

## Clinical Policy: Mipomersen (Kynamro)

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Line of Business: Illinois Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

### Description

Mipomersen (Kynamro<sup>®</sup>) 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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions<sup>™</sup> that Kynamro is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

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

1. Diagnosis of HoFH defined as one of the following (a, b, or c):
  - a. Genetic mutation indicating HoFH (e.g., mutations in low density lipoprotein receptor [LDLR] gene, proprotein convertase subtilisin kexin 9 [PCSK9] gene, apo B gene, low density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene);
  - b. Treated LDL-C  $\geq$  300 mg/dL or non-HDL-C  $\geq$  330 mg/dL;
  - c. Untreated LDL-C  $\geq$  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  $\geq$  190 mg/dL prior to lipid-lowering therapy);
2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
3. Age  $\geq$  18 years;
4. Documentation of recent (within the last 60 days) LDL-C  $\geq$  70 mg/dL;
5. For members on statin therapy, both of the following (a and b):
  - a. Kynamro is prescribed in conjunction with a statin at the maximally tolerated dose;
  - b. Member has been adherent for at least the last 4 months to maximally tolerated doses of one of the following statin regimens (i, ii, or iii):
    - i. A high intensity statin (*see Appendix D*);
    - ii. A moderate intensity statin (*see Appendix D*), and member has one of the following (a or b):

- a) Intolerance to two high intensity statins;
- b) A statin risk factor (see *Appendix F*);
- iii. A low intensity statin, and member has one of the following (a or b):
  - a) Intolerance to one high and one moderate intensity statins;
  - b) A statin risk factor (see *Appendix F*) and history of intolerance to two moderate intensity statins;
6. For members not on statin therapy, member meets one of the following (a or b):
  - a. Statin therapy is contraindicated per *Appendix E*;
  - b. For members who are statin intolerant, member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin), and member meets one of the following (i or ii):
    - i. Member has documented statin risk factors (see *Appendix F*);
    - ii. Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
      - a) Documentation of intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
      - b) Documentation of re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);
7. Member has been adherent to ezetimibe therapy used concomitantly with a statin at the maximally tolerated dose for at least the last 4 months, unless contraindicated per Appendix E or member has a history of ezetimibe intolerance (e.g., associated diarrhea or upper respiratory tract infection);
8. Treatment plan does not include coadministration with Juxtapid®, Praluent®, or Repatha;
9. Dose not exceed 200 mg per week.

**Approval duration: 6 months**

**B. Other diagnoses/indications**

1. Refer to ERX.PA.01 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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. If statin tolerant, documentation of adherence to a statin at the maximally tolerated dose;
3. Member is responding positively to therapy as evidenced by lab results within the last 3 months showing an LDL-C reduction since initiation of Kynamro therapy;
4. If request is for a dose increase, new dose does not exceed 200 mg per week.

**Approval duration: 12 months**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

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

2. Refer to ERX.PA.01 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 – ERX.PA.01 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                | LDLRAP1: low density lipoprotein receptor adaptor protein 1 |
| HDL-C: high-density lipoprotein cholesterol      | PCSK9: proprotein convertase subtilisin kexin 9             |
| HeFH: heterozygous familial hypercholesterolemia | SAMS: statin-associated muscle symptoms                     |
| HoFH: homozygous familial hypercholesterolemia   | TC: total cholesterol                                       |
| LDL-C: low density lipoprotein cholesterol       | ULN: upper limit of normal                                  |
| LDLR: low density lipoprotein receptor           |   |

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ezetimibe/simvastatin (Vytorin <sup>®</sup> )	10/40 mg PO QD	10 mg-40 mg/day (use of the 10/80 mg dose is restricted to patients who have been taking simvastatin 80 mg for ≥ 12 months without evidence of muscle toxicity)
ezetimibe (Zetia <sup>®</sup> )	10 mg PO QD	10 mg/day
atorvastatin (Lipitor <sup>®</sup> )	40 mg PO QD	80 mg/day
rosuvastatin (Crestor <sup>®</sup> )	5 - 40 mg PO QD	40 mg/day

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Moderate or severe hepatic impairment (Child-Pugh B or C) or active liver disease, including unexplained persistent elevations of serum transaminases
  - Known sensitivity to product components
- Boxed warning(s): risk of hepatotoxicity

*Appendix D: High and Moderate Intensity Daily Statin Therapy for Adults*

<p><b>High Intensity Statin Therapy</b> <i>Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%</i></p> <ul style="list-style-type: none"> <li>• Atorvastatin 40-80 mg</li> <li>• Rosuvastatin 20-40 mg</li> </ul>
<p><b>Moderate Intensity Statin Therapy</b> <i>Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%</i></p> <ul style="list-style-type: none"> <li>• Atorvastatin 10-20 mg</li> <li>• Fluvastatin XL 80 mg</li> <li>• Fluvastatin 40 mg 2x/day</li> <li>• Lovastatin 40 mg</li> <li>• Pitavastatin 1-4 mg</li> <li>• Pravastatin 40-80 mg</li> <li>• Rosuvastatin 5-10 mg</li> <li>• Simvastatin 20-40 mg</li> </ul>
<p><b>Low Intensity Statin Therapy</b> <i>Daily dose shown to lower LDL-C, on average, by &lt; 30%</i></p> <ul style="list-style-type: none"> <li>• Simvastatin 10 mg</li> <li>• Pravastatin 10-20 mg</li> </ul>

Low Intensity Statin Therapy Daily dose shown to lower LDL-C, on average, by < 30%
<ul style="list-style-type: none"> <li>• Lovastatin 20 mg</li> <li>• Fluvastatin 20-40 mg</li> </ul>

*Appendix E: Statin and Ezetimibe Contraindications*

Statins
<ul style="list-style-type: none"> <li>• Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy)</li> <li>• Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment</li> <li>• Pregnancy, actively trying to become pregnant, or nursing</li> <li>• 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</li> </ul>
Ezetimibe
<ul style="list-style-type: none"> <li>• Moderate or severe hepatic impairment [Child-Pugh classes B and C]</li> <li>• Hypersensitivity to ezetimibe (e.g., anaphylaxis, angioedema, rash, urticaria)</li> </ul>

*Appendix F: Statin Risk Factors*

Statin Risk Factors
<ul style="list-style-type: none"> <li>• Multiple or serious comorbidities, including impaired renal or hepatic function</li> <li>• Unexplained alanine transaminase (ALT) elevations &gt; 3 times upper limit of normal, or active liver disease</li> <li>• Concomitant use of drugs adversely affecting statin metabolism</li> <li>• Age &gt; 75 years, or history of hemorrhagic stroke</li> <li>• Asian ancestry</li> </ul>

*Appendix G: General Information*

- Because of the risk of hepatotoxicity, Kynamro is available only through a Risk Evaluation and Mitigation Strategy (REMS) program.
- Low density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene is also known as autosomal recessive hypercholesterolemia (ARH) adaptor protein 1 gene.
- The diagnosis of SAMS is often on the basis of clinical criteria. Typical SAMS include muscle pain and aching (myalgia), cramps, and weakness. Symptoms are usually bilateral and involve large muscle groups, including the thigh, buttock, back, and shoulder girdle musculature. In contrast, cramping is usually unilateral and may involve small muscles of the hands and feet. Symptoms may be more frequent in physically active patients. Symptoms often appear early after starting statin therapy or after an increase in dose and usually resolve or start to dissipate within weeks after cessation of therapy, although it may take several months for symptoms to totally resolve. Persistence of symptoms for more than 2 months after drug cessation should prompt a search for other causes or for underlying muscle disease possibly provoked by statin therapy. The reappearance of symptoms with statin rechallenge and their disappearance with drug cessation offers the best evidence that the symptoms are truly SAMS.
- Pravastatin, fluvastatin, and rosuvastatin are hydrophilic statins which have been reported to confer fewer adverse drug reactions than lipophilic statins.

**V. Dosage and Administration**

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

**VI. Product Availability**

Single-use pre-filled syringe: 200 mg/mL

**VII. References**

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10. Thompson PD, Panza G, Zaleski A, et al. Statin-associated side effects. *JACC* 2016;67(20):2395-2410.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.19.21	05.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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