Clinical Policy: Lomitapide (Juxtapid)
Reference Number: ERX.SPMN.185
Effective Date: 01/2017

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that lomitapide (Juxtapid®) 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 homozygous familial hypercholesterolemia (HoFH) defined as one of the following (a, b, or c):
         a. Genetic mutation indicating HoFH (LDLR, PCSK9, apoB, 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. Member meets one of the following (a or b):
         a. Age < 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 ≥ 18 years and recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) ≥ 70 mg/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 C 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 Kynamro (mipomersen), Repatha (evolocumab), or Praluent (alirocumab);
9. Prescribed dose of Juxtapid does not exceed 60 mg daily.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. Continued Approval
A. Homozygous Familial Hypercholesterolemia (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. If member has been taking Juxtapid for at least 6 months, lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of Juxtapid therapy;
   3. Prescribed dose of Juxtapid does not exceed 60 mg daily.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
   2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
Juxtapid capsules contain lomitapide mesylate, a synthetic lipid-lowering agent for oral administration. Juxtapid directly binds and inhibits microsomal triglyceride transfer protein (MTP), 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 VLDL. The inhibition of the synthesis of VLDL leads to reduced levels of plasma LDL-C.

Formulations:
Each Juxtapid capsule contains lomitapide mesylate equivalent to 5, 10, 20, 30, 40 or 60 mg lomitapide free base.

FDA Approved Indications:
Juxtapid is a microsomal triglyceride transfer protein inhibitor/oral capsule formulation 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 (LDLC), total cholesterol, apolipoprotein B (apoB), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).
Limitations of use

- The safety and effectiveness of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effect of Juxtapid on cardiovascular morbidity and mortality has not been determined.

Safety Information:
Due to the risk of hepatotoxicity, Juxtapid is available only through a restricted program called the Juxtapid Risk Evaluation and Mitigation Strategy (REMS) program.

Appendices

Appendix A: Abbreviation Key

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>apoB</td>
<td>apolipoprotein B</td>
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<tr>
<td>ASCVD</td>
<td>atherosclerotic cardiovascular disease</td>
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<tr>
<td>CVD</td>
<td>cardiovascular disease</td>
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<tr>
<td>FH</td>
<td>familial hypercholesterolemia</td>
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<tr>
<td>HDL-C</td>
<td>high-density lipoprotein cholesterol</td>
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<tr>
<td>HeFH</td>
<td>heterozygous familial hypercholesterolemia</td>
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<tr>
<td>HoFH</td>
<td>homozygous familial hypercholesterolemia</td>
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<tr>
<td>LD-C</td>
<td>low-density lipoprotein cholesterol</td>
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<tr>
<td>LDLR</td>
<td>low-density lipoprotein receptor</td>
</tr>
<tr>
<td>LDLRAP1</td>
<td>low-density lipoprotein receptor adaptor protein 1</td>
</tr>
<tr>
<td>MTP</td>
<td>microsomal triglyceride transfer protein</td>
</tr>
<tr>
<td>PCSK9</td>
<td>proprotein convertase subtilisin kexin 9</td>
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<tr>
<td>VLDL-C</td>
<td>very low-density lipoprotein cholesterol</td>
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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 10-20 mg
    - 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 mg

Appendix C: Statin and Zetia Contraindications

- Statins
  - Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy);
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- 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.

Reviews, Revisions, and Approvals

<table>
<thead>
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<th>Policy split from USS.SPMN.32 Juxtapid and Kynamro, and converted to new template. Removed age criteria. Changed signs from “&gt;” to “≥” for following criteria per NLA FH guidelines: treated LDL-C ≥ 300 mg/dL or non-HDL-C ≥ 330 mg/dL; untreated LDL-C ≥ 500 mg/dL, and one of the following (i or ii): o Tendinous or cutaneous xanthoma prior to age 10 years; o Evidence of HeFH in both parents (e.g., documented history of elevated LDL-C ≥ 190 mg/dL prior to lipid-lowering therapy). Added examples of Zetia intolerance. Incorporated HOFH and TLC appendices into the criteria. Combined Zetia and statin contraindications (App C) and added nursing as a contraindication. Statin risk factors are listed at App D. Added requirement for the use of statin and Zetia therapy for the last 4 months. Modified approval duration to 6 months initial/12 month renewal.</th>
<th>Date</th>
<th>Approval Date</th>
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<tr>
<td>11/16</td>
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References


**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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