Clinical Policy: Obeticholic acid (Ocaliva)

Reference Number: PA.CP.PHAR.287
Effective Date: 01/2018
Last Review Date: 07/17/19 Revision Log

Description
Obeticholic acid (Ocaliva®) is a farnesoid X receptor agonist.

FDA Approved Indication(s)
Ocaliva is 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.

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 Pennsylvania Health and Wellness® that Ocaliva is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Primary biliary cholangitis (must meet all)**:**

1. Diagnosis of PBC;
2. Prescribed by or in consultation with a hepatologist or gastrointestinal (GI) specialist;
3. Failure (as evidenced by sustained elevation in liver function tests) of ≥ 12 month trial of UDCA (ursodiol) at a dose of ≥ 13 mg/kg/day, unless contraindicated or clinically significant adverse effects are experienced;
4. Prescribed in combination with UDCA, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 10mg/day (1 tablet/day).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Primary biliary cholangitis (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as evidenced by (a or b):
   a. Initial reauthorization: reduction in alkaline phosphatase level from pretreatment level;
   b. Subsequent reauthorization: continued reduction or maintenance of initial reduction in alkaline phosphatase level;
3. If request is for a dose increase, new dose does not exceed 10 mg/day (1 tablet/day).
4. ;

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Obeticholic acid is an agonist for farnesoid X receptor (FXR), a nuclear receptor expressed in the liver and intestine. FXR is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. FXR activation decreases the intracellular hepatocyte concentrations of bile acids by suppressing de novo synthesis from cholesterol as well as by increased transport of bile acids out of the hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
ALP: alkaline phosphatase
FDA: Food and Drug Administration
GI: gastrointestinal
ICER: Institute for Clinical and Economic Review
NASH: non-alcoholic steatohepatitis
PBC: primary biliary cholangitis
UDCA: ursodeoxycholic acid
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
ursodiol (Urso®, Urso Forte®, Actigall®)	13-15 mg/kg/day PO in 2-4 divided doses	15 mg/kg/day

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

- Complete biliary obstruction

Appendix D: General Information

- Ocaliva is approved under accelerated approval based on a reduction in ALP. An improvement in survival or disease-related symptoms has not been established.

Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- Ocaliva is being evaluated for the treatment of non-alcoholic steatohepatitis (NASH). Results of a phase II trial are available. A Phase III trial is ongoing. Based on an ICER (Institute for Clinical and Economic Review) review, obeticholic acid as an off-label treatment for adults with NASH with fibrosis is not currently recommended. The limited evidence was deemed insufficient based on uncertainty regarding the long-term clinical effects of changes in surrogate endpoints and conflicting physiological outcomes while taking the drug (e.g., insulin resistance in one trial versus another trial).
- According to the AASLD Primary Biliary Cirrhosis 2009 practice guidelines, UDCA dosed at 13-15 mg/kg/day orally is recommended for all patients with PBC who have abnormal liver enzyme values regardless of histological stage. Improvement in liver tests will be seen within a matter of a few weeks and 90% of the improvement usually occurs within 6-9 months. The eligibility criteria in the Ocaliva efficacy trial required enrolled patients to have a minimum 12 month history of taking UDCA.
- Ocaliva prescribing information includes a black box warning for hepatic decompensation and failure (in some cases fatal) in incorrectly dosed PBC patients with Child-Pugh Class B or C or decompensated cirrhosis. The recommended starting dose is 5 mg once weekly for these patients titrated to 10mg twice weekly (at least 3 days apart) based on response and tolerability.
- In the PBC clinical trial, response was defined as a composite of three criteria: ALP less than 1.67-times the ULN, total bilirubin less than or equal to ULN, and an ALP decrease of at least 15%. The ULN for ALP was defined as 118 U/L for females and 124 U/L for males. The ULN for total bilirubin was defined as 1.1 mg/dL for females and 1.5 mg/dL for males.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PBC	5 mg PO QD titrated after 3 months to 10 mg PO QD based on efficacy and tolerability Dose adjustments required for Child-Pugh Class B/C or patients with prior decompensation event	10 mg/day

V. Product Availability

Tablets: 5 mg, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
3Q 2018 annual review: added prescriber requirement; removed criteria confirming diagnosis; modified UDCA monotherapy trial duration to 12 months from 6 months based on Ocaliva package labeling and treatment guideline recommendations; references reviewed and updated	08/18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

References

1. Ocaliva Prescribing Information. New York, NY: Intercept Pharmaceuticals, Inc.; February 2018. Available at https://ocaliva.com/. Accessed May 8, 2018.
2. Lindor, KD, Gershwin ME, Poupon R et al. AASLD Practice Guidelines: Primary biliary cirrhosis. Hepatology. 2009; 50(1): 291-308.
3. European Association for the Study of the Liver (EASL). EASL clinical practice guidelines: the diagnosis and management of patients with primary biliary cholangitis. J Hepatology. 2017;67:145-72.