Pharmacy Policy

Homozygous Familial Hypercholesterolemia – Juxtapid™, Kynamro™

Policy Number: 9.039
Version Number: 6.0
Version Effective Date: 09/07/2017

Product Applicability  □ All Plan* Products

<table>
<thead>
<tr>
<th>Well Sense Health Plan</th>
<th>Boston Medical Center HealthNet Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>☒ New Hampshire Medicaid</td>
<td>☒ MassHealth</td>
</tr>
<tr>
<td>☒ NH Health Protection Program</td>
<td>☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct</td>
</tr>
<tr>
<td>☐ Senior Care Options</td>
<td>☐ Senior Care Options</td>
</tr>
</tbody>
</table>

Note: Disclaimer and audit information is located at the end of this document.

Policy Summary

The Plan will authorize coverage Juxtapid™ and Kynamro™ when appropriate criteria are met.

Description of Item or Service

Familial hypercholesterolemia (FH) is a genetic syndrome characterized by high LDL-C levels apparent from birth and is associated with early onset coronary heart disease (CHD). Heterozygous FH affects approximately 1 in 500 persons in the United States while homozygous FH is a rare disorder affecting approximately 1 in 1 million persons in the United States and 1 in 250,000 births. FH is associated with a high risk of premature CHD and aggressive lipid management is necessary to slow the progression of coronary atherosclerosis. Homozygous individuals often require early initiation of combination therapy including LDL apheresis, high dose statin therapy and cholesterol absorption inhibitors, typically initiated in childhood. Some patients may also require bile acid sequestrants and nicotinic acid.

* Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.
LDL apheresis is a procedure which removes apo B- lipoproteins from circulation. Methods for LDL apheresis include the use of dextran sulfate cellulose absorption, heparin induced extracorporeal LDL-C precipitation, immunoadsorption, and double filtration plasma apheresis of lipoproteins. It is performed weekly or biweekly and is available in approximately 40 centers in the United States. The cost can vary from between $ 3,000 - $ 4,000 per session and side effects include hypotension, anemia, nausea, flushing and headache. Patients may require the formation of an AV fistula, which increases the risk of long-term complications.

The National Lipid Association Expert Panel on Familial Hypercholesterolemia recommends the use of lipid apheresis in patients with functional homozygous FH with LDL cholesterol >300 mg/dL or non-HDL cholesterol >330 mg/dL who have not had an adequate response to maximum tolerated drug therapy.

Juxtapid™ (lopitamide) and Kynamro™ (mipomersen) are FDA-approved to treat patients with homozygous FH, as adjunctive therapies to a low-fat diet and other lipid-lowering treatments. Of note, Juxtapid™ is approved for use in combination with lipid apheresis, where the safety and efficacy of Kynamro™ in combination with lipid apheresis has not been established. In clinical trials, Juxtapid™ demonstrated a reduction in LDL-C levels of approximately 40% while Kynamro™ demonstrated reductions of approximately 25%; both were in combination with other lipid-lowering therapies. Juxtapid™ and Kynamro™ have not yet been incorporated into NCEP guidelines.

In August 2015 the FDA approved the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor Repatha™ (evolocumab) as an adjunct to other LDL lowering therapies (including LDL apheresis) for the treatment of homozygous familial hypercholesterolemia. Repatha™ is administered as a once monthly subcutaneous injection. At this time outcomes data for cardiovascular morbidity and mortality Repatha™, Juxtapid®, or Kynamro® is not available.

Policy

The Plan may authorize coverage of Juxtapid™ and Kynamro™ for members meeting the following criteria:

**Prior Authorization – (Duration of Approval: Maximum of 1 year)**

A prior authorization request will be required for all prescriptions for Juxtapid™ and Kynamro™. These requests will be approved when the following criteria are met:

**Initial Therapy:**

**Kynamro™**

Documentation of the following:

1. Diagnosis of homozygous FH; **AND**
2. Either of the following:
   a. Inadequate LDL reduction while adherent to a minimum of 90 day continuous use of atorvastatin 80mg or rosuvastatin 40mg in combination with Zetia evidenced by:

---

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.**
Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.

Homozygous FH

i. Current LDL-C greater than or equal to 100mg/dL; **AND**
ii. Less than a 50 percent reduction in LDL-C from baseline; **OR**

b. Inability to tolerate a high intensity statin (atorvastatin 80mg or rosuvastatin 40mg); **AND**
   Inadequate response while adherent to a minimum of 90 day continuous use of a maximum tolerated dose of a non-high intensity statin and Zetia evidenced by:
   i. Current LDL-C greater than or equal to 100mg/dL; **AND**
   iv. Less than a 50 percent reduction in LDL-C from baseline; **OR**

3. An inadequate response to Repatha™ while adherent to a minimum of 90 day continuous use as evidenced by current LDL-C greater than or equal to 100 mg/dL **OR** an adverse effect or contraindication to Repatha™

**Juxtapid™**

Documentation of the following:
1. Diagnosis of homozygous FH; **AND**
2. Either of the following:
   a. Inadequate LDL reduction while adherent to a minimum of 90 day continuous use of atorvastatin 80mg or rosuvastatin 40mg in combination with Zetia evidenced by:
      iii. Current LDL-C greater than or equal to 100mg/dL; **AND**
      iv. Less than a 50 percent reduction in LDL-C from baseline; **OR**
   b. Inability to tolerate a high intensity statin (atorvastatin 80mg or rosuvastatin 40mg); **AND**
      Inadequate response while adherent to a minimum of 90 day continuous use of a maximum tolerated dose of a non-high intensity statin and Zetia evidenced by:
      ii. Current LDL-C greater than or equal to 100mg/dL; **AND**
3. An inadequate response to Repatha™ while adherent to a minimum of 90 day continuous use as evidenced by current LDL-C greater than or equal to 100 mg/dL **OR** an adverse effect or contraindication to Repatha™; **AND**
4. Inadequate response, adverse effect or contraindication to Kynamro™ **OR** the member is concurrently receiving lipid apheresis.

**Re-authorization:**

**Juxtapid™, Kynamro™**

Documentation of the following:
1. Clinical response to therapy as defined by a decrease in LDL-C levels from baseline; **AND**
2. Member has been compliant with therapy (confirmed by pharmacy claims)

**Quantity Limitations Apply – see Appendix A**

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.*

Homoygous FH

3 of 6
Limitations

The Plan will not approve coverage of Juxtapid™ or Kynamro™ in the following instances:

1. When the above criteria are not met
2. Concurrent use with PCSK-9 inhibitors

Clinical Background Information and References


Appendix A – Quantity Limitations for Juxtapid™ and Kynamro™

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Quantity Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juxtapid™ 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 60 mg capsules</td>
<td>1 capsule per day</td>
</tr>
<tr>
<td>Kynamro™ 200 mg</td>
<td>4 syringes per 28 days</td>
</tr>
</tbody>
</table>

Original Approval Date | Original Effective Date | Policy Owner | Approved by
-----------------------|-------------------------|--------------|-----------------
05/09/2013             | 10/01/2013              | Pharmacy Services | Pharmacy & Therapeutics (P&T) Committee
12/01/2013             | 12/01/2013              | Pharmacy Services | NH DHHS

Policy Revisions History

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
<th>Revision Effective Date</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/13/2013</td>
<td>Policy applied to</td>
<td>04/01/2014</td>
<td>P&amp;T Committee</td>
</tr>
</tbody>
</table>

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.
Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.

<table>
<thead>
<tr>
<th>Policy Revisions History</th>
<th>ConnectorCare/Qualified Health Plan (QHP)</th>
<th>05/08/2014</th>
<th>P&amp;T Annual Review, added bile acid sequestrant and nicotinic acid as acceptable drug trial</th>
<th>09/01/2014</th>
<th>P&amp;T Committee NH DHHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/14/2015</td>
<td>P&amp;T Annual Review, no changes required</td>
<td>09/01/2015 (BMCHP) and 10/01/2015 (Well Sense)</td>
<td>P&amp;T Committee NH DHHS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>05/12/2016</td>
<td>P&amp;T Annual Review, added quantity limit for Juxtapid 30 mg, 40 mg, and 60 mg capsules; changed quantity limit for Juxtapid 20 mg capsules; revised step therapy criteria for Juxtapid™ and Kynamro™ to require step therapy with Repatha™; added concurrent use with PCSK9 inhibitors to the limitations section of the policy</td>
<td>09/15/2016</td>
<td>P&amp;T Committee NH DHHS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/11/2017</td>
<td>P&amp;T Annual Review, changed Kynamro QL from 4 vials/syringes per month to 4 vials per 28 days</td>
<td>09/07/2017</td>
<td>P&amp;T Committee</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Next Review Date

05/10/2018

Other Applicable Policies

9.002 Mandatory Generic Substitution Policy
9.015 Quantity Limitation Policy

Reference to Applicable Laws and Regulations, If Any

Disclaimer Information

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.
Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.*