BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 8/16/13**
SECTION: DRUGS	**LAST REVIEW DATE: 8/02/18**
	LAST CRITERIA REVISION DATE: 8/02/18
	ARCHIVE DATE:

JUXTAPID® (lomitapide) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

JUXTAPID® (lomitapide) oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Juxtapid (lomitapide) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Age is 18 years or older

2. A confirmed diagnosis of homozygous familial hypercholesterolemia (HoFH) by **ONE** of the following
   - Genetic confirmation of a homozygous mutation of LDLR gene
   - An untreated LDL-C greater than 500 mg/dL (or greater than 300 mg/dL if on treatment) with **EITHER:**
     - Cutaneous or tendon xanthomas before age 10
     - Documented evidence of heterozygous familial hypercholesterolemia in **both** parents

3. Individual is currently on and adherent with other lipid lowering treatment

4. Individual is currently on and adherent with a low-fat diet

5. Individual is currently on and adherent with use of a supplement(s) that contains 400 IU vitamin E, 200 mg linoleic acid, 210 mg alpha-linoleic acid (ALA), 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA)

6. **ALL** of the following baseline tests have been obtained before initiation of treatment:
   - Negative pregnancy test, in females of reproductive potential
   - ALT, AST, alkaline phosphatase, and total bilirubin as required by the Juxtapid Risk Evaluation and Mitigation Strategy (REMS) Program

7. There are **NO** contraindications:
   - Contraindications include:
     - Pregnancy
     - Simultaneous use of strong to moderate CYP3A4 inhibitors (see Definitions section)
     - Moderate or severe hepatic impairment (Child-Pugh Class B or C)
     - Active liver disease including unexplained persistent abnormal liver function tests

8. Individual does not have hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption

9. Will not be used to treat individuals who do not have a diagnosis of homozygous familial hypercholesterolemia

10. Will not be used with Praluent (alirocumab) or Repatha (evolocumab)

11. Women of child bearing potential must be using adequate contraception during therapy

12. Woman who is breast feeding an infant or child should stop breast feeding

JUXTAPID® (lomitapide) oral capsule (cont.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Juxtapid (lomitapide) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition responded
    - Response is defined as:
        - Achieved and maintains at least a 50% in LDL-C from baseline
2. Individual has been adherent with the medication
3. Individual has been adherent with other lipid lowering therapy
4. Individual has been adherent with low fat diet
5. Individual has been adherent with use of a supplement(s) that contains 400 IU vitamin E, 200 mg linoleic acid, 210 mg alpha-linoleic acid (ALA), 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA)
6. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect such as:
        - Liver toxicity
7. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Juxtapid (lomitapide) is a microsomal triglyceride transfer protein (MTP) inhibitor 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).

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

HoFH is a rare inherited disorder in which the body cannot remove low-density lipoprotein cholesterol (LDL-C). HoFH is caused by a loss of function mutations in both alleles of the low-density lipoprotein receptor (LDLR) gene that encodes the LDLR protein. HoFH may also be considered in an individual with untreated LDL of greater than

JUXTAPID® (lomitapide) oral capsule (cont.)

500 mg/dL (or an LDL-C 300 mg/dL if on treatment) and one of the following: cutaneous or tendinous xanthomas before age 10, untreated LDL-C of greater than 190 mg/dL in both parents, or evidence of HeFH in both parents.

Individuals with HoFH have markedly impaired removal of LDL-C from the circulation that results from reduced or absent hepatic LDL receptor activity. The hepatic LDL receptor plays a critical role in regulating the concentration of LDL-C in the blood. In the absence of functional LDL receptors, the uptake of LDL-C from the blood is impaired and concentrations of LDL-C are extremely elevated. As a direct consequence to markedly elevated LDL-C blood levels, individuals with HoFH develop dramatically early and severe atherosclerotic cardiovascular disease (ASCVD) and often, early cardiac-related death. Symptomatic ASCVD often presents during the first 2 decades of life. HoFH affects approximately 1 in 1,000,000 individuals.

MTP plays a key role in the assembly and release of apo B-containing lipoproteins, including LDL-C, and inhibition of this protein significantly lowers associated plasma lipid levels. It is an intracellular lipid-transfer protein found in the lumen of the endoplasmic reticulum and is responsible for binding and shuttling individual lipid molecules between membranes. Normal concentrations and function of MTP in the liver and intestine are necessary for the proper assembly and secretion of apo B-containing lipoproteins from the liver and chylomicrons from the intestine. Inhibition of MTP leads directly to decreases in circulating levels of apo B-containing lipoproteins, including LDL-C.

Juxtapid (lomitapide) directly binds and inhibits MTP. Juxtapid (lomitapide) prevents the assembly of apo B-containing lipoproteins in enterocytes and hepatocytes. The result is inhibition of the synthesis of chylomicrons and very-low density lipoproteins (VLDL). The inhibition of the synthesis of VLDL leads to reduced levels of plasma LDL-C.

Juxtapid (lomitapide) is only available through a restricted program called JUXTAPID REMS PROGRAM and therefore, it is only available from certified pharmacies that are enrolled in the program. Providers must be enrolled in the program in order to prescribe Juxtapid (lomitapide).

Definitions:

Homozygous familial hypercholesterolemia:
Loss of function mutations in both alleles of the LDLR gene

Heterozygous familial hypercholesterolemia:
Loss of function mutation in one allele of the LDLR gene

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The Child-Pugh classification system:

	Score: 1 point	**Score: 2 points**	**Score: 3 points**
Serum Albumin (g/dL)	>3.5	3.0 - 3.5	<3.0
Serum Bilirubin (mg/dL)	<2.0	2.0 - 3.0	>3.0
Prothrombin time (seconds)	1 - 4	4 - 6	>6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:

- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease

Inhibitors of Juxtapid metabolism; concurrent use is contraindicated (list is not all inclusive):

3A4 inhibitors:

Strong inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, tipranavir/ritonavir, voriconazole

Moderate inhibitors: amprenavir, aprepitant, atazanavir, ciprofloxacin, crizotinib, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, verapamil

Resources:

Juxtapid package insert, revised by manufacturer 05/2016, reviewed on 06-20-2016, 06-26-17.

Juxtapid package insert, revised by manufacturer 04/2015, reviewed on 06/13/2015

Juxtapid package insert, revised by manufacturer 05/2014, reviewed on 08/13/2014

Juxtapid package insert, revised by manufacturer 12/2012, reviewed on 01/09/2013

Juxtapid package insert, revised by manufacturer 08/2017, reviewed on 07/09/2018

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.