



Louisiana

obeticholic acid (Ocaliva[®])

Policy # 00538

Original Effective Date: 11/16/2016

Current Effective Date: 12/11/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider obeticholic acid (Ocaliva[®])[‡] for the treatment of primary biliary cholangitis (PBC) to be **eligible for coverage**.**

Patient Selection Criteria

Initial Authorization (6 months):

Coverage eligibility for obeticholic acid (Ocaliva) will be considered when the following criteria (I, II, III, and IV) are met:

- I. Patient has a diagnosis of primary biliary cholangitis (PBC) confirmed by meeting at least TWO of the following criteria (a, b, and/or c):
 - a. Alkaline phosphatase (ALP) elevated above the upper limit of normal as defined by normal laboratory reference values; AND/OR
 - b. Positive anti-mitochondrial antibodies (AMAs); AND/OR
 - c. Histologic evidence of PBC from a liver biopsy; AND
- II. Patient does NOT have cirrhosis OR patient has compensated cirrhosis withOUT evidence of portal hypertension; AND
- III. Patient is 18 years of age or older; AND
- IV. Patient meets ONE of the following (a or b):
 - a. Patient is using Ocaliva in combination with ursodeoxycholic acid (URSO[®]‡, URSO Forte[®], ursodiol)[‡] due to an inadequate response to ursodeoxycholic acid (URSO, URSO Forte, ursodiol) AFTER 1 year of therapy with ursodeoxycholic acid (URSO, URSO Forte, ursodiol). Inadequate response is defined as meeting ONE of the following (i or ii):

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- i. ALP greater than or equal to 1.67 times the upper limit of normal; OR
- ii. Total bilirubin greater than the upper limit of normal but less than two times the upper limit of normal; OR
- b. Patient is using Ocaliva as monotherapy due to an intolerance to ursodeoxycholic acid (URSO, URSO Forte, ursodiol)

Re-authorization (1 year)

Coverage eligibility for obeticholic acid (Ocaliva) will be considered when the following criteria are met:

- I. Patient has responded to Ocaliva therapy as determined by the prescribing physician (e.g., improved biochemical markers of primary biliary cholangitis [PBC] {e.g., alkaline phosphatase (ALP), bilirubin, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels}); AND
- II. Patient does NOT have cirrhosis OR patient has compensated cirrhosis without evidence of portal hypertension.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers obeticholic acid (Ocaliva) for any use other than its FDA approved indication OR when the patient selection criteria are not met to be **investigational.***

Background/Overview

Ocaliva is a farnesoid X receptor (FXR) agonist indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. The FDA approved Ocaliva under an accelerated approval based on a reduction in ALP. An improvement in survival or disease related symptoms has NOT been established. The FDA also states that continued approval for Ocaliva for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In 2021, a boxed warning was added to Ocaliva. Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with Ocaliva treatment in

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PBC patients with cirrhosis, either compensated or decompensated. Among post-marketing cases reporting it, median time to hepatic decompensation (e.g., new onset ascites) was 4 months for patients with compensated cirrhosis; median time to a new decompensation event (e.g., hepatic encephalopathy) was 2.5 months for patients with decompensated cirrhosis. It is recommended to discontinue Ocaliva in patients who develop hepatic decompensation, who have compensated cirrhosis and portal hypertension, who experience clinically significant hepatic adverse reactions, or who develop complete biliary obstruction. Ocaliva is supplied as 5 mg and 10 mg tablets. The starting dose of Ocaliva is 5 mg once daily in adults who have not achieved an adequate response to an appropriate dosage of UDCA for at least 1 year or are intolerant to UDCA. If an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of Ocaliva 5 mg daily and the patient is tolerating the medication, the dosage of Ocaliva can be increased to 10 mg once daily (which is also the maximum dosage).

Primary Biliary Cholangitis

Primary biliary cholangitis (previously referred to as primary biliary cirrhosis) is characterized by an ongoing immunologic attack in the intralobular ducts. This immunologic attack eventually leads to cirrhosis and liver failure. A number of complications occur in primary biliary cholangitis and these include pruritis, metabolic bone disease, hypercholesterolemia and xanthomas, malabsorption, vitamin deficiencies, hypothyroidism and anemia. There are currently only two products that are FDA approved for the treatment of this condition. Those include ursodeoxycholic acid (URSO, URSO Forte, ursodiol) and Ocaliva. The mainstay of therapy for the last couple of decades has been treatment with ursodeoxycholic acid.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Ocaliva was approved in May of 2016 for the treatment of primary biliary cholangitis in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. In 2021, a boxed warning was added to Ocaliva. It states: "Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with Ocaliva treatment in primary biliary cholangitis patients with either compensated or decompensated cirrhosis. Ocaliva is contraindicated in primary biliary cholangitis patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension. Permanently discontinue Ocaliva in patients who develop laboratory or clinical

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evidence of hepatic decompensation, have compensated cirrhosis and develop evidence of portal hypertension, or experience clinically significant hepatic adverse reactions while on treatment.”

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Ocaliva’s safety and efficacy was evaluated in a randomized, double-blind, placebo-controlled, 12 month trial in 216 patients with primary biliary cholangitis who were taking ursodeoxycholic acid for at least 12 months or who were unable to tolerate ursodeoxycholic acid. Patients included in the trial had an alkaline phosphatase (ALP) of 1.67 times the upper limit or normal or greater and/or if the total bilirubin was greater than 1 times the upper limit of normal, but less than 2 times the upper limit of normal. Patients were randomized to receive either Ocaliva 10 mg once daily for the entire 12 months of the trial, Ocaliva titration (5 mg once daily for the initial 6 months, with the option to increase to 10 mg once daily for the last 6 months if the patient was tolerating Ocaliva but had ALP 1.67 times the upper limit of normal or greater and/or total bilirubin greater than the upper limit of normal, or less than 15% ALP reduction), or placebo. Ocaliva was administered with ursodeoxycholic acid in 93% of patients during the trial, while 7% were unable to tolerate the ursodeoxycholic acid. The primary endpoint was a responder analysis at month 12. The response included three criteria: ALP less than 1.67 times the upper limit of normal, total bilirubin less than or equal to the upper limit of normal, and an ALP decrease of at least 15%. The responder rate was 48% in the Ocaliva 10 mg group, 46% in the Ocaliva titration group, and 10% in the placebo group.

References

1. Ocaliva [package insert]. Intercept Pharmaceuticals, Inc. New York, New York. May 2021.
2. UpToDate. Primary Biliary Cholangitis. Accessed October 2016.

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| 11/03/2016 | Medical Policy Committee review |
| 11/16/2016 | Medical Policy Implementation Committee approval. New policy. |
| 11/02/2017 | Medical Policy Committee review |
| 11/15/2017 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/08/2018 | Medical Policy Committee review |
| 11/21/2018 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/07/2019 | Medical Policy Committee review |
| 11/13/2019 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/05/2020 | Medical Policy Committee review |
| 11/11/2020 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/04/2021 | Medical Policy Committee review |
| 11/10/2021 | Medical Policy Implementation Committee approval. Added a criterion to note that patients should either have no cirrhosis OR compensated cirrhosis withOUT evidence of portal hypertension due to a new boxed warning for Ocaliva. |
| 11/03/2022 | Medical Policy Committee review |
| 11/09/2022 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/02/2023 | Medical Policy Committee review |
| 11/08/2023 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |

Next Scheduled Review Date: 11/2024

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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