Washington State Health Care Authority

Antihyperlipidemics – Apolipoprotein B Synthesis Inhibitors: mipomersen sodium

Medical policy no. 39.50.00-1 Effective: October 1, 2018

Related medical policies:

- **Antihyperlipidemics – Apolipoprotein B Synthesis Inhibitors: lomitapide mesylate**
- **Antihyperlipidemics – Proprotein Converatase Subtilisin Kexin type 9 (PCSK-9) Inhibitors**

Background:

Apolipoprotein B is a protein that in humans is encoded by the APOB gene. Apolipoprotein B is the primary apolipoprotein of chylomicrons, VLDL, IDL, and LDL particles, which is responsible for carrying fat molecules, including cholesterol, around the body to all cells within all tissues. While all the functional roles of ApoB within the LDL particles remains somewhat unclear, it is the primary organizing protein component of the particles and is required for the formation of these particles. What is also clear is that the ApoB on the LDL particle acts as a ligand for LDL receptors, in various cells throughout the body.

Medical necessity

Drug	Medical Necessity
Mipomersen sodium (KYNAMRO®)	May be considered medically necessary when: Used for the treatment of homozygous familial hypercholesterolemia (HoFH) following a trial of a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
Mipomersen sodium (KYNAMRO ®)	1. Homozygous familial hypercholesterolemia (HoFH) confirmed by **ONE** of the following: a. Genetic confirmation of two mutant alleles at the LDLR, APOB, PCSK9, or LDLRAP1 gene locus. b. Documented DNA test for functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality c. An untreated low density lipoprotein (LDL) cholesterol > 500mg/dL and TG < 300 mg/dL and both parents with documented untreated TC > 250 mg/dL with either: i. Cutaneous or tendon xanthoma before age 10 years ii. Evidence of heterozygous familial hypercholesterolemia in both parents 2. History of failure after 3 months of **two** PCSK9 inhibitors with different active ingredients without decrease of LDL to patient specific goal, unless contraindication or intolerance due to severe adverse side effects.

	3. Greater than or equal to (≥) 18 years of age 4. Prescribed by or in consultation with a provider specializing in lipid management (e.g. cardiologist, lipid specialist, or endocrinologist) **Approve for 6 months**
	Criteria (Reauthorization)
	1. Continued clinical benefit (e.g. LDL reduction over baseline) 2. Prescribed by or in consultation with a provider specializing in lipid management (e.g. cardiologist, lipid specialist, or endocrinologist) **Approve for 12 months**

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
Kynamro 200mg/mL solution	200mg SQ injection once weekly; #4 vials/syringe in 28-days

References

1. Cuchel, M, Bruckert, E, Ginsberg, HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. European heart journal. 2014;35:2146-57. PMID: 25053660
2. Raal, FJ, Santos, RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8. PMID: 22398274
3. Kynamro Risk Evaluation and Mitigation Strategy [cited 5/26/2017]; Available from: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM337472.pdf. .
4. Juxtapid Risk Evaluation and Mitigation Strategy [cited 5/26/2017]; Available from: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM333438.pdf.
5. Raal, FJ, Santos, RD, Blom, DJ, et al. Mipomersen, an apolipoprotein B synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomised, double-blind, placebo-controlled trial. Lancet. 2010;375:998-1006. PMID: 20227758
6. Stein, EA, Dufour, R, Gagne, C, et al. Apolipoprotein B synthesis inhibition with mipomersen in heterozygous familial hypercholesterolemia: results of a randomized, double-blind, placebo-controlled trial to assess efficacy and safety as add-on therapy in patients with coronary artery disease. Circulation. 2012;126:2283-92. PMID: 23060426
7. Akdim, F, Visser, ME, Tribble, DL, et al. Effect of mipomersen, an apolipoprotein B synthesis inhibitor, on low-density lipoprotein cholesterol in patients with familial hypercholesterolemia. The American journal of cardiology. 2010;105:1413-9. PMID: 20451687
8. Panta, R, Dahal, K, Kunwar, S. Efficacy and safety of mipomersen in treatment of dyslipidemia: A meta-analysis of randomized controlled trials. Journal of clinical lipidology. 2015 Mar-Apr;9(2):217-25. PMID: 25911078
9. Kynamro® [Prescribing Information]. Cambridge, MA: Genzyme; March 2015

10. Samaha, FF, McKenney, J, Bloedon, LT, Sasiela, WJ, Rader, DJ. Inhibition of microsomal triglyceride transfer protein alone or with ezetimibe in patients with moderate hypercholesterolemia. Nat Clin Pract Cardiovasc Med. 2008;5:497-505. PMID: 18506154
11. Juxtapid® [Prescribing Information]. Cambridge, MA: Aegerion Pharmaceuticals; May 2016

History

Date	Action and Summary of Changes
11/02/2018	Trial of PCSK-9 added
04/18/2018	New Policy