This drug requires a written request for prior authorization. All requests for Kynamro (mipomersen) require review by a pharmacist prior to final approval.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of homozygous familial hypercholesterolemia as determined by meeting ONE of the following criteria?
   - Simon Broome diagnostic criteria (definite) [example: genetic testing consistent with HoFH and pretreatment baseline LDL cholesterol is greater than 190 mg/dL]
   - Cascade screening
   - Dutch Lipid Network criteria with a score at least 6
   - History of untreated cholesterol >500mg/dL (or treated >300mg/dL) and cutaneous xanthoma before age 10, or
   - Patient has undergone regular apheresis treatments in the past for extremely elevated LDL cholesterol levels and has a history of untreated cholesterol >500mg/dL (or treated >300mg/dL)

   If yes, continue to #2.
   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

2. Does patient meet ALL of the following criteria?
   - Age 12 or older
   - Patient does NOT have any of the following contraindications to Kynamro (mipomersen): moderate or severe hepatic impairment or active liver disease, including unexplained persistent elevations of serum transaminases
   - LDL cholesterol level is at least 160mg/dL
   - Kynamro is prescribed by, or in consultation with a cardiologist, endocrinologist, or lipidologist.

   If yes, continue to #3.
   If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

   **CONTINUED ON NEXT PAGE**
3. Has the patient had a previous trial of a PCSK9 inhibitor (e.g., Praluent (alirocumab) or Repatha (evolocumab))?
   - If yes, continue to #5.
   - If no, continue to #4.

4. Does patient have non-functioning LDL receptors?
   - If yes, continue to #5.
   - If no, do not approve.
   **DENIAL TEXT:** See the initial denial text at the end of the guideline.

5. Will Kynamro (mipomersen) be used in combination with Zetia (ezetimibe) and at least **ONE** of the following drugs:
   - a high intensity statin (e.g., atorvastatin 40mg or 80mg, Crestor (rosuvastatin) 20mg or 40mg),
   - a maximally tolerated dose of atorvastatin or Crestor (rosuvastatin),
   - a maximally tolerated dose of any statin if patient has previously failed either atorvastatin or Crestor (rosuvastatin)?
   - If yes, continue to #7.
   - If no, continue to #6.
6. Will Kynamro ( mipomersen) be used in combination with Zetia ( ezetimibe) and another LDL-lowering agent ( bile acid sequestrant, gemfibrozil or other fibrate, or niacin) given that patient has previously failed at least two statin agents or has absolute contraindication to statins? **Note:** If patient has not previously failed at least two statin agents, documentation must include an absolute contraindication to statin therapy ( active, decompensated liver disease; nursing female, pregnancy or plans to become pregnant; hypersensitivity reaction). If patient has previously failed statins, documentation of failure must include **ALL** of the following for each statin:

- Severe and intolerable adverse effects, with other potential causes ruled out ( low vitamin D levels, sudden increase in intense or prolonged physical activity, drug interactions with statins, other metabolic or inflammatory causes), **AND**
- Failed rechallenge with a second statin agent, including alternate dosing strategies such as every-other-day statin dosing), **AND**
- **ONE** of the following lab values or incidents
  - CK exceeds 10 times upper limit of normal
  - LFTs exceed 3 times upper limit of normal
  - Hospitalization due to severe adverse event such as rhabdomyolysis
  - Severe muscle weakness leading to temporary disability, fall, or inability to use a major muscle group ( e.g., unable to stand from a seated position or inability to exit a motor vehicle without assistance.)

If yes, continue to #7.
If no, do not approve.
**DENIAL TEXT:** See the initial denial text at the end of the guideline.

7. Is Kynamro ( mipomersen) being prescribed in conjunction with LDL apheresis?

If yes, do not approve.
**DENIAL TEXT:** See the initial denial text at the end of the guideline.
If no, approve for 7 months by HICL for #4 syringes per 28 day supply.

**CONTINUED ON NEXT PAGE**
INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: Our guideline for MIPOMERSEN requires that the patient is at least 12 years of age, has a LDL cholesterol level of at least 160mg/dL, and has a diagnosis of homozygous familial hypercholesterolemia (HoFH) as determined by meeting ONE of the following criteria:

- Simon Broome diagnostic criteria (definite)
- Cascade screening
- Dutch Lipid Network criteria with a score at least 6
- History of untreated cholesterol >500 (or treated >300) and cutaneous xanthoma before age 10, or
- Patient has undergone regular apheresis treatments in the past for extremely elevated LDL cholesterol levels, with a history of untreated cholesterol >500mg/dL (or treated >300mg/dL).

Additional guideline requirements apply.

Approval also requires that ALL of the following criteria are met:

- Patient must have had a previous trial of a PCSK9 inhibitor (e.g., Praluent (alirocumab) or Repatha (evolocumab)), unless patient has non-functioning LDL receptors.
- Patient does NOT have any of the following contraindications to Kynamro (mipomersen): moderate or severe hepatic impairment or active liver disease, including unexplained persistent elevations of serum transaminases
- Kynamro is prescribed by, or in consultation with, a cardiologist, endocrinologist or lipidologist.
- Patient is not concurrently receiving apheresis.

(Initial denial text continued on next page)

CONTINUED ON NEXT PAGE
Kynamro must be used in combination with Zetia (ezetimibe) and **ONE** of the following drugs:

- a high intensity statin (e.g., atorvastatin 40mg or 80mg, Crestor (rosuvastatin) 20mg or 40mg),
- a maximally tolerated dose of atorvastatin or Crestor (rosuvastatin),
- a maximally tolerated dose of any statin given that if patient has previously failed either atorvastatin or rosuvastatin,
- an LDL-lowering agent (bile acid sequestrant, gemfibrozil or other fibrate, or niacin) given that patient has previously failed at least 2 statin agents or an absolute contraindication to statins (active, decompensated liver disease; nursing female, pregnancy or plans to become pregnant; hypersensitivity reaction). For patients unable to take a statin that do not have an absolute contraindication to therapy, documentation of statin trial/failure must include **ALL** of the following for each statin trial:
  - Severe and intolerable adverse effects, with other potential causes ruled out (low vitamin D levels, sudden increase in intense or prolonged physical activity, drug interactions with statins, other metabolic or inflammatory causes), **AND**
  - Failed rechallenge with a second statin agent, including alternate dosing strategies such as every-other-day statin dosing), **AND**
  - **ONE** of the following lab values or incidents
    - CK level exceed 10 times upper limit of normal
    - LFTs exceed 3 times upper limit of normal
    - Hospitalization due to severe adverse event such as rhabdomyolysis
    - Severe muscle weakness leading to temporary disability, fall, or inability to use a major muscle group (e.g., unable to get up)

RENWEAL CRITERIA

1. Is the request for a patient who has had at least 26 weeks of therapy?

   If yes, continue to #2.
   If no, do not approve.

   **DENIAL TEXT:** See the renewal denial text at the end of the guideline.

   **CONTINUED ON NEXT PAGE**
MIPOMERSEN SODIUM

RENEWAL CRITERIA (CONTINUED)

2. Is the patient adherent to Kynamro ( mipomersen) therapy and statin therapy (or Kynamro ( mipomersen) and other lipid-lowering agent if patient is statin intolerant)?
   
   If yes, continue to #3.
   If no, do not approve.
   **DENIAL TEXT:** See the renewal denial text at the end of the guideline.

3. Has the patient had an LDL reduction of at least 20% from baseline, at or after 26 weeks of treatment?
   
   If yes, **approve for 12 months by HICL for #4 syringes per 28 day supply.**
   If no, do not approve.
   **DENIAL TEXT:** See the renewal denial text at the end of the guideline.

**RENEWAL DENIAL TEXT:** Our guideline for **MIPOMERSEN** renewal requires that the patient has had at least 26 weeks of therapy, with a LDL reduction of at least 20% from baseline after Kynamro ( mipomersen) therapy for 26 weeks. Patient must also be adherent to Kynamro ( mipomersen) and statin therapy (or Kynamro and other lipid-lowering agent, if patient is statin intolerant).

**RATIONALE**
To ensure appropriate use of Kynamro based on FDA approved indication and prescribing information.

The recommended dosage is 200mg injected subcutaneously once weekly. The first dose should be administered under the supervision of a healthcare provider. Prior to initiating therapy, patient ALT, AST, alkaline phosphatase, and total bilirubin should be measured.

Kynamro may increase risk of hepatic toxicity. Kynamro contains a boxed warning regarding the risk of elevated transaminases and hepatic steatosis. Kynamro also has a mandatory REMS program to educate prescribers about the risk of hepatotoxicity and the importance of monitoring patients while taking Kynamro as well as to limit the use of Kynamro to patients with HoFH.

**FDA APPROVED INDICATION**
Kynamro ( mipomersen) 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).

**CONTINUED ON NEXT PAGE**
MIPOMERSEN SODIUM

FDA APPROVED INDICATION (CONTINUED)

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.

REFERENCES

<table>
<thead>
<tr>
<th>Library</th>
<th>Commercial</th>
<th>NSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Created: 03/13
Effective: 01/01/16
Client Approval: 11/15