KYNAMRO® (mipomersen sodium) Injection 200mg/mL

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).

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

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) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR) or partial thromboplastin time (PTT).

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

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

Because of the risk of hepatotoxicity, KYNAMRO is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the KYNAMRO REMS.

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.

WARNINGS AND PRECAUTIONS

KYNAMRO can cause elevations in transaminases and hepatic steatosis.

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

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.

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.

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.

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. To minimize the potential for injection site reactions, proper technique for subcutaneous administration should be followed. Injection site reactions do not occur with all injections but resulted in discontinuation of therapy in 5% of patients in pooled Phase 3 trials.

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.

USE IN SPECIFIC POPULATIONS

Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. KYNAMRO should be used during pregnancy only if clearly needed.
Nursing Mothers: It is not known whether KYNAMRO is excreted in human milk. Because many drugs are excreted in human milk a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
Pediatric Use: Safety and effectiveness have not been established in pediatric patients.
Females of Reproductive Potential: KYNAMRO may cause fetal harm. Females who become pregnant during KYNAMRO therapy should notify their healthcare provider. Females of reproductive potential should use effective contraception during KYNAMRO therapy.
Renal Impairment: The safety and efficacy of KYNAMRO treatment in patients with known renal impairment or in patients undergoing renal dialysis have not been established. Due to the lack of clinical data and KYNAMRO's renal safety profile, KYNAMRO is not recommended in patients with severe renal impairment, clinically significant proteinuria, or on renal dialysis.

ADVERSE REACTIONS

In clinical trials the most commonly-reported adverse reactions were injection site reactions (84%), flu-like symptoms (30%), nausea (14%), headache (12%), and elevations in serum transaminases, specifically ALT (10%).

See full Prescribing Information and Medication Guide, including Boxed Warning, for more details.