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

KYNAMRO REMS Program Pharmacy Certification Training Module and Knowledge Assessment
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KYNAMRO Knowledge Assessment

This training contains important information about your Specialty Pharmacy’s role in the KYNAMRO REMS program
INTRODUCTION
Introduction

• This training module has been developed as part of the KYNAMRO REMS Program to:
  – Educate pharmacists on the risk of hepatotoxicity associated with the use of KYNAMRO
  – Provide information on the KYNAMRO REMS Program requirements, including how to enroll in the KYNAMRO REMS Program, and requirements for dispensing KYNAMRO

• 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
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)

• Selected Limitations of use
  – The safety and effectiveness of KYNAMRO have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH)
Appropriate Patient Selection

- KYNAMRO is only indicated for use in patients with HoFH
- Patients must have a clinical or laboratory diagnosis consistent with HoFH
Contraindication

• 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

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.
Boxed Warning for Hepatotoxicity

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 ≥3x ULN. Discontinue KYNAMRO for clinically significant liver toxicity.

Because of the risk of hepatotoxicity, KYNAMRO is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the KYNAMRO REMS. Prescribe KYNAMRO only to patients with a clinical or laboratory diagnosis consistent with HoFH. The safety and effectiveness of KYNAMRO have not been established in patients with hypercholesterolemia who do not have HoFH.
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.
  - In the clinical trial, 4 (12%) of the 34 subjects with HoFH treated with KYNAMRO compared to 0% of the 17 subjects treated with placebo had an elevation in ALT >3x ULN, and 3 (9%) of those treated with KYNAMRO compared to 0% treated with placebo had at least one elevation in ALT >5x ULN.
Risk of Hepatotoxicity

• Hepatic steatosis
  – KYNAMRO increases hepatic fat (steatosis) with or without concomitant increases in transaminases.
  – Hepatic steatosis is a risk factor for advanced liver disease including steatohepatitis and cirrhosis
  – During the clinical trial 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% baseline, measured by magnetic resonance imaging (MRI).
**Dosing and Administration**

- The recommended dose of KYNAMRO is 200 mg once weekly as a subcutaneous injection:
  - KYNAMRO is available in a pre-filled syringe
  - Each 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
Adverse Reaction Reporting

• To report SUSPECTED ADVERSE REACTIONS, contact Kastle Therapeutics at 877-279-2308 or FDA at 800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)
KYNAMRO REMS PROGRAM

KYNAMRO®
(mipomersen sodium) injection
200mg/ml
Program Goals

• The goal of the KYNAMRO REMS Program is to mitigate the risk of hepatotoxicity associated with the use of KYNAMRO by ensuring that:
  – Prescribers are educated about:
    o The approval indication of KYNAMRO
    o The risk of hepatotoxicity associated with the use of KYNAMRO
    o The need to monitor patients during treatment with KYNAMRO per product labeling
  – KYNAMRO is dispensed only to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)
  – Patients are informed about the risk of hepatotoxicity associated with the use of KYNAMRO and the need for baseline and periodic monitoring
Program 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:
  - Certified Prescriber
    - ONLY prescribers trained, enrolled and thereby certified can prescribe KYNAMRO
  - Patient Education
    - Patients must be educated on the approved indication, the risks and the need for regular monitoring
  - Certified Pharmacies
    - ONLY pharmacies trained and thereby certified can dispense KYNAMRO
    - Restrict access to therapy with KYNAMRO to patients with a clinical or laboratory diagnosis consistent with Homozygous familial hypercholesterolemia (HoFH)
    - KYNAMRO can ONLY be dispensed to patients with evidence or other documentation of safe use conditions. This is confirmed on the KYNAMRO Prescription Authorization Form.
Each pharmacy must be REMS certified before KYNAMRO may be dispensed:

**Pharmacy TRAINING**
- Review the KYNAMRO Prescribing Information and **KYNAMRO REMS Program: An Introduction**
- Complete the **KYNAMRO REMS Program Pharmacy Certification Training Module**, successfully complete the **Knowledge Assessment** and fax to the KYNAMRO REMS Program Coordinating Center

**Pharmacy ENROLLMENT**
- Complete the **KYNAMRO REMS Program Pharmacy Enrollment Form** and submit the form to the KYNAMRO REMS Program Coordinating Center

**Pharmacy Dispensing Process**
- The prescriber is certified in the KYNAMRO REMS Program by checking the REMS Certified Prescriber Report prior to dispensing
- The **KYNAMRO REMS Program Prescription Authorization Form** is received for each new prescription
- The **KYNAMRO REMS Program Patient-Prescriber Acknowledgement Form** is on file with the REMS Program Coordinating Center
Pharmacy Roles and Responsibilities

Each Certified Pharmacy must:

• Agree to be audited to ensure that all processes and procedures are in place and are being followed for the KYNAMRO REMS program
• Agree to cooperate with Kastle for the investigation of root causes of noncompliance with KYNAMRO REMS program-required dispensing/reporting and any corrective and/or preventive actions taken to address noncompliance;
• Provide KYNAMRO prescription data to Kastle that includes:
  – Number of KYNAMRO prescriptions dispensed, including quantity of pre-filled syringes; number of prescriptions dispensed without a signed attestation on the Prescription Authorization Form
  – Number and demographics (e.g. gender, age, geographic location) of patients who received KYNAMRO;
  – Report of the number, length, and reasons for shipment delays to patients, if any
  – Provide reports in a format and frequency required by Kastle

NOTE: Only Specialty Pharmacy Providers and locations who have received written notification from the Kastle REMS Administrator that they have been REMS certified in the KYNAMRO REMS program, can dispense KYNAMRO.
• Authorized Pharmacy Representative (APR) must complete the following KYNAMRO REMS Program training before SPP location may dispense KYNAMRO:
  1. Review Prescribing Information
  2. Review **KYNAMRO REMS Program: An Introduction**, which summarizes the risks and requirements of the REMS program
  3. Complete this **KYNAMRO REMS Program Pharmacy Certification Training Module**
  4. Complete, sign, and fax the **KYNAMRO REMS Program Knowledge Assessment** and **KYNAMRO REMS Program Pharmacy Enrollment Form** to KYNAMRO REMS Program Coordinating Center
  5. APR must educate all pharmacy staff involved in the dispensing of KYNAMRO on the KYNAMRO REMS Program requirements and putting in appropriate processes to ensure compliance with the REMS program.

• APR needs to only do complete the KYNAMRO REMS Program training **once** before first dispensing KYNAMRO
  • Recertification is required if there is a change in the authorized representative.
Required Dispensing Process – Receipt of Prescription Authorization Form Directly From Kastle

- KYNAMRO is only available through a designated network of Specialty Pharmacy Providers (SPPs) that are certified in the KYNAMRO REMS Program.
- Prescriptions for KYNAMRO must be written by the prescriber using the REMS Prescription Authorization Form (PAF) and sent to the KYNAMRO REMS Coordinating Center.
- Upon receipt of a completed Prescription Authorization Form, KYNAMRO REMS Coordinating Center will:
  - Confirm prescriber is REMS-certified
  - Perform complete insurance benefit investigation, prior authorization support, etc.
  - Confirm SPP is REMS-certified
- When above work is completed, KYNAMRO REMS Program Coordinating Center will send the Prescription Authorization Form to REMS-certified SPP.
- Upon receipt of the Prescription Authorization Form, the SPP will:
  1. Verify the prescriber is REMS-certified in the KYNAMRO REMS Program by checking the REMS Certified Prescriber Report prior to dispensing.
  2. The KYNAMRO REMS Program Prescription Authorization Form is received for each new prescription.
  3. The KYNAMRO REMS Program Patient-Prescriber Acknowledgement Form is on file with the REMS Program Coordinating Center.

Note: SPP are to redirect any Prescription Authorization Forms received directly from prescribers to the KYNAMRO REMS Program Coordinating Center.
Dispensing Process – Filling a Prescription

• SPP will order Kynamro from Kastle’s 3PL provider, and maintain adequate inventory to service its current patient census without delay in prescription shipments or interruption in patient treatment.

• SPP will only dispense prescriptions written on Prescription Authorization Forms from REMS Certified prescribers that have been triaged to them from the KYNAMRO REMS Program Coordinating Center.

• Refills for existing patients can continue uninterrupted until refills are exhausted and a new Prescription Authorization Form is required. The new Prescription Authorization Form should be sent by the prescriber to the KYNAMRO REMS Program Coordinating Center and not directly to the SPP.
Records and Reporting

SPPs are required to provide the following information to the KYNAMRO REMS Program Coordinating Center on a weekly basis, as specified by Kastle:

- **Information on Kynamro prescriptions dispensed:**
  - PrescriptionNumber
  - Prescriber name and NPI number
  - Confirmation of Prescriber REMS Certification
  - Confirmation of Completed Prescription Authorization Form with Prescriber signature to attest for patient qualification
  - Date dispensed, number of cartons and sizes dispensed
  - Dispensing Pharmacy address
  - Ship-To address

- **Information on patients who received KYNAMRO:**
  - Kynamro Cornerstone Program Patient ID
  - Patient First and Last Names
  - Patient Date of Birth
  - Patient Gender
  - Patient Address

- **Information on special alerts:**
  - Initial fill/New Patient Flag
  - Refill/Existing Patient Flag

- **Information on shipping delays to patients (including number, length, and reasons)**

Copies of submitted information must be retained by the SPP for at least 2 years from the date of report submittal to the REMS program.
Summary – Points to Remember

• Only Pharmacies that are REMS-Certified can dispense KYNAMRO
• Only prescribers that are REMS-Certified can prescribe KYNAMRO and only by using the Prescription Authorization Form
  – Be sure to check the weekly REMS certification report for list of certified prescribers
• Pharmacy staff must be trained on the dispensing process for KYNAMRO
  – Documentation showing compliance (training, dispensing records, etc) will be needed for auditing
• Pharmacies must provide prescription information to Kastle on a weekly basis

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

KYNAMRO is a registered trademark of Kastle Therapeutics LLC
KYNAMRO REMS PROGRAM
Pharmacist Training, Enrolling and Prescribing Summary

TRAIN

Review the KYNAMRO Prescribing Information and KYNAMRO REMS Program: An Introduction

Complete the KYNAMRO REMS Program Pharmacy Certification Training Module

Complete the Knowledge Assessment Form

ENROLL

Complete the KYNAMRO REMS Program Pharmacy Enrollment Form

Fax both completed Knowledge Assessment Form and Pharmacy Enrollment Form to 1-877-778-9008

Train all pharmacy staff at pharmacy location on the KYNAMRO REMS Program requirements & ensure processes for program compliance

DISPENSE

Review & ensure all information on KYNAMRO REMS Program Prescription Authorization Form is complete

Before dispensing KYNAMRO, confirm:

1. The prescriber is certified in the KYNAMRO REMS Program by checking the REMS Certified Prescriber Report prior to dispensing
2. The KYNAMRO REMS Program Prescription Authorization Form is received for each new prescription
3. The KYNAMRO REMS Program Patient-Prescriber Acknowledgement Form is on file with the REMS Program Coordinating Center

Ensure all data requirements are reported back to the KYNAMRO REMS Program Coordinating Center

Reference ID: 4171886
Knowledge Assessment
Knowledge Assessment

• You must answer all 5 questions correctly

• 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.

• Fax both completed Knowledge Assessment Form & Pharmacy Enrollment Form to KYNAMRO REMS Program Coordinating Center
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
2. KYNAMRO is indicated for the following patients. Check all that apply

- Patients must have a laboratory diagnosis consistent with HoFH
- KYNAMRO is only indicated for use in patients with HoFH
- Patients with moderate or severe hepatic impairment
- Patients must have a clinical or laboratory diagnosis consistent with HoFH
3. KYNAMRO is available from any pharmacy

- True
- False

Reference ID: 4171886
4. Each REMS-certified pharmacy must: (Check all that apply)

- Agree to be audited to ensure that all REMS processes and procedures are in place
- Provide detailed prescription data to Kastle on a weekly basis
- May receive prescriptions directly from prescribers and dispense
- Recertify every year
Knowledge Assessment– Question 5

5. Prior to dispensing KYNAMRO, every certified SPP must do the following:

- Verify the prescriber is certified in the KYNAMRO REMS Program by checking the REMS-Certified Prescriber Report distributed by the REMS Coordinating Center
- Receive a Prescription Authorization Form for each new prescription
- Confirm that a Patient-Prescriber Acknowledgement Form is on file with the REMS Coordinating Center
- All of the above
Now that you’ve reviewed and completed the Training Module, please submit the Knowledge Assessment Form & Pharmacy Enrollment Form and fax both to 1-877-778-9008.

The REMS Coordinating Center will review your answers and fax back a confirmation that you are REMS certified to prescribe KYNAMRO along with the Knowledge Assessment Answer Key.

For additional information on the KYNAMRO REMS Program, call 1-877-596-2676 or visit www.KYNAMROREMS.com

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