Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, gender or quantity restrictions. Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:
The intent of this policy is to communicate the medical necessity criteria for lomitapide (Juxtapid) and mipomersen (Kynamro) as provided under the member's pharmacy benefit.

Description:
Lomitapide is a synthetic lipid-lowering agent, directly binds and inhibits microsomal triglyceride transfer protein, which resides in the lumen of the endoplasmic reticulum, thereby preventing the assembly of apo B-containing lipoproteins in enterocytes and hepatocytes. This inhibits the synthesis of chylomicrons and very low-density lipoprotein (VLDL). The inhibition of the synthesis of VLDL leads to reduced levels of plasma LDL-C.

Lomitapide (Juxtapid) is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

Mipomersen sodium is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis. Apo B is the principal apolipoprotein of LDL and its metabolic precursor, very low density lipoprotein (VLDL). Mipomersen Sodium inhibits synthesis of apo B by binding to its mRNA, resulting in degradation of the mRNA.

Mipomersen sodium (Kynamro®) is indicated as 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).

Policy:
Mipomersen sodium (Kynamro®) and Lomitapide (Juxtapid) are approved when documentation is provided of ALL of the following:
1. Diagnosis of Homozygous Familial Hypercholesterolemia; and
2. Used as an adjunct to lipid lowering treatments and a low fat diet with ONE of the following:
   a. Genetic confirmation of 2 mutant alleles at the LDL receptor. Apo B, PCSK9, or ARH adaptor protein gene locus
   b. Untreated LDL-C > 500 mg/dL or treated LDL cholesterol ≥ 300 mg/dL or treated non-HDL cholesterol ≥330 mg/dL together with either of the following:
      i. Cutaneous or tendonous xanthoma prior to 10 years of age
      ii. Elevated LDL cholesterol prior to lipid-lowering therapy consistent with
HeFH in both parents as listed below:

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total cholesterol (LDL cholesterol) (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18</td>
<td>220 (155)</td>
</tr>
<tr>
<td>20-29</td>
<td>240 (170)</td>
</tr>
<tr>
<td>30-39</td>
<td>270 (190)</td>
</tr>
<tr>
<td>≥ 40</td>
<td>290 (205)</td>
</tr>
</tbody>
</table>

3. ONE of the following:
   a. Inadequate response to one of the following medications in combination with ezetimibe:
      i. simvastatin (daily dose ≥ 40mg)
      ii. atorvastatin (daily dose ≥ 20mg)
      iii. rosuvastatin (Crestor) (daily dose ≥ 10mg)
   b. Member has experienced ONE of the following:
      i. Rhabdomyolysis or muscle symptoms with creatine kinase (CK) elevations >10 times upper limit of normal (ULN) on any statin OR
      ii. Myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations <10 times ULN) with TWO statins

Authorization length for mipomersen sodium and lomitapide is 6 months.

Re-authorization criteria: Mipomersen sodium and lomitapide are re-approved when there is a reduction in LDL level of at least 25% since initiation of therapy with respective drug.

**Black Box Warning:**
Risk of hepatotoxicity:

**Mipomersen and Lomitapide** can cause elevations in transaminases. In clinical trials, 12% of patients treated with mipomersen and 34% of patients treated with lomitapide had at least 1 elevation in ALT or AST at least 3 times the upper limit of normal (ULN) or higher. There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), alkaline phosphatase or partial thromboplastin time (PTT).

Mipomersen and Lomitapide also increase hepatic fat, with or without concomitant increase in transaminases. In the trials of patients with heterozygous familial hypercholesterolemia and hyperlipidemia, the median absolute increase in hepatic fat was 10% (mipomersen) and 6% (lomitapide) after 26 weeks of treatment from 0% at baseline, measured by magnetic resonance imaging (MRI) and 1% at baseline, measured by magnetic resonance spectroscopy (MRS) respectively. Hepatic steatosis is a risk factor for advanced liver disease, including steatohepatitis and cirrhosis.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended. During treatment, adjust the dose of mipomersen and lomitapide if the ALT or AST are at least 3 times the ULN. Discontinue mipomersen and lomitapide for clinically significant liver toxicity.

Because of the risk of hepatotoxicity, mipomersen and lomitapide are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

**Guidelines:**
Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**
Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the pharmacy benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**


**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Generic name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kynamro</td>
<td>Mipomersen Sodium</td>
</tr>
<tr>
<td>Juxtapid</td>
<td>Lomitapide</td>
</tr>
</tbody>
</table>

**Cross References:**
The Policy Bulletins on this website were developed to assist Independence Blue Cross ("Independence") in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Independence organization, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Independence does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of Independence. If you have a specific medical condition, please consult with your doctor. Independence reserves the right at any time to change or update its Policy Bulletins. ©2016 Independence Blue Cross. All Rights Reserved.

Independence Blue Cross is an independent licensee of the Blue Cross and Blue Shield Association.