

## Clinical Policy: Lomitapide (Juxtapid)

Reference Number: IL.PHAR.283

Effective Date: 1.1.20

Last Review Date: 4.13.2021

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Lomitapide (Juxtapid<sup>®</sup>) 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 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).

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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> 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 (e.g., mutations in low density lipoprotein receptor [LDLR] gene, proprotein convertase subtilisin kexin 9 [PCSK9] gene, apo B gene, low density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene);
  - b. Treated LDL-C  $\geq$  300 mg/dL or non-HDL-C  $\geq$  330 mg/dL;
  - c. Untreated LDL-C  $\geq$  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  $\geq$  190 mg/dL prior to lipid-lowering therapy);
2. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist;

3. Age  $\geq$  18 years;
4. Documentation of recent (within the last 60 days) LDL-C  $\geq$  70 mg/dL;
5. For members on statin therapy, both of the following (a and b):
  - a. Juxtapid is prescribed in conjunction with a statin at the maximally tolerated dose;
  - b. Member has been adherent for at least the last 4 months to maximally tolerated doses of one of the following statin regimens (i, ii, or iii):
    - i. A high intensity statin (*see Appendix C*);
    - ii. A moderate intensity statin (*see Appendix C*) and member has one of the following (a or b):
      - a) Intolerance to two high intensity statins;
      - b) A statin risk factor (*see Appendix E*);
    - iii. A low intensity statin and member has one of the following (a or b):
      - a) Intolerance to one high and one moderate intensity statins;
      - b) A statin risk factor (*see Appendix E*) and history of intolerance to two moderate intensity statins;
6. For members not on statin therapy, member meets one of the following (a or b):
  - a. Statin therapy is contraindicated per Appendix D;
  - b. For members who are statin intolerant, member has tried at least two statins, 1 of which must be hydrophilic statins (pravastatin or rosuvastatin), and member meets one of the following (i or ii):
    - i. Member has documented statin risk factors (*see Appendix E*);
    - ii. Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
      - a) Documentation of intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
      - b) Documentation of re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);
7. Member has been adherent to ezetimibe therapy used concomitantly with a statin at the maximally tolerated dose for at least the last 4 months, unless contraindicated per Appendix D or member has a history of ezetimibe intolerance (e.g., associated diarrhea or upper respiratory tract infection);
8. Treatment plan does not include coadministration with Repatha<sup>®</sup>, or Praluent<sup>®</sup>;
9. Dose not exceed 60 mg per day.

**Approval duration: 6 months**

#### **B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

## **II. Continued Therapy**

### **A. Homozygous Familial Hypercholesterolemia (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

2. If statin tolerant, documentation of adherence to a statin at the maximally tolerated dose;
3. Member is responding positively to therapy as evidenced by lab results within the last 3 months showing an LDL-C reduction since initiation of Juxtapid therapy;
4. If request is for a dose increase, new dose does not exceed 60 mg per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.  
**Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

**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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ALT: alanine aminotransferase	LDLR: low density lipoprotein receptor
apoB: apolipoprotein B	LDLRAP1: low density lipoprotein receptor adaptor protein 1
FDA: Food and Drug Administration	PCSK9: proprotein convertase subtilisin kexin 9
HDL-C: high-density lipoprotein cholesterol	SAMS: statin-associated muscle symptoms
HeFH: heterozygous familial hypercholesterolemia	TC: total cholesterol
HoFH: homozygous familial hypercholesterolemia	ULN: upper limit of normal
LDL-C: low density lipoprotein cholesterol	

*Appendix B: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Pregnancy
  - Concomitant use with strong or moderate CYP3A4 inhibitors
  - Moderate or severe hepatic impairment (Child-Pugh B or C) or active liver disease, including unexplained persistent elevations of serum transaminases
- Boxed warning(s): risk of hepatotoxicity

*Appendix C: High and Moderate Intensity Daily Statin Therapy for Adults*

**High Intensity Statin Therapy**

<b><i>Daily dose shown to lower LDL-C, on average, by approximately <math>\geq</math>50%</i></b>
<ul style="list-style-type: none"> <li>• Atorvastatin 40-80 mg</li> <li>• Rosuvastatin 20-40 mg</li> </ul>
<b>Moderate Intensity Statin Therapy</b>
<b><i>Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%</i></b>
<ul style="list-style-type: none"> <li>• Atorvastatin 10-20mg</li> <li>• Fluvastatin XL 80 mg</li> <li>• Fluvastatin 40 mg BID</li> <li>• Lovastatin 40 mg</li> <li>• Pitavastatin 1-4 mg</li> <li>• Pravastatin 40-80 mg</li> <li>• Rosuvastatin 5-10 mg</li> <li>• Simvastatin 20-40 mg</li> </ul>
<b>Low Intensity Statin Therapy</b>
<b><i>Daily dose shown to lower LDL-C, on average, by <math>&lt;</math>30%</i></b>
<ul style="list-style-type: none"> <li>• Simvastatin 10 mg</li> <li>• Pravastatin 10–20 mg</li> <li>• Lovastatin 20 mg</li> <li>• Fluvastatin 20–40 mg</li> </ul>

*Appendix D: Statin and Ezetimibe Contraindications*

<b>Statins</b>
<ul style="list-style-type: none"> <li>• Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy)</li> <li>• Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment</li> <li>• Pregnancy, actively trying to become pregnant, or nursing</li> <li>• 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</li> </ul>
<b>Ezetimibe</b>
<ul style="list-style-type: none"> <li>• Moderate or severe hepatic impairment [Child-Pugh classes B and C]</li> <li>• Hypersensitivity to ezetimibe (e.g., anaphylaxis, angioedema, rash, urticaria)</li> </ul>

*Appendix E: Statin Risk Factors*

<b>Statin Risk Factors</b>
<ul style="list-style-type: none"> <li>• Multiple or serious comorbidities, including impaired renal or hepatic function</li> <li>• Unexplained alanine transaminase (ALT) elevations <math>&gt;</math> 3 times upper limit of normal, or active liver disease</li> <li>• Concomitant use of drugs adversely affecting statin metabolism</li> <li>• Age <math>&gt;</math> 75 years, or history of hemorrhagic stroke</li> <li>• Asian ancestry</li> </ul>

*Appendix F: General Information*

- The safety and effectiveness of Juxtapid have not been established in pediatric patients.
- Because of the risk of hepatotoxicity, Juxtapid is available only through a Risk Evaluation and Mitigation Strategy (REMS) program called the Juxtapid REMS Program.
- Low density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene is also known as autosomal recessive hypercholesterolemia (ARH) adaptor protein 1 gene.
- The diagnosis of SAMS is often on the basis of clinical criteria. Typical SAMS include muscle pain and aching (myalgia), cramps, and weakness. Symptoms are usually bilateral and involve large muscle groups, including the thigh, buttock, back, and shoulder girdle musculature. In contrast, cramping is usually unilateral and may involve small muscles of the hands and feet. Symptoms may be more frequent in physically active patients. Symptoms often appear early after starting statin therapy or after an increase in dose and usually resolve or start to dissipate within weeks after cessation of therapy, although it may take several months for symptoms to totally resolve. Persistence of symptoms for more than 2 months after drug cessation should prompt a search for other causes or for underlying muscle disease possibly provoked by statin therapy. The reappearance of symptoms with statin rechallenge and their disappearance with drug cessation offers the best evidence that the symptoms are truly SAMS.
- Pravastatin, fluvastatin, and rosuvastatin are hydrophilic statins which have been reported to confer fewer adverse drug reactions than lipophilic statins.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
HoFH	5 mg PO QD up to maximum dose following a specific titration schedule as follows:  Dosage – duration of administration before considering increase to next dosage: 5 mg QD – at least 2 weeks 10 mg, 20mg, 40 mg QD – at least 4 weeks for each dose <ul style="list-style-type: none"> <li>• Doses should be escalated gradually based on acceptable safety and tolerability.</li> <li>• Modify dosing for patients taking concomitant cytochrome P450 (CYP) 3A4 inhibitors, renal impairment, or baseline hepatic impairment.</li> <li>• Dose adjustments are also required for patients who develop transaminase values at least 3x ULN during Juxtapid treatment.</li> </ul>	60 mg/day

**VI. Product Availability**

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

**VII. References**

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted CP.PHAR.283 Lomitapide (Juxtapid) policy.	12.13.19	
1Q 2020 annual review: increased the timeframe for LDL-C lab draws from 30 days to 60 days; concomitant statin usage section modified to more clearly delineate between patients who are currently on statin therapy vs. those who are not, and for the latter, to require documentation of a prior trial of two statins with documentation of statin risk factors or intolerance; criteria for statin-rechallenge in the setting of SAMS are added; Appendix D	12.30.19	1.7.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
updated based on 2018 ACC/AHA guidelines; references reviewed and updated.		
2Q 2021 annual review. added requirement for adherence to statin therapy on re-auth; references reviewed and updated. Reference reviewed.	4.13.2021	
2Q 2022 annual review: remove reference to Kynamro as removed from the market, removed 40 and 60mg capsules per updated PI, references reviewed and updated	4.27.2022	

**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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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