Clinical Policy: Mipomersen (Kynamro)

Reference Number: PA.CP.PHAR.284
Effective Date: 01/18
Last Review Date: 10/17
Line of Business: Medicaid

Revision Log

Description
Mipomersen (Kynamro®) is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis.

FDA Approved Indication(s)
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).

Limitation(s) of use:
- The safety and effectiveness of Kynamro have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH)
- 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

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that Kynamro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Homozygous Familial Hypercholesterolemia (must meet all)**:**

1. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist;
2. Diagnosis of HoFH defined as one of the following (a, b or c):
   a. Genetic mutation indicating HoFH [low density lipoprotein receptor (LDLR), proprotein convertase subtilisin kexin 9 (PCSK9), apoB, low density lipoprotein receptor adaptor protein 1 (LDLRAP1)];
   b. Treated LDL-C ≥ 300 mg/dL or non-HDL-C ≥ 330 mg/dL;
   c. Untreated LDL-C ≥ 500 mg/dL, and one of the following (i or ii):
      i. Tendinous or cutaneous xanthoma prior to age 10 years;
      ii. Evidence of HeFH in both parents (e.g., documented history of elevated LDL-C ≥ 190 mg/dL prior to lipid-lowering therapy);
3. Meets a or b:
   a. Age is < 18 years and LDL-C ≥ 130 mg/dL within the last 30 days despite statin and Zetia therapy unless a contraindication (Appendix D) or history of intolerance to each such therapy;

b. Age is ≥ 18 years and recent (within the last 30 days) LDL-C ≥ 70mg/dL;

4. If member is ≥ 18 years, has received a high intensity statin (Appendix C) adherently for at least the last 4 months, unless one of the following applies (a, b, or c):
   a. Statin therapy is contraindicated per Appendix D;
   b. Member has received a moderate intensity statin (Appendix C) adherently for at least the last 4 months due to (i or ii):
      i. Intolerance to two high intensity statins;
      ii. A statin risk factor (Appendix E);
   c. Member is unable to take a high or moderate intensity statin due to (i or ii):
      i. Intolerance to two high and two moderate intensity statins;
      ii. A statin risk factor (Appendix E) and history of intolerance to two moderate intensity statins;
5. If member is ≥ 18 years, has received Zetia therapy adherently for at least the last 4 months, unless contraindicated per Appendix D or a history of Zetia intolerance (e.g., associated diarrhea or upper respiratory tract infection);
6. Member has received counseling on therapeutic lifestyle changes (i.e., heart healthy diet; regular exercise; avoidance of tobacco products; maintenance of a healthy weight);
7. Failure of Repatha (evolocumab), unless contraindicated or intolerant;
8. Treatment plan does not include coadministration with Juxtapid (lomitapide), Repatha (evolocumab), Praluent (alirocumab), or LDL-C apheresis;
9. Prescribed dose of Kynamro is 200 mg once weekly;
10. Member does not have severe renal impairment or clinically significant proteinuria, and is not on renal dialysis.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Homozygous Familial Hypercholesterolemia (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or Continuity of Care policy applies;
2. If member has been taking Kynamro for at least 6 months, lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of Kynamro therapy;
3. Prescribed dose of Kynamro does not exceed 200 mg once weekly.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: alanine aminotransferase
apoB: apolipoprotein B
FDA: Food and Drug Administration
FH: familial hypercholesterolemia
HDL-C: high-density lipoprotein cholesterol
HeFH: heterozygous familial hypercholesterolemia
HoFH: homozygous familial hypercholesterolemia
LDL-C: low density lipoprotein cholesterol
LDLR: low density lipoprotein receptor
LDLRAP1: low density lipoprotein receptor adaptor protein 1
PCSK9: proprotein convertase subtilisin kexin 9
ULN: upper limit of normal

Appendix B: High and Moderate Intensity Daily Statin Therapy for Adults

- High Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by approximately ≥50%
  - Atorvastatin 40-80 mg
  - Rosuvastatin 20-40 mg
- Moderate Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%
  - Atorvastatin 10-20mg
  - Fluvastatin XL 80 mg
  - Fluvastatin 40 mg 2x/day
  - Lovastatin 40 mg
  - Pitavastatin 2-4 mg
  - Pravastatin 40-80 mg
  - Rosuvastatin 5-10 mg
  - Simvastatin 20-40 mg
- Low Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by <30%
  - Simvastatin 10 mg
  - Pravastatin 10–20 mg
  - Lovastatin 20 mg
  - Fluvastatin 20–40 mg
  - Pitavastatin 1 m

Appendix C: Statin and Zetia Contraindications

- Statins
  - Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy);
  - Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment;
  - Pregnancy, actively trying to become pregnant, or nursing;

  - Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins;
- Zetia
  - Moderate or severe hepatic impairment [Child-Pugh classes B and C];
  - Hypersensitivity to Zetia (e.g., anaphylaxis, angioedema, rash, urticaria).

Appendix D: Statin Risk Factors

- Multiple or serious comorbidities, including impaired renal or hepatic function;
- Unexplained ALT elevations > 3 times ULN, or active liver disease;
- Concomitant use of drugs adversely affecting statin metabolism;
- Age > 75 years, or history of hemorrhagic stroke;
- Asian ancestry.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HoFH	200 mg SC once per week	

VI. Product Availability

Pre-filled syringe: 1 mL of 200 mg/mL solution

VII. References

1. Kynamro Prescribing Information. Chicago, IL: Kastle Therapeutics; May 2016. Available at http://media.wix.com/ugd/f993a5_29c41370bdd14b1bb113d196a124c497.pdf. Accessed on September 11, 2017.
2. Stone NJ, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. November 2013. DOI: 10.1161/01.cir.0000437738.63853.7a
3. Jacobson TA, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 – full report. Journal of Clinical Lipidology. March-April 2015; 9(2): 129-169. http://dx.doi.org/10.1016/j.jacl.2015.02.003
4. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. Journal of Clinical Lipidology. June 2011; 5(3S): 1-15.
5. Jacobson TA. National Lipid Association Task Force on Statin Therapy – 2014 update. Journal of Clinical Lipidology. 2014; 8(S1-S4): 1-81.
6. Zetia Prescribing Information. Whitehouse Station, NJ: Merck and Company, Inc.; August 2013. Available at http://www.merck.com/product/usa/pi_circulars/z/zetia/zetia_pi.pdf. Accessed May 10, 2017.

Reviews, Revisions, and Approvals	Date	Approval Date