# Clinical Policy: Lomitapide (Juxtapid)

Reference Number: CP.PHAR.283
Effective Date: 10.01.16
Last Review Date: 02.24
Line of Business: Commercial, Medicaid

Revision Log

**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 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® 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 ≥ 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. Age ≥ 18 years;

4. Documentation of recent (within the last 60 days) LDL-C of one of the following (a or b):
   a. ≥ 70 mg/dL;
   b. ≥ 55 mg/dL if member has ASCVD and is at very high risk (*see Appendix H*);
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 D*);
      ii. A moderate intensity statin (*see Appendix D*), and member has one of the following (a or b):
         a) Intolerance to two high intensity statins;
         b) A statin risk factor (*see Appendix F*);
      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 F*) 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 E;
   b. For members who are statin intolerant, both of the following (i and ii):
      i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin),
      ii. Member meets one of the following (a or b):
         a) Member has documented statin risk factors (*see Appendix F*);
         b) Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (1 and 2):
            1) Documentation of intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
            2) 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 E or member has a history of ezetimibe intolerance (e.g., associated diarrhea or upper respiratory tract infection);
8. Failure of a preferred PCSK9 inhibitor, if applicable, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for PCSK9 inhibitors*
9. Treatment plan does not include coadministration with Leqvio®, Repatha®, or Praluent®;
10. Dose not exceed (a and b):
    a. 60 mg per day;
    b. 2 capsules per day.

**Approval duration: 6 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. Homozygous Familial Hypercholesterolemia** (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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. Treatment plan does not include coadministration with Leqvio, Repatha, or Praluent;
5. If request is for a dose increase, new dose does not exceed (a and b):
   a. 60 mg per day;
   b. 2 capsules per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and 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.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

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

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| ezetimibe/simvastatin (Vytorin®) | 10/40 mg PO QD | 10 mg-40 mg/day (use of the 10/80 mg dose is restricted to patients who have been taking simvastatin 80 mg for 12 months or more without evidence of muscle toxicity) |
| ezetimibe (Zetia®) | 10 mg PO QD | 10 mg/day |
| atorvastatin (Lipitor®) | 40 mg PO QD | 80 mg/day |
| rosuvastatin (Crestor®) | 5 - 40 mg PO QD | 40 mg/day |
| Repatha® (evolocumab) | 420 mg SC once monthly | 420 mg/month |
| Praluent® (alirocumab) | 150 mg SC every 2 weeks | 300 mg/month |

*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.*

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

| **High Intensity Statin Therapy**<br>***Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%*** |
|---|
| • Atorvastatin 40-80 mg<br>• Rosuvastatin 20-40 mg |
| **Moderate Intensity Statin Therapy**<br>***Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%*** |
| • Atorvastatin 10-20 mg<br>• Fluvastatin XL 80 mg<br>• Fluvastatin 40 mg BID<br>• Lovastatin 40 mg<br>• Pitavastatin 1-4 mg<br>• Pravastatin 40-80 mg<br>• Rosuvastatin 5-10 mg<br>• Simvastatin 20-40 mg |
| **Low Intensity Statin Therapy**<br>***Daily dose shown to lower LDL-C, on average, by < 30%*** |
| • Simvastatin 10 mg<br>• Pravastatin 10–20 mg<br>• Lovastatin 20 mg<br>• Fluvastatin 20–40 mg |

*Appendix E: Statin and Ezetimibe Contraindications*

| **Statins** |
|---|
| • Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy)<br>• Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment<br>• Pregnancy*, actively trying to become pregnant, or nursing<br>• 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 |
| **Ezetimibe** |
| • Moderate or severe hepatic impairment [Child-Pugh classes B and C]<br>• Hypersensitivity to ezetimibe (e.g., anaphylaxis, angioedema, rash, urticaria) |

**In July 2021, the FDA requested removal of the contraindication against use of statins in pregnant women. Because the benefits of statins may include prevention of serious or potentially fatal events in a small group of very high-risk pregnant patients, contraindicating these drugs in all pregnant women is not appropriate. https://www.fda.gov/safety/medical-product-safety-information/statins-drug-safety-communication-fda-requests-removal-strongest-warning-against-using-cholesterol*

*Appendix F: Statin Risk Factors*

| Statin Risk Factors |
| --- |
| • Multiple or serious comorbidities, including impaired renal or hepatic function<br>• Unexplained alanine transaminase (ALT) elevations > 3 times upper limit of normal, or active liver disease<br>• Concomitant use of drugs adversely affecting statin metabolism<br>• Age > 75 years, or history of hemorrhagic stroke<br>• Asian ancestry |

*Appendix G: General Information*

- 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 stain 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.

*Appendix H: Criteria for Defining Patients at Very High Risk of Future ASCVD Events*[3, 16, 13]
Very high risk is defined as having either a history of multiple major ASCVD events **OR** 1 major ASCVD event and multiple high-risk conditions:

- Major ASCVD events:
  - Recent acute coronary syndrome (within the past 12 months)
  - History of myocardial infarction (other than recent acute coronary syndrome event listed above)
  - History of ischemic stroke
  - Symptomatic peripheral artery disease (history of claudication with ankle-brachial index < 0.85 or previous revascularization or amputation)
- High-risk conditions:
  - Age ≥ 65 years
  - FH

- History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
- Diabetes
- Hypertension
- Chronic kidney disease (estimated glomerular filtration rate [eGFR] 15-59 mL/min/1.73 $m^2$)
- Current tobacco smoking
- Persistently elevated LDL-C (LDL-C ≥ 100 mg/dL [≥ 2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
- History of congestive heart failure

## 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:<br><br>Dosage – duration of administration before considering increase to next dosage:<br>5 mg QD – at least 2 weeks<br>10 mg, 20 mg, 40 mg QD – at least 4 weeks for each dose<br><br>• Doses should be escalated gradually based on acceptable safety and tolerability.<br>• Modify dosing for patients taking concomitant cytochrome P450 (CYP) 3A4 inhibitors, renal impairment, or baseline hepatic impairment.<br>• Dose adjustments are also required for patients who develop transaminase values at least 3x ULN during Juxtapid treatment. | 60 mg/day |

## VI. Product Availability

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

## VII. References

1. Juxtapid Prescribing Information. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; September 2020. Available at: http://www.juxtapidpro.com/prescribing-information. Accessed November 28, 2023.
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3. Jacobson TA, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 – full report. Journal of Clinical Lipidology. March-April 2015; 9(2): 129-169. http://dx.doi.org/10.1016/j.jacl.2015.02.003.

4. Goldber AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. Journal of Clinical Lipidology. June 2011; 5(3S): 1-15
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10. Thompson PD, Panza G, Zaleski A, et al. Statin-associated side effects. JACC 2016;67(20):2395-2410.
11. Lloyd-Jones DM, Morris PB, Ballntyne CM, et al. 2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2022; 80 (14): 1366-1418.
12. Warden BA, Guyton JR, Kovacs AC, et al. Assessment and management of statin-associated muscle symptoms (SAMS): A clinical perspective from the National Lipid Association. Published September 9, 2022. Available at: https://www.lipid.org/nla/clinical-perspective-assessment-management-statin-associated-muscle-symptoms-sams. Accessed October 18, 2022.
13. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines [published correction appears in Circulation. 2023 Sep 26;148(13):e148]. Circulation. 2023;148(9):e9-e119.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 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 | 11.05.19 | 02.20 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| updated based on 2018 ACC/AHA guidelines; references reviewed and updated. | | |
| 1Q 2021 annual review: added requirement for adherence to statin therapy on re-auth; references reviewed and updated. | 11.02.20 | 02.21 |
| 1Q 2022 annual review: no significant changes; removed references to Kynamro since it has been withdrawn from market; removed 40 mg and 60 mg capsules per updated PI; references reviewed and updated. | 10.01.21 | 02.22 |
| Template changes applied to other diagnoses/indications and continued therapy section. | 09.20.22 | |
| 1Q 2023 annual review: per 2022 ACC expert consensus decision pathway, lowered minimum LDL requirement to 55 mg/dL for members with ASCVD at very high risk and added corresponding Appendix H; references reviewed and updated. | 10.18.22 | 02.23 |
| Revised redirection to Repatha to instead state "failure of a preferred PCSK9 inhibitor, if applicable." | 11.16.23 | 12.23 |
| 1Q 2024 annual review: added Leqvio to list of drugs where coadministration is not allowed; added the following requirement from initial approval criteria to also require for continuation of therapy "Treatment plan does not include coadministration with Leqvio, Repatha, or Praluent"; Appendix I clarified that smoking is specific to tobacco and revised HeFH to FH; references reviewed and updated. | 11.28.23 | 02.24 |

**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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.