

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203568Orig1s000**

**REMS**

**Initial REMS Approval: 01/2013**

**NDA 203568**

**KYNAMRO™ (mipomersen sodium)**

**Drug Class: Oligonucleotide Inhibitor of Apolipoprotein B-100 Synthesis**

Genzyme Corporation  
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## **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](http://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.
  - vi. To facilitate prescriber certification, Genzyme will communicate information to HCPs and professional associations through the KYNAMRO REMS Program website and *Dear Healthcare Provider* and *Dear Professional Association* letters.

- 1) *Dear Healthcare Provider* letter - Genzyme will distribute a *Dear Healthcare Provider* letter within 60 days of KYNAMRO REMS approval to inform potential prescribers about the REMS and the REMS requirements. The *Dear Healthcare Provider* letter will be distributed to HCPs certified by the American Board of Clinical Lipidology, directors of apheresis centers, and to HCPs known to be experienced in treating patients with HoFH. The letter will be accompanied by the PI, the *Healthcare Professional Information Brochure*, and the *Summary of Monitoring Recommendations* and will be available from the KYNAMRO REMS Program website ([www.KynamroREMS.com](http://www.KynamroREMS.com)) at the time of the mailing and will remain on the website for 12 months after the mailing, or can be requested from the KYNAMRO REMS Program coordinating center by phone at 877-596-2676. Genzyme will distribute the letter via electronic mail, mail, or facsimile.
  
- 2) *Dear Professional Association* letter - Genzyme will send a *Dear Professional Association* letter within 60 days of KYNAMRO REMS approval to the leadership of the following professional associations and will request that these associations disseminate the content of the letter to their professional membership:
  - a) National Lipid Association
  - b) The Endocrine Society
  - c) The American Association of Clinical Endocrinologists
  - d) American Heart Association
  - e) American College of Cardiology
  - f) American Society of Preventive Cardiology
  - g) Preventive Cardiology Nurses Association
  - h) American Society for Apheresis

The letter will be provided to MedWatch at the same time it is provided to the professional associations.

- 3) KYNAMRO REMS website - A KYNAMRO REMS website ([www.KynamroREMS.com](http://www.KynamroREMS.com)) will be available at the time of approval.

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

- *Dear Healthcare Provider* letter
- *Healthcare Professional Information Brochure*
- *Dear Professional Association* letter
- 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](http://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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## An Overview of the KYNAMRO™ Risk Evaluation and Mitigation Strategy (REMS) Program

Prescriber Training

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  - 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



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## 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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## 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

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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)  $\geq 3$ x 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  $\geq 3$  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  $\geq 2x$  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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## 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  $\geq 3$  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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# KYNAMRO™ (mipomersen sodium) injection

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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

KYNAMRO™  
(mipomersen sodium) injection

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## Monitoring of Hepatic Transaminases

PERIOD ON TREATMENT	TREATMENT AND MONITORING RECOMMENDATIONS
Beginning treatment	<ul style="list-style-type: none"><li>• Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin</li></ul>
During first year	<ul style="list-style-type: none"><li>• Conduct liver-related tests monthly (ALT and AST, at a minimum)</li></ul>
After first year	<ul style="list-style-type: none"><li>• Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)</li></ul>



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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	<ul style="list-style-type: none"><li>Confirm elevation with a repeat measurement within 1 week</li><li>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</li><li>If resuming KYNAMRO after transaminases resolve to &lt;3x ULN, consider monitoring liver-related laboratory tests more frequently</li></ul>
≥5x ULN	<ul style="list-style-type: none"><li>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</li><li>If resuming KYNAMRO after transaminases resolve to &lt; 3x ULN, monitor liver-related laboratory tests more frequently</li></ul>



\* 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](http://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](http://www.KynamroREMS.com) or call 877-596-2676



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## Prescriber Enrollment Form

**KYNAMRO** 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 material 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 877-775-3008 or scan and email to [kynamroREMS@lsdgroup.com](mailto:kynamroREMS@lsdgroup.com).

**1** Prescriber Information (Please print. All information required.)

Name (Last, Middle, First)		Telephone: ( ) - - x - x	
Name of your institution (Name)		Physician Specialty	
Office Address			
City	State	Zip Code	Physician Contact at Office <input type="checkbox"/> Home <input type="checkbox"/> Other
Home Address	Office Phone Number	Home Phone Number	Street or Number
Primary State License Number (State of Issue)			
National Provider Identifier (NPI) Number			

**2** By signing this form, I certify that:

- I understand that KYNAMRO is indicated as an adjunct to lipid-lowering medication and not to reduce the density (LDL-C) or apoB lipoprotein (apoB) or total cholesterol (TC), and to raise density lipoprotein (HDL-C) in patients with heterozygous familial hypercholesterolemia (FH).
- I understand that KYNAMRO is only available through the KYNAMRO REMS Program and that its use is subject to program requirements as outlined by the KYNAMRO REMS Program.
- I have completed the KYNAMRO REMS Prescriber Training.
- I understand that there is a risk of myopathy associated with KYNAMRO.
- I understand that there is a risk of myopathy associated with KYNAMRO, and that clinical events are tracked before starting therapy with KYNAMRO.
- I understand that during the first year of treatment with KYNAMRO, we should monitor for ALT and AST at a minimum within the listed intervals.
- I understand that after the first year, liver parameters should be monitored at least every 3 months.
- I agree that patients from the KYNAMRO REMS Program may contact me to gather patient information or receive drug samples or to provide other information related to KYNAMRO or the KYNAMRO REMS Program.
- I will complete and submit KYNAMRO REMS Prescription Authorization Form for each new prescription.
- I agree that Genzyme, its agents, and contractors are not its primary provider and may contact me via phone, mail, or email to ensure that the effective use of the program requirements for the KYNAMRO REMS Program.

**3** Prescriber Signature \_\_\_\_\_ Date \_\_\_\_\_

If you have any questions, contact the KYNAMRO REMS Program.  
Phone: 877-556-2676 | Fax: 877-775-3008 | [www.kynamroREMS.com](http://www.kynamroREMS.com)

The KYNAMRO Prescriber Enrollment Form is available at [www.kynamroREMS.com](http://www.kynamroREMS.com).  
Please see Prescribing Information for KYNAMRO.  
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- 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



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## Prescriber Enrollment Form

**KYNAMRO** 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](mailto:KynamroREMS@LashGroup.com).

**Prescriber Information (Please print, all information required.)**

Name (Last, middle, first) \_\_\_\_\_ Date: MM / DD / YY, 8 AM - 8 PM, 8 Time \_\_\_\_\_

Name of your institution (Name) \_\_\_\_\_ Physician Specialty \_\_\_\_\_

Street Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ Zip Code \_\_\_\_\_ Phone (Area/Number of Country)  Day  Even

Home Address \_\_\_\_\_ Office Phone Number \_\_\_\_\_ Mobile Phone Number \_\_\_\_\_ Check # of Number \_\_\_\_\_

Phone (Area/Number of State) \_\_\_\_\_ Check # of Number \_\_\_\_\_

Specialty (Please print) \_\_\_\_\_

By signing this form, I certify that:

- I understand that KYNAMRO is indicated as an adjunct to statin therapy and not to replace the daily statin therapy (rosuvastatin (CRU-C), atorvastatin (CRU-C), simvastatin (CRU-C), and pravastatin (CRU-C)) and high-dose statin therapy (rosuvastatin (CRU-C)) and high-dose statin therapy (rosuvastatin (CRU-C)).
- I understand that KYNAMRO is only available through the KYNAMRO REMS Program and that it is not to be used in conjunction with the program requirements to 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 certain ALT, AST, alkaline phosphatase, and bilirubin levels are checked before starting therapy with KYNAMRO.
- I understand that during the first year of therapy with KYNAMRO, liver-related laboratory tests (ALT and AST at a minimum) are checked monthly.
- I understand that after the first year, liver-related laboratory tests (ALT and AST at a minimum) are checked every 3 months.
- I agree that prescribers from the KYNAMRO REMS Program may contact me to gather further information or receive assistance or to provide other information related to KYNAMRO or the KYNAMRO REMS Program.
- I will complete and submit KYNAMRO REMS Prescription Authorization Form for each new prescription.
- I agree that Genzyme, its agents, and contractors will be the primary provider(s) to contact me in person, mail, or email to ensure me the effectiveness of the program requirements for the KYNAMRO REMS Program.

Prescriber Signature \_\_\_\_\_ Date \_\_\_\_\_

If you have any questions, contact the KYNAMRO REMS Program.  
Phone: 877-556-2576 | Fax: 877-778-9008 | [www.KynamroREMS.com](http://www.KynamroREMS.com)

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**4** Fax the signed form to the KYNAMRO REMS Program at 877-778-9008 or scan and email to [KynamroREMS@LashGroup.com](mailto: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

**KYNAMRO**  
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.

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

**2** Insurance Information (Please print.)

**3** Attestation of REMS Requirements

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

**3** KYNAMRO Prescriber (Please print. All information marked with an \* is required.)

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

### 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

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



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## LEARNING CHECK



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## 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



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## Learning Check – Question 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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## 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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## 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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## 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  $\geq 3x$  and  $< 5x$  ULN, the elevation should be confirmed with a repeat measurement within 1 month
- All of the above



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## 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  $\geq 3x$  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  $\geq 3x$  and  $< 5x$  ULN, the elevation should be confirmed with a repeat measurement within 1 week.



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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



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## 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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## 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.



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## Learning Check – Question 6

6. **KYNAMRO** is available from any pharmacy.

- True
- False



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## 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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## Summary

For additional information on the KYNAMRO REMS Program,  
call 877-596-2676 or visit [www.KynamroREMS.com](http://www.KynamroREMS.com)



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**APPENDIX 2**

**PRESCRIBER TRAINING SLIDE SET**



# 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



# 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



# 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



# 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.



# 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)  $\geq 3$ x 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  $\geq 3$  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  $\geq 2x$  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  $\geq 3$  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.



# 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	<ul style="list-style-type: none"><li>• Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin</li></ul>
During first year	<ul style="list-style-type: none"><li>• Conduct liver-related tests monthly (ALT and AST, at a minimum)</li></ul>
After first year	<ul style="list-style-type: none"><li>• Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)</li></ul>



# 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*
$\geq 3x$ and $< 5x$ ULN	<ul style="list-style-type: none"><li>Confirm elevation with a repeat measurement within 1 week</li><li>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</li><li>If resuming KYNAMRO after transaminases resolve to <math>&lt; 3x</math> ULN, consider monitoring liver-related laboratory tests more frequently</li></ul>
$\geq 5x$ ULN	<ul style="list-style-type: none"><li>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</li><li>If resuming KYNAMRO after transaminases resolve to <math>&lt; 3x</math> ULN, monitor liver-related laboratory tests more frequently</li></ul>



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

**KYNAMRO**<sup>™</sup>  
(mipomersen sodium) injection

# KYNAMRO REMS 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:
  - 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

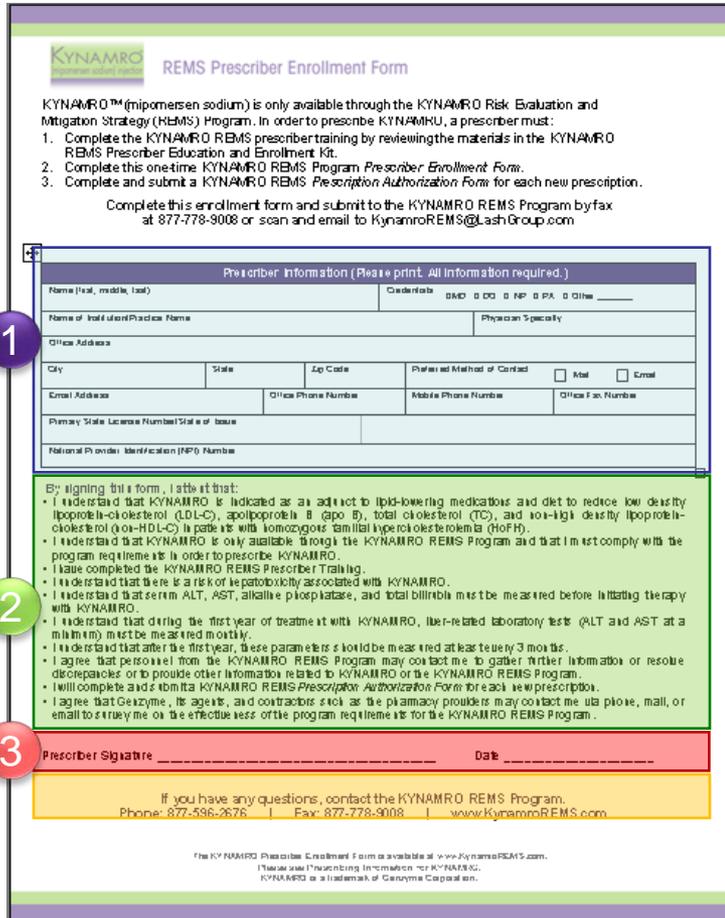


# Prescriber Certification and Enrollment

- 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](http://www.KynamroREMS.com) or call 877-596-2676



# Prescriber Enrollment Form



**KYNAMRO**  
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](mailto:KynamroREMS@LashGroup.com)

**1** Prescriber Information (Please print. All information required.)

Name (last, middle, first)		Credentials: MD <input type="checkbox"/> DO <input type="checkbox"/> NP <input type="checkbox"/> PA <input type="checkbox"/> Other _____	
Name of Institution/Practice Name		Physician Specialty	
Office Address			
City	State	Zip Code	Preferred Method of Contact: <input type="checkbox"/> Mail <input type="checkbox"/> Email
Email Address	Office Phone Number	Mobile Phone Number	Office Fax Number
Primary State License Number/State of Issue			
National Provider Identification (NPI) Number			

**2** By signing this form, I state 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 the KYNAMRO REMS Program 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 the KYNAMRO REMS Program.
- 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 determine the effectiveness of the program requirements for the KYNAMRO REMS Program.

**3** Prescriber Signature \_\_\_\_\_ Date \_\_\_\_\_

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

The KYNAMRO Prescriber Enrollment Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
For more prescribing information on KYNAMRO, KYNAMRO is a trademark of Genzyme Corporation.

- 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

# 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**<sup>™</sup>  
(mipomersen sodium) injection

# Prescriber Enrollment Form

**KYNAMRO** (mipomersen sodium) injection

**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](mailto:KynamroREMS@LashGroup.com)

Prescriber Information (Please print. All information required.)

Name (Last, middle, first)		Credentials: MD, DO, NP, PA, Other _____	
Name of Institution/Practice Name		Physician Specialty	
Office Address			
City	State	Zip Code	Preferred Method of Contact: <input type="checkbox"/> Mail <input type="checkbox"/> Email
Email Address	Office Phone Number	Mobile Phone Number	Office Fax Number
Primary State License Number/State of Issue			
National Provider Identification (NPI) Number			

By signing this form, I state 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 the KYNAMRO REMS Program 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 the KYNAMRO REMS Program.
- 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 determine the effectiveness of the program requirements for the KYNAMRO REMS Program.

Prescriber Signature \_\_\_\_\_ Date \_\_\_\_\_

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

The KYNAMRO Prescriber Enrollment Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
 Please see the accompanying information for KYNAMRO.  
 KYNAMRO is a trademark of Genzyme Corporation.

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Fax the signed form to the KYNAMRO REMS Program at 877-778-9008 or scan and email to [KynamroREMS@LashGroup.com](mailto:KynamroREMS@LashGroup.com)

5

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

4

Reference ID: 3252315

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# Prescription Authorization Form

**KYNAMRO**  
(mipomersen sodium) injection

## 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.)**

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

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

Name      Address      City      State      Zip      Phone Number

**Insurance Information (Please print.)**

**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

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

Prescriber's Full Name\*      NPI\*  
Phone Number\*      Fax Number\*  
Practice Street Address\*      City\*      State\*      Zip\*

**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.)**

Dosing Instructions\*      Refills: NR 1 2 3 4 5 6  
DATE\*      PRESCRIBER SIGNATURE\*       Dispense as Written

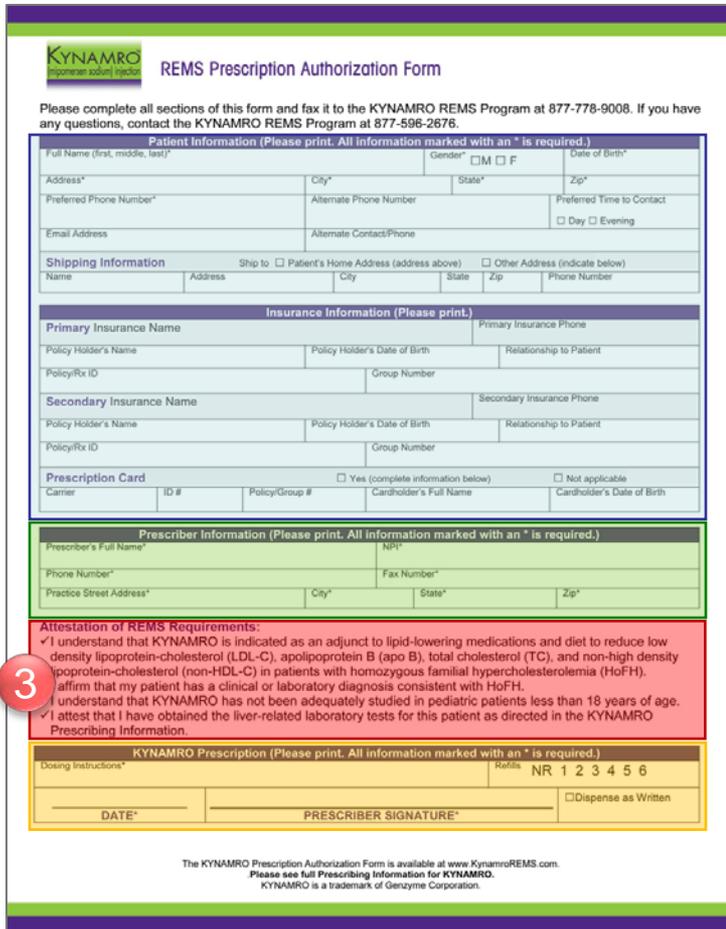
The KYNAMRO Prescription Authorization Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
Please see full Prescribing Information for KYNAMRO.  
KYNAMRO is a trademark of Genzyme Corporation.

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

**KYNAMRO**  
(mipomersen sodium) injection

# Prescription Authorization Form Requirements



**KYNAMRO**  
(mipomersen sodium) injection

**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.)**

Full Name (first, middle, last)\*      Gender\*  M  F      Date of Birth\*

Address\*      City\*      State\*      Zip\*

Preferred Phone Number\*      Alternate Phone Number      Preferred Time to Contact  
 Day  Evening

Email Address      Alternate Contact/Phone

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

Name      Address      City      State      Zip      Phone Number

**Insurance Information (Please print.)**

**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

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

Prescriber's Full Name\*      NPI\*

Phone Number\*      Fax Number\*

Practice Street Address\*      City\*      State\*      Zip\*

**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.)**

Dosing Instructions\*      Route      NR 1 2 3 4 5 6

DATE\*      PRESCRIBER SIGNATURE\*       Dispense as Written

The KYNAMRO Prescription Authorization Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
Please see full Prescribing Information for KYNAMRO.  
KYNAMRO is a trademark of Genzyme Corporation.

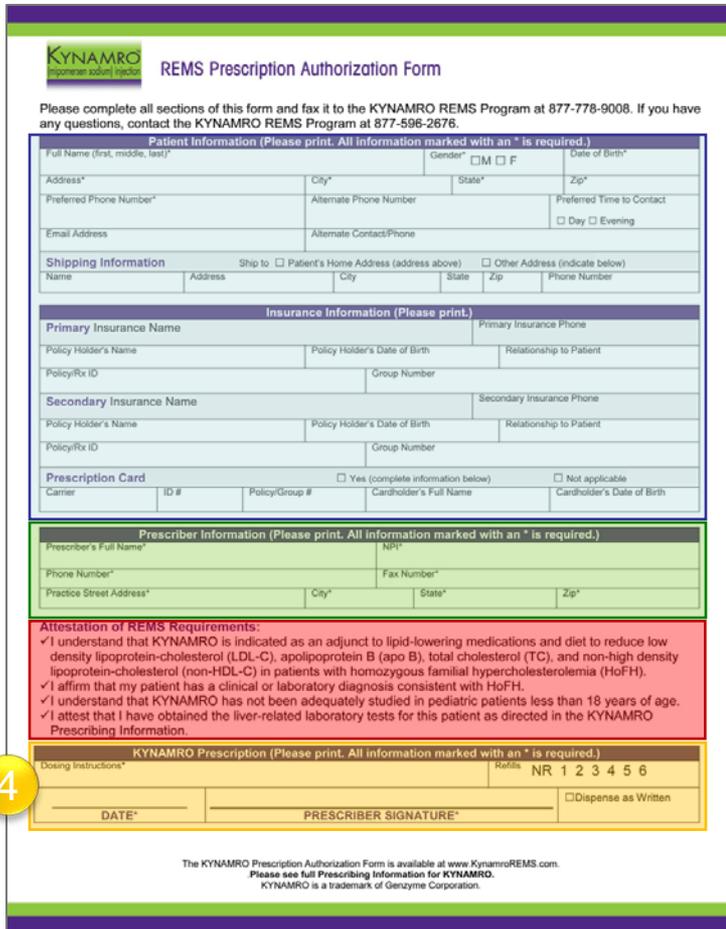
3

## 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**  
(mipomersen sodium) injection

## 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.)**

Full Name (first, middle, last)\*      Gender\*  M  F      Date of Birth\*

Address\*      City\*      State\*      Zip\*

Preferred Phone Number\*      Alternate Phone Number      Preferred Time to Contact  
 Day  Evening

Email Address      Alternate Contact/Phone

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

Name      Address      City      State      Zip      Phone Number

**Insurance Information (Please print.)**

**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

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

Prescriber's Full Name\*      NPI\*

Phone Number\*      Fax Number\*

Practice Street Address\*      City\*      State\*      Zip\*

**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.)**

Dosing Instructions\*      Refills NR 1 2 3 4 5 6

DATE\*      PRESCRIBER SIGNATURE\*       Dispense as Written

The KYNAMRO Prescription Authorization Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
Please see full Prescribing Information for KYNAMRO.  
KYNAMRO is a trademark of Genzyme Corporation.

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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

4



# 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



# 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



# 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



# 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.



# 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  $\geq 3x$  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  $\geq 3x$  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  $\geq 3x$  and  $< 5x$  ULN, the elevation should be confirmed with a repeat measurement within 1 week.



# 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 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.



# 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.



# Summary

For additional information on the KYNAMRO REMS Program,  
call 877-596-2676 or visit [www.KynamroREMS.com](http://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	<input type="checkbox"/> Measure transaminases (ALT,AST), alkaline phosphatase, and total bilirubin
During the first year of treatment	<input type="checkbox"/> Instruct patients to report symptoms of possible liver problems <input type="checkbox"/> Conduct liver-related tests monthly (ALT and AST, at minimum)
After the first year of treatment	<input type="checkbox"/> Instruct patients to report symptoms of possible liver problems <input type="checkbox"/> Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)
If liver enzyme elevations are observed:	<ul style="list-style-type: none"> <li>• If elevations in ALT or AST levels <math>\geq 3X</math> and <math>&lt; 5X</math> 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</li> <li>• If elevations in ALT or AST levels <math>\geq 5X</math> 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</li> <li>• If resuming KYNAMRO after transaminases resolve to <math>&lt; 3X</math> ULN, consider monitoring liver-related laboratory tests more frequently</li> </ul>
For patients with:	<ul style="list-style-type: none"> <li>• Persistent or clinically significant elevations in transaminases</li> <li>• Transaminase elevations accompanied by clinical symptoms of liver injury, increases in bilirubin <math>\geq 2x</math> ULN, or active liver disease</li> <li>• Clinically significant liver toxicity</li> </ul> <p>Discontinue treatment with KYNAMRO and investigate to identify the probable cause</p>
<p><i>*Please see the Prescribing Information for more information.</i></p> <p>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 <a href="http://www.fda.gov/medwatch">www.fda.gov/medwatch</a>.</p>	



**APPENDIX 4**

**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](mailto:KynamroREMS@LashGroup.com)**

Prescriber Information (Please print. All information required.)				
Name (first, middle, last)		Credentials <input type="checkbox"/> MD <input type="checkbox"/> DO <input type="checkbox"/> NP <input type="checkbox"/> PA <input type="checkbox"/> Other _____		
Name of Institution/Practice Name			Physician Specialty	
Office Address				
City	State	Zip Code	Preferred Method of Contact <input type="checkbox"/> Mail <input type="checkbox"/> Email	
Email Address		Office Phone Number	Mobile Phone Number	Office Fax Number
Primary State License Number/State of Issue				
National Provider Identification (NPI) Number				

**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 the KYNAMRO REMS Program 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 the KYNAMRO REMS Program.
- 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 the KYNAMRO REMS Program.

Prescriber Signature \_\_\_\_\_

Date \_\_\_\_\_

**If you have any questions, contact the KYNAMRO REMS Program.  
Phone: 877-596-2676 | Fax: 877-778-9008 | [www.KynamroREMS.com](http://www.KynamroREMS.com)**

The KYNAMRO Prescriber Enrollment Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com).  
**Please see Prescribing Information for KYNAMRO.**  
KYNAMRO is a trademark of Genzyme Corporation.

**APPENDIX 5**

**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.)					
Full Name (first, middle, last)*			Gender* <input type="checkbox"/> M <input type="checkbox"/> F		Date of Birth*
Address*		City*	State*		Zip*
Preferred Phone Number*		Alternate Phone Number			Preferred Time to Contact <input type="checkbox"/> Day <input type="checkbox"/> Evening
Email Address		Alternate Contact/Phone			
Shipping Information					
Ship to <input type="checkbox"/> Patient's Home Address (address above) <input type="checkbox"/> Other Address (indicate below)					
Name	Address	City	State	Zip	Phone Number

Insurance Information (Please print.)					
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					
<input type="checkbox"/> Yes (complete information below)			<input type="checkbox"/> Not applicable		
Carrier	ID #	Policy/Group #	Cardholder's Full Name		Cardholder's Date of Birth

Prescriber Information (Please print. All information marked with an * is required.)					
Prescriber's Full Name*			NPI*		
Phone Number*			Fax Number*		
Practice Street Address*		City*	State*		Zip*

### 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.)		
Dosing Instructions*		Refills NR 1 2 3 4 5 6
_____ DATE*	_____ PRESCRIBER SIGNATURE*	<input type="checkbox"/> Dispense as Written

The KYNAMRO Prescription Authorization Form is available at [www.KynamroREMS.com](http://www.KynamroREMS.com)

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

**APPENDIX 6**

**DEAR HEALTHCARE PROVIDER LETTER**

Genzyme Corporation  
500 Kendall Street  
Cambridge, MA 02142

[insert date]

### IMPORTANT DRUG WARNING

SUBJECT: - Risk of hepatotoxicity with KYNAMRO™ (mipomersen sodium) injection  
- Appropriate patient selection and monitoring  
- Prescriber Action: Training and enrollment as part of KYNAMRO REMS Program

Dear Healthcare Provider:

Genzyme Corporation, a Sanofi company, would like to inform you of the approval of KYNAMRO™ (mipomersen sodium) by the Food and Drug Administration (FDA). 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), and non-high density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for KYNAMRO. The purpose of the REMS is to help ensure that the benefits of treatment with KYNAMRO outweigh the **risk of hepatotoxicity**. **Please see enclosed brochure for detailed risk information.**

KYNAMRO has a **Boxed Warning** in the prescribing information.

#### 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)  $\geq 3$ x 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 regularly as recommended. During treatment, withhold the dose of KYNAMRO if the ALT or AST are  $\geq 3$  x 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.

KYNAMRO is a trademark of Genzyme Corporation.

### **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

### **Prescriber Action**

KYNAMRO will only be available through the KYNAMRO REMS Program. In order to prescribe KYNAMRO, prescribers must:

- Review the KYNAMRO Prescribing Information and complete the Prescriber Training;
- Complete and submit the one-time KYNAMRO REMS Program Prescriber Enrollment Form;
- Complete and submit a KYNAMRO REMS Prescription Authorization Form for each new prescription; and
- Comply with the requirements of the KYNAMRO REMS Program.

KYNAMRO REMS training materials are available at the KYNAMRO REMS Program website ([www.KynamroREMS.com](http://www.KynamroREMS.com)) or by contacting the KYNAMRO REMS Program by phone at 877-596-2676.

### **Certified Pharmacies**

- KYNAMRO is only dispensed through certified pharmacies.

For more information regarding KYNAMRO REMS Program enrollment or general questions regarding the KYNAMRO REMS Program, visit [www.KynamroREMS.com](http://www.KynamroREMS.com) or call 877-596-2676.

### **Reporting Adverse Events**

HCPs should report all suspected adverse events associated with the use of KYNAMRO. Please contact Genzyme at 800-745-4447 or the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

The information in this letter is not a comprehensive description of the risks associated with the use of KYNAMRO. Please see the enclosed Prescribing Information and Medication Guide for a complete description of these risks.

Sincerely,

[Signature, Name, Title]  
Genzyme Corporation

Enclosures: KYNAMRO Prescribing Information, Medication Guide, KYNAMRO Healthcare Professional Information Brochure

**APPENDIX 7**

**DEAR PROFESSIONAL ASSOCIATION LETTER**

Genzyme Corporation  
500 Kendall Street  
Cambridge, MA 02142

[insert date]

### IMPORTANT DRUG WARNING

SUBJECT: - Risk of hepatotoxicity with KYNAMRO™ (mipomersen sodium) injection  
- Appropriate patient selection and monitoring  
- Prescriber Action: Training and enrollment as part of KYNAMRO REMS Program

Dear Professional Association:

This letter highlights important safety information your members need to know when prescribing KYNAMRO™ (mipomersen sodium). To ensure the safe and appropriate use of KYNAMRO, it is important that you share the information included in this letter with your members who may treat patients with homozygous familial hypercholesterolemia (HoFH).

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), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with HoFH.

FDA has required a Risk Evaluation and Mitigation Strategy (REMS) for KYNAMRO. The purpose of the REMS is to help ensure that the benefits of treatment with KYNAMRO outweigh the **risk of hepatotoxicity**.

KYNAMRO has a **Boxed Warning** in the prescribing information.

#### 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)  $\geq 3$ x 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 regularly as recommended. During treatment, withhold the dose of KYNAMRO if the ALT or AST are  $\geq 3$  x 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.

KYNAMRO is a trademark of Genzyme Corporation.

## 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

## Prescriber Action

In order to prescribe KYNAMRO, prescribers must review the Prescribing Information and complete the Prescriber Training, and enroll in the KYNAMRO REMS Program.

## Certified Pharmacies

KYNAMRO is only dispensed through certified pharmacies.

More specific details about prescriber responsibilities, enrollment and educational materials for the KYNAMRO REMS Program can be found at [www.KynamroREMS.com](http://www.KynamroREMS.com). For more information, you may also contact KYNAMRO REMS Program at 877-596-2676.

The information in this letter is not a comprehensive description of the benefits and risks associated with the use of KYNAMRO. Please see accompanying Prescribing Information and Medication Guide.

Please share the information on the KYNAMRO REMS Program and the materials referenced above with your membership in order to ensure the safe and appropriate use of KYNAMRO. Thank you for your consideration of this request.

Sincerely,

[Signature, Name, Title]  
Genzyme Corporation

Enclosures: KYNAMRO Prescribing Information, KYNAMRO Medication Guide

**APPENDIX 8**

**HEALTHCARE PROFESSIONAL INFORMATION BROCHURE**

## Patient Counseling

Before initiating treatment with KYNAMRO, prescribers must discuss the risks of KYNAMRO with patients and their caregivers:

- Patients should be advised about the risk of hepatotoxicity and the need to have regular blood tests to monitor for evidence of liver injury or dysfunction
- For additional information on patient counseling, please see the Prescribing Information

## Reporting Adverse Events

Healthcare professionals should 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](http://www.fda.gov/medwatch).

Please see accompanying Prescribing Information for KYNAMRO for complete information on all the risks associated with KYNAMRO.



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## RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM

KYNAMRO™ (mipomersen sodium) and risk of hepatotoxicity

Healthcare Professional Information Brochure  
Important REMS Information for Healthcare Professionals



## About this Brochure

This brochure has been developed as a part of the Risk Evaluation and Mitigation Strategy (REMS) to help educate healthcare professionals on the risk of hepatotoxicity associated with the use of KYNAMRO (mipomersen sodium). Prescribers of KYNAMRO must review training materials and enroll in the KYNAMRO REMS Program in order to prescribe KYNAMRO. Please visit [www.KynamroREMS.com](http://www.KynamroREMS.com) to find out more information about the KYNAMRO REMS Program.

The brochure includes information about this risk and how to mitigate this risk through liver transaminase monitoring and dosing recommendations in the presence of increased hepatic transaminases.

This brochure focuses on elevations of hepatic transaminases and hepatic steatosis that have been observed in patients treated with KYNAMRO. These are not the only risks associated with KYNAMRO. Please see the accompanying Prescribing Information for KYNAMRO.

## Introduction

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), and non-high density lipoprotein-cholesterol (non HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). HoFH is a rare genetic disorder that causes extremely elevated cholesterol levels and premature cardiovascular disease as a result of genetic mutations that impair the liver's ability to clear LDL particles from the bloodstream.

Use of KYNAMRO in patients with moderate or severe hepatic impairment, or active liver disease, including unexplained persistent elevations of serum transaminases is contraindicated. KYNAMRO was approved with a required REMS to ensure that the benefits of KYNAMRO outweigh the risks.

## Elevated Hepatic Transaminases and Hepatic Steatosis

Elevated hepatic transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) were observed in patients who received KYNAMRO in clinical trials. In phase 3 placebo-controlled trials, 8.4% and 4.2% of patients receiving KYNAMRO experienced elevated ALT and AST enzymes, respectively,  $\geq 3$  times the upper limit of normal (ULN) on 2 or more consecutive measurements at least 7 days apart.

	KYNAMRO (N=261)	Placebo (N=129)
<b>ALT*</b>		
Maximum $\geq 3$ x ULN and $< 5$ x ULN	11.9%	0.8%
Maximum $\geq 5$ x ULN and $< 10$ x ULN	3.4%	0.0%
Maximum $\geq 10$ x ULN	1.1%	0.0%
<b>AST*</b>		
Maximum $\geq 3$ x ULN and $< 5$ x ULN	7.3%	0.8%
Maximum $\geq 5$ x ULN and $< 10$ x ULN	2.7%	0.0%
Maximum $\geq 10$ x ULN	0.0%	0.0%

\*Measurement taken on any single occasion

Hepatic steatosis was observed in patients who received KYNAMRO in clinical trials. In clinical trials in patients with heterozygous familial hypercholesterolemia and hyperlipidemia where both baseline and 6-month MRI data were available, a median absolute increase in fat fraction of 9.6% relative to baseline was observed in patients following KYNAMRO therapy versus a nominal 0.02% change observed for patients in the placebo group (mean increases were 12.2% for KYNAMRO-treated patients versus 0.4% for patients who received placebo). The maximum change in fat fraction was 46% for the KYNAMRO group and 28% for the placebo group.

## Monitoring for Hepatotoxicity

- Before beginning treatment with KYNAMRO, measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin
- During the first year of treatment with KYNAMRO
  - Conduct liver-related tests monthly (ALT and AST, at a minimum)
- After the first year of treatment with KYNAMRO
  - Conduct liver-related tests at least every 3 months (ALT and AST, at a minimum)
- For patients who develop elevated transaminases during therapy with KYNAMRO, follow the monitoring recommendations summarized below:

### Monitoring for Patients With Elevated Transaminases

ALT OR AST	TREATMENT AND MONITORING RECOMMENDATIONS*
$\geq 3x$ and $< 5x$ ULN	<ul style="list-style-type: none"> <li>• Confirm elevation with a repeat measurement within 1 week</li> <li>• 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</li> <li>• If resuming KYNAMRO after transaminases resolve to <math>&lt; 3x</math> ULN, consider monitoring liver-related laboratory tests more frequently</li> </ul>
$\geq 5x$ ULN	<ul style="list-style-type: none"> <li>• 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</li> <li>• If resuming KYNAMRO after transaminases resolve to <math>&lt; 3x</math> ULN, consider monitoring liver-related laboratory tests more frequently</li> </ul>

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

- Advise patients to promptly report symptoms of possible liver injury
- Discontinue treatment with KYNAMRO and investigate to identify the probable cause for patients with:
  - Persistent or clinically significant elevations in transaminases
  - Transaminase elevations accompanied by clinical symptoms of liver injury, increases in bilirubin  $\geq 2x$  ULN, or active liver disease
  - Clinically significant liver toxicity

**APPENDIX 9**

**WEBSITE SCREEN SHOT – LANDING PAGE**



[Prescribing Information](#) [Important Safety Information](#)

## 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 the KYNAMRO REMS program is:

- To educate prescribers about the risk of hepatotoxicity associated with the use of KYNAMRO
- To educate prescribers about the need to monitor patients during treatment with KYNAMRO as per the [Full Prescribing Information](#)
- To restrict access to therapy with KYNAMRO to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH)

### Healthcare Provider Training

This comprehensive online program provides important safety information and REMS program enrollment requirements that must be completed before you can prescribe Kynamro to your patients with a clinical or laboratory diagnosis of homozygous familial hypercholesterolemia (HoFH).

[Get Started Now](#)

## Download and Print Resources

### Healthcare Providers

[KYNAMRO Full Prescribing Information](#)

[Prescriber Enrollment Form](#)

[Healthcare Professional Information Brochure](#)

[Dear Healthcare Provider Letter](#)

[Prescriber Training Slide Set](#)

[Prescription Authorization Form](#)

[Summary of Monitoring Recommendations](#)

### Patients

[Medication Guide](#)

## INDICATIONS

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), and 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.

## Important Safety Information

### 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)  $\geq 3$ x 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  $\geq 3$  x 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.**

## OTHER WARNINGS AND PRECAUTIONS

Patients are advised to read the KYNAMRO medication guide before starting treatment with KYNAMRO, and each time they receive a refill. There may be new information. This information does not take the place of talking to a doctor about a medical condition or treatment.

KYNAMRO may cause serious side effects, including liver problems. A doctor should be informed of any liver problems, including liver problems while taking other medicines, or if a patient has any of these symptoms of liver problems while taking KYNAMRO: nausea, vomiting, fever, loss of appetite, being (or feeling) more tired than usual, yellowing of eyes or skin, dark urine, itching, or stomach pain.

Alcohol may increase levels of hepatic fat and induce or exacerbate liver injury. It is recommended that 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.

KYNAMRO should be used during pregnancy only if clearly needed. Females who become pregnant during KYNAMRO therapy should notify their healthcare provider. Safety and effectiveness have not been established in pediatric patients.

KYNAMRO is not recommended in patients with severe renal impairment, clinically significant proteinuria, or on renal dialysis.

The safety and effectiveness of KYNAMRO as an adjunct to LDL apheresis have not been established; therefore, the use of KYNAMRO as an adjunct to LDL apheresis is not recommended.

## CONTRAINDICATIONS

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.
- Patients with a known hypersensitivity to any component of this product.

## COMMON SIDE EFFECTS

In clinical trials the most commonly-reported adverse reactions were injection site reactions occurring in 84% of patients receiving KYNAMRO versus 33% of placebo treated patients. The most common injection site reactions were erythema (59%), pain (56%), hematoma (32%), pruritus (29%), swelling (18%) and discoloration (17%). Injection site reactions did not occur with every injection but resulted in discontinuation of therapy in 5% of patients in pooled phase 3 trials.

Flu-like symptoms, defined as any one of the following: influenza-like illness, pyrexia, chills, myalgia, arthralgia, malaise or fatigue and occurring within 2 days of injection, have been reported more frequently in patients receiving KYNAMRO (30%) versus placebo (16%) in the pooled Phase 3 trials. Flu-like symptoms did not occur with all injections but resulted in discontinuation of therapy in 3% of patients in pooled phase 3 trials.

[See full prescribing information for more details about Warnings & Precautions, complete list of Adverse Reactions and Boxed Warning.](#)

**genzyme**  
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NP0022-0113

 This website is intended for US audiences only.



[Prescribing Information](#) [Important Safety Information](#)

## KYNAMRO™ Risk Evaluation and Mitigation Strategy (REMS) Program

You're almost there! Please fill in the information below then print and sign the downloadable enrollment form to complete the training and certification program. After completing and signing the enrollment form, you can finalize your REMS registration by faxing it to **877-778-9008** or scan and email your form to [KynamroREMS@LashGroup.com](mailto:KynamroREMS@LashGroup.com).

All fields required unless specified.

Email Address:

Telephone:

First Name:

City:

Last Name:

State / Province:

Job Title:

Institution / Facility:

**Submit**

  
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NP0022-0113

**KYNAMRO™**  
(mipomersen sodium) injection

[Prescribing Information](#) [Important Safety Information](#)

## KYNAMRO™ Risk Evaluation and Mitigation Strategy (REMS) Program

**Thank you for finalizing your enrollment in the KYNAMRO™ (mipomersen sodium) REMS Program.**

Don't forget to fax your signed copy of the [REMS Prescriber Enrollment Form](#) to 877-778-9008, or scan and email your form to [KynamroREMS@LashGroup.com](mailto:KynamroREMS@LashGroup.com).

**genzyme**

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NP0022-0113

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

CHRISTINE P NGUYEN  
01/29/2013