HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KYNAMRO safely and effectively. See full prescribing information for KYNAMRO.

KYNAMRO (mipomersen sodium) Injection
Solution for Subcutaneous Injection
Initial U.S. Approval: 2013

WARNING: RISK OF HEPATOTOXICITY
See full prescribing information for complete boxed warning.

KYNAMRO can cause elevations in transaminases (5.1).
- **Measure alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended (2.3, 5.1)**
- **During treatment, withhold the dose of KYNAMRO if the ALT or AST is ≥3 times the upper limit of normal (ULN) (2.3, 5.1).**
- **Discontinue KYNAMRO for clinically significant liver toxicity (2.3, 5.1).**

KYNAMRO increases hepatic fat (hepatic steatosis) with or without concomitant increases in transaminases (5.1).
- **Hepatic steatosis associated with KYNAMRO may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis (5.1).**

Because of the risk of hepatotoxicity, KYNAMRO is available only through a restricted program called the KYNAMRO REMS (5.2).

----------INDICATIONS AND USAGE----------
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) (1).

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.

----------DOSAGE AND ADMINISTRATION----------
- 200 mg once weekly as a subcutaneous injection (2.1)
- Before treatment, measure ALT, AST, alkaline phosphatase, and total bilirubin (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
- Single-use vial containing 1 mL of a 200 mg/mL solution (3)
- Single-use pre-filled syringe containing 1 mL of a 200 mg/mL solution (3)

----------CONTRAINDICATIONS----------
- Moderate or severe hepatic impairment, or active liver disease, including unexplained persistent elevations of serum transaminases (4)
- Known sensitivity to product components (4)

----------WARNINGS AND PRECAUTIONS----------
- Injection site reactions occur in 84% of patients and typically consist of one or more of the following: erythema, pain, tenderness, pruritus and local swelling (5.3)
- Flu-like symptoms, which typically occur within 2 days after an injection, occur in 30% of patients and include one or more of the following: influenza-like illness, pyrexia, chills, myalgia, arthralgia, malaise or fatigue (5.4)

----------ADVERSE REACTIONS----------
The most commonly reported adverse reactions (incidence ≥ 10% and greater than placebo) are injection site reactions, flu-like symptoms, nausea, headache and elevations in serum transaminases, specifically ALT (5.4, 6).

----------USE IN SPECIFIC POPULATIONS ----------
- Nursing mothers: Discontinue drug or nursing (8.3).
- Pediatric Patients: Safety and effectiveness not established (8.4).

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 2/2015

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FULL 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) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR) or partial thromboplastin time (PTT) [see *Warnings and Precautions (5.1)]*.

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 [see *Warnings and Precautions (5.1)*].

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT, AST regularly as recommended. During treatment, withhold the dose of KYNAMRO if the ALT or AST are ≥3 x ULN. Discontinue KYNAMRO for clinically significant liver toxicity [see *Dosage and Administration (2.3) and Warnings and Precautions (5.1)*].

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 [see *Warnings and Precautions (5.2)*].

1 INDICATIONS AND USAGE

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).

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 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.

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

Before beginning treatment with KYNAMRO, measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin [see *Warnings and Precautions (5.1)*].

The recommended dose of KYNAMRO is 200 milligrams (mg) once weekly as a subcutaneous injection.

KYNAMRO is intended for subcutaneous use only. Do not administer intramuscularly or intravenously.

The injection should be given on the same day every week, but if a dose is missed, the injection should be given at least 3 days from the next weekly dose.

After initiation of KYNAMRO therapy lipid levels should be monitored at least every 3 months for the first year. Maximal reduction of LDL-C may be seen with KYNAMRO therapy after approximately 6 months (based on the time to steady state seen in clinical studies). Health care providers should assess the patient's LDL-C level after 6 months to determine if the LDL-C reduction achieved with KYNAMRO is sufficiently robust to warrant the potential risk of liver toxicity.

2.2 Administration

Each vial or pre-filled syringe of KYNAMRO provides 200 mg of mipomersen sodium in a deliverable volume of 1 milliliter (mL) of solution and is intended for single-use only.

The KYNAMRO vial or pre-filled syringe should be removed from 2-8°C (36-46°F) refrigerated storage and allowed to reach room temperature for at least 30 minutes prior to administration.

Parenteral drug products should be inspected visually prior to administration. If the solution is cloudy or contains visible particulate matter, the contents must not be injected and the product should be returned to the pharmacy.

The first injection administered by the patient or caregiver should be performed under the guidance and supervision of an appropriately qualified health care professional.

KYNAMRO should be injected into the abdomen, thigh region, or outer area of the upper arm. KYNAMRO should not be injected in areas of active skin disease or injury such as sunburns, skin rashes, inflammation, skin infections, active areas of psoriasis, etc. Areas of tattooed skin and scarring should also be avoided.

2.3 Adjustments for Patients Developing Transaminase Elevations

Table 1 summarizes recommendations for monitoring for patients who develop elevated transaminases during therapy with KYNAMRO [see *Warnings and Precautions (5.1)*].

Table 1: Monitoring for Patients With Elevated Transaminases

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

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

If transaminase elevations are accompanied by clinical symptoms of liver injury (e.g., nausea, vomiting, abdominal pain, fever, jaundice, lethargy, flu-like symptoms), increases in bilirubin ≥2x ULN, or active liver disease, discontinue treatment with KYNAMRO and investigate to identify the probable cause [see *Warnings and Precautions (5.1)*].

3 DOSAGE FORMS AND STRENGTHS

- Single-use vial containing 1 mL of a 200 mg/mL clear, colorless to slightly yellow solution.
- Single-use pre-filled syringe containing 1 mL of a 200 mg/mL clear, colorless to slightly yellow solution.

4 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 [see *Warnings and Precautions (5.1) and Use in Specific Populations (8.8*)]
- Patients with a known hypersensitivity to any component of this product [see *Adverse Reactions (6.1)*].

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Hepatotoxicity

KYNAMRO can cause elevations in transaminases and hepatic steatosis, as described below. To what extent KYNAMRO-associated hepatic steatosis promotes the elevations in transaminases is unknown. There is concern that KYNAMRO could induce steatohepatitis, which can progress to cirrhosis over several years. The clinical studies

supporting the safety and efficacy of KYNAMRO in HoFH would have been unlikely to detect this adverse outcome given their size and duration [see *Clinical Studies (14)*].

Elevation of Transaminases

KYNAMRO can cause increases in serum transaminases (alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]). In the clinical trial, 4 (12%) of the 34 subjects with HoFH treated with KYNAMRO compared to 0% of the 17 subjects treated with placebo had an elevation in ALT ≥ 3x ULN, and 3 (9%) of those treated with KYNAMRO compared to 0% treated with placebo had at least one elevation in ALT ≥ 5x ULN.

Measure a full liver panel to include ALT, AST, total bilirubin, and alkaline phosphatase before initiation of treatment with KYNAMRO [see *Dosage and Administration (2.1)*]. KYNAMRO is contraindicated in patients with moderate or severe hepatic impairment, or active liver disease, including unexplained persistent elevations of serum transaminases. If the baseline liver-related tests are abnormal, consider initiating KYNAMRO after an appropriate work-up and the baseline abnormalities are explained or resolved. During the first year, conduct liver-related tests monthly (ALT and AST, at a minimum). After the first year, conduct these tests at least every 3 months. Discontinue KYNAMRO for persistent or clinically significant elevations [see *Dosage and Administration (2.3)*].

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

Hepatic Steatosis

KYNAMRO increases hepatic fat (steatosis) with or without concomitant increases in transaminases [see *Adverse Reactions* (6.1)]. Hepatic steatosis is a risk factor for advanced liver disease, including steatohepatitis and cirrhosis. The long-term consequences of hepatic steatosis associated with KYNAMRO therapy are unknown. During the clinical 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).

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

Mipomersen 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.

5.2 KYNAMRO REMS

Because of the risk of hepatotoxicity, KYNAMRO is available only through a limited program under the REMS. Under the KYNAMRO REMS, only certified healthcare providers and pharmacies may prescribe and distribute KYNAMRO. Further information is available at www.KynamroREMS.com or by telephone at 1-877-KYNAMRO (1-877-596-2676).

5.3 Injection Site Reactions

Injection site reactions have been reported in 84% of patients receiving KYNAMRO therapy. These local reactions typically consist of one or more of the following: erythema, pain, tenderness, pruritus and local swelling. Injection site reactions do not occur with all injections but resulted in discontinuation of therapy in 5% of patients in pooled Phase 3 trials. [see *Adverse Reactions (6.1)*] To minimize the potential for injection site reactions, proper technique for subcutaneous administration should be followed. [see *Patient Counseling Information (17)*]

5.4 Flu-Like Symptoms

Flu-like symptoms have been reported in 30% of patients receiving KYNAMRO therapy and include one or more of the following: influenza-like illness, pyrexia, chills, myalgia, arthralgia, malaise or fatigue. Flu-like symptoms, which typically occur within 2 days after an injection, do not occur with all injections but resulted in discontinuation of therapy in 3% of patients in pooled Phase 3 trials. [see *Adverse Reactions (6.1)*]

6 ADVERSE REACTIONS

The following important adverse reactions have been observed and are discussed in detail in other sections of the label:

- Risk of hepatotoxicity [see *Warnings and Precautions (5.1)*]

6.1 Clinical Trials

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trial of another drug and may not reflect the rates observed in patients in clinical practice.

Safety data are based on pooled results from four Phase 3, randomized, double-blind, placebo-controlled trials with a total of 390 patients of which 261 patients received weekly subcutaneous injections of 200 mg of KYNAMRO and 129 patients received placebo for a median treatment duration of 25 weeks (age range 12-81 years, 47% women, 84% Caucasian, 10% Blacks, 3% Asian, 3% other). For the 141 participants who subsequently were treated in the open-label extension trial, the mean length of study treatment, including exposure to KYNAMRO in the index study, was 19.8 months and

the median was 18.2 months. A total of 41 individuals with HoFH were exposed to KYNAMRO for at least 6 months and 25 were exposed for at least 12 months.

Eighteen percent of patients on KYNAMRO and 2% of patients on placebo discontinued treatment due to adverse reactions. The five most common adverse reactions in patients treated with KYNAMRO that led to treatment discontinuation and occurred at a rate greater than placebo were: injection site reactions (5.0%), alanine aminotransferase increased (3.4%), flu-like symptoms (2.7%), aspartate aminotransferase increased (2.3%), and liver function test abnormal (1.5%).

Common Adverse Reactions

Table 2 enumerates adverse reactions that occurred among pooled Phase 3 patients treated with KYNAMRO at an incidence that was at least 2% more than that observed in the placebo-treated patients, listed by system organ class and frequency (MedDRA v.13.0). Similar types and severities of adverse reactions were observed across all populations in this pooled table including the subset of patients with HoFH.

Table 2: Summary of Adverse Reactions for Pooled Phase 3 Placebo-Controlled Trials

System Organ Class Preferred Term	**Treatment Group**	
	KYNAMRO (%) (N=261)	**Placebo (%) (N=129)**
Total Patients with Events	**95%**	**85%**
Cardiac disorders	**9%**	**6%**
Angina pectoris	4%	2%
Palpitations	3%	0%
Gastrointestinal disorders	**30%**	**29%**
Nausea	14%	8%
Vomiting	4%	2%
Abdominal pain	3%	1%
General disorders and administration site conditions	**87%**	**47%**
Injection site reactions*	84%	33%
Fatigue	15%	8%
Influenza like illness	13%	3%
Pyrexia	8%	3%
Chills	6%	1%
Edema peripheral	5%	2%
Hepatobiliary disorders	**9%**	**5%**
Hepatic steatosis	7%	2%
Investigations	**30%**	**15%**
Alanine aminotransferase increased	10%	1%
Aspartate aminotransferase increased	6%	2%
Liver function test abnormal	5%	1%
Hepatic enzyme increased	3%	1%
Musculoskeletal and connective tissue disorders	**26%**	**26%**
Pain in extremity	7%	3%
Musculoskeletal pain	4%	2%

System Organ Class Preferred Term	Treatment Group	
	KYNAMRO (%) (N=261)	**Placebo (%) (N=129)**
Nervous system disorders	**25%**	**17%**
Headache	12%	9%
Psychiatric disorders	**10%**	**3%**
Insomnia	3%	1%
Vascular disorders	**11%**	**5%**
Hypertension	7%	3%

* Preferred Terms include: Injection site erythema, Injection site pain, Injection site hematoma, Injection site pruritus, Injection site swelling, Injection site discoloration, Injection site nodule, Injection site rash, Injection site warmth, Injection site induration, Injection site recall reaction, Injection site edema, Injection site hemorrhage, Injection site discomfort, Injection site reaction, Injection site papule, Injection site inflammation, Injection site macule, Injection site vesicles, Injection site urticaria

In the pooled Phase 3 trials, neoplasms (benign and malignant) were reported in 4% of patients receiving KYNAMRO and 0% of patients receiving placebo. In addition, 9% of patients receiving KYNAMRO and 3% of patients receiving placebo developed 1+ or greater proteinuria by dipstick measurement by the end of the trial.

In the open-label extension trial, one case of hypersensitivity reaction with angioedema and one case of glomerular nephritis were reported.

Platelets

In the phase 3 trial in patients with HoFH, the mean change in platelet count from baseline to Week 28/Early Termination was -30.6 x 10^3/uL in the mipomersen group and +8.1 x 10^3/uL in the placebo group. In the pooled Phase 3 trials the mean change in platelet count from baseline to Week 28/Early Termination was -23.8 x 10^3/μL in the mipomersen group and -3.5 x 10^3/μL in the placebo group.

Transaminase Elevations

In the pooled, placebo-controlled clinical trials with KYNAMRO, elevated serum transaminase levels, mainly ALT, have been observed as presented in Table 3. Elevated ALT levels ≥ 3X ULN have been reported on two consecutive occasions at least 7 days apart in 8.4% of patients receiving KYNAMRO therapy (versus 0% of placebo patients) with 16.5% of patients receiving KYNAMRO therapy having at least 1 result that was ≥ 3X ULN (versus 0.8% for placebo patients). The ALT elevations observed in the pooled, placebo-controlled trials were generally accompanied by lesser AST elevations and were not associated with increased total bilirubin, changes in INR or PTT, nor by decreased albumin levels. After stopping therapy, in the patients in whom an elevation was observed, transaminase elevations trended toward baseline over a period of weeks to months.

Table 3: Transaminase Results for Pooled Phase 3 Placebo-Controlled Trials

Parameter	Statistic	Kynamro (%) (N=261)	Placebo (%) (N=129)
ALT maximum	Incidence rate, %		
	≥ 3 x ULN and < 5 x ULN	12%	1%
	≥ 5 x ULN and < 10 x ULN	3%	0%
	≥ 10 x ULN	1%	0%
ALT	≥ 3 x ULN, two consecutive results (at least 7 days apart), %	8%	0%
AST maximum	Incidence rate, %		
	≥ 3 x ULN and < 5 x ULN	7%	1%
	≥ 5 x ULN and < 10 x ULN	3%	0%
	≥ 10 x ULN	0%	0%
AST	≥ 3 x ULN, two consecutive results (at least 7 days apart), %	4%	0%

Adults: ALT ULN= 41 U/L; AST ULN = 34 U/L

Hepatic Steatosis

Increases in liver fat as measured by MRI were greater in patients receiving KYNAMRO therapy than in patients receiving placebo. Data from Phase 3 supportive trials in patients with heterozygous familial hypercholesterolemia and coronary artery disease and in patients with high risk hypercholesterolemia demonstrated after 26 weeks of treatment, a median nominal increase in fat fraction of 9.6% relative to baseline following KYNAMRO therapy versus a nominal 0.02% change in the placebo group (mean increases were 12.2% mipomersen vs 0.4% placebo). The maximum change in fat fraction was 46% for the KYNAMRO group and 28% for the placebo group. Sixty-two percent of patients receiving KYNAMRO developed a 5% or greater increase in hepatic fat versus 8% of patients receiving placebo. In general, these elevations in fat fraction decreased when assessed by MRI performed 24 weeks after cessation of KYNAMRO in the Phase 3 trial of patients with high-risk hypercholesterolemia. In the open-label extension trial, among individuals with a measurement at baseline and at 12 months or longer on KYNAMRO, 25% had an average liver fat fraction > 20% on at least one occasion.

Injection Site Reactions

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. Injection site reactions resulted in discontinuation of KYNAMRO in 5% of patients. Recall reactions, consisting of local erythema, tenderness and/or pruritus at previous injection sites when subsequent injections were administered, were observed in 8% of patients, all of whom were receiving KYNAMRO.

Flu-like Symptoms

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 (29.9%) versus placebo (16.3%) in the pooled Phase 3 studies. Flu-like symptoms did not occur with all injections. Flu-like symptoms resulted in discontinuation of KYNAMRO in 2.7% of patients. In the open-label extension trial, in which all patients received KYNAMRO therapy, 66% reported flu-like symptoms, 25% discontinued treatment due to flu-like symptoms and 9% experienced severe flu-like symptoms.

Immunogenicity

In the pooled Phase 3 trials, 38% of KYNAMRO-treated patients tested positive for anti-KYNAMRO antibodies during the 6-month trials. Efficacy results in the Phase 3 trials in patients who tested positive for anti-KYNAMRO antibodies were similar to patients who remained negative for antibodies (mean LDL-C percent change from baseline was -32% for antibody-positive and -34% for antibody-negative participants). In the open-label extension trial, approximately 72% of patients receiving KYNAMRO therapy tested positive for anti-KYNAMRO antibodies (35% with titers >3200). The incidence of flu-like symptoms and the incidence of discontinuation of KYNAMRO were higher in antibody-positive patients. Antibodies to KYNAMRO were associated with higher trough levels for the drug. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to KYNAMRO with the incidence of antibodies to other products may be misleading.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of KYNAMRO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Idiopathic thrombocytopenic purpura

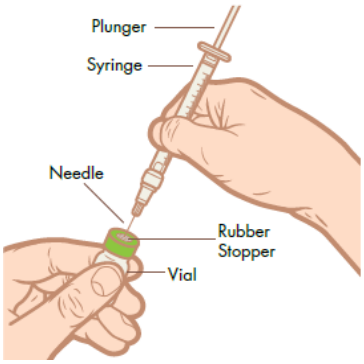
7 DRUG INTERACTIONS

No clinically relevant pharmacokinetic interactions were reported between KYNAMRO and warfarin, or between KYNAMRO and simvastatin or ezetimibe [see *Clinical Pharmacology (12.3)*]. Additionally, coadministration of KYNAMRO with warfarin did not result in a pharmacodynamic interaction as determined by INR, aPTT and PT.

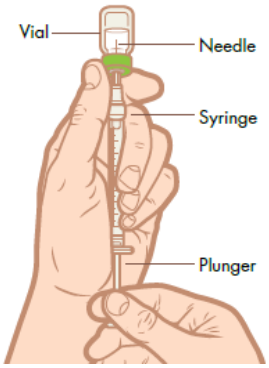
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

above the liquid.



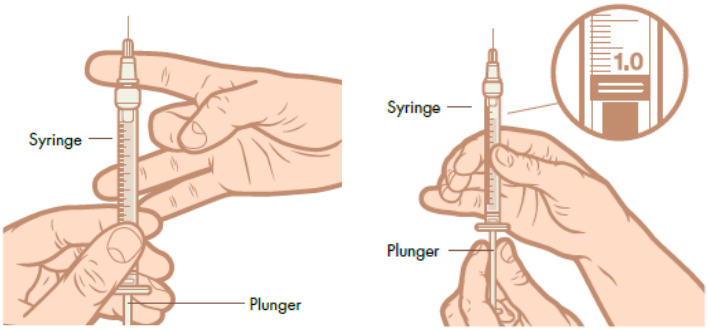
Step 6. Fill syringe. Turn the vial upside down. Position the syringe so the needle is in the liquid. Pull back on the plunger to fill the syringe to the 1 mL mark.
NOTE: Make sure the needle remains in the liquid while drawing the medicine into the syringe.



Step 7. Check the syringe.

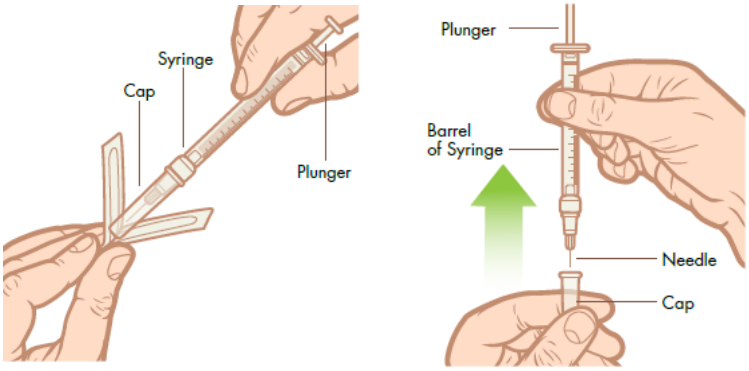
a. Remove the syringe from the vial.
b. Check for air bubbles in the syringe by gently tapping on the syringe with your fingertips to make any air bubbles rise to the top (see Figure E).
c. With your other hand gently push the plunger to remove the air bubbles without accidently pushing out the medicine.

d. Check to be sure that the right amount of medicine is in the syringe. If needed, repeat the steps above until 1 mL of the medicine is in the syringe without air bubbles (see Figure F).



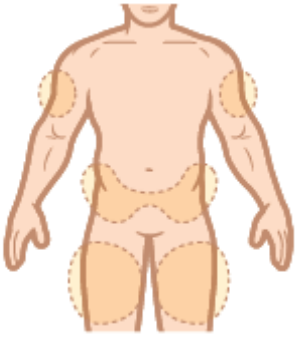
Step 8. Remove and dispose of needle. Remove the needle from the syringe and carefully throw away the needle in a puncture-proof container.

Step 9. Attach 30-gauge needle. Put a 30-gauge needle onto the syringe (see Figure G) and remove the cap by pulling it straight off the syringe to avoid bending the needle (see Figure H).
NOTE: Hold the barrel of the syringe in one hand like a pencil or a dart. **Do not** touch the needle itself.



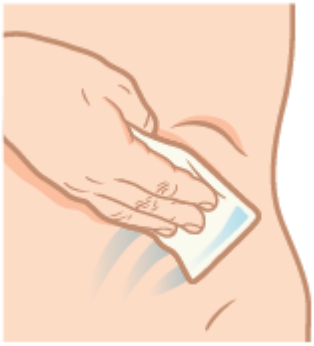
Step 10. Choose an injection site. KYNAMRO is injected under the skin and into the fat layer between the skin and muscles (subcutaneous tissue). KYNAMRO should be injected in the abdomen (belly), thigh, or back of the upper arm. If you choose your abdomen, do not use the area 2 inches around your belly button (navel).
NOTE: Choose a different site each time you give yourself an injection to reduce the chance of redness or pain. Avoid injecting KYNAMRO into areas of skin that are damaged, such as scars, tattoos, active skin disease, sunburns, rashes, inflammation, skin infections, or active areas

of psoriasis.

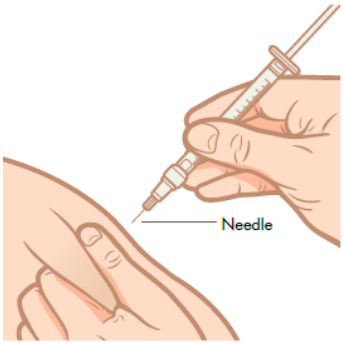


INJECT:

Step 11. Clean the injection site. Use an alcohol wipe and allow the site to dry.

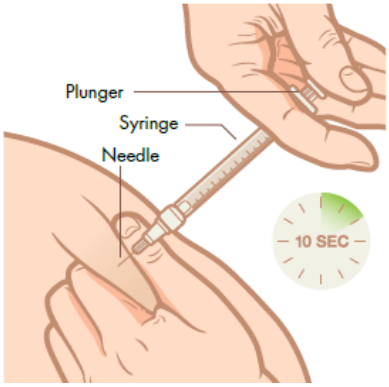


Step 12. Insert the needle. Gently pinch and lift the skin around the injection site. Stick the needle straight down into your skin with a quick, firm motion. Be careful not to stick the needle into the fingers of your other hand.



Step 13. Slowly, over a period of at least 10 seconds, push down the plunger with your thumb until the syringe is empty. Once the

syringe is empty, pull the needle straight out, release the skin, and hold a clean cotton ball at the injection site. **Do not** rub the area because rubbing may cause reddening or pain at your injection site.



DISPOSE:

Step 14. Dispose of used syringes, needles and vials.

- Put your used needles, syringes, and vials in a FDA-cleared sharps disposal container right away after use.
- **Do not** throw away (dispose of) loose needles, syringes, or vials in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic
    - can be closed with a tight-fitting, puncture-proof lid, without sharps being able to come out
    - upright and stable during use
    - leak resistant
    - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal
- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.
- **Do not** recycle your used sharps disposal container.

How should I store KYNAMRO?

- Store KYNAMRO in a refrigerator between 36°F to 46°F (2°C to 8°C). If a refrigerator is not available, KYNAMRO can be stored at or below 86°F (30°C) for up to 14 days if it is kept away from heat.
- Protect KYNAMRO from light and store in the original carton.
- Safely throw away medicine that is out of date or no longer needed.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

KYNAMRO is manufactured for:

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
1-800-745-4447 (phone)

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