MEDICAL MUTUAL®

Drug Policy

Policy:	Juxtapid® (lomitapide) capsules	Annual Review Date: 05/16/2024 Last Revised Date: 05/16/2024

OVERVIEW

Juxtapid, a microsomal triglyceride transfer protein inhibitor, is indicated as an adjunct to a low fat diet and other lipid modifying therapies, including low-density lipoprotein (LDL) apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol, apolipoprotein B, and non-high-density lipoprotein cholesterol in adults with **homozygous familial hypercholesterolemia** (HoFH).[1] Limitations of use include that the safety and efficacy of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH).[1] Also, the effect of Juxtapid on cardiovascular (CV) morbidity and mortality have not been determined.

Repatha® (evolocumab subcutaneous [SC] injection) and Praluent® (alirocumab SC injection), two proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors, are indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with HoFH who require additional LDL-C lowering.[2,3] It is notable that patients known to have two LDL-receptor negative alleles (little or no residual function) did not respond or had minimal response to these agents. PCSK9 inhibitors are well tolerated and not associated with hepatotoxicity.[2] Simvastatin, atorvastatin, and rosuvastatin are statins that are indicated for the management of patients with HoFH.[4-6] Ezetimibe is also indicated for use in combination with atorvastatin or simvastatin in patients with HoFH.[7] Ezetimibe/simvastatin tablets are indicated for use in HoFH.[8]

POLICY STATEMENT

This policy involves the use of Juxtapid. Prior authorization is recommended for pharmacy benefit coverage of Juxtapid. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Juxtapid as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Juxtapid be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Juxtapid is recommended in those who meet the following criteria:

1. **Initial Homozygous Familial Hypercholesterolemia**

Patient must meet the following criteria (A, B, C, D, E, and F):

A) Patient is ≥ 18 years of age; AND

B) Patient meets one of the following (i, ii, or iii):

i. Patient has phenotypic confirmation of homozygous familial hypercholesterolemia; OR
Note: Examples include pathogeneic variants at the low-density lipoprotein receptor (LDLR), apolipoprotein B (apo B), proprotein convertase subtilisin kexin type 9 (PCSK9), or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene; OR

ii. Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level > 400 mg/dL AND meets one of the following [documentation required] (a or b):
Note: Untreated refers to prior therapy with any antihyperlipidemic agent.

a) Patient had clinical manifestation of HoFH before 10 years of age [documentation required]; OR
Note: Clinical manifestations of HoFH are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma.

b) At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with heterozygous familial hypercholesterolemia (HeFH) [documentation required]; OR
Note: An example of familial hypercholesterolemia is an untreated low-density LDL-C level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL.

iii. Patient has a treated LDL-C level ≥ 300 mg/dL AND meets one of the following [documentation required] (a or b):
Note: Treated refers to after therapy with at least one antihyperlipidemic agent. Some examples of antihyperlipidemic agents include statins (e.g., atorvastatin, rosuvastatin, lovastatin, simvastatin, pravastatin), ezetimibe, PCSK9 inhibitors (i.e., Repatha [evolocumab injection for subcutaneous use], Praluent [alirocumab injection for subcutaneous use]), and Evkeeza (evinacumab-dgnb injection for intravenous use).

a) Patient had clinical manifestations of HoFH before 10 years of age [documentation required]; OR
Note: Examples of clinical manifestations of HoFH are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma.

b) At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with HeFH [documentation required]; AND
Note: An example of familial hypercholesterolemia is an untreated LDL-C ≥ 190 mg/dL and/or an untreated total cholesterol > 250 mg/dL.

C) Patient meets one of the following (i or ii):

i. Patient meets both of the following (a and b):

a) Patient has tried at least one proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor for ≥ 8 continuous weeks [documentation required]; AND
Note: Examples of PCSK9 inhibitors include Repatha and Praluent.

b) LDL-C level after this PCSK9 inhibitor therapy remains ≥ 70 mg/dL [documentation required]; OR

ii. Patient is known to have two LDL-receptor negative alleles [documentation required]; AND

D) Patient meets one of the following criteria (i or ii):

i. Patient meets all of the following criteria (a, b and c):
- **a)** Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin tablets ≥ 20 mg daily [as a single-entity or as a combination product]) [documentation required]; AND
- **b)** Patient has tried one high-intensity statin along with ezetimibe (as a single entity or as a combination product) for ≥ 8 continuous weeks [documentation required]; AND
- **c)** LDL-C level after this treatment regimen remains ≥ 70 mg/dL [documentation required]; OR

ii. Patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):
- **a)** Patient experienced statin-related rhabdomyolysis [documentation required]; OR
  Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
- **b)** Patient meets all of the following criteria [(1), (2), and (3)]:
  - **(1)** Patient experienced skeletal-related muscle symptoms [documentation required]; AND
    Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).
  - **(2)** The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) [documentation required]; AND
  - **(3)** When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin) [documentation required]; AND
    Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

2. Continuation of Treatment for Homozygous Familial Hypercholesterolemia

Patient must meet the following criteria (A, B, and C):
- **A)** The above initial criteria are still met; AND
- **B)** Provider has checked ALT and AST (at a minimum) since initiation and monthly within the first year or every 3 months after the first year and adjusted the dose of Juxtapid if the ALT or AST are ≥3x ULN. (Note: for clinically significant liver toxicity the prescriber should discontinue Juxtapid).
- **C)** The patient is having a beneficial response (as determined by the prescriber) as well as a reduction in LDL levels.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 90 days (3 months)
B) *Extended Approval:* 180 days (6 months)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Juxtapid has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Heterozygous Familial Hypercholesterolemia (HeFH).** The safety and effectiveness of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH, including those with HeFH.[1]

2. **Hyperlipidemia.** The safety and efficacy of Juxtapid have not been established in patients with hypercholesterolemia who do not have HoFH.[1]

   Note: This is not associated with homozygous familial hypercholesterolemia and may be referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), mixed dyslipidemia, or increased/elevated low-density lipoprotein cholesterol (LDL-C) levels.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Juxtapid® capsules [prescribing information]. Dublin, Ireland: Amryt; September 2020.
2. Repatha® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; September 2021.
3. Praluent® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; April 2021.
4. Zocor® tablets [prescribing information]. Jersey City, NJ: Organon; March 2022.
5. Lipitor® tablets [prescribing information]. New York, NY: Pfizer; November 2021.
6. Crestor® tablets [prescribing information]. Wilmington, DE: AstraZeneca; September 2021.
7. Zetia® tablets [prescribing information]. Jersey City, NJ: June 2021.
8. Vytorin® tablets [prescribing information]. Whitehouse Station, NJ: Merck; September 2020.
9. Cuchel M, Bruckert E, Ginsberg HN, et al, for the European Atherosclerosis Society Consensus Panel on Familial Hypercholesterolaemia. Homozygous familial hypercholesterolemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolemia of the European Atherosclerosis Society. *Eur Heart J*. 2014;35:2146-2157.
10. Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. *J Clin Lipidol*. 2011;5:S1-S8.
11. Raal FJ, Hovingh GK, Catapano AL. Familial hypercholesterolemia treatments: guidelines and new therapies. *Atherosclerosis*. 2018;277:483-492.

12. Lloyd-Jones DM, Morris PB, Ballantyne CM. 2017 focused update of the 2016 ACC Expert Consensus Decision Pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *J Am Coll Cardiol*. 2017;70(14):1785-1822.