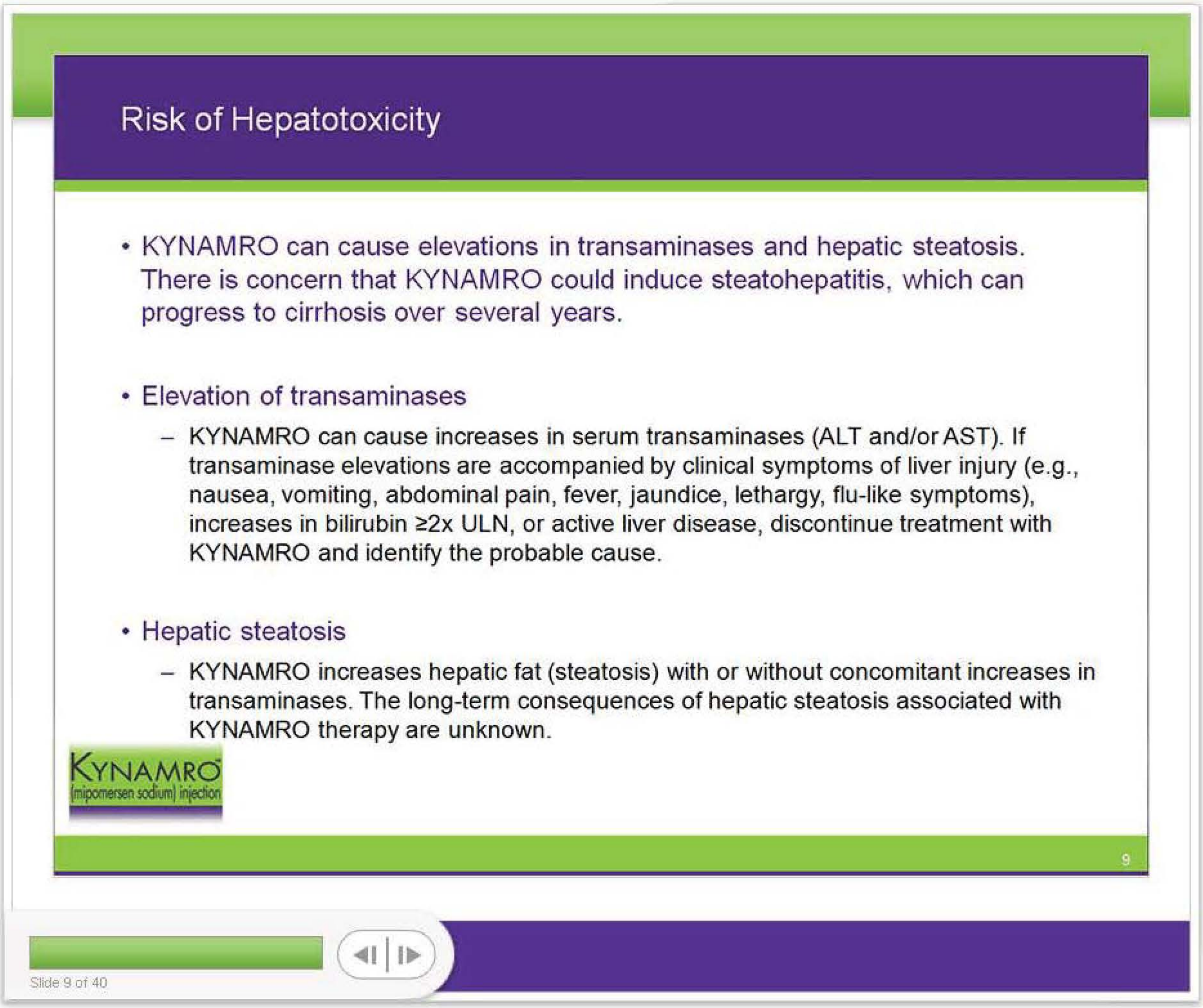

Risk of Hepatotoxicity

- KYNAMRO can cause elevations in transaminases and hepatic steatosis. There is concern that KYNAMRO could induce steatohepatitis, which can progress to cirrhosis over several years.
- Elevation of transaminases
  - KYNAMRO can cause increases in serum transaminases (ALT and/or AST). If transaminase elevations are accompanied by clinical symptoms of liver injury (e.g., nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like symptoms), increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with KYNAMRO and identify the probable cause.
- Hepatic steatosis
  - KYNAMRO increases hepatic fat (steatosis) with or without concomitant increases in transaminases. The long-term consequences of hepatic steatosis associated with KYNAMRO therapy are unknown.

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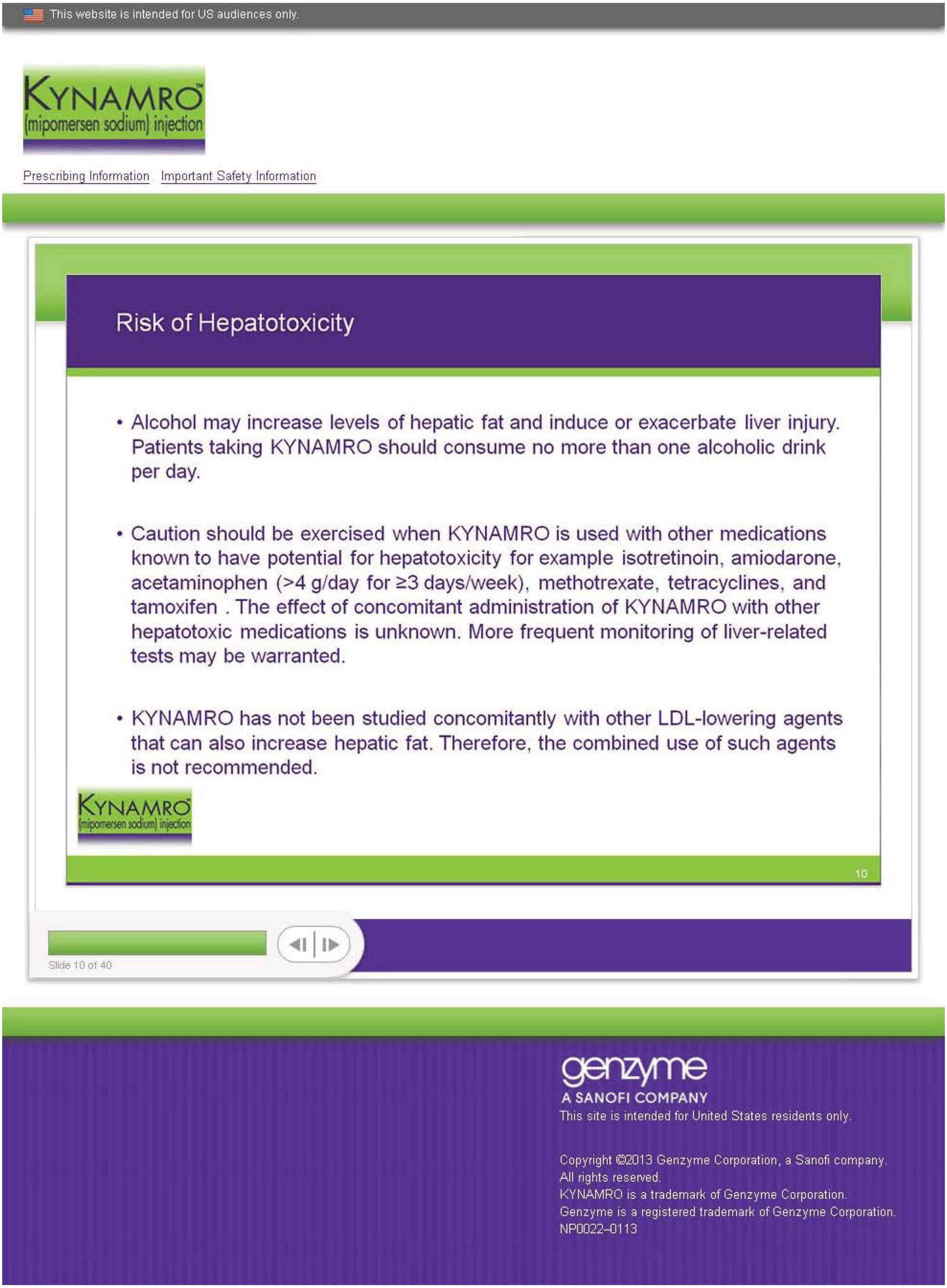

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Prescribing Information Important Safety Information

Risk of Hepatotoxicity

- Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than one alcoholic drink per day.
- Caution should be exercised when KYNAMRO is used with other medications known to have potential for hepatotoxicity for example isotretinoin, amiodarone, acetaminophen (>4 g/day for ≥3 days/week), methotrexate, tetracyclines, and tamoxifen . The effect of concomitant administration of KYNAMRO with other hepatotoxic medications is unknown. More frequent monitoring of liver-related tests may be warranted.
- KYNAMRO 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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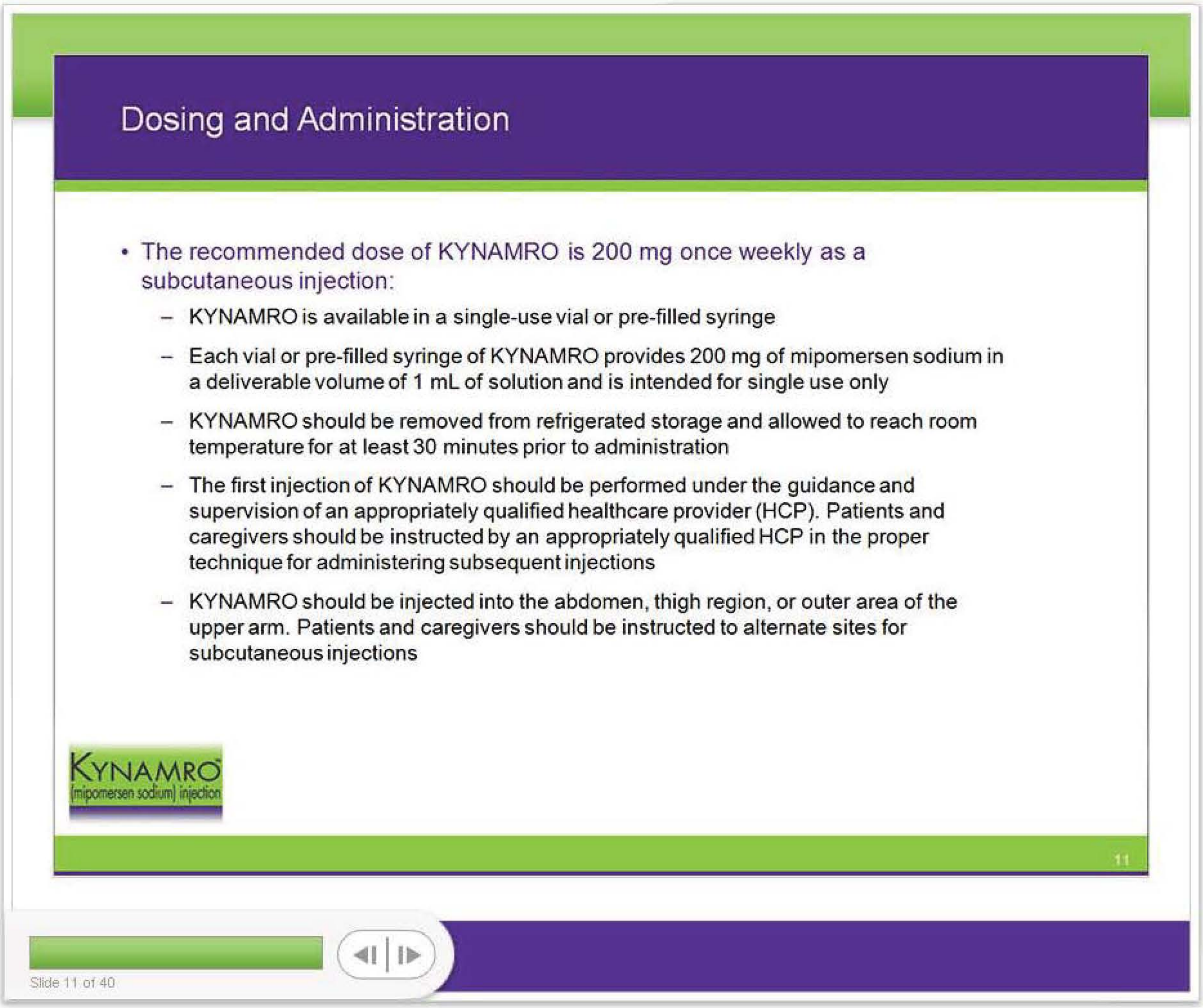

Dosing and Administration

- The recommended dose of KYNAMRO is 200 mg once weekly as a subcutaneous injection:
  - KYNAMRO is available in a single-use vial or pre-filled syringe
  - Each vial or pre-filled syringe of KYNAMRO provides 200 mg of mipomersen sodium in a deliverable volume of 1 mL of solution and is intended for single use only
  - KYNAMRO should be removed from refrigerated storage and allowed to reach room temperature for at least 30 minutes prior to administration
  - The first injection of KYNAMRO should be performed under the guidance and supervision of an appropriately qualified healthcare provider (HCP). Patients and caregivers should be instructed by an appropriately qualified HCP in the proper technique for administering subsequent injections
  - KYNAMRO should be injected into the abdomen, thigh region, or outer area of the upper arm. Patients and caregivers should be instructed to alternate sites for subcutaneous injections

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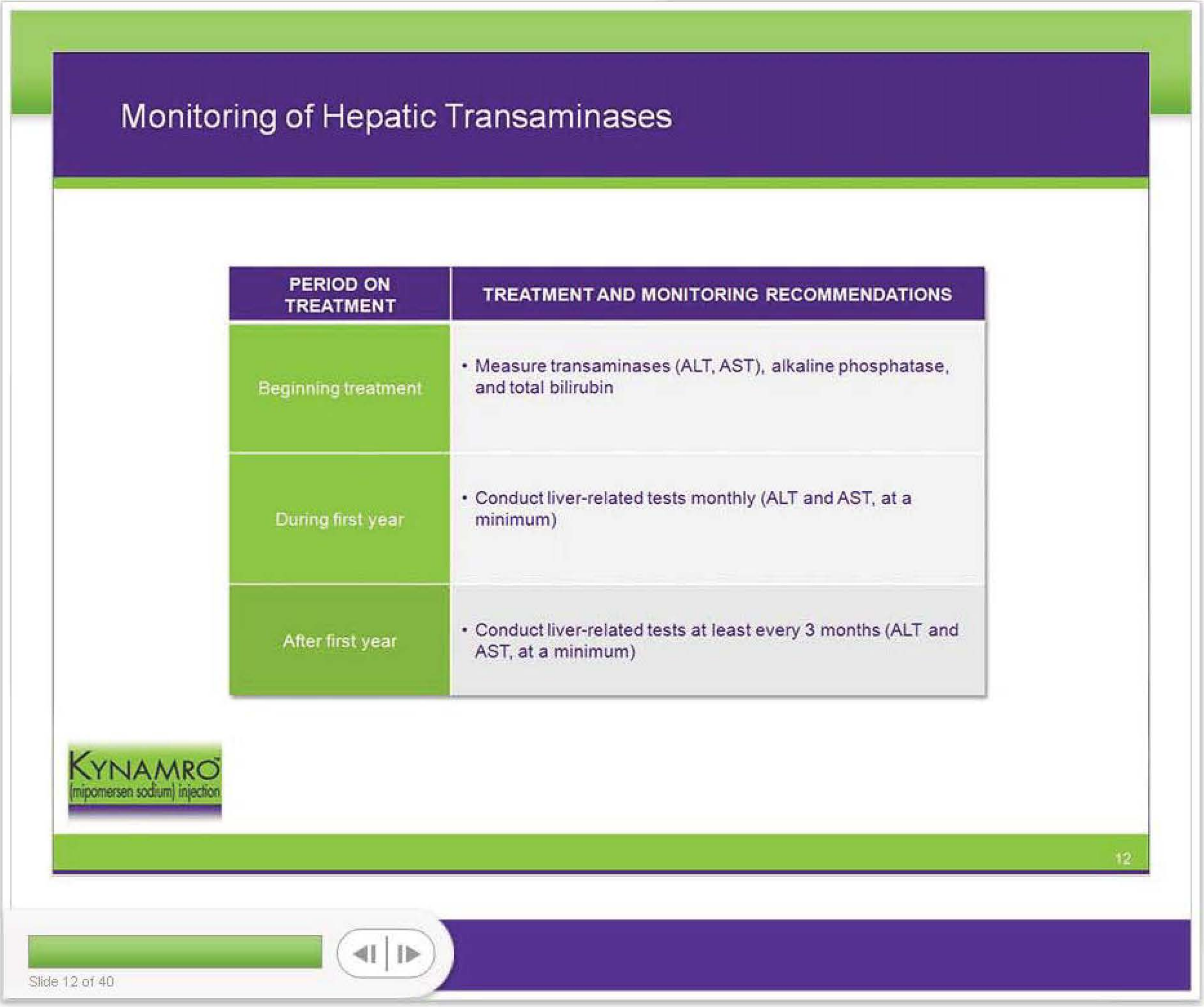

Monitoring of Hepatic Transaminases

PERIOD ON TREATMENT	TREATMENT AND MONITORING RECOMMENDATIONS
Beginning treatment	• Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin
During first year	• Conduct liver-related tests monthly (ALT and AST, at a minimum)
After first year	• Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)

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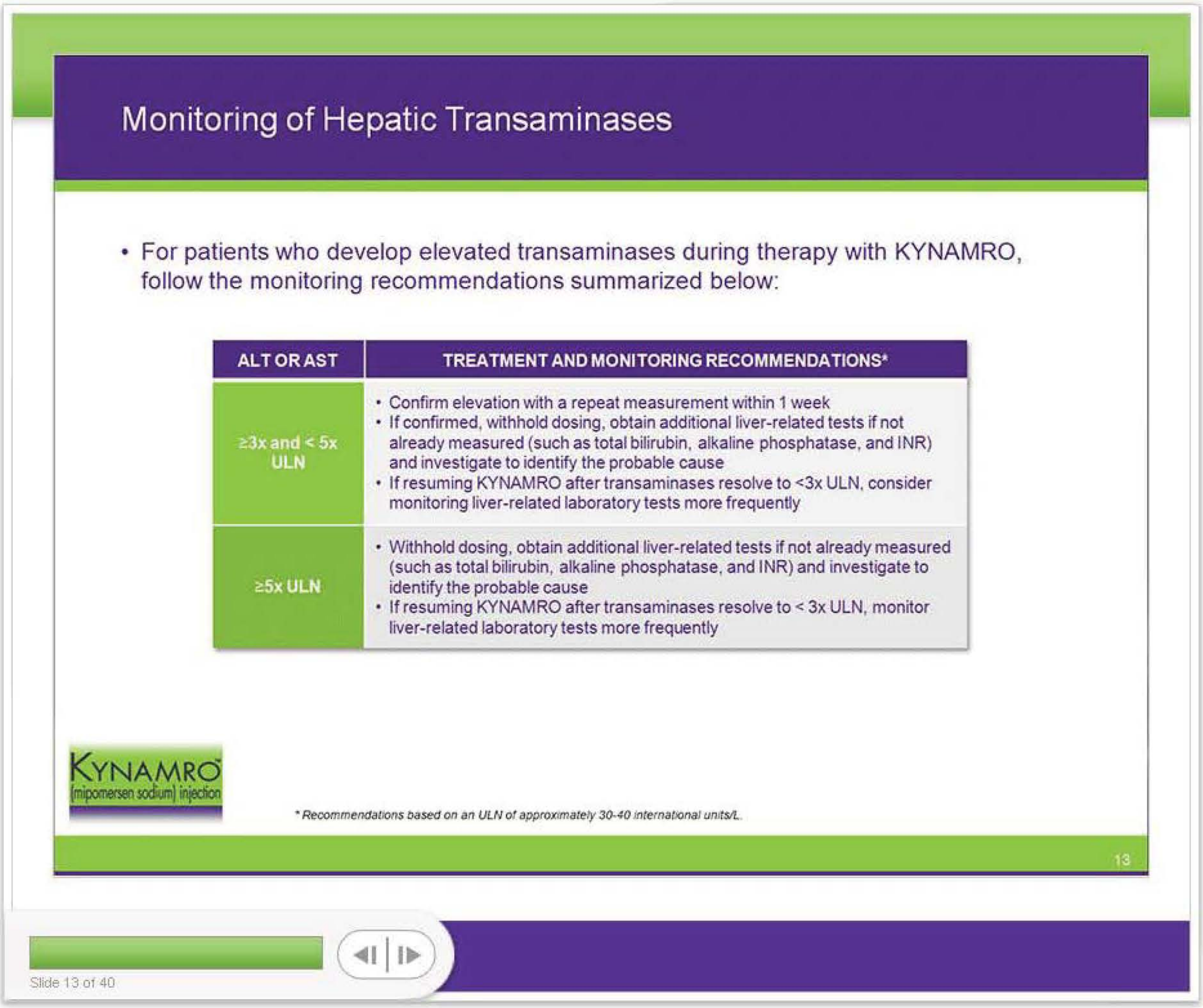

Monitoring of Hepatic Transaminases

- For patients who develop elevated transaminases during therapy with KYNAMRO, follow the monitoring recommendations summarized below:

ALT OR AST	TREATMENT AND MONITORING RECOMMENDATIONS*
≥3x and < 5x ULN	• Confirm elevation with a repeat measurement within 1 week • If confirmed, withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If resuming KYNAMRO after transaminases resolve to <3x ULN, consider monitoring liver-related laboratory tests more frequently
≥5x ULN	• Withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If resuming KYNAMRO after transaminases resolve to < 3x ULN, monitor liver-related laboratory tests more frequently

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

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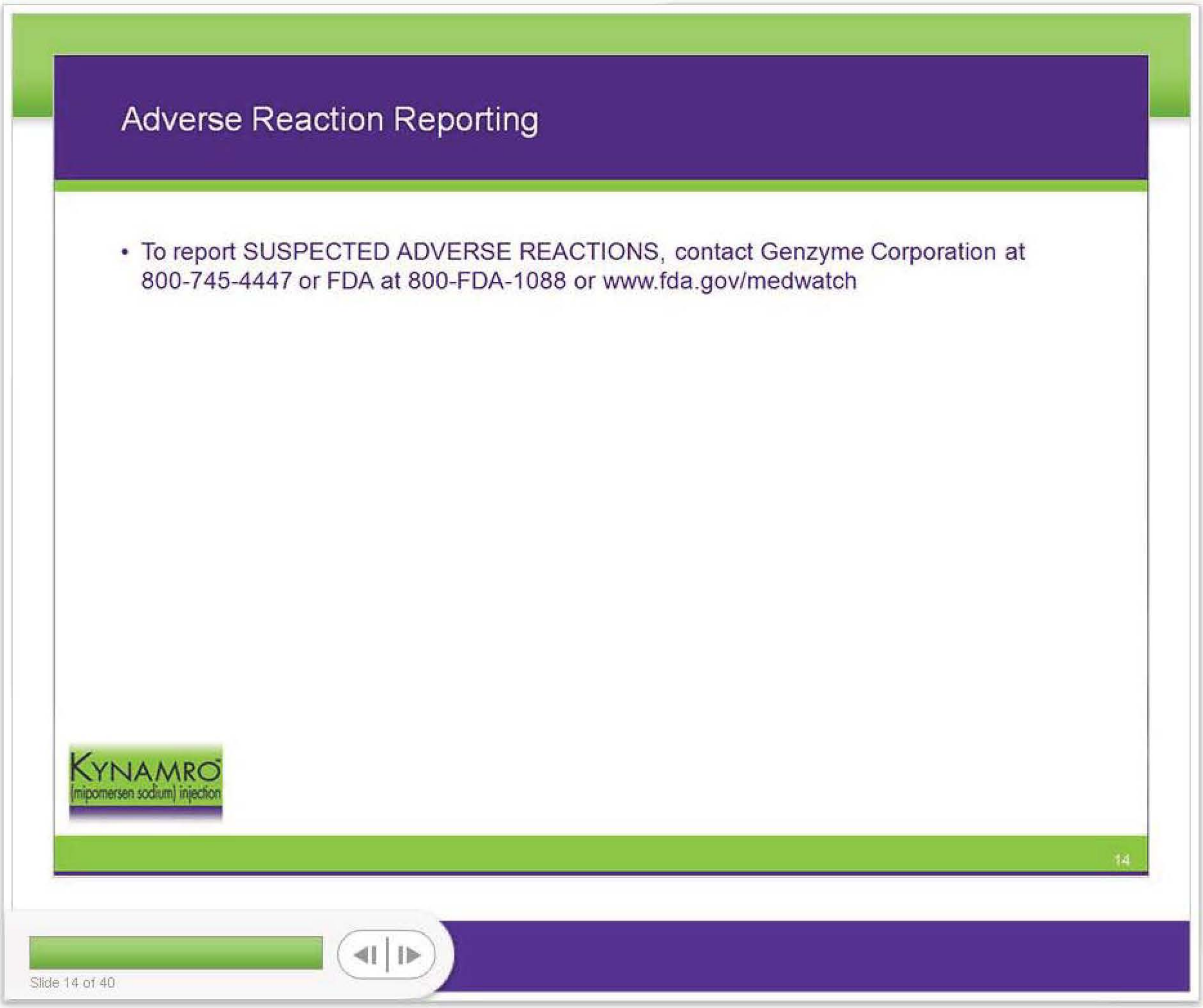

Adverse Reaction Reporting

- To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 800-745-4447 or FDA at 800-FDA-1088 or www.fda.gov/medwatch

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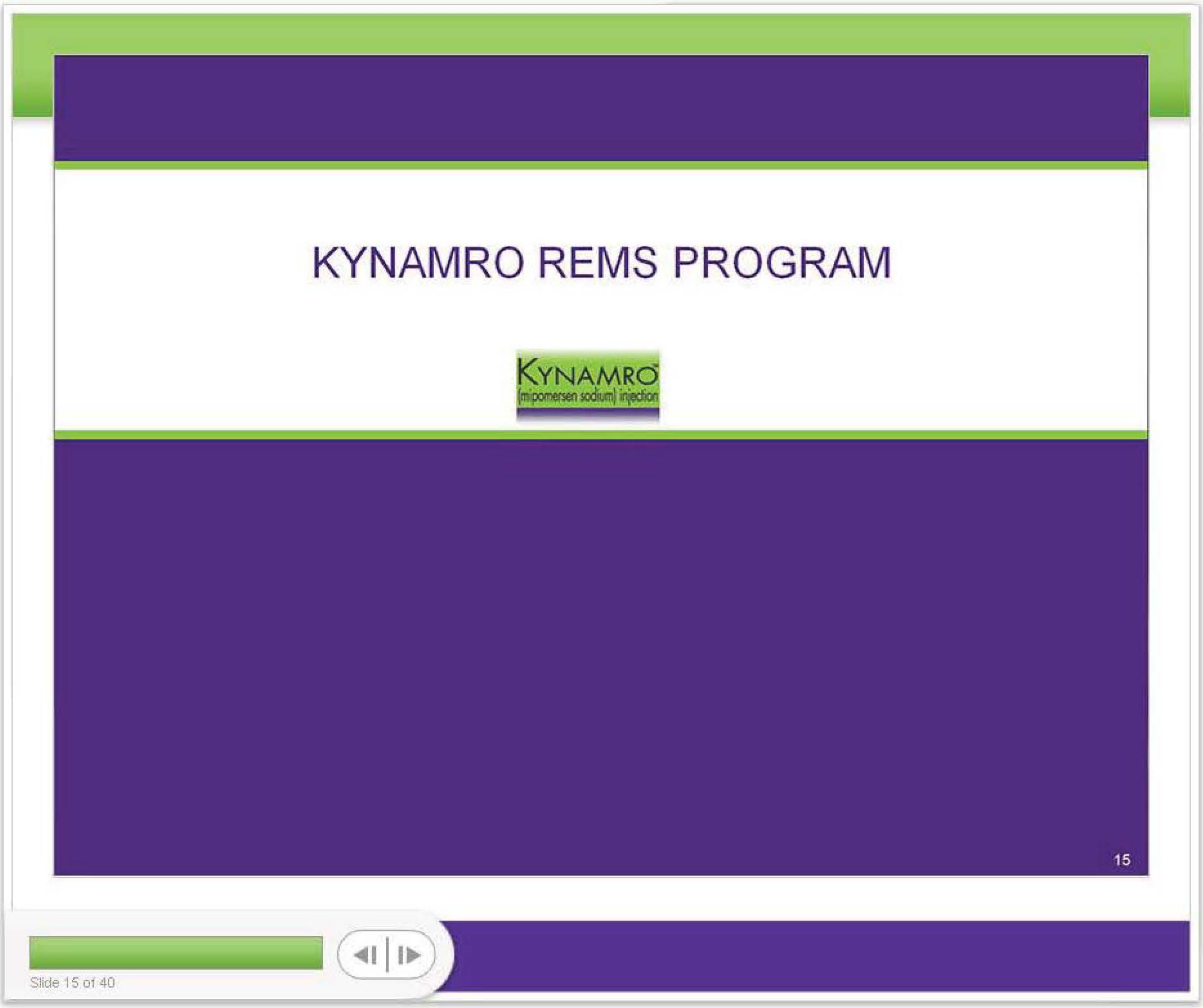

KYNAMRO REMS PROGRAM

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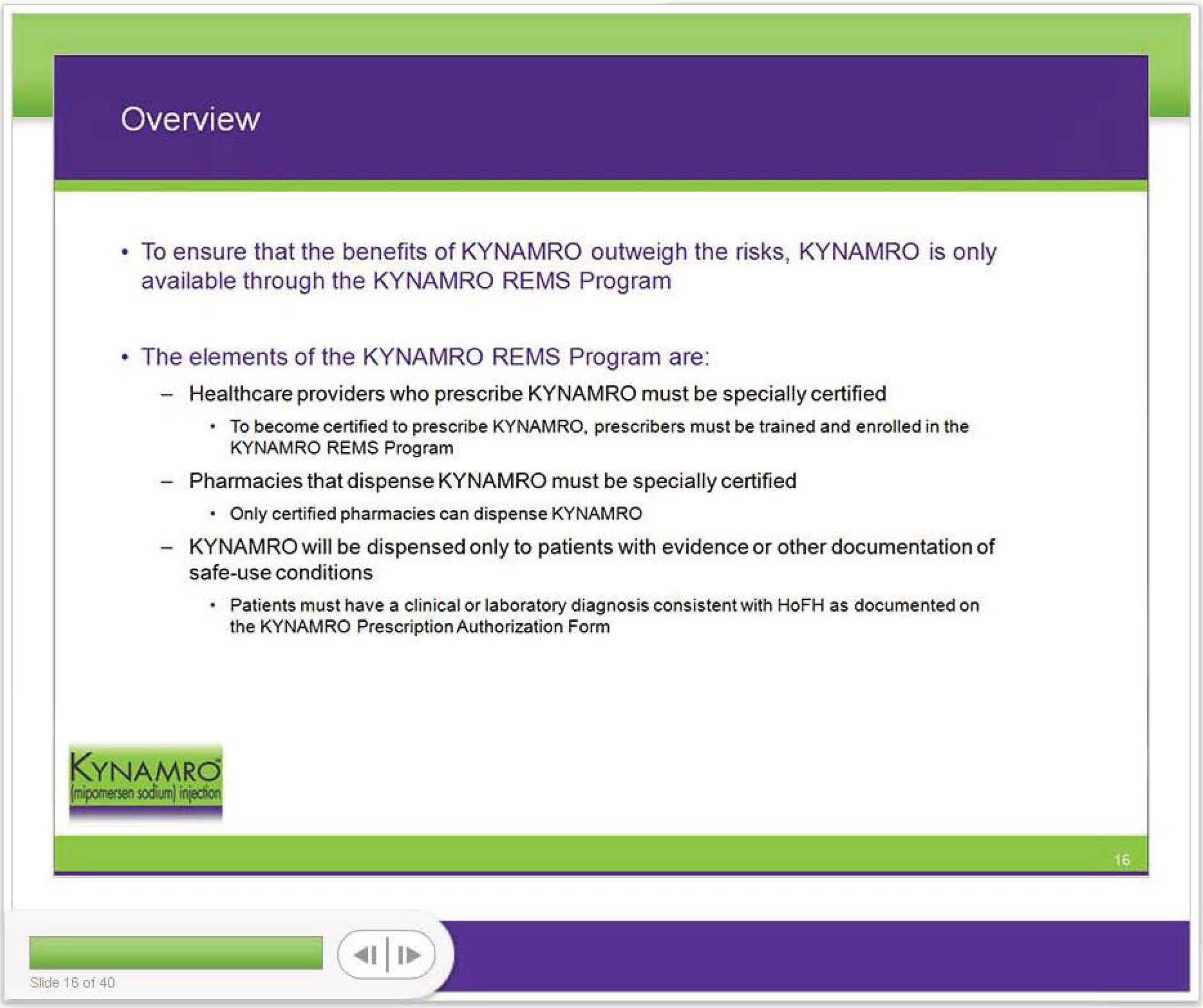

Overview

- To ensure that the benefits of KYNAMRO outweigh the risks, KYNAMRO is only available through the KYNAMRO REMS Program
- The elements of the KYNAMRO REMS Program are:
  - Healthcare providers who prescribe KYNAMRO must be specially certified
    - To become certified to prescribe KYNAMRO, prescribers must be trained and enrolled in the KYNAMRO REMS Program
  - Pharmacies that dispense KYNAMRO must be specially certified
    - Only certified pharmacies can dispense KYNAMRO
  - KYNAMRO will be dispensed only to patients with evidence or other documentation of safe-use conditions
    - Patients must have a clinical or laboratory diagnosis consistent with HoFH as documented on the KYNAMRO Prescription Authorization Form

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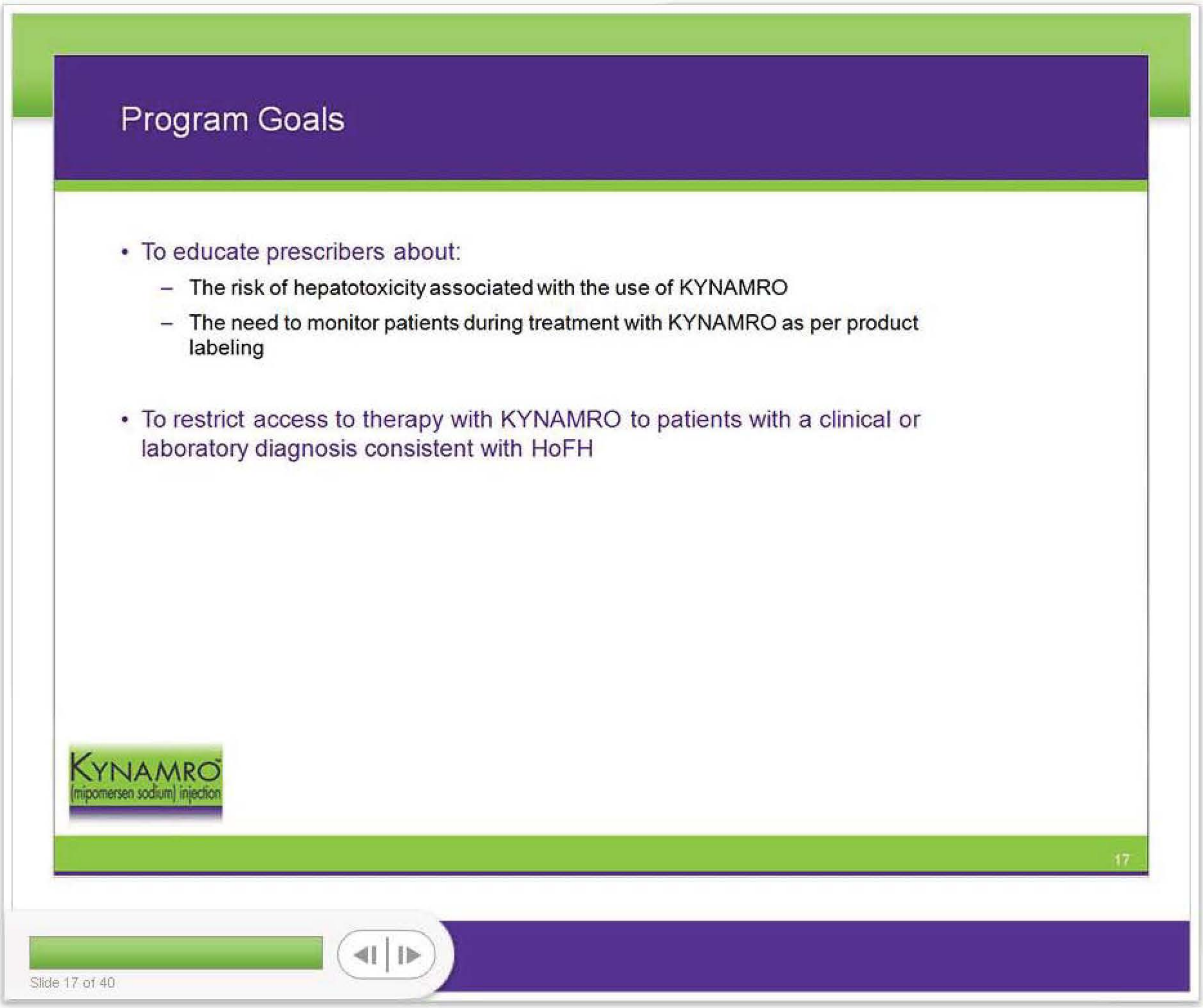

Program Goals

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

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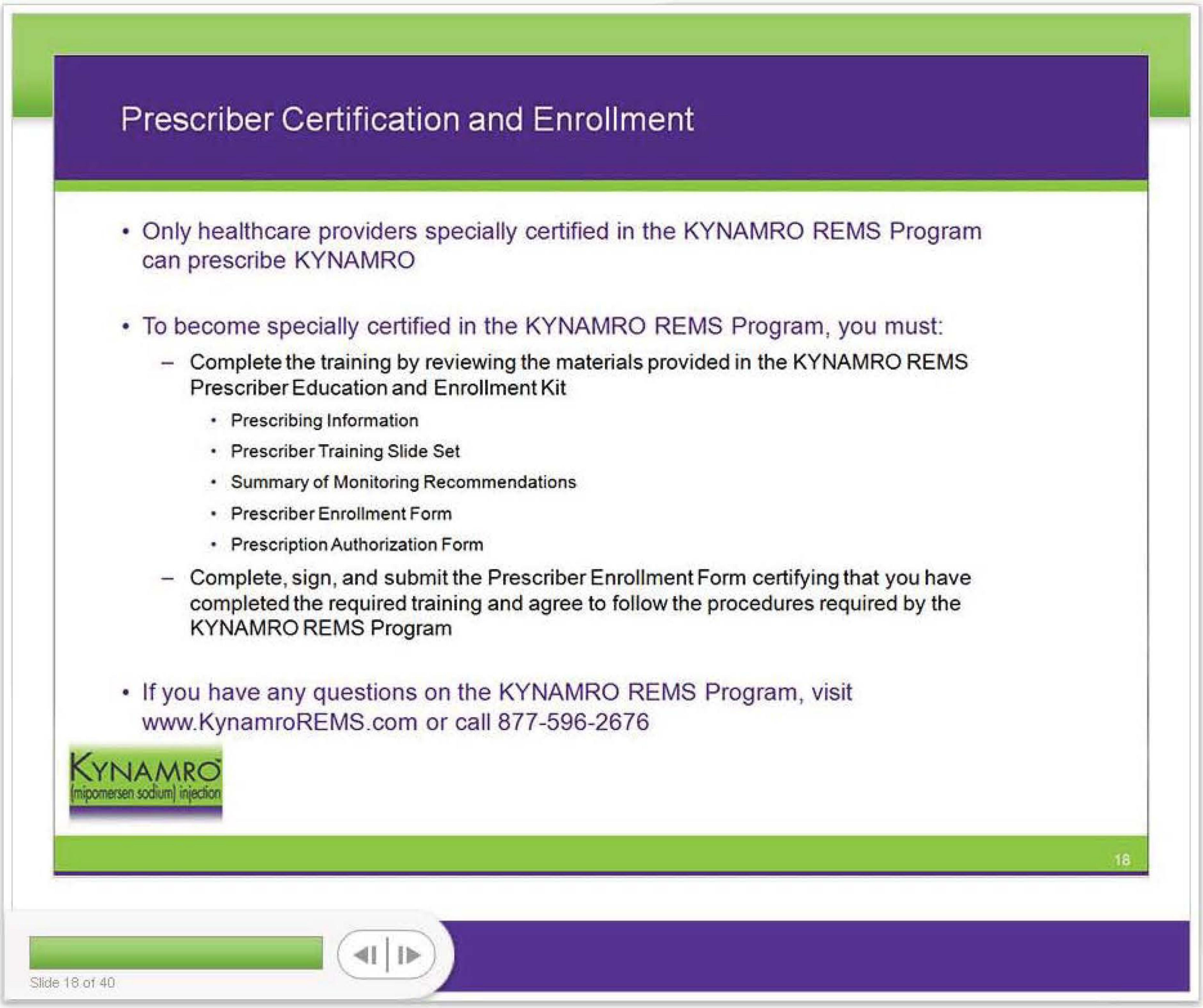

Prescriber Certification and Enrollment

- Only healthcare providers specially certified in the KYNAMRO REMS Program can prescribe KYNAMRO
- To become specially certified in the KYNAMRO REMS Program, you must:
  - Complete the training by reviewing the materials provided in the KYNAMRO REMS Prescriber Education and Enrollment Kit
    - Prescribing Information
    - Prescriber Training Slide Set
    - Summary of Monitoring Recommendations
    - Prescriber Enrollment Form
    - Prescription Authorization Form
  - Complete, sign, and submit the Prescriber Enrollment Form certifying that you have completed the required training and agree to follow the procedures required by the KYNAMRO REMS Program
- If you have any questions on the KYNAMRO REMS Program, visit www.KynamroREMS.com or call 877-596-2676

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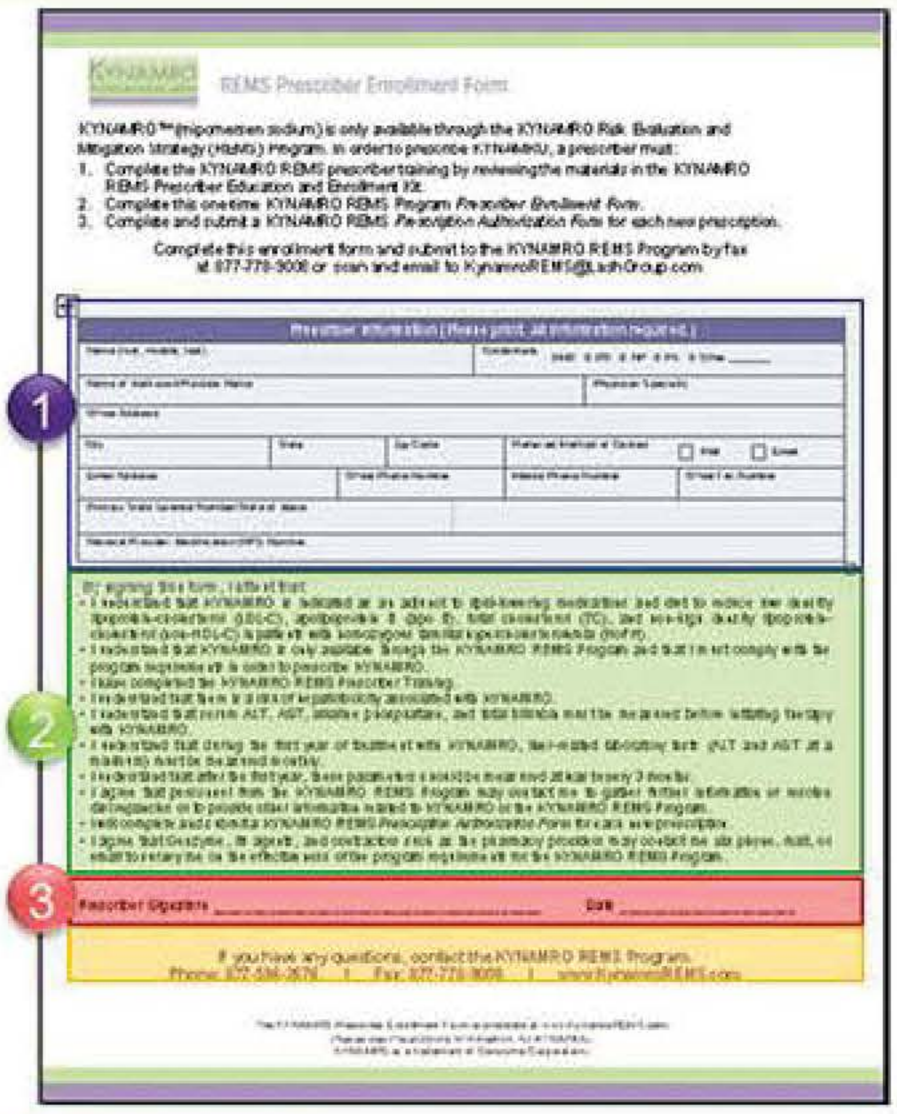
Prescribing Information   Important Safety Information

Prescriber Enrollment Form



REMS Prescriber Enrollment Form

KYNAMRO™ (mipomersen sodium) is only available through the KYNAMRO Risk Evaluation and Mitigation Strategy (REMS) Program. In order to prescribe KYNAMRO, a prescriber must:

1. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.
2. Complete this one-time KYNAMRO REMS Program *Prescriber Enrollment Form*.
3. Complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.

Complete this enrollment form and submit to the KYNAMRO REMS Program by fax at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

Prescriber Information (Please print, all information required.)

By signing this form, I attest that:

Prescriber Signature ____________ Date ____________

If you have any questions, contact the KYNAMRO REMS Program.
Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

1. Complete the Prescriber Information at the top of the form
2. Carefully review the attestations on the bottom half of the form
3. Sign and date the form to attest and agree to comply with the KYNAMRO REMS Program requirements

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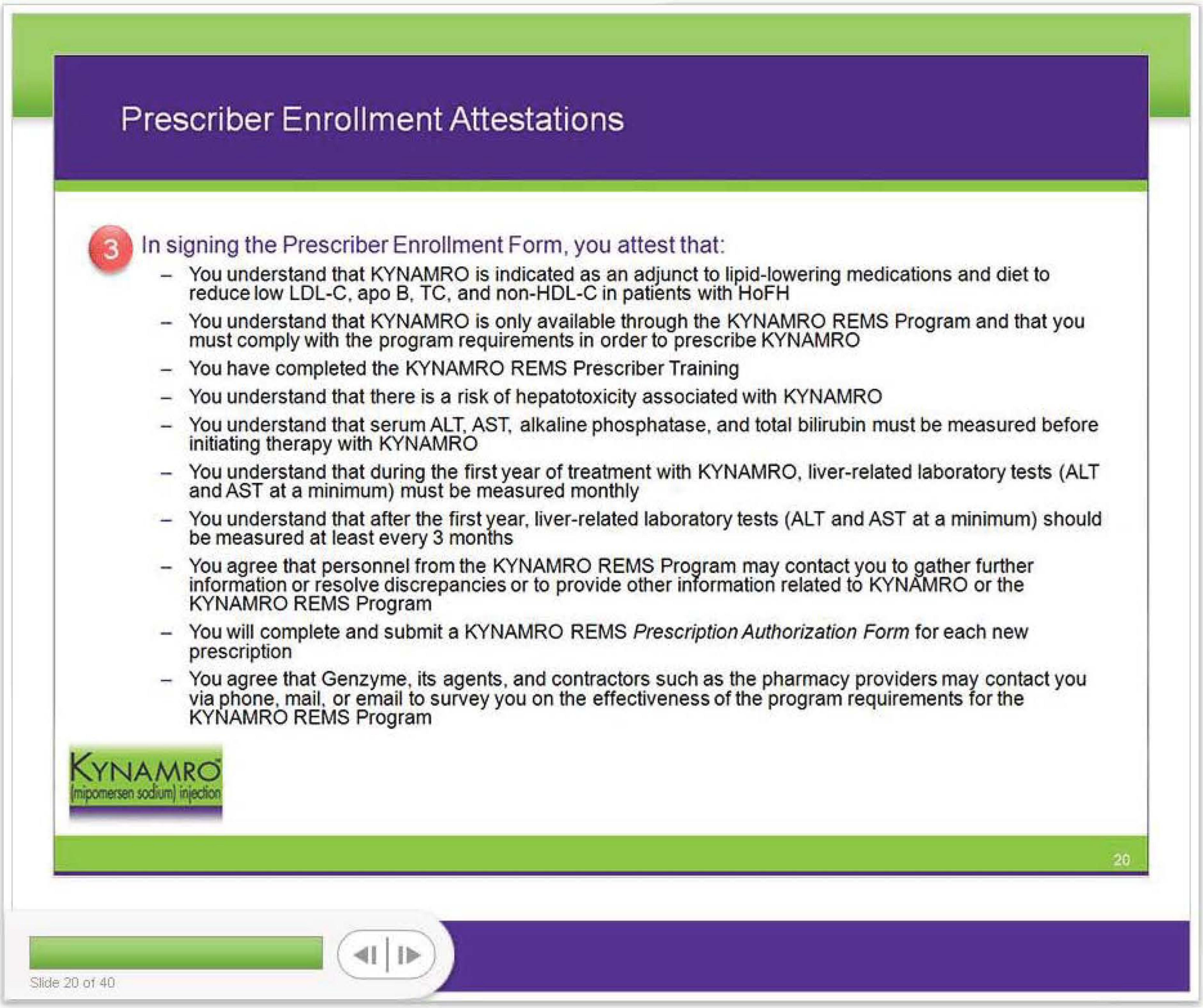

Prescriber Enrollment Attestations

③ In signing the Prescriber Enrollment Form, you attest that:

- You understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low LDL-C, apo B, TC, and non-HDL-C in patients with HoFH
- You understand that KYNAMRO is only available through the KYNAMRO REMS Program and that you must comply with the program requirements in order to prescribe KYNAMRO
- You have completed the KYNAMRO REMS Prescriber Training
- You understand that there is a risk of hepatotoxicity associated with KYNAMRO
- You understand that serum ALT, AST, alkaline phosphatase, and total bilirubin must be measured before initiating therapy with KYNAMRO
- You understand that during the first year of treatment with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) must be measured monthly
- You understand that after the first year, liver-related laboratory tests (ALT and AST at a minimum) should be measured at least every 3 months
- You agree that personnel from the KYNAMRO REMS Program may contact you to gather further information or resolve discrepancies or to provide other information related to KYNAMRO or the KYNAMRO REMS Program
- You will complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription
- You agree that Genzyme, its agents, and contractors such as the pharmacy providers may contact you via phone, mail, or email to survey you on the effectiveness of the program requirements for the KYNAMRO REMS Program

KYNAMRO (mipomersen sodium) injection

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Prescriber Enrollment Form

REMS Prescriber Enrollment Form

KYNAMRO™ (mipomersen sodium) is only available through the KYNAMRO Risk Evaluation and Mitigation Strategy (REMS) Program. In order to prescribe KYNAMRO, a prescriber must:

1. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.
2. Complete the one-time KYNAMRO REMS Program *Prescriber Enrollment Form*.
3. Complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.

Complete this enrollment form and submit to the KYNAMRO REMS Program by fax at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

4

4 Fax the signed form to the KYNAMRO REMS Program at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

5 *A confirmation letter will be sent when the form has been received and verified*

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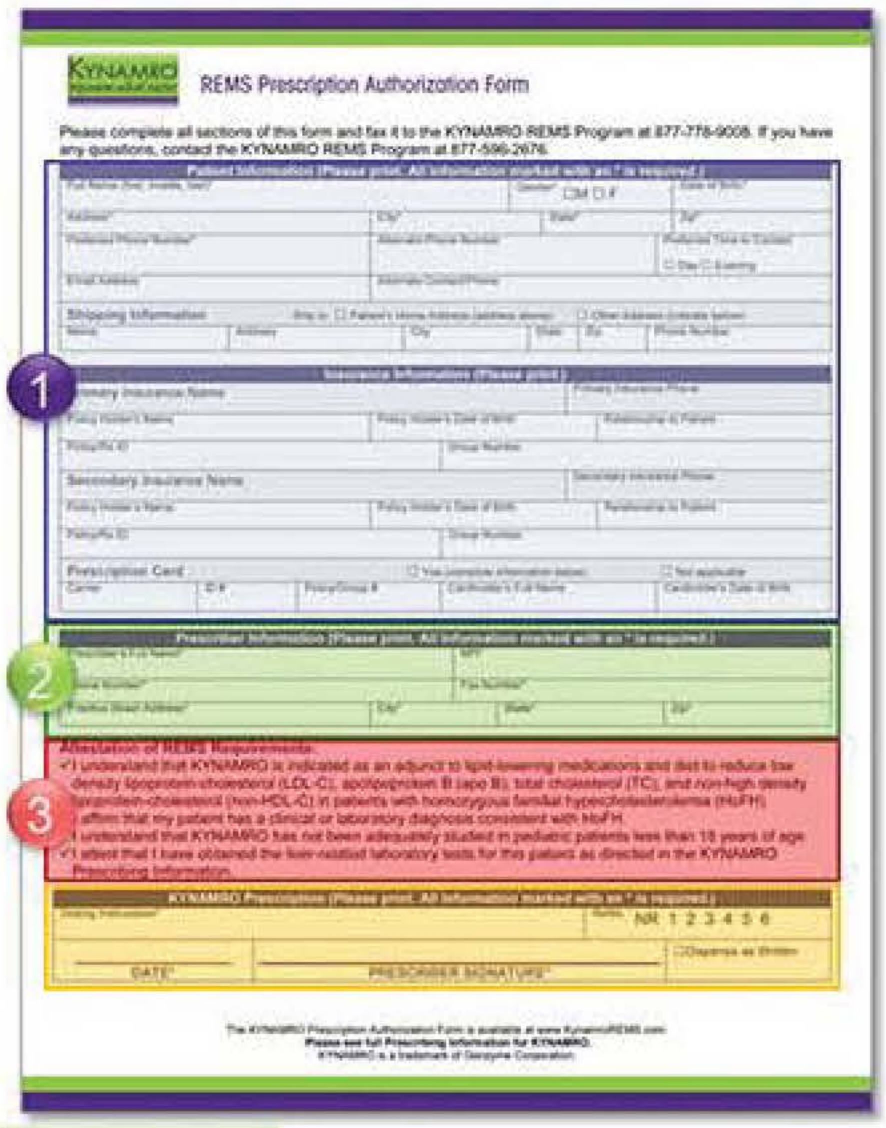
Prescription Authorization Form



REMS Prescription Authorization Form

Please complete all sections of this form and fax it to the KYNAMRO REMS Program at 877-778-9008. If you have any questions, contact the KYNAMRO REMS Program at 877-596-2676.

Patient Information (Please print. All information marked with an * is required.)

Shipping Information

Insurance Information (Please print.)

Primary Insurance Name

Secondary Insurance Name

Prescription Card

Prescriber Information (Please print. All information marked with an * is required.)

Attestation of REMS Requirements:

✓I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age

✓I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information

KYNAMRO Prescription (Please print. All information marked with an * is required.)

NR 1 2 3 4 5 6

DATE*

PRESCRIBER SIGNATURE*

For a patient to receive KYNAMRO, the Prescription Authorization Form must be completed by the prescriber

1. Patient Information and Insurance Information should be completed at the top of the form
2. Prescriber Information should be completed within the third box of the form
3. Carefully review the Attestation of REMS Requirements on the bottom half of the form

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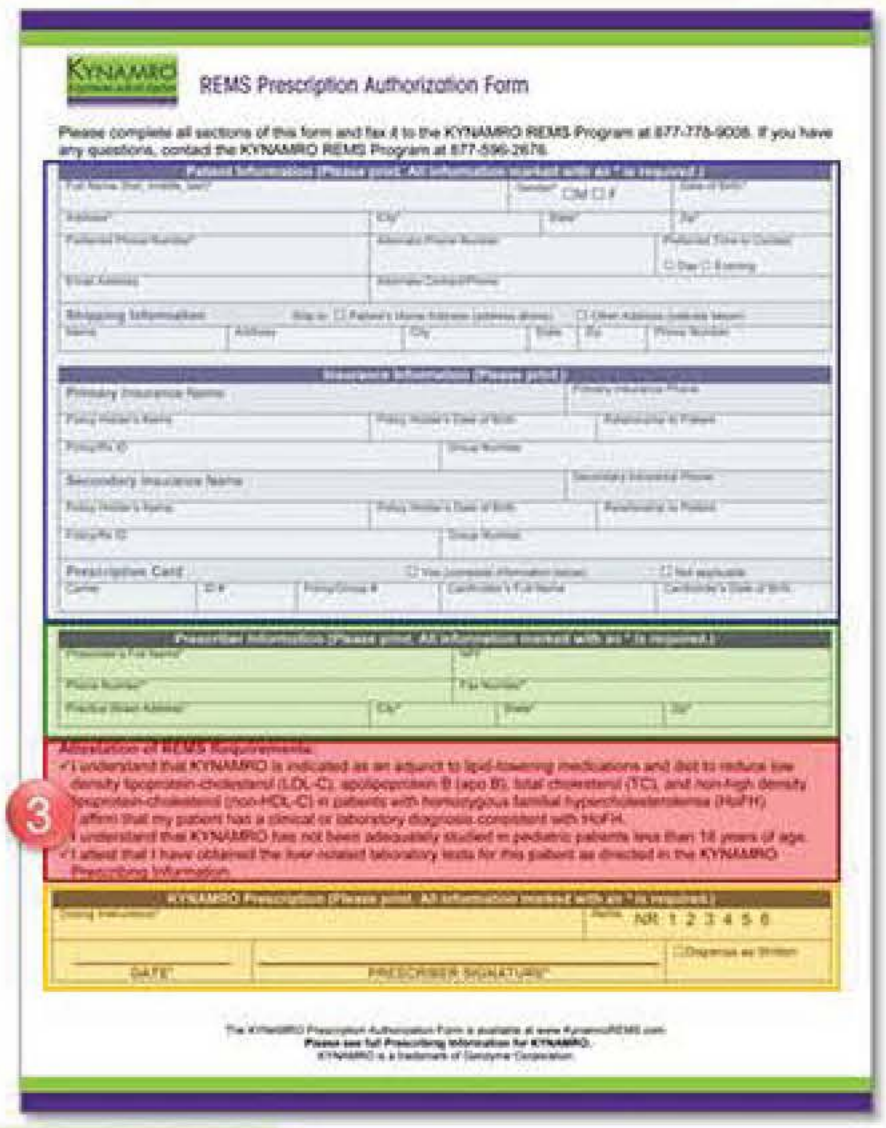
Prescription Authorization Form Requirements



REMS Prescription Authorization Form

Please complete all sections of this form and fax it to the KYNAMRO REMS Program at 877-778-9008. If you have any questions, contact the KYNAMRO REMS Program at 877-596-2676.

3 In completing the Prescription Authorization Form, you attest that:

- You understand that KYNAMRO is indicated as an adjunct to lipid lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with HoFH
- The patient has a clinical or laboratory diagnosis consistent with HoFH
- You understand that KYNAMRO has not been adequately studied in pediatric patients <18 years of age
- You have obtained the appropriate liver-related laboratory tests for the patient as directed in the KYNAMRO PI

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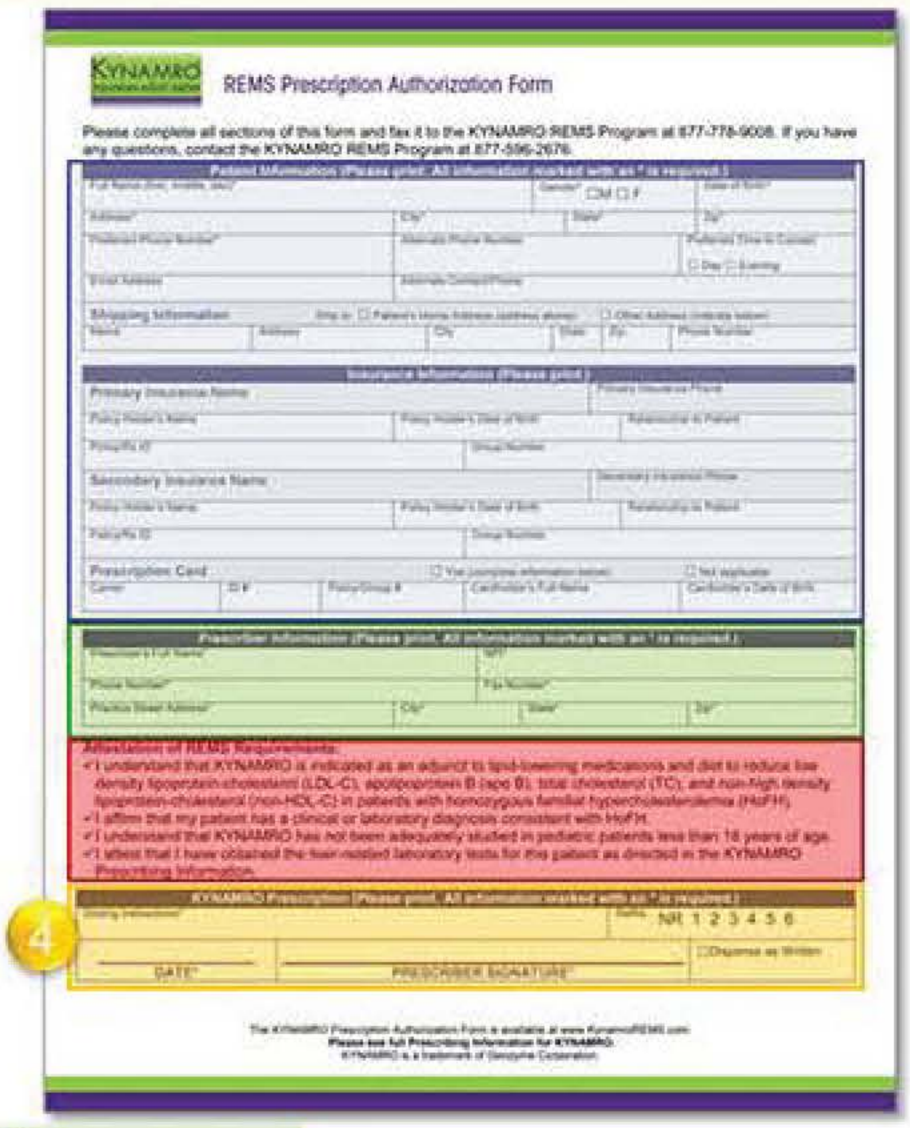
Prescription Authorization Form



REMS Prescription Authorization Form

Please complete all sections of this form and fax it to the KYNAMRO REMS Program at 877-778-9008. If you have any questions, contact the KYNAMRO REMS Program at 877-596-2676.

Attestation of REMS Requirements:

- ✓ I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age.
- ✓ I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information.

KYNAMRO Prescription (Please print. All information marked with an * is required.)

Refills: NR 1 2 3 4 5 6

☐ Dispense as Written

DATE*

PRESCRIBER SIGNATURE*

4 The KYNAMRO Prescription should be written in the last box on the form

The Prescription Authorization Form should be provided by the prescriber to a certified pharmacy via the KYNAMRO REMS Program by faxing the completed form to the KYNAMRO REMS Program at 877-778-9008

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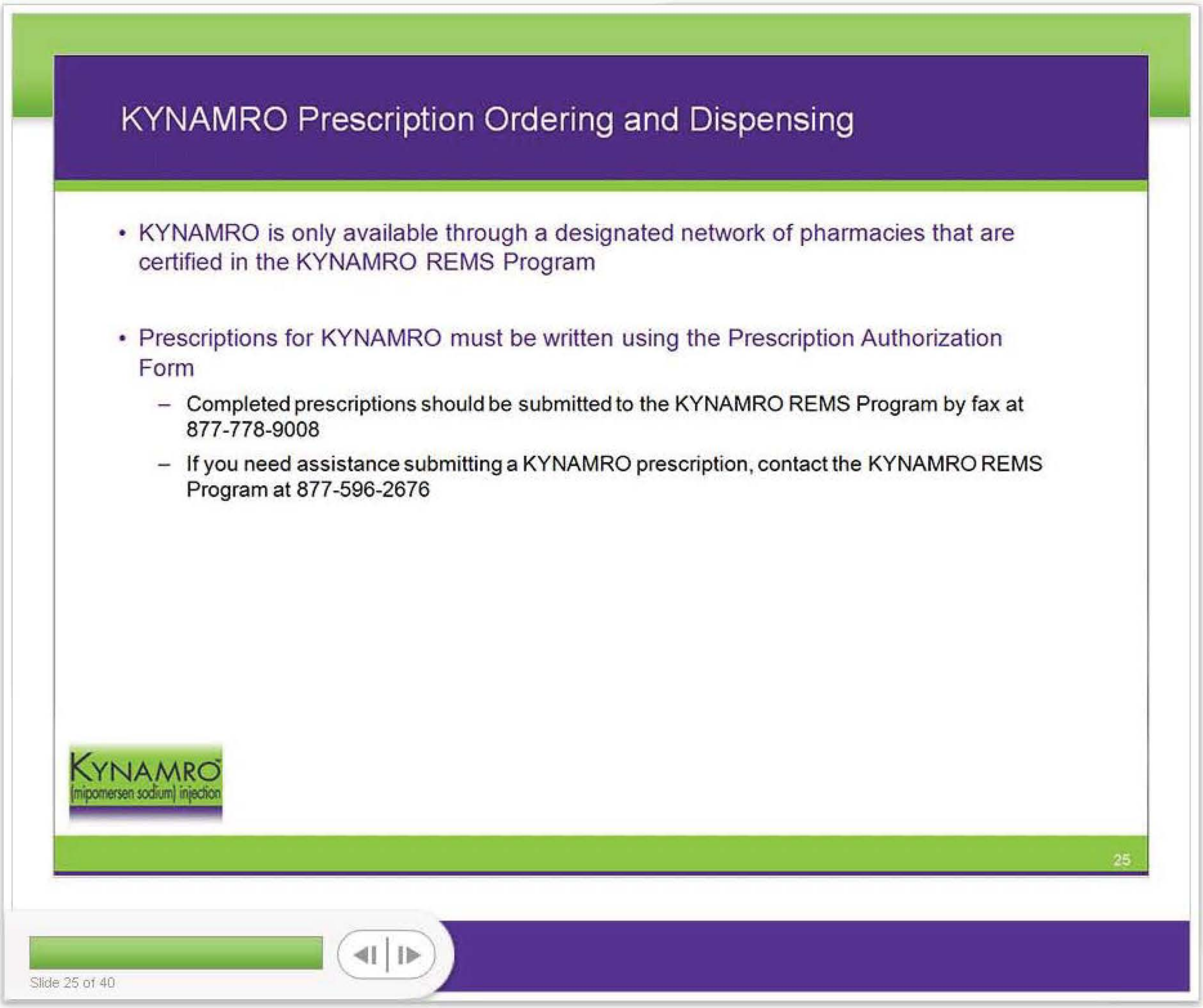
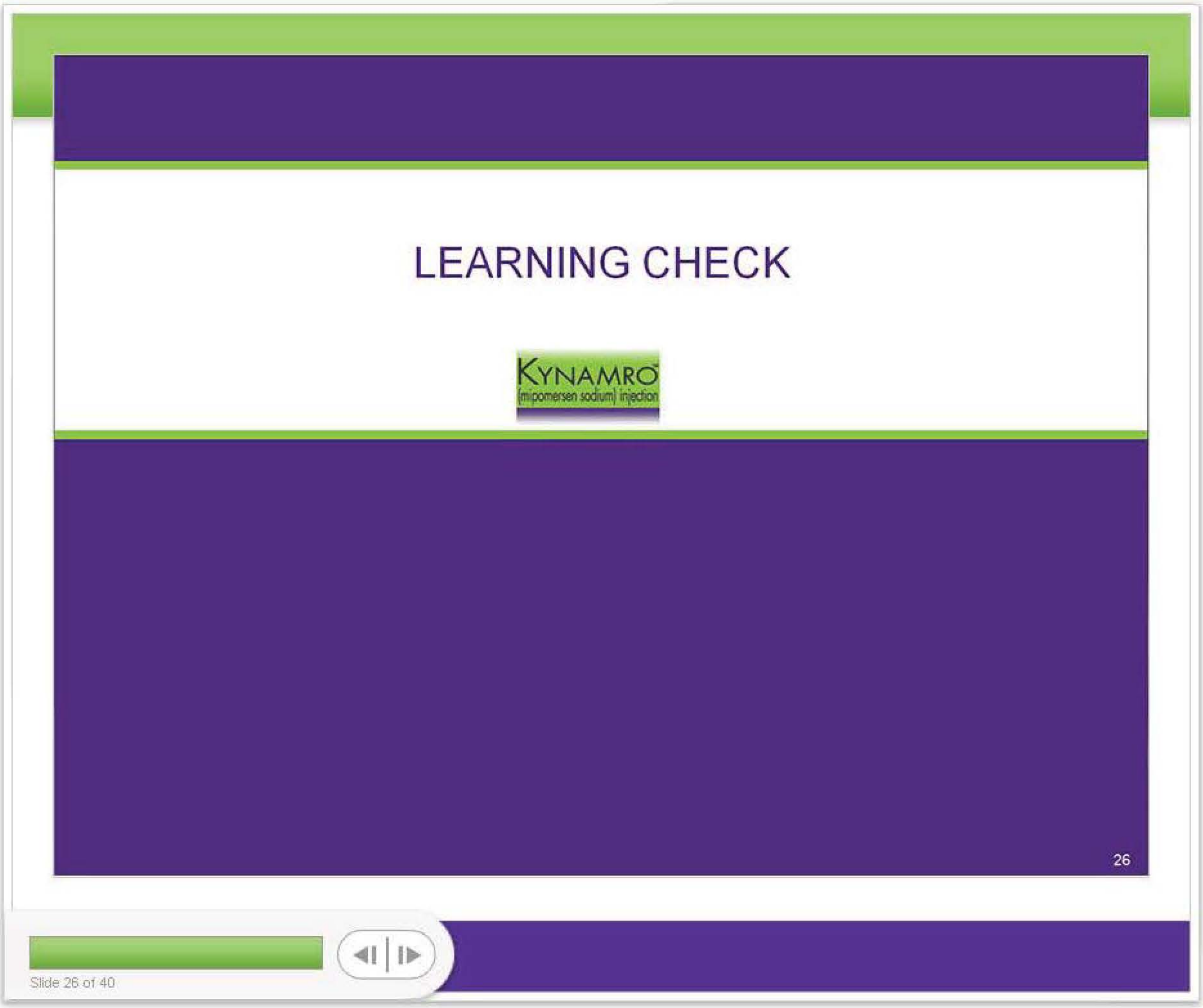


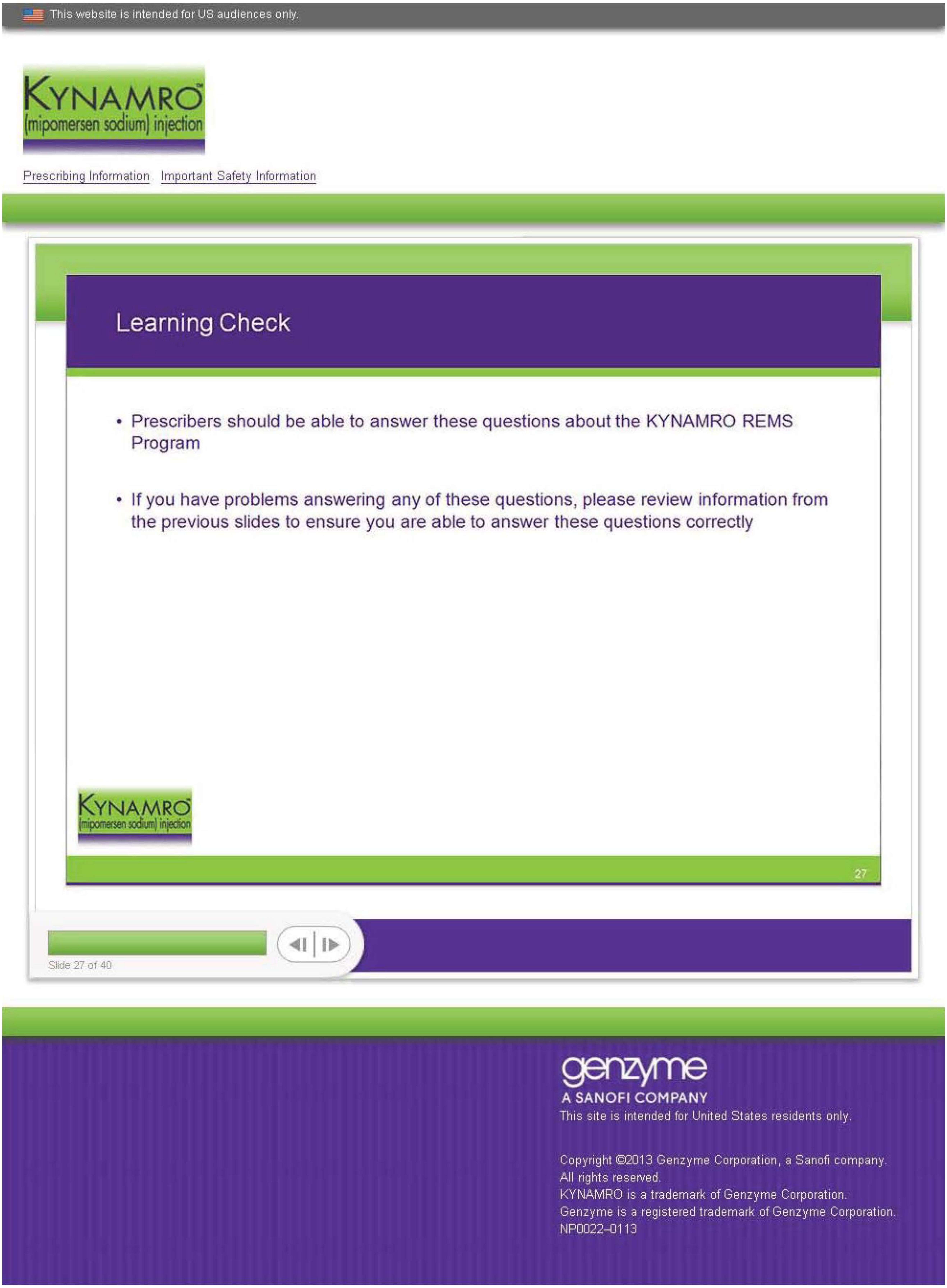
KYNAMRO Prescription Ordering and Dispensing

- KYNAMRO is only available through a designated network of pharmacies that are certified in the KYNAMRO REMS Program
- Prescriptions for KYNAMRO must be written using the Prescription Authorization Form
  - Completed prescriptions should be submitted to the KYNAMRO REMS Program by fax at 877-778-9008
  - If you need assistance submitting a KYNAMRO prescription, contact the KYNAMRO REMS Program at 877-596-2676



LEARNING CHECK

KYNAMRO™
(mipomersen sodium) injection

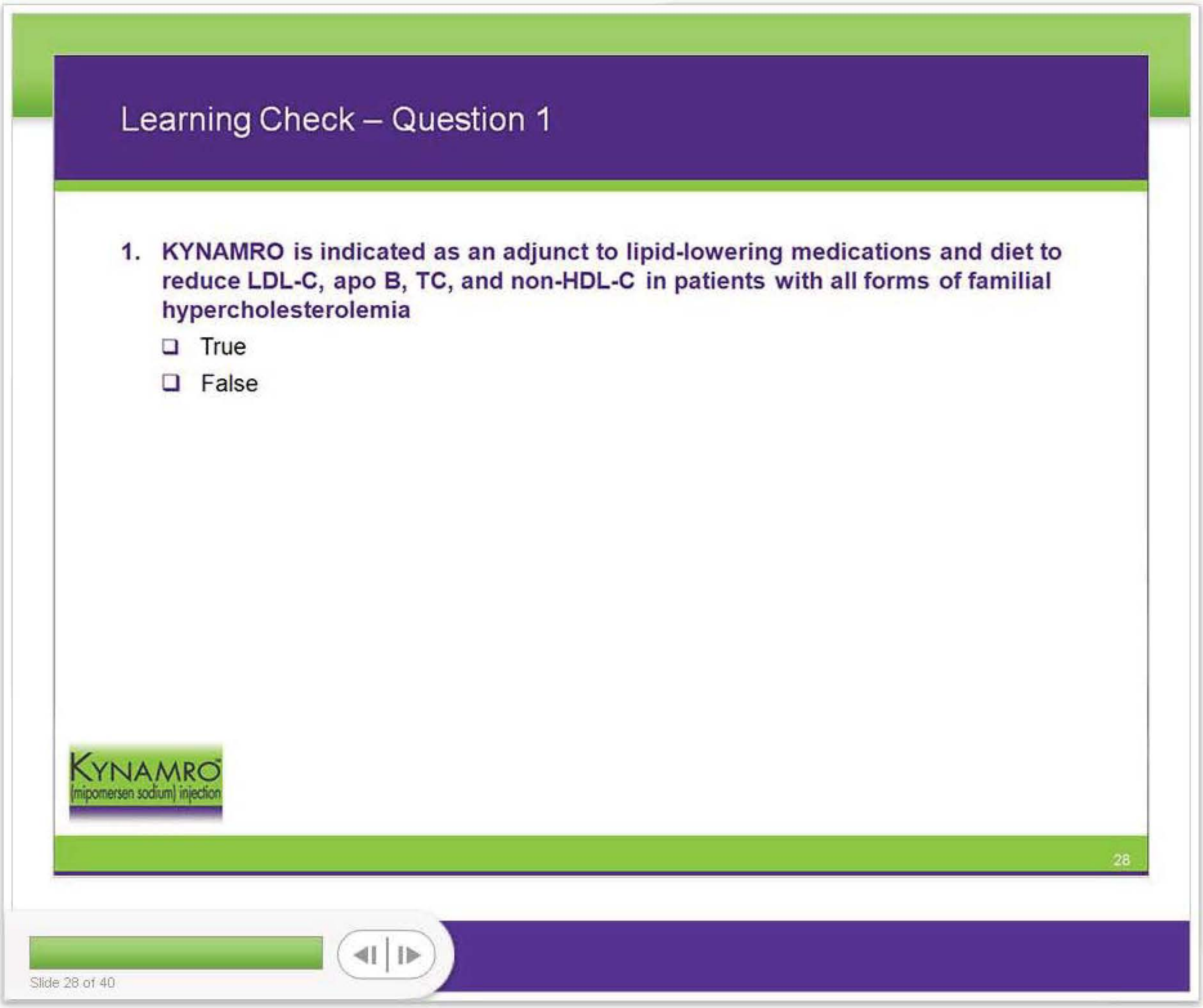


Learning Check

- Prescribers should be able to answer these questions about the KYNAMRO REMS Program
- If you have problems answering any of these questions, please review information from the previous slides to ensure you are able to answer these questions correctly

KYNAMRO™
(mipomersen sodium) injection

Prescribing Information Important Safety Information



Learning Check – Question 1

1. **KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with all forms of familial hypercholesterolemia**
   - ☐ True
   - ☐ False

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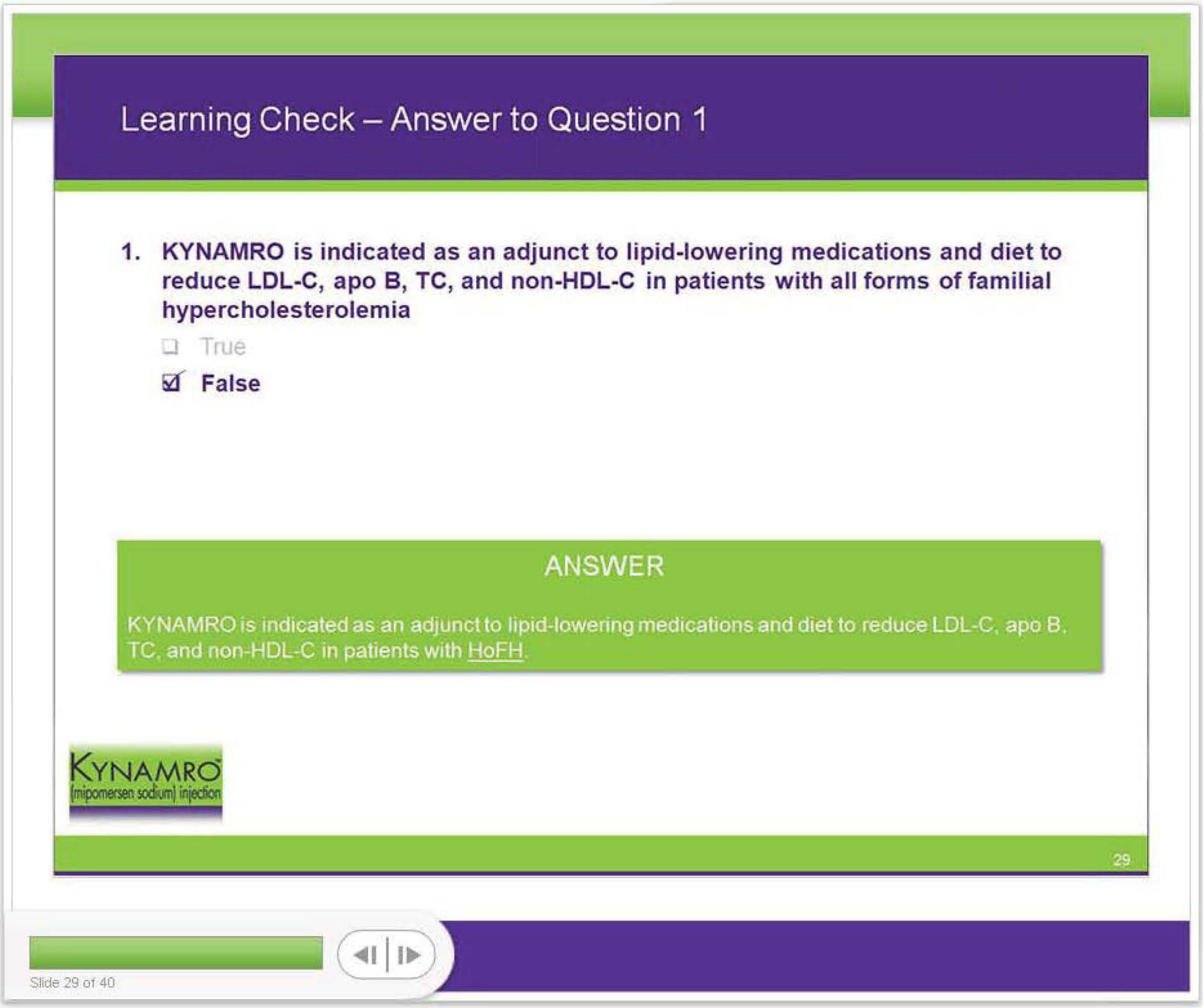
Prescribing Information Important Safety Information



Learning Check – Answer to Question 1

1. **KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with all forms of familial hypercholesterolemia**
   - ☐ True
   - ☑ **False**

ANSWER

KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with HoFH.

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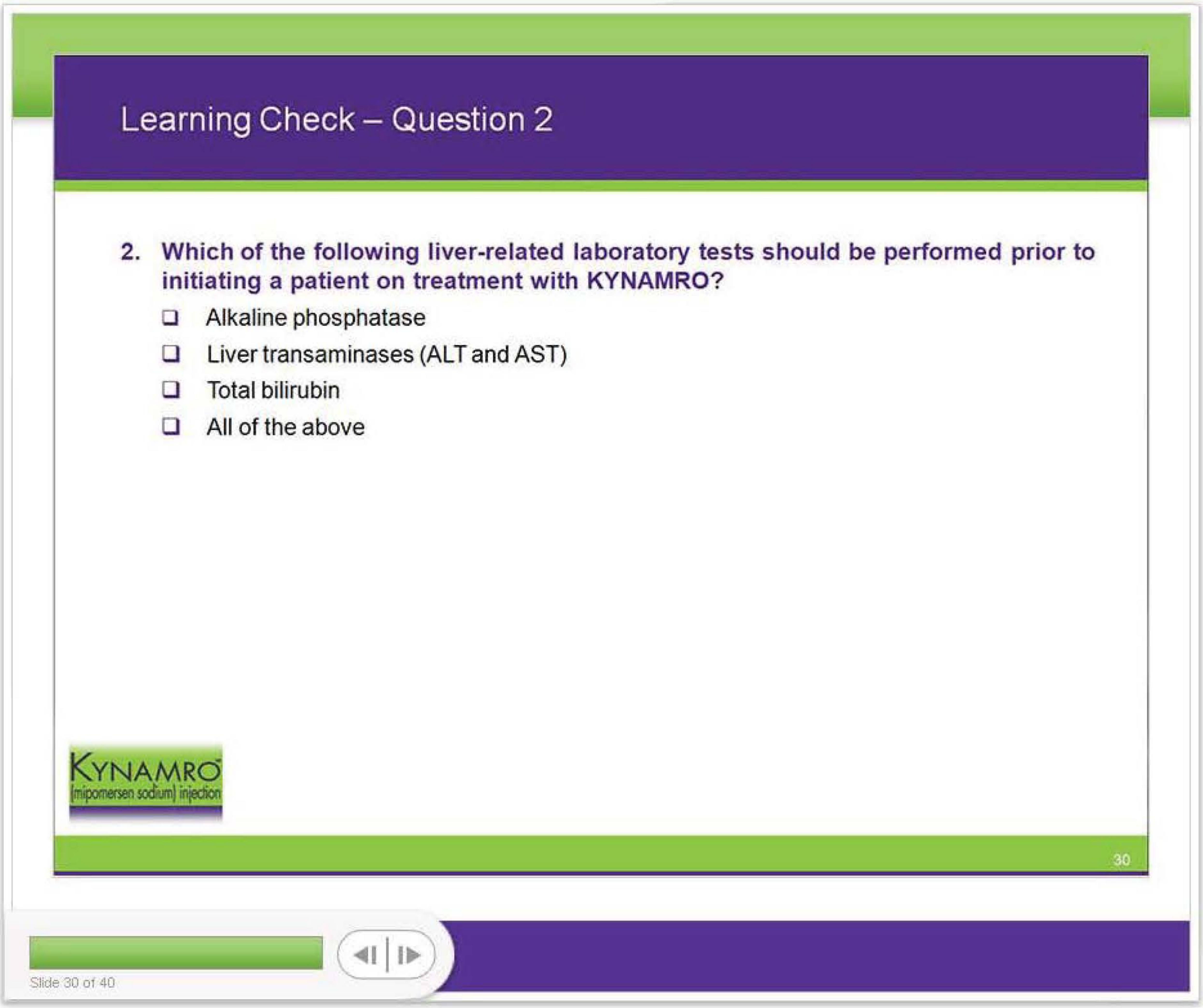
Prescribing Information Important Safety Information



Learning Check – Question 2

2. **Which of the following liver-related laboratory tests should be performed prior to initiating a patient on treatment with KYNAMRO?**
   - ☐ Alkaline phosphatase
   - ☐ Liver transaminases (ALT and AST)
   - ☐ Total bilirubin
   - ☐ All of the above

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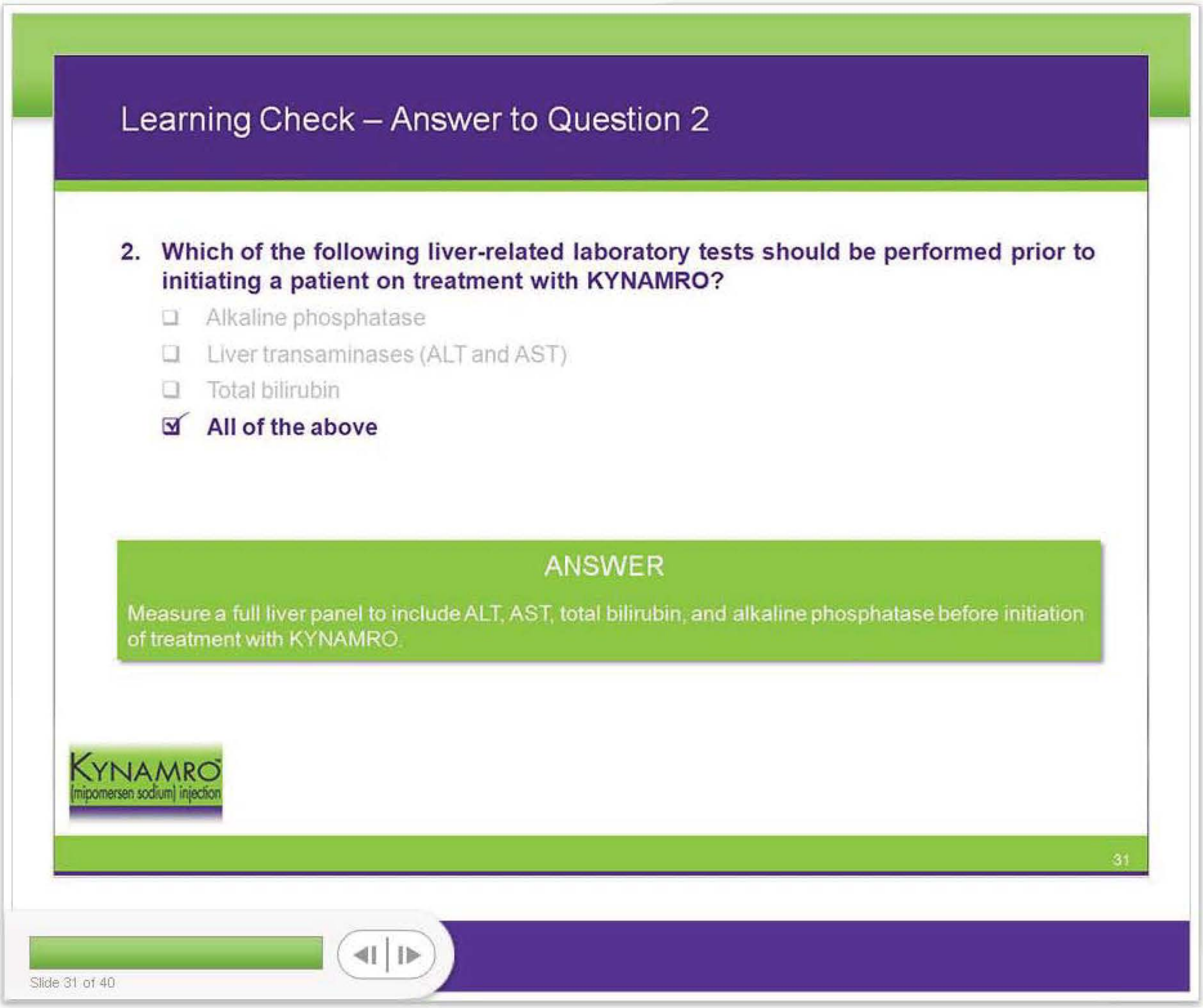
Prescribing Information Important Safety Information



Learning Check – Answer to Question 2

2. Which of the following liver-related laboratory tests should be performed prior to initiating a patient on treatment with KYNAMRO?

- ☐ Alkaline phosphatase
- ☐ Liver transaminases (ALT and AST)
- ☐ Total bilirubin
- ☑ **All of the above**

ANSWER

Measure a full liver panel to include ALT, AST, total bilirubin, and alkaline phosphatase before initiation of treatment with KYNAMRO.

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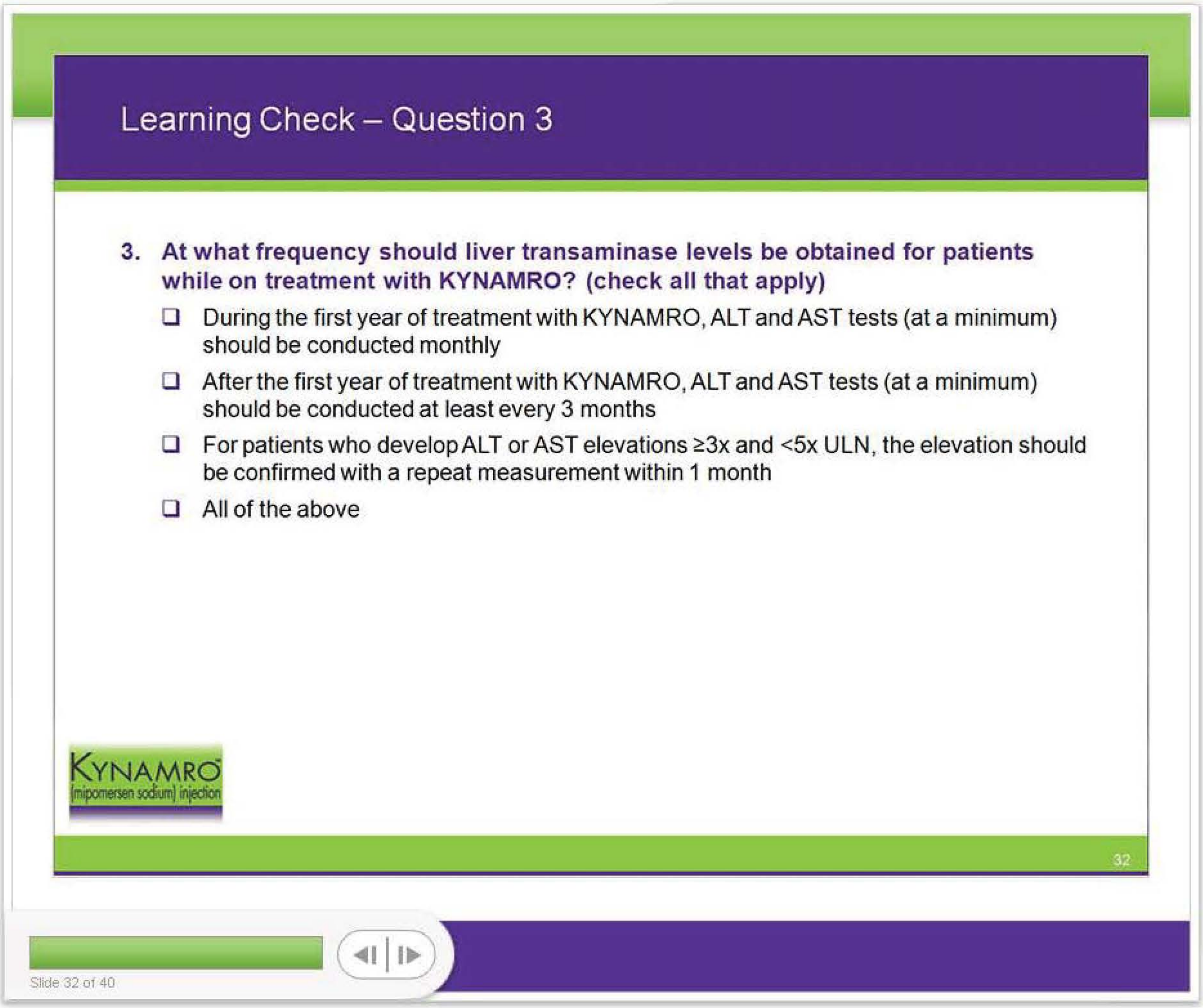

Learning Check – Question 3

3. At what frequency should liver transaminase levels be obtained for patients while on treatment with KYNAMRO? (check all that apply)

- ☐ During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly
- ☐ After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months
- ☐ For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 month
- ☐ All of the above

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KYNAMRO™
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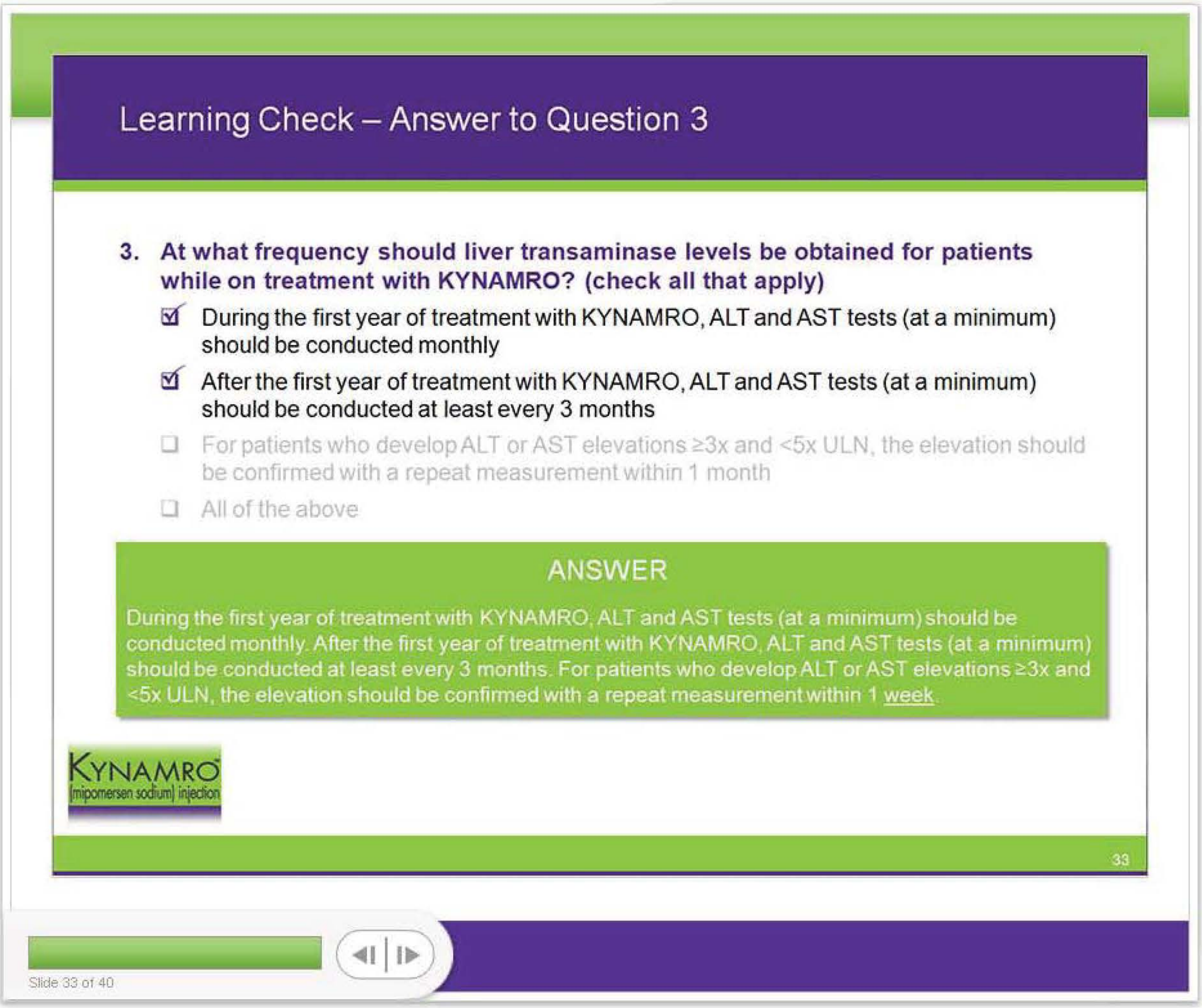
Prescribing Information Important Safety Information



Learning Check – Answer to Question 3

3. At what frequency should liver transaminase levels be obtained for patients while on treatment with KYNAMRO? (check all that apply)

- ☑ During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly
- ☑ After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months
- ☐ For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 month
- ☐ All of the above

ANSWER

During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly. After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months. For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 week.

KYNAMRO
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Slide 33 of 40

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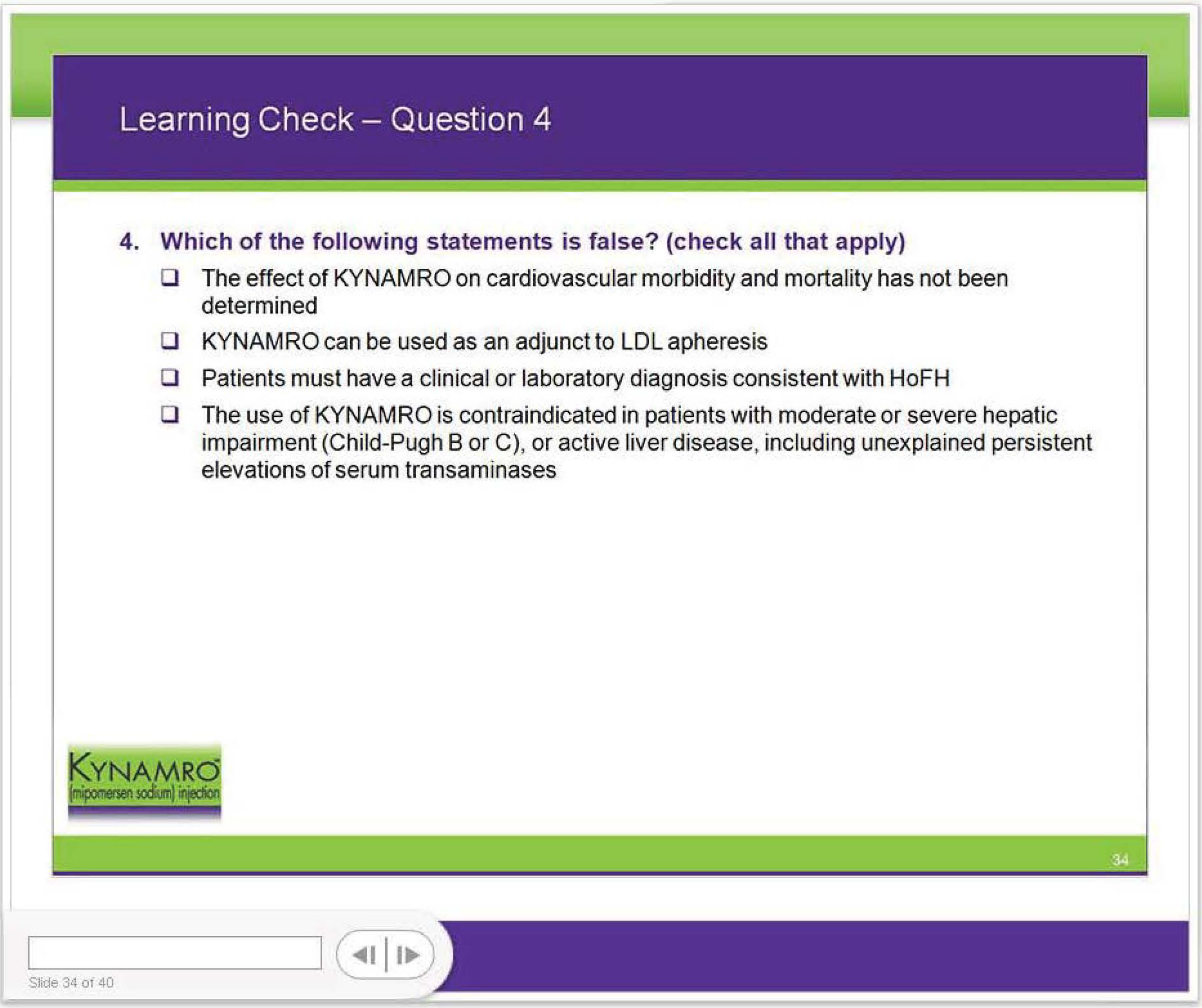


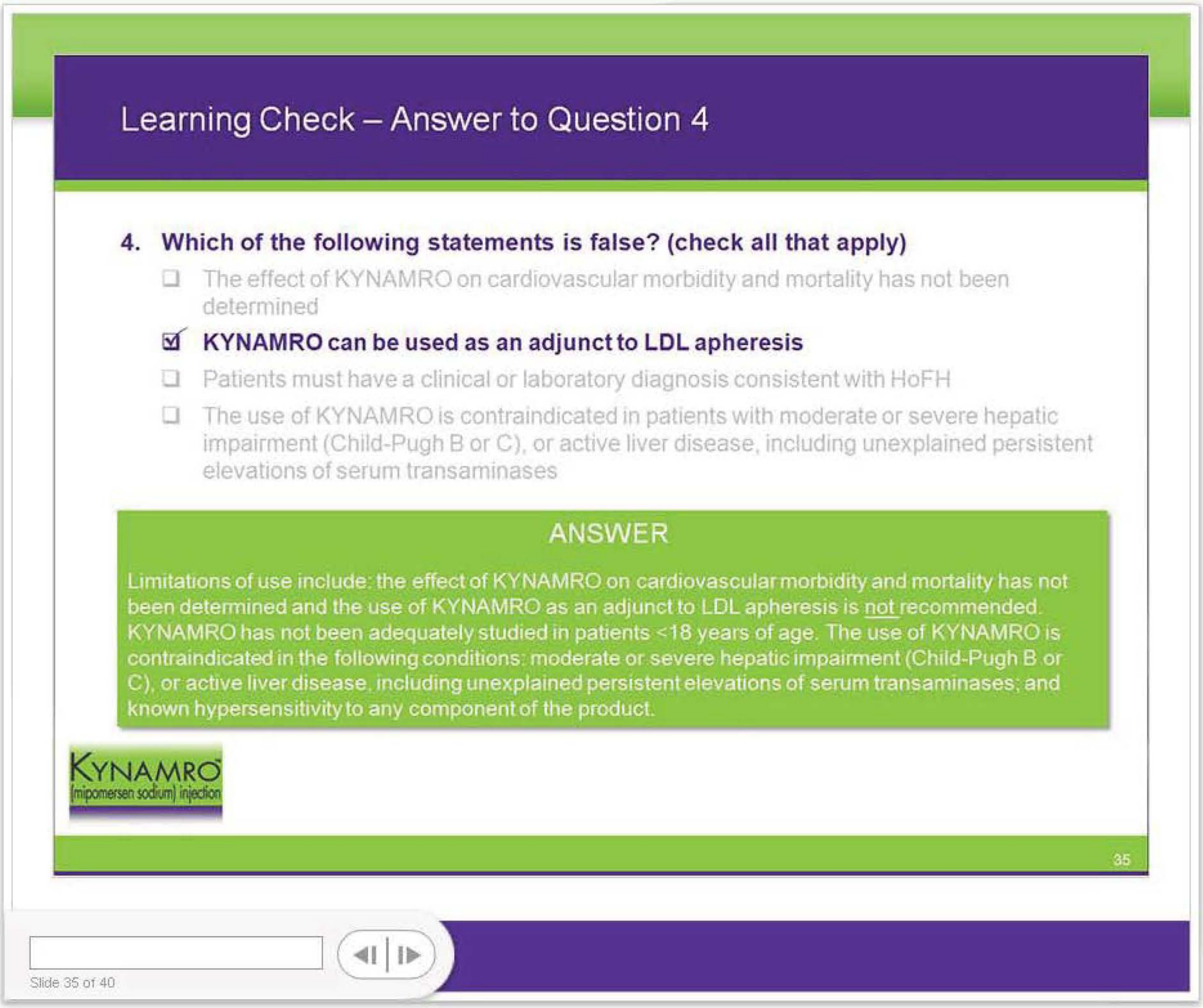
Learning Check – Question 4

4. Which of the following statements is false? (check all that apply)

- ☐ The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
- ☐ KYNAMRO can be used as an adjunct to LDL apheresis
- ☐ Patients must have a clinical or laboratory diagnosis consistent with HoFH
- ☐ The use of KYNAMRO is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases

KYNAMRO™
(mipomersen sodium) injection

Prescribing Information Important Safety Information



Learning Check – Answer to Question 4

4. Which of the following statements is false? (check all that apply)

- ☐ The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
- ☑ **KYNAMRO can be used as an adjunct to LDL apheresis**
- ☐ Patients must have a clinical or laboratory diagnosis consistent with HoFH
- ☐ The use of KYNAMRO is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases

ANSWER

Limitations of use include: the effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined and the use of KYNAMRO as an adjunct to LDL apheresis is not recommended. KYNAMRO has not been adequately studied in patients <18 years of age. The use of KYNAMRO is contraindicated in the following conditions: moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases; and known hypersensitivity to any component of the product.

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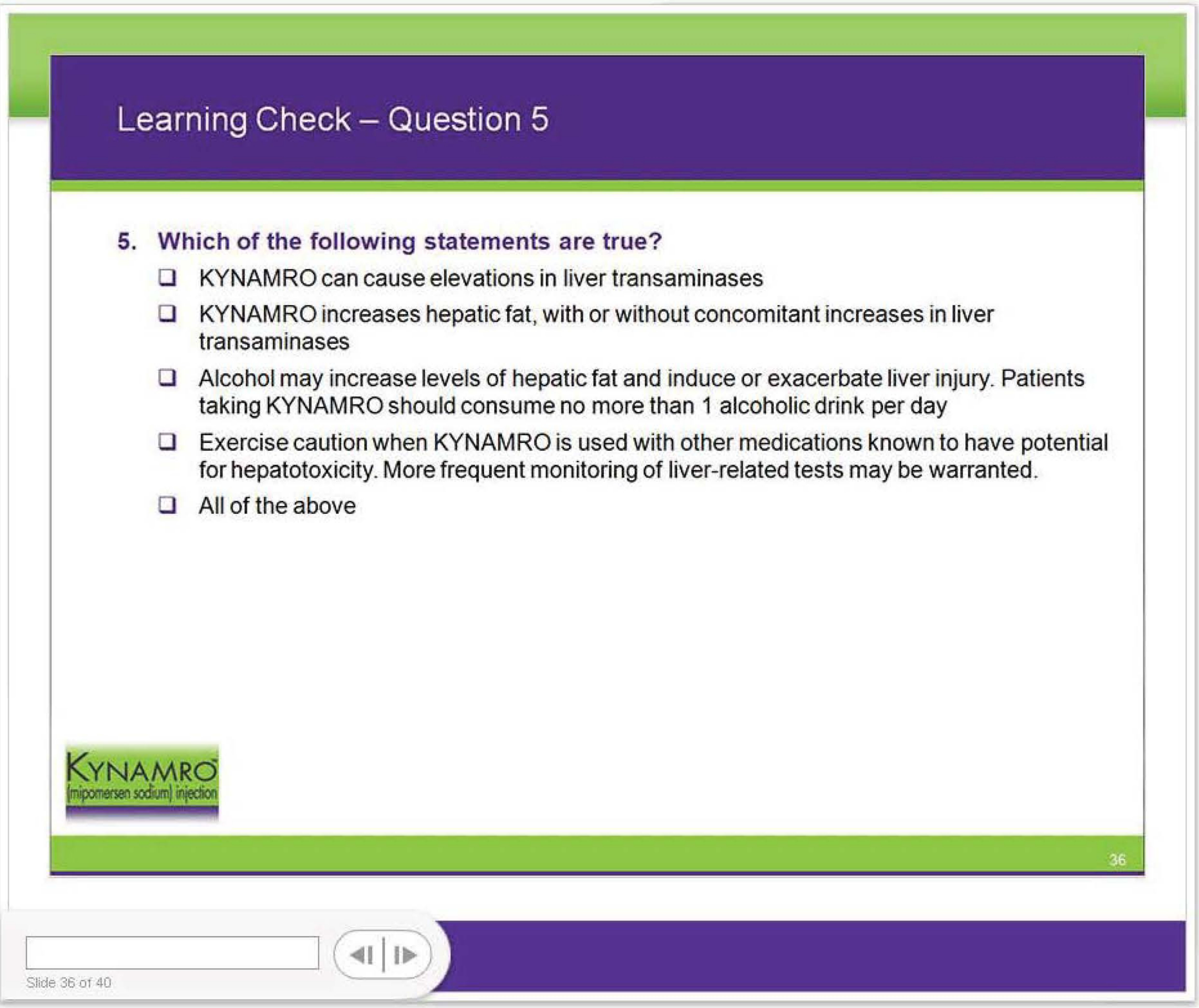
Prescribing Information Important Safety Information



Learning Check – Question 5

5. Which of the following statements are true?

- ☐ KYNAMRO can cause elevations in liver transaminases
- ☐ KYNAMRO increases hepatic fat, with or without concomitant increases in liver transaminases
- ☐ Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than 1 alcoholic drink per day
- ☐ Exercise caution when KYNAMRO is used with other medications known to have potential for hepatotoxicity. More frequent monitoring of liver-related tests may be warranted.
- ☐ All of the above

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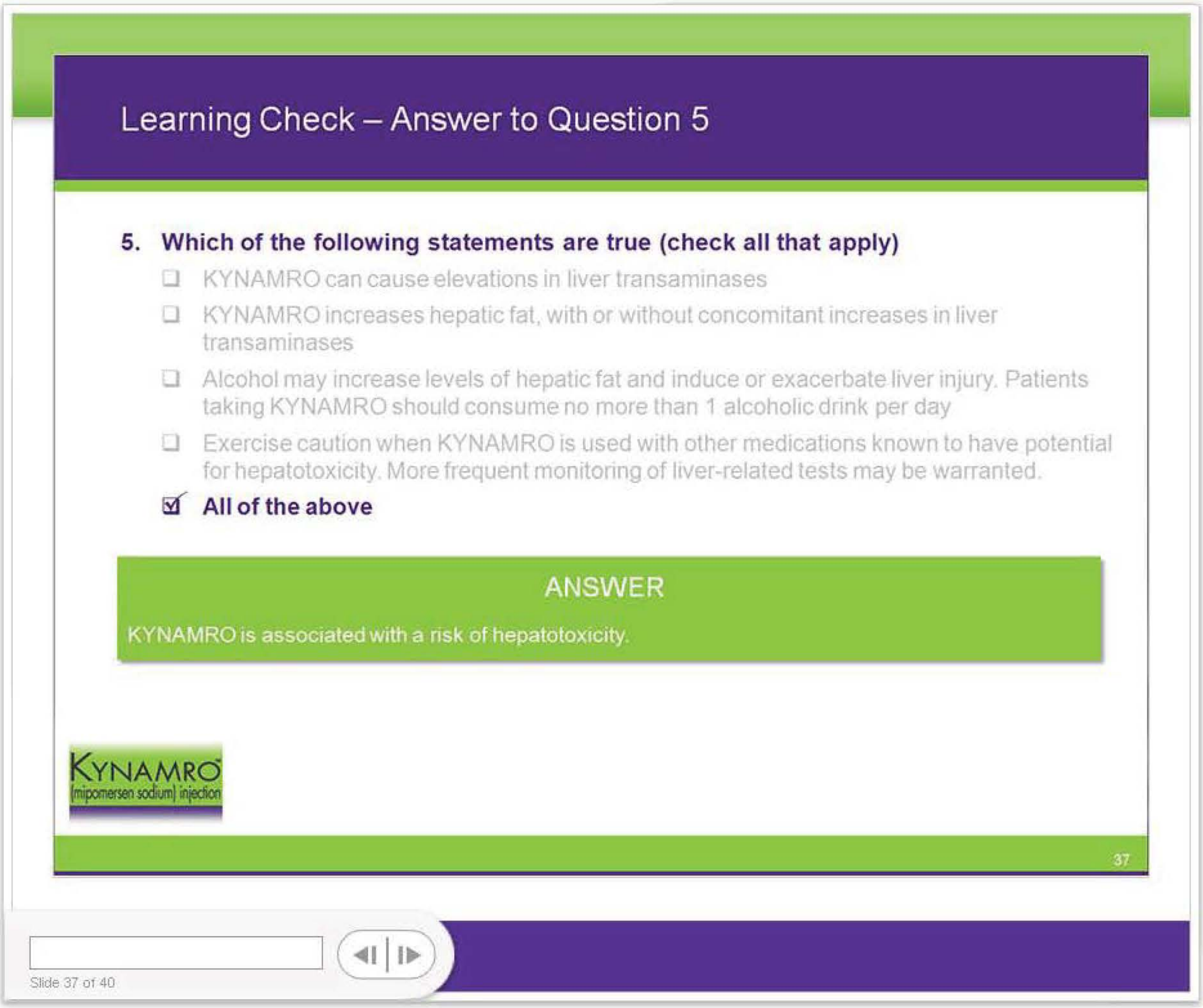


Learning Check – Answer to Question 5

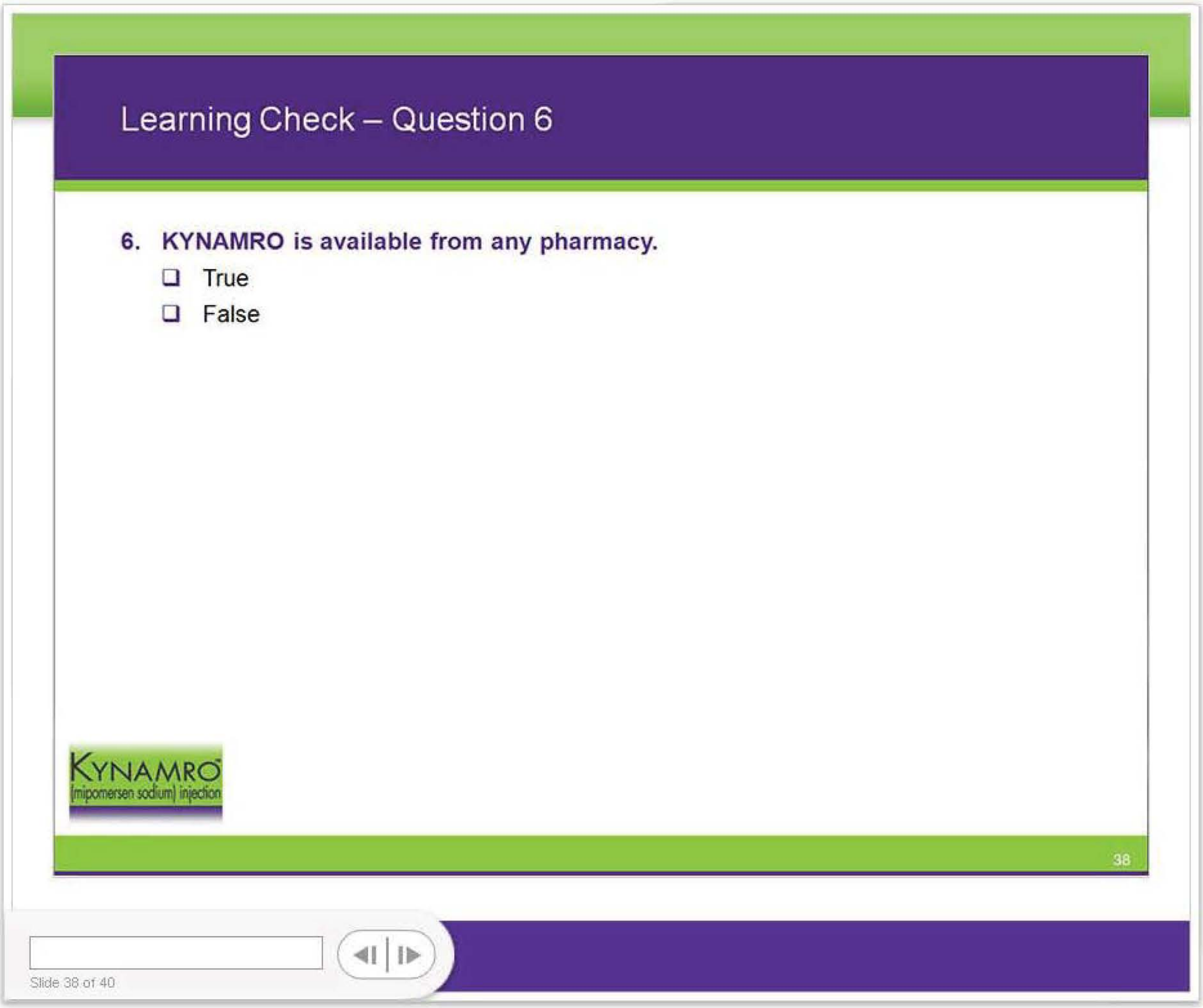
5. Which of the following statements are true (check all that apply)

- ☐ KYNAMRO can cause elevations in liver transaminases
- ☐ KYNAMRO increases hepatic fat, with or without concomitant increases in liver transaminases
- ☐ Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than 1 alcoholic drink per day
- ☐ Exercise caution when KYNAMRO is used with other medications known to have potential for hepatotoxicity. More frequent monitoring of liver-related tests may be warranted.
- ☑ **All of the above**

ANSWER

KYNAMRO is associated with a risk of hepatotoxicity.

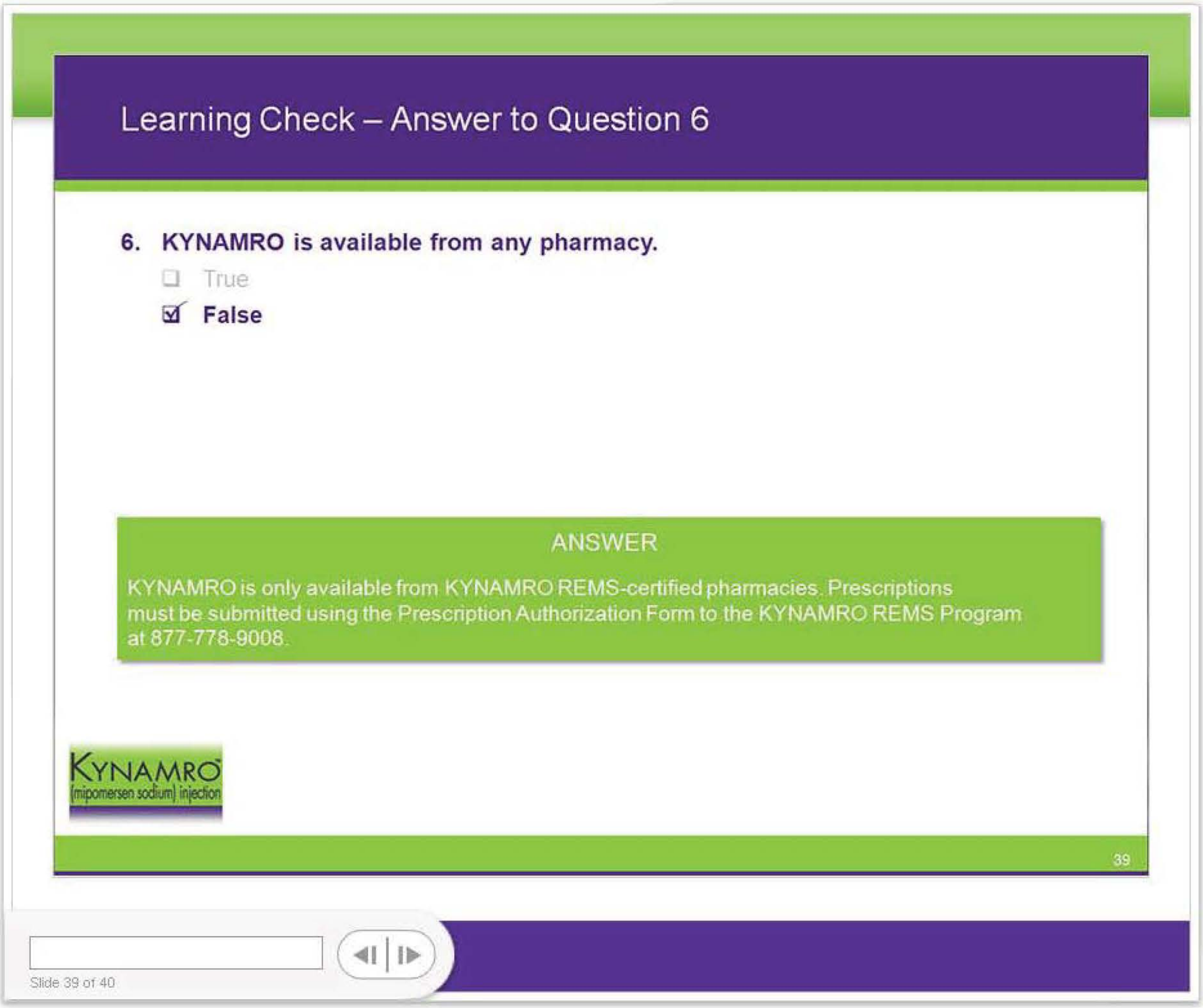
KYNAMRO
(mipomersen sodium) injection



Learning Check – Question 6

6. KYNAMRO is available from any pharmacy.

- ☐ True
- ☐ False



Learning Check – Answer to Question 6

6. KYNAMRO is available from any pharmacy.

- ☐ True
- ☑ **False**

ANSWER

KYNAMRO is only available from KYNAMRO REMS-certified pharmacies. Prescriptions must be submitted using the Prescription Authorization Form to the KYNAMRO REMS Program at 877-778-9008.

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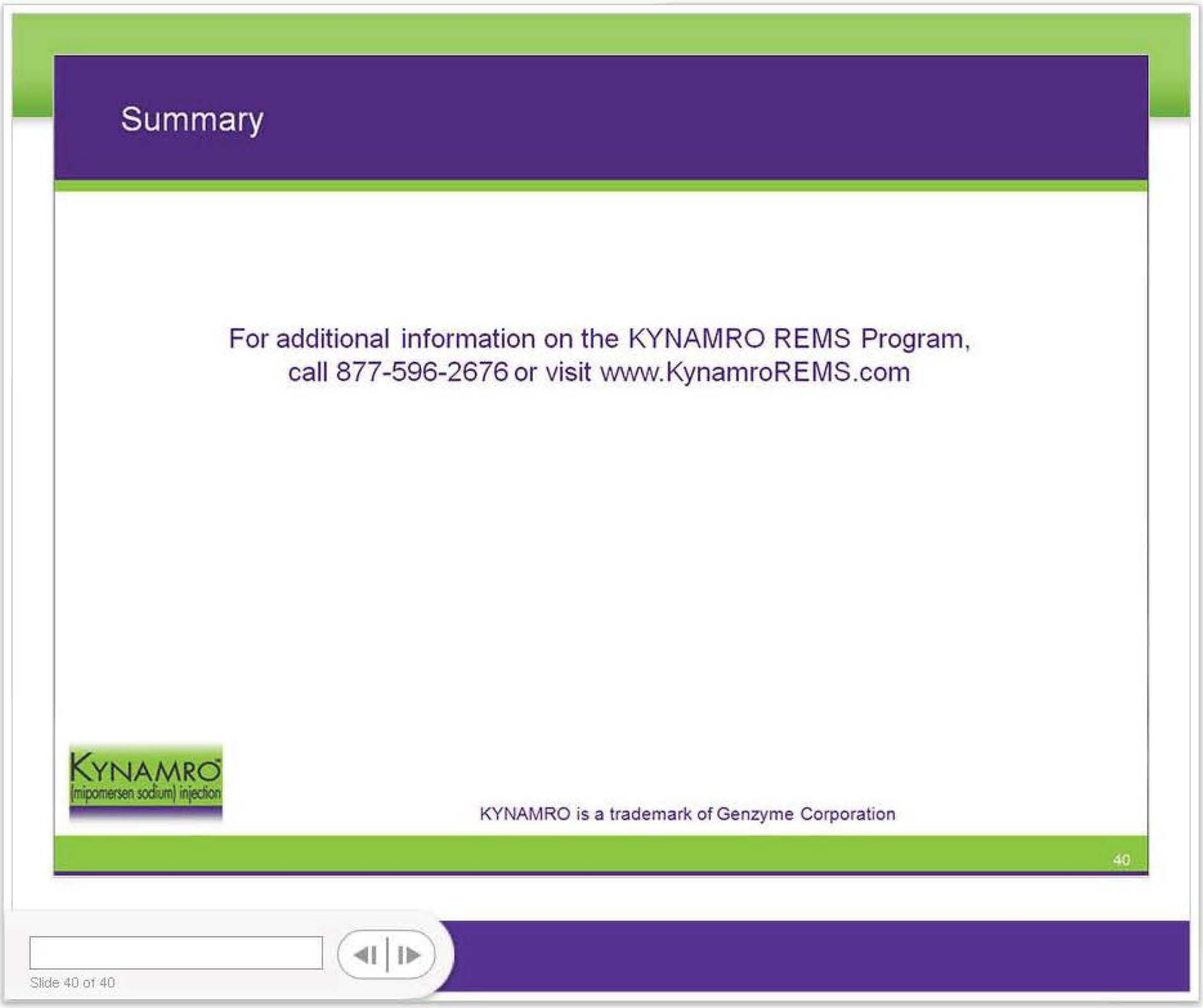
KYNAMRO™
(mipomersen sodium) injection

Prescribing Information Important Safety Information



Summary

For additional information on the KYNAMRO REMS Program, call 877-596-2676 or visit www.KynamroREMS.com

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APPENDIX 2

PRESCRIBER TRAINING SLIDE SET

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KYNAMRO™
(mipomersen sodium) injection

An Overview of the KYNAMRO™ Risk Evaluation and Mitigation Strategy (REMS) Program

Prescriber Training

Contents

- Introduction
- KYNAMRO Product Information
  - Indication and Limitations of Use
  - Appropriate Patient Selection
  - Serious Risks
  - Warnings and Precautions
  - Dosing and Administration
  - Patient Monitoring
- KYNAMRO REMS Program
  - Overview
  - Program Goals
  - Prescriber Certification and Enrollment
  - Prescription Authorization Form
  - Prescription Ordering and Dispensing
  - Learning Check

This training module contains important information about the risk of hepatotoxicity associated with the use of KYNAMRO and the need to monitor patients during treatment, and about the KYNAMRO REMS Program requirements

KYNAMRO™
(mipomersen sodium) injection

Introduction

- This training module has been developed as part of the KYNAMRO REMS Program to:
  - Educate prescribers on the risk of hepatotoxicity associated with the use of KYNAMRO and the need to monitor patients during treatment with KYNAMRO per product labeling
  - Provide information to prescribers on the KYNAMRO REMS Program requirements, including how to enroll in the KYNAMRO REMS Program
- This training module focuses on the risk of hepatotoxicity associated with KYNAMRO. This is not the only risk associated with the use of KYNAMRO. Please see the Prescribing Information (PI) for a complete description of risks associated with the use of KYNAMRO.

KYNAMRO PRODUCT INFORMATION

KYNAMRO™
(mipomersen sodium) injection

Indication and Limitations of Use

- KYNAMRO is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis indicated as an adjunct to lipid-lowering medications and diet to reduce low-density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)

- Limitations of use
  - The safety and effectiveness of KYNAMRO have not been established in patients with hypercholesterolemia who do not have HoFH
  - The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
  - The use of KYNAMRO as an adjunct to LDL apheresis is not recommended

KYNAMRO™ (mipomersen sodium) injection

Appropriate Patient Selection

- KYNAMRO is indicated for use in patients with HoFH
- Patients must have a clinical or laboratory diagnosis consistent with HoFH
- KYNAMRO has not been adequately studied in patients less than 18 years of age

Serious Risks, Warnings and Precautions

- The use of KYNAMRO is contraindicated in the following conditions:
  - Moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases
  - Known hypersensitivity to any component of the product

This is not a comprehensive description of the risks associated with the use of KYNAMRO. Please see the Prescribing Information for a complete description of risks associated with the use of KYNAMRO.

KYNAMRO™
(mipomersen sodium) injection

Boxed Warning for Serious Risk

WARNING: RISK OF HEPATOTOXICITY

KYNAMRO can cause elevations in transaminases. In the KYNAMRO clinical trial in patients with HoFH, 4 (12%) of the 34 patients treated with KYNAMRO compared with 0% of the 17 patients treated with placebo had at least one elevation in alanine aminotransferase (ALT) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), or partial thromboplastin time (PTT).

KYNAMRO also increases hepatic fat, with or without concomitant increases in transaminases. In the trials in patients with heterozygous familial hypercholesterolemia (HeFH) and hyperlipidemia, the median absolute increase in hepatic fat was 10% after 26 weeks of treatment, from 0% at baseline, measured by magnetic resonance imaging (MRI). Hepatic steatosis is a risk factor for advanced liver disease, including steatohepatitis and cirrhosis.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT, AST regularly as recommended. During treatment, withhold the dose of KYNAMRO if the ALT or AST are ≥3 x ULN. Discontinue KYNAMRO for clinically significant liver toxicity.

Risk of Hepatotoxicity

- KYNAMRO can cause elevations in transaminases and hepatic steatosis. There is concern that KYNAMRO could induce steatohepatitis, which can progress to cirrhosis over several years.

- Elevation of transaminases
  - KYNAMRO can cause increases in serum transaminases (ALT and/or AST). If transaminase elevations are accompanied by clinical symptoms of liver injury (e.g., nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like symptoms), increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with KYNAMRO and identify the probable cause.

- Hepatic steatosis
  - KYNAMRO increases hepatic fat (steatosis) with or without concomitant increases in transaminases. The long-term consequences of hepatic steatosis associated with KYNAMRO therapy are unknown.

Risk of Hepatotoxicity

- Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than one alcoholic drink per day.

- Caution should be exercised when KYNAMRO is used with other medications known to have potential for hepatotoxicity for example isotretinoin, amiodarone, acetaminophen (>4 g/day for ≥3 days/week), methotrexate, tetracyclines, and tamoxifen . The effect of concomitant administration of KYNAMRO with other hepatotoxic medications is unknown. More frequent monitoring of liver-related tests may be warranted.

- KYNAMRO 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.

KYNAMRO™
(mipomersen sodium) injection

Dosing and Administration

- The recommended dose of KYNAMRO is 200 mg once weekly as a subcutaneous injection:
  - KYNAMRO is available in a single-use vial or pre-filled syringe
  - Each vial or pre-filled syringe of KYNAMRO provides 200 mg of mipomersen sodium in a deliverable volume of 1 mL of solution and is intended for single use only
  - KYNAMRO should be removed from refrigerated storage and allowed to reach room temperature for at least 30 minutes prior to administration
  - The first injection of KYNAMRO should be performed under the guidance and supervision of an appropriately qualified healthcare provider (HCP). Patients and caregivers should be instructed by an appropriately qualified HCP in the proper technique for administering subsequent injections
  - KYNAMRO should be injected into the abdomen, thigh region, or outer area of the upper arm. Patients and caregivers should be instructed to alternate sites for subcutaneous injections

Monitoring of Hepatic Transaminases

PERIOD ON TREATMENT	TREATMENT AND MONITORING RECOMMENDATIONS
Beginning treatment	• Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin
During first year	• Conduct liver-related tests monthly (ALT and AST, at a minimum)
After first year	• Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)

KYNAMRO™
(mipomersen sodium) injection

Monitoring of Hepatic Transaminases

- For patients who develop elevated transaminases during therapy with KYNAMRO, follow the monitoring recommendations summarized below:

ALT OR AST	TREATMENT AND MONITORING RECOMMENDATIONS*
≥3x and < 5x ULN	• Confirm elevation with a repeat measurement within 1 week • If confirmed, withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If resuming KYNAMRO after transaminases resolve to <3x ULN, consider monitoring liver-related laboratory tests more frequently
≥5x ULN	• Withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If resuming KYNAMRO after transaminases resolve to < 3x ULN, monitor liver-related laboratory tests more frequently

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

Adverse Reaction Reporting

- To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 800-745-4447 or FDA at 800-FDA-1088 or www.fda.gov/medwatch

KYNAMRO REMS PROGRAM

KYNAMRO™
(mipomersen sodium) injection

Overview

- To ensure that the benefits of KYNAMRO outweigh the risks, KYNAMRO is only available through the KYNAMRO REMS Program

- The elements of the KYNAMRO REMS Program are:
  - Healthcare providers who prescribe KYNAMRO must be specially certified
    - To become certified to prescribe KYNAMRO, prescribers must be trained and enrolled in the KYNAMRO REMS Program
  - Pharmacies that dispense KYNAMRO must be specially certified
    - Only certified pharmacies can dispense KYNAMRO
  - KYNAMRO will be dispensed only to patients with evidence or other documentation of safe-use conditions
    - Patients must have a clinical or laboratory diagnosis consistent with HoFH as documented on the KYNAMRO Prescription Authorization Form

Program Goals

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

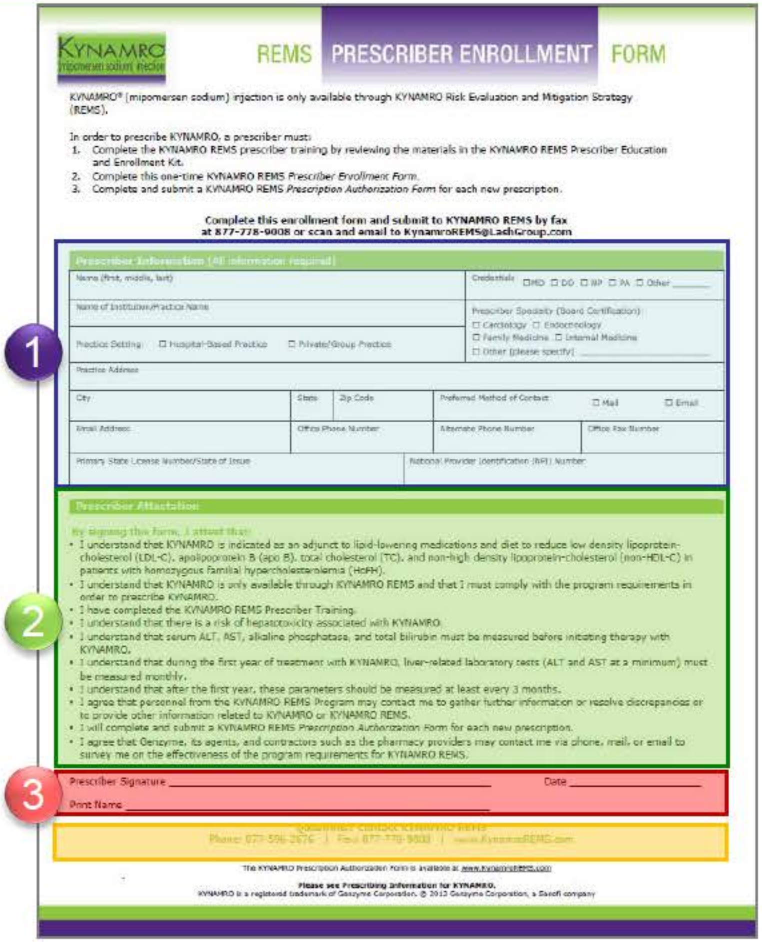
Prescriber Certification and Enrollment

- Only healthcare providers specially certified in the KYNAMRO REMS Program can prescribe KYNAMRO

- To become specially certified in the KYNAMRO REMS Program, you must:
  - Complete the training by reviewing the materials provided in the KYNAMRO REMS Prescriber Education and Enrollment Kit
    - Prescribing Information
    - Prescriber Training Slide Set
    - Summary of Monitoring Recommendations
    - Prescriber Enrollment Form
    - Prescription Authorization Form
  - Complete, sign, and submit the Prescriber Enrollment Form certifying that you have completed the required training and agree to follow the procedures required by the KYNAMRO REMS Program

- If you have any questions on the KYNAMRO REMS Program, visit www.KynamroREMS.com or call 877-596-2676

Prescriber Enrollment Form



KYNAMRO (mipomersen sodium) injection

REMS **PRESCRIBER ENROLLMENT** FORM

KYNAMRO® (mipomersen sodium) injection is only available through KYNAMRO Risk Evaluation and Mitigation Strategy (REMS).

In order to prescribe KYNAMRO, a prescriber must:

1. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.
2. Complete this one-time KYNAMRO REMS *Prescriber Enrollment Form.*
3. Complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.

Complete this enrollment form and submit to KYNAMRO REMS by fax at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

Prescriber Information (All information required)

Name (first, middle, last)		Credentials ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other ______	
Name of Institution/Practice Name		Prescriber Specialty (Board Certification) ☐ Cardiology ☐ Endocrinology ☐ Family Medicine ☐ Internal Medicine ☐ Other (please specify) ______	
Practice Setting: ☐ Hospital-Based Practice ☐ Private/Group Practice			
Practice Address			
City	State / Zip Code	Preferred Method of Contact ☐ Mail ☐ Email	
Email Address	Office Phone Number	Alternate Phone Number	Office Fax Number
Primary State License Number/State of Issue		National Provider Identification (NPI) Number	

Prescriber Attestation

By signing this form, I attest that:

- I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).
- I understand that KYNAMRO is only available through KYNAMRO REMS and that I must comply with the program requirements in order to prescribe KYNAMRO.
- I have completed the KYNAMRO REMS Prescriber Training.
- I understand that there is a risk of hepatotoxicity associated with KYNAMRO.
- I understand that serum ALT, AST, alkaline phosphatase, and total bilirubin must be measured before initiating therapy with KYNAMRO.
- I understand that during the first year of treatment with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) must be measured monthly.
- I understand that after the first year, these parameters should be measured at least every 3 months.
- I agree that personnel from the KYNAMRO REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to KYNAMRO or KYNAMRO REMS.
- I will complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.
- I agree that Genzyme, 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 KYNAMRO REMS.

Prescriber Signature ______________________ Date ____________

Print Name ______________________

Questions? Contact KYNAMRO REMS
Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

The KYNAMRO Prescription Authorization Form is available at www.KynamroREMS.com

Please see Prescribing Information for KYNAMRO.
KYNAMRO is a registered trademark of Genzyme Corporation. © 2013 Genzyme Corporation, a Sanofi company

1. Complete the Prescriber Information at the top of the form
2. Carefully review the attestations on the bottom half of the form
3. Sign and date the form to attest and agree to comply with the KYNAMRO REMS Program requirements

KYNAMRO™
(mipomersen sodium) injection

Reference ID: 3502923

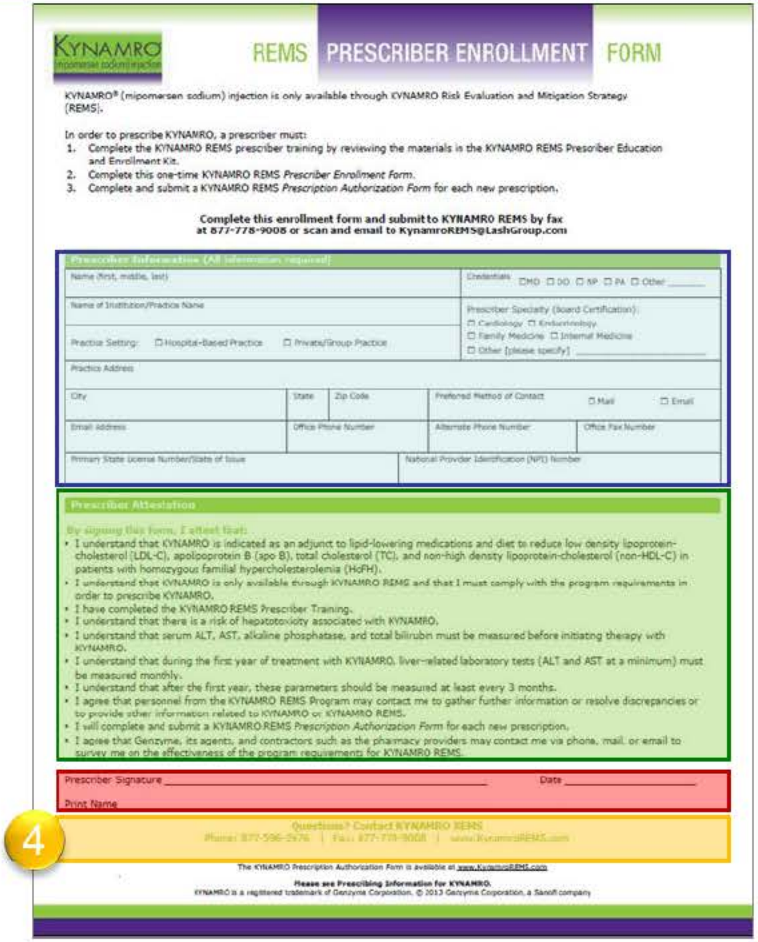
Prescriber Enrollment Attestations

3 In signing the Prescriber Enrollment Form, you attest that:

- You understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low LDL-C, apo B, TC, and non-HDL-C in patients with HoFH
- You understand that KYNAMRO is only available through the KYNAMRO REMS Program and that you must comply with the program requirements in order to prescribe KYNAMRO
- You have completed the KYNAMRO REMS Prescriber Training
- You understand that there is a risk of hepatotoxicity associated with KYNAMRO
- You understand that serum ALT, AST, alkaline phosphatase, and total bilirubin must be measured before initiating therapy with KYNAMRO
- You understand that during the first year of treatment with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) must be measured monthly
- You understand that after the first year, liver-related laboratory tests (ALT and AST at a minimum) should be measured at least every 3 months
- You agree that personnel from the KYNAMRO REMS Program may contact you to gather further information or resolve discrepancies or to provide other information related to KYNAMRO or the KYNAMRO REMS Program
- You will complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription
- You agree that Genzyme, its agents, and contractors such as the pharmacy providers may contact you via phone, mail, or email to survey you on the effectiveness of the program requirements for the KYNAMRO REMS Program

KYNAMRO™
(mipomersen sodium) injection

Prescriber Enrollment Form



KYNAMRO (mipomersen sodium) injection

REMS PRESCRIBER ENROLLMENT FORM

KYNAMRO® (mipomersen sodium) injection is only available through KYNAMRO Risk Evaluation and Mitigation Strategy (REMS).

In order to prescribe KYNAMRO, a prescriber must:

1. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.
2. Complete this one-time KYNAMRO REMS *Prescriber Enrollment Form*.
3. Complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.

Complete this enrollment form and submit to KYNAMRO REMS by fax at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

Prescriber Information (All information required)

Name (first, middle, last)

Credentials ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other ______

Name of Institution/Practice Name

Prescriber Specialty (Board Certification):
☐ Cardiology ☐ Endocrinology
☐ Family Medicine ☐ Internal Medicine
☐ Other (please specify) ______

Practice Setting: ☐ Hospital-Based Practice ☐ Private/Group Practice

Practice Address

City | State | Zip Code | Preferred Method of Contact ☐ Mail ☐ Email

Email Address | Office Phone Number | Alternate Phone Number | Office Fax Number

Primary State License Number/State of Issue | National Provider Identification (NPI) Number

Prescriber Attestation

By signing this form, I attest that:

- I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).
- I understand that KYNAMRO is only available through KYNAMRO REMS and that I must comply with the program requirements in order to prescribe KYNAMRO.
- I have completed the KYNAMRO REMS Prescriber Training.
- I understand that there is a risk of hepatotoxicity associated with KYNAMRO.
- I understand that serum ALT, AST, alkaline phosphatase, and total bilirubin must be measured before initiating therapy with KYNAMRO.
- I understand that during the first year of treatment with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) must be measured monthly.
- I understand that after the first year, these parameters should be measured at least every 3 months.
- I agree that personnel from the KYNAMRO REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to KYNAMRO or KYNAMRO REMS.
- I will complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.
- I agree that Genzyme, 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 KYNAMRO REMS.

Prescriber Signature ______________________ Date ______________

Print Name

4

Questions? Contact KYNAMRO REMS
Phone: 877-596-3976 | Fax: 877-778-9008 | www.KynamroREMS.com

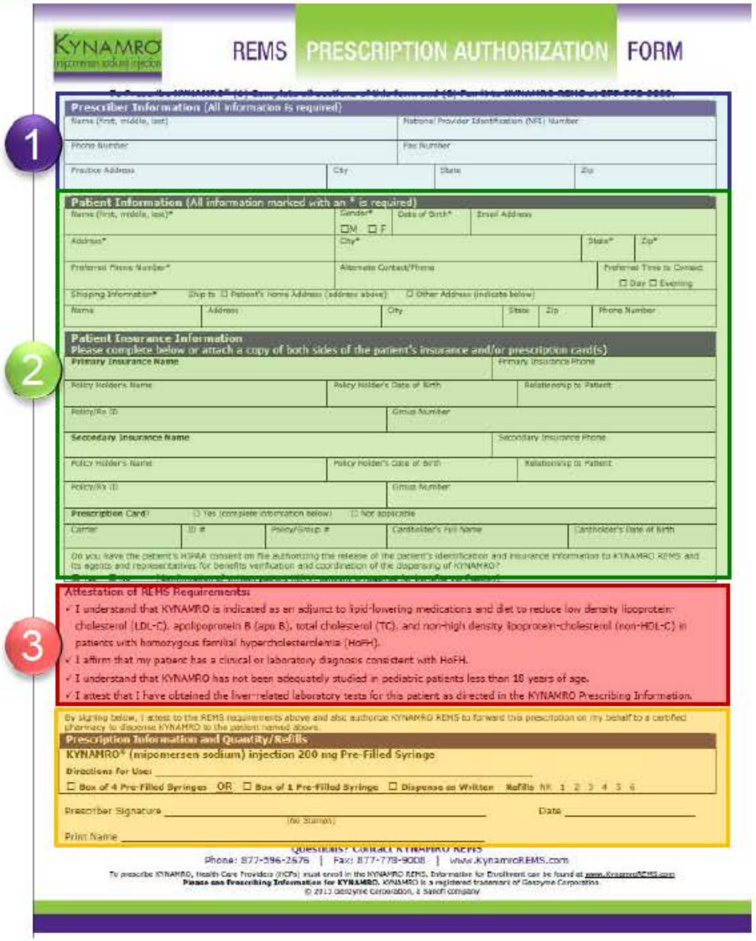
The KYNAMRO Prescription Authorization Form is available at www.KynamroREMS.com

Please see Prescribing Information for KYNAMRO.

4 Fax the signed form to the KYNAMRO REMS Program at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

5 *A confirmation letter will be sent when the form has been received and verified*

Prescription Authorization Form



KYNAMRO (mipomersen sodium) injection

REMS PRESCRIPTION AUTHORIZATION FORM

Prescriber Information (All information is required)

Name (first, middle, last) | National Provider Identification (NPI) Number
Phone Number | Fax Number
Practice Address | City | State | Zip

Patient Information (All information marked with an * is required)

Name (first, middle, last)* | Gender* ☐M ☐F | Date of Birth* | Email Address
Address* | City* | State* | Zip*
Preferred Phone Number* | Alternate Contact/Phone | Preferred Time to Contact ☐ Day ☐ Evening
Shipping Information* Ship to ☐ Patient's Home Address (address above) ☐ Other Address (indicate below)
Name | Address | City | State | Zip | Phone Number

Patient Insurance Information
Please complete below or attach a copy of both sides of the patient's insurance and/or prescription card(s)

Primary Insurance Name | Primary Insurance Phone
Policy Holder's Name | Policy Holder's Date of Birth | Relationship to Patient
Policy/Rx ID | Group Number
Secondary Insurance Name | Secondary Insurance Phone
Policy Holder's Name | Policy Holder's Date of Birth | Relationship to Patient
Policy/Rx ID | Group Number
Prescription Card? ☐ Yes (complete information below) ☐ Not applicable
Carrier | ID # | Policy/Group # | Cardholder's Full Name | Cardholder's Date of Birth

Do you have the patient's HIPAA consent on file authorizing the release of the patient's identification and insurance information to KYNAMRO REMS and its agents and representatives for benefits verification and coordination of the dispensing of KYNAMRO?

Attestation of REMS Requirements:

- ✓ I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age.
- ✓ I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information.

By signing below, I attest to the REMS requirements above and also authorize KYNAMRO REMS to forward this prescription on my behalf to a certified pharmacy to dispense KYNAMRO to the patient named above.

Prescription Information and Quantity/Refills

KYNAMRO® (mipomersen sodium) injection 200 mg Pre-Filled Syringe

Directions For Use: ____________________

☐ **Box of 4 Pre-Filled Syringes** OR ☐ **Box of 1 Pre-Filled Syringe** ☐ **Dispense as Written** **Refills** NR 1 2 3 4 5 6

Prescriber Signature ____________________ Date ____________
(No Stamps)

Print Name ____________________

Questions? Contact KYNAMRO REMS
Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

To prescribe KYNAMRO, Health Care Providers (HCPs) must enroll in the KYNAMRO REMS. Information for Enrollment can be found at www.KynamroREMS.com
Please see Prescribing Information for KYNAMRO. KYNAMRO is a registered trademark of Genzyme Corporation.
© 2013 Genzyme Corporation, a Sanofi company

For a patient to receive KYNAMRO, the Prescription Authorization Form must be completed by the prescriber

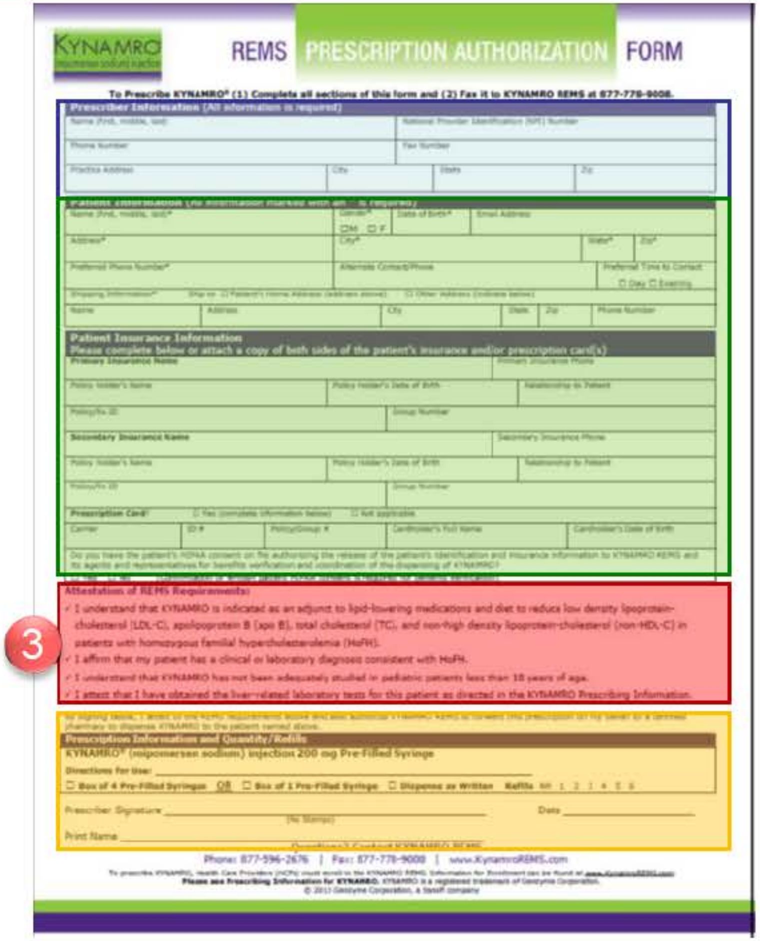
① Prescriber Information should be completed at the top of the form

② Patient Information and Insurance Information should be completed in the second and third box of the form

③ Carefully review the Attestation of REMS Requirements on the bottom half of the form

KYNAMRO™
(mipomersen sodium) injection

Prescription Authorization Form Requirements



KYNAMRO

REMS PRESCRIPTION AUTHORIZATION FORM

To Prescribe KYNAMRO® (1) Complete all sections of this form and (2) Fax it to KYNAMRO REMS at 877-778-9008.

Prescriber Information (All information is required)

Name (first, middle, last)	National Provider Identification (NPI) Number
Phone Number	Fax Number

Practice Address	City	State	Zip

Patient Insurance Information
Please complete below or attach a copy of both sides of the patient's insurance and/or prescription card(s)

Attestation of REMS Requirements:

✓ I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age.
✓ I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information.

Prescription Information and Quantity/Refills

KYNAMRO® (mipomersen sodium) injection 200 mg Pre-Filled Syringe

Directions for Use: ____________________

☐ **Box of 4 Pre-Filled Syringes** OR ☐ **Box of 1 Pre-Filled Syringe** ☐ **Dispense as Written** **Refills** NR 1 2 3 4 5 6

Prescriber Signature ____________________ Date ____________________

Print Name ____________________

Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

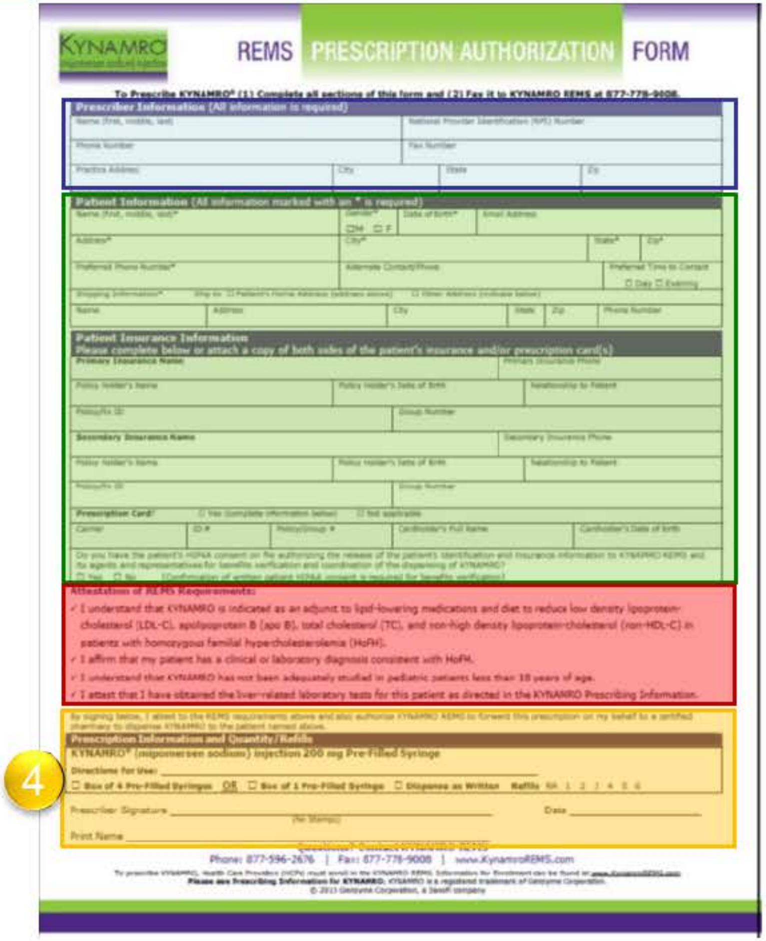
3

In completing the Prescription Authorization Form, you attest that:

- You understand that KYNAMRO is indicated as an adjunct to lipid lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with HoFH
- The patient has a clinical or laboratory diagnosis consistent with HoFH
- You understand that KYNAMRO has not been adequately studied in pediatric patients <18 years of age
- You have obtained the appropriate liver-related laboratory tests for the patient as directed in the KYNAMRO PI

KYNAMRO™
(mipomersen sodium) injection

Prescription Authorization Form



KYNAMRO

REMS PRESCRIPTION AUTHORIZATION FORM

To Prescribe KYNAMRO® (1) Complete all sections of this form and (2) Fax it to KYNAMRO REMS at 877-778-9008.

Prescriber Information (All information is required)

Name (first, middle, last)		National Provider Identification (NPI) Number	
Phone Number		Fax Number	
Practice Address	City	State	Zip

Patient Information (All information marked with an * is required)

Name (first, middle, last)*	Gender* ☐M ☐F	Date of Birth*	Email Address	
Address*	City*		State*	Zip*
Preferred Phone Number*	Alternate Contact/Phone		Preferred Time to Contact ☐ Day ☐ Evening	

Shipping Information* Ship to: ☐ Patient's Home Address (address above) ☐ Other Address (indicate below)

Name	Address	City	State	Zip	Phone Number

Patient Insurance Information
Please complete below or attach a copy of both sides of the patient's insurance and/or prescription card(s)

Primary Insurance Name		Primary Insurance Phone
Policy holder's Name	Policy Holder's Date of Birth	Relationship to Patient
Policy/Rx ID	Group Number	
Secondary Insurance Name		Secondary Insurance Phone
Policy holder's Name	Policy Holder's Date of Birth	Relationship to Patient
Policy/Rx ID	Group Number	

Prescription Card? ☐ Yes (complete information below) ☐ Not applicable

Carrier	ID #	Policy/Group #	Cardholder's Full Name	Cardholder's Date of Birth

Do you have the patient's HIPAA consent on file authorizing the release of the patient's identification and insurance information to KYNAMRO REMS and its agents and representatives for benefits verification and coordination of the dispensing of KYNAMRO?
☐ Yes ☐ No (Confirmation of written patient HIPAA consent is required for benefits verification)

Attestation of REMS Requirements:

✓ I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age.
✓ I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information.

By signing below, I attest to the REMS requirements above and also authorize KYNAMRO REMS to forward this prescription on my behalf to a certified pharmacy to dispense KYNAMRO to the patient named above.

Prescription Information and Quantity/Refills

KYNAMRO® (mipomersen sodium) injection 200 mg Pre-Filled Syringe

Directions for Use: ____________________

☐ **Box of 4 Pre-Filled Syringes** OR ☐ **Box of 1 Pre-Filled Syringe** ☐ **Dispense as Written** **Refills** NR 1 2 3 4 5 6

Prescriber Signature ____________________ Date ____________
(No Stamps)

Print Name ____________________

Questions? Contact KYNAMRO REMS

Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

To prescribe KYNAMRO, Health Care Providers (HCPs) must enroll in the KYNAMRO REMS. Information for Enrollment can be found at www.KynamroREMS.com

Please see Prescribing Information for KYNAMRO. KYNAMRO is a registered trademark of Genzyme Corporation.

4

4 The KYNAMRO Prescription should be written in the last box on the form

The Prescription Authorization Form should be provided by the prescriber to a certified pharmacy via the KYNAMRO REMS Program by faxing the completed form to the KYNAMRO REMS Program at 877-778-9008

KYNAMRO™
(mipomersen sodium) injection

KYNAMRO Prescription Ordering and Dispensing

- KYNAMRO is only available through a designated network of pharmacies that are certified in the KYNAMRO REMS Program

- Prescriptions for KYNAMRO must be written using the Prescription Authorization Form
  - Completed prescriptions should be submitted to the KYNAMRO REMS Program by fax at 877-778-9008
  - If you need assistance submitting a KYNAMRO prescription, contact the KYNAMRO REMS Program at 877-596-2676

LEARNING CHECK

KYNAMRO™
(mipomersen sodium) injection

Learning Check

- Prescribers should be able to answer these questions about the KYNAMRO REMS Program
- If you have problems answering any of these questions, please review information from the previous slides to ensure you are able to answer these questions correctly

KYNAMRO™
(mipomersen sodium) injection

Learning Check – Question 1

1. **KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with all forms of familial hypercholesterolemia**
   - ☐ True
   - ☐ False

KYNAMRO™
(mipomersen sodium) injection

Learning Check – Answer to Question 1

1. **KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with all forms of familial hypercholesterolemia**
   - ☐ True
   - ☑ **False**

ANSWER

KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, TC, and non-HDL-C in patients with HoFH.

Learning Check – Question 2

2. Which of the following liver-related laboratory tests should be performed prior to initiating a patient on treatment with KYNAMRO?

- ☐ Alkaline phosphatase
- ☐ Liver transaminases (ALT and AST)
- ☐ Total bilirubin
- ☐ All of the above

Learning Check – Answer to Question 2

2. Which of the following liver-related laboratory tests should be performed prior to initiating a patient on treatment with KYNAMRO?

- ☐ Alkaline phosphatase
- ☐ Liver transaminases (ALT and AST)
- ☐ Total bilirubin
- ☑ **All of the above**

ANSWER

Measure a full liver panel to include ALT, AST, total bilirubin, and alkaline phosphatase before initiation of treatment with KYNAMRO.

KYNAMRO™
(mipomersen sodium) injection

Learning Check – Question 3

3. At what frequency should liver transaminase levels be obtained for patients while on treatment with KYNAMRO? (check all that apply)

☐ During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly

☐ After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months

☐ For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 month

☐ All of the above

Learning Check – Answer to Question 3

3. At what frequency should liver transaminase levels be obtained for patients while on treatment with KYNAMRO? (check all that apply)

- ☑ During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly
- ☑ After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months
- ☐ For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 month
- ☐ All of the above

ANSWER

During the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted monthly. After the first year of treatment with KYNAMRO, ALT and AST tests (at a minimum) should be conducted at least every 3 months. For patients who develop ALT or AST elevations ≥3x and <5x ULN, the elevation should be confirmed with a repeat measurement within 1 week.

KYNAMRO™
(mipomersen sodium) injection

Learning Check – Question 4

4. Which of the following statements is false? (check all that apply)

- ☐ The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
- ☐ KYNAMRO can be used as an adjunct to LDL apheresis
- ☐ Patients must have a clinical or laboratory diagnosis consistent with HoFH
- ☐ The use of KYNAMRO is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases

Learning Check – Answer to Question 4

4. Which of the following statements is false? (check all that apply)

- ☐ The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined
- ☑ **KYNAMRO can be used as an adjunct to LDL apheresis**
- ☐ Patients must have a clinical or laboratory diagnosis consistent with HoFH
- ☐ The use of KYNAMRO is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases

ANSWER

Limitations of use include: the effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined and the use of KYNAMRO as an adjunct to LDL apheresis is <u>not</u> recommended. KYNAMRO has not been adequately studied in patients <18 years of age. The use of KYNAMRO is contraindicated in the following conditions: moderate or severe hepatic impairment (Child-Pugh B or C), or active liver disease, including unexplained persistent elevations of serum transaminases; and known hypersensitivity to any component of the product.

KYNAMRO™
(mipomersen sodium) injection

Learning Check – Question 5

5. Which of the following statements are true?

- ☐ KYNAMRO can cause elevations in liver transaminases
- ☐ KYNAMRO increases hepatic fat, with or without concomitant increases in liver transaminases
- ☐ Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than 1 alcoholic drink per day
- ☐ Exercise caution when KYNAMRO is used with other medications known to have potential for hepatotoxicity. More frequent monitoring of liver-related tests may be warranted.
- ☐ All of the above

Learning Check – Answer to Question 5

5. Which of the following statements are true (check all that apply)

- ☐ KYNAMRO can cause elevations in liver transaminases
- ☐ KYNAMRO increases hepatic fat, with or without concomitant increases in liver transaminases
- ☐ Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. Patients taking KYNAMRO should consume no more than 1 alcoholic drink per day
- ☐ Exercise caution when KYNAMRO is used with other medications known to have potential for hepatotoxicity. More frequent monitoring of liver-related tests may be warranted.
- ☑ **All of the above**

ANSWER

KYNAMRO is associated with a risk of hepatotoxicity.

Learning Check – Question 6

6. KYNAMRO is available from any pharmacy.

- ☐ True
- ☐ False

Learning Check – Answer to Question 6

6. KYNAMRO is available from any pharmacy.

☐ True

☑ **False**

ANSWER

KYNAMRO is only available from KYNAMRO REMS-certified pharmacies. Prescriptions must be submitted using the Prescription Authorization Form to the KYNAMRO REMS Program at 877-778-9008.

KYNAMRO™
(mipomersen sodium) injection

Summary

For additional information on the KYNAMRO REMS Program, call 877-596-2676 or visit www.KynamroREMS.com

KYNAMRO is a trademark of Genzyme Corporation

APPENDIX 3

SUMMARY OF MONITORING RECOMMENDATIONS

SUMMARY OF RECOMMENDATIONS*

Monitoring Patients Receiving KYNAMRO™

TIMING	RECOMMENDATION
Prior to initiating treatment	☐ Measure transaminases (ALT,AST), alkaline phosphatase, and total bilirubin
During the first year of treatment	☐ Instruct patients to report symptoms of possible liver problems ☐ Conduct liver-related tests monthly (ALT and AST, at minimum)
After the first year of treatment	☐ Instruct patients to report symptoms of possible liver problems ☐ Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)
If liver enzyme elevations are observed:	• If elevations in ALT or AST levels ≥3X and <5X ULN are observed, confirm elevation with a repeat measurement within 1 week. If confirmed, withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If elevations in ALT or AST levels ≥5X ULN are observed, withhold dosing, obtain additional liver-related tests if not already measured (such as total bilirubin, alkaline phosphatase, and INR) and investigate to identify the probable cause • If resuming KYNAMRO after transaminases resolve to <3X ULN, consider monitoring liver-related laboratory tests more frequently

For patients with:

- Persistent or clinically significant elevations in transaminases
- Transaminase elevations accompanied by clinical symptoms of liver injury, increases in bilirubin ≥2x ULN, or active liver disease
- Clinically significant liver toxicity

Discontinue treatment with KYNAMRO and investigate to identify the probable cause

**Please see the Prescribing Information for more information.*

Report all suspected adverse events associated with KYNAMRO. Please contact Genzyme at 1-800-745-4447 or the FDA at 1-800-FDA-1088 (332-1088) or www.fda.gov/medwatch.

KYNAMRO™
(mipomersen sodium) injection

APPENDIX 4

PRESCRIBER ENROLLMENT FORM

KYNAMRO
(mipomersen sodium) injection

REMS PRESCRIBER ENROLLMENT FORM

KYNAMRO® (mipomersen sodium) injection is only available through KYNAMRO Risk Evaluation and Mitigation Strategy (REMS).

In order to prescribe KYNAMRO, a prescriber must:

1. Complete the KYNAMRO REMS prescriber training by reviewing the materials in the KYNAMRO REMS Prescriber Education and Enrollment Kit.
2. Complete this one-time KYNAMRO REMS *Prescriber Enrollment Form.*
3. Complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.

Complete this enrollment form and submit to KYNAMRO REMS by fax at 877-778-9008 or scan and email to KynamroREMS@LashGroup.com

Prescriber Information (All information required)

Name (first, middle, last)

Credentials ☐MD ☐ DO ☐ NP ☐ PA ☐ Other _______

Name of Institution/Practice Name

Prescriber Specialty (Board Certification):
☐ Cardiology ☐ Endocrinology
☐ Family Medicine ☐ Internal Medicine
☐ Other [please specify] ________________________

Practice Setting: ☐ Hospital-Based Practice ☐ Private/Group Practice

Practice Address

City

State

Zip Code

Preferred Method of Contact ☐ Mail ☐ Email

Email Address

Office Phone Number

Alternate Phone Number

Office Fax Number

Primary State License Number/State of Issue

National Provider Identification (NPI) Number

Prescriber Attestation

By signing this form, I attest that:

- I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).
- I understand that KYNAMRO is only available through KYNAMRO REMS and that I must comply with the program requirements in order to prescribe KYNAMRO.
- I have completed the KYNAMRO REMS Prescriber Training.
- I understand that there is a risk of hepatotoxicity associated with KYNAMRO.
- I understand that serum ALT, AST, alkaline phosphatase, and total bilirubin must be measured before initiating therapy with KYNAMRO.
- I understand that during the first year of treatment with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) must be measured monthly.
- I understand that after the first year, these parameters should be measured at least every 3 months.
- I agree that personnel from the KYNAMRO REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to KYNAMRO or KYNAMRO REMS.
- I will complete and submit a KYNAMRO REMS *Prescription Authorization Form* for each new prescription.
- I agree that Genzyme, 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 KYNAMRO REMS.

Prescriber Signature ____ Date ____________________

Print Name ____

Questions? Contact KYNAMRO REMS
Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

The KYNAMRO Prescription Authorization Form is available at www.KynamroREMS.com

Please see Prescribing Information for KYNAMRO.

APPENDIX 5

PRESCRIPTION AUTHORIZATION FORM

KYNAMRO
(mipomersen sodium) injection

REMS PRESCRIPTION AUTHORIZATION FORM

To Prescribe KYNAMRO® (1) Complete all sections of this form and (2) Fax it to KYNAMRO REMS at 877-778-9008.

Prescriber Information (All information is required)

Name (first, middle, last)		National Provider Identification (NPI) Number	
Phone Number		Fax Number	
Practice Address	City	State	Zip

Patient Information (All information marked with an * is required)

Name (first, middle, last)*	Gender* ☐M ☐F	Date of Birth*	Email Address		
Address*	City*			State*	Zip*
Preferred Phone Number*	Alternate Contact/Phone			Preferred Time to Contact ☐ Day ☐ Evening	

Shipping Information* Ship to ☐ Patient's Home Address (address above) ☐ Other Address (indicate below)

Name	Address	City	State	Zip	Phone Number

Patient Insurance Information

Please complete below or attach a copy of both sides of the patient's insurance and/or prescription card(s)

Primary Insurance Name		Primary Insurance Phone
Policy Holder's Name	Policy Holder's Date of Birth	Relationship to Patient
Policy/Rx ID	Group Number	
Secondary Insurance Name		Secondary Insurance Phone
Policy Holder's Name	Policy Holder's Date of Birth	Relationship to Patient
Policy/Rx ID	Group Number	

Prescription Card? ☐ Yes (complete information below) ☐ Not applicable

Carrier	ID #	Policy/Group #	Cardholder's Full Name	Cardholder's Date of Birth

Do you have the patient's HIPAA consent on file authorizing the release of the patient's identification and insurance information to KYNAMRO REMS and its agents and representatives for benefits verification and coordination of the dispensing of KYNAMRO?
☐ Yes ☐ No [Confirmation of written patient HIPAA consent is required for benefits verification]

Attestation of REMS Requirements:

- ✓ I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), 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 KYNAMRO has not been adequately studied in pediatric patients less than 18 years of age.
- ✓ I attest that I have obtained the liver-related laboratory tests for this patient as directed in the KYNAMRO Prescribing Information.

By signing below, I attest to the REMS requirements above and also authorize KYNAMRO REMS to forward this prescription on my behalf to a certified pharmacy to dispense KYNAMRO to the patient named above.

Prescription Information and Quantity/Refills

KYNAMRO® (mipomersen sodium) injection 200 mg Pre-Filled Syringe

Directions for Use: ____________________

☐ **Box of 4 Pre-Filled Syringes** **OR** ☐ **Box of 1 Pre-Filled Syringe** ☐ **Dispense as Written** **Refills** NR 1 2 3 4 5 6

Prescriber Signature ____________________ Date ____________________
(No Stamps)

Print Name ____________________

Questions? Contact KYNAMRO REMS

Phone: 877-596-2676 | Fax: 877-778-9008 | www.KynamroREMS.com

To prescribe KYNAMRO, Health Care Providers (HCPs) must enroll in the KYNAMRO REMS. Information for Enrollment can be found at www.KynamroREMS.com
Please see Prescribing Information for KYNAMRO. KYNAMRO is a registered trademark of Genzyme Corporation.

APPENDIX 6

WEBSITE SCREEN SHOT – LANDING PAGE

KYNAMRO
(mipomersen sodium) injection

Prescribing Information   Important Safety Information   Medication Guide

KYNAMRO Risk Evaluation and Mitigation Strategy (REMS)

The FDA has required a REMS program for KYNAMRO so that the benefits of the drug outweigh the risks to patients.

The purpose of KYNAMRO REMS is to:

- Educate prescribers about:
  - the risk of hepatotoxicity associated with the use of KYNAMRO
  - the need to monitor patients during treatment with KYNAMRO as per product labeling
- Restrict access to therapy with KYNAMRO to patients with a clincal or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)

Only health care providers trained, enrolled and thereby certified in KYNAMRO REMS may prescribe KYNAMRO

For health care providers to become certified in KYNAMRO REMS:

1

Train

Click to open and review all of the educational materials below, including the question-and-answer section of the Prescriber Training Slide Set.

Prescriber Training Slide Set

Summary of Monitoring Recommendations

Prescribing Information

2

Enroll

Download and complete the Prescriber Enrollment Form below.

Fax completed form to 877-778-9008 or scan and **email to KynamroREMS@LashGroup.com.**

Prescriber Enrollment Form

For every new prescription for KYNAMRO:

LINE BREAK

Rx

Prescribe

For every new prescription for KYNAMRO, REMS-Certified Prescribers must use the Prescription Authorization Form below.

Download, complete, and **Fax completed form to 877-778-9008.**

Prescription Authorization Form

Prescriber Education and Enrollment Kit

Click Below to Download Materials

- Prescriber Training Slide Set
- Summary of Monitoring Recommendations
- Prescribing Information
- Prescriber Enrollment Form
- Prescription Authorization Form

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MP0021-0113

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Toll free: 800-745-4447

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JENNIFER R PIPPINS
05/07/2014