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

Description
Lomitapide (Juxtapid®) is a microsomal triglyceride transfer protein inhibitor.

FDA Approved Indication(s)
Juxtapid is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including low-density lipoprotein (LDL) apheresis where available, to reduce LDL 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).

Limitation(s) 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.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Juxtapid 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 (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);
      2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
      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 there is a contraindication (see Appendix D) or history of intolerance to each such therapy;
         b. Age ≥ 18 years and recent (within the last 30 days) LDL-C ≥ 100 mg/dL;
      4. If member is ≥ 18 years, has received a high intensity statin (see 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 (see 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 (see 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 (see 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 member has a history of Zetia intolerance (e.g., associated diarrhea or upper respiratory tract infection);
6. Failure of a trial of Repatha, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 60 mg daily.

**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. Lab results within the last 3 months show an LDL-C reduction (defined as at least 25% LDL reduction from baseline, LDL< 70 mg/dL for high risk patients, or LDL < 100 mg/dL for medium risk patients, see Appendix E) since initiation of Juxtapid
   3. If request is for a dose increase, new does not exceed 60 mg daily.

**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;
B. Coadministration with Kynamro ( mipomersen), Repatha (evolocumab), or Praluent (alirocumab).

IV. **Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*
- apoB: apolipoprotein B
- ASCVD: atherosclerotic cardiovascular disease
- CVD: cardiovascular disease
- FDA: Food and Drug Administration
- FH: familial hypercholesterolemia
- HDL-C: high-density lipoprotein cholesterol
- HeFH: heterozygous familial hypercholesterolemia
- LDL-C: low density lipoprotein cholesterol
- LDLR: low density lipoprotein receptor
- LDLRAP1: low density lipoprotein receptor adaptor protein 1
- MTP: microsomal triglyceride transfer protein
- PCSK9: proprotein convertase subtilisin kexin 9
- VLDL-C: very low-density lipoprotein cholesterol

*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 10-20mg
    - Fluvastatin XL 80 mg
    - Fluvastatin 40 mg 2x/day
    - Lovastatin 40 mg
    - Pitavastatin 2-4 mg
    - Pravastatin 40-80 mg
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- 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

- **Statin**
  - Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy);
  - 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

- Multiplor or serious comorbidities, including impaired renal or hepatic function;
- Unexplained alanine aminotransferase (ALT) elevations > 3 times the upper limit of normal, or active liver disease;
- Concomitant use of drugs adversely affecting statin metabolism;
- Age > 75 years, or history of hemorrhagic stroke;
- Asian ancestry.

Appendix E: High and Moderate Risk of ASCVD:

- Patients with high risk of ASCVD include the following:
  - History of clinical atherosclerotic cardiovascular disease (as defined in section II)
  - Diabetes with an estimated 10-year ASCVD risk ≥ 7.5% for adults 40-75 years of age
  - Untreated LDL ≥ 190 mg/dL
- Patients with moderate risk of ASCVD include the following:
  - Diabetes with an estimated 10-year ASCVD risk < 7.5% for adults 40-75 years of age
  - Estimated 10-year ASCVD risk ≥ 5% for adults 40-75 years of age
- The calculator for the 10-year ASCVD risk estimator can be found here: [http://tools.cardiosource.org/ASCVD-Risk-Estimator/](http://tools.cardiosource.org/ASCVD-Risk-Estimator/). Information needed to complete the ASCVD Risk Estimator include: gender, race (white, African American, other), systolic blood pressure, diabetes, age, total cholesterol, HDL-Cholesterol, treatment for hypertension, current smoker.

Appendix F: Therapeutic Alternatives

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vytorin® (ezetimibe/simvastatin)</td>
<td>10/40 mg PO QD</td>
<td>10/40 mg PO QD (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)</td>
</tr>
<tr>
<td>atorvastatin (Lipitor®)</td>
<td>40 mg PO QD</td>
<td>80 mg PO QD</td>
</tr>
<tr>
<td>rosuvastatin (Crestor®)</td>
<td>5 - 40 mg PO QD</td>
<td>40 mg PO QD</td>
</tr>
<tr>
<td>Repatha® (evolocumab)*</td>
<td>HoFH 420 mg SC once monthly</td>
<td>420 mg SC once monthly</td>
</tr>
</tbody>
</table>

*Requires prior authorization

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
V. **Dosage and Administration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOFH</td>
<td>PO QD, following a specific titration schedule (below).</td>
<td>60 mg/day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Duration of administration before considering increase to next dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mg QD</td>
<td>At least 2 weeks</td>
</tr>
<tr>
<td>10 mg QD</td>
<td>At least 4 weeks</td>
</tr>
<tr>
<td>20 mg QD</td>
<td>At least 4 weeks</td>
</tr>
<tr>
<td>40 mg QD</td>
<td>At least 4 weeks</td>
</tr>
<tr>
<td>60 mg QD</td>
<td>Max recommended dosage</td>
</tr>
</tbody>
</table>

Doses should be escalated gradually based on acceptable safety and tolerability. Transaminases should be measured prior to any increase in dose.

VI. **Product Availability**

Capsules: 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 60 mg

VII. **References**


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.16</td>
<td>12.16</td>
</tr>
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</table>

- Policy split from USS.SPMN.32 Juxtapid and Kynamro, and converted to new template. Removed age criteria. Changed signs from “>” 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):
  - Tendinous or cutaneous xanthoma prior to age 10 years;
  - 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.
- 4Q17 Annual Review
  - Converted to new template
<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changed LDL level from ≥ 70 mg/dL to ≥ 100 mg/dL for age 18 and above</td>
<td></td>
<td></td>
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<tr>
<td>Coadministration with Juxtapid (lomitapid), Kynamro (mipomersen), or Repatha (evolocumab) moved to section III from section I</td>
<td></td>
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</tr>
<tr>
<td>Specified LDL-C reduction required at re-authorization</td>
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<tr>
<td>Removed initial criterion requiring counseling on therapeutic lifestyle changes</td>
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**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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