Clinical Policy Title:	Obeticholic acid
Policy Number:	RxA.246
Drug(s) Applied:	Ocaliva®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
obeticholic acid (Ocaliva®)	PBC	5 mg PO once daily titrated after 3 months to 10 mg PO once daily based on efficacy and tolerability. Dose adjustments required for Child-Pugh Class B/C or patients with prior decompensation event.	10 mg/day

Dosage Forms

- Tablets: 5 mg, 10 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 gastroenterologist;
3. Age ≥ 18 years;
4. 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;
5. Prescribed in combination with UDCA, unless contraindicated or clinically significant adverse effects are

experienced;
6. Dose does not exceed 10 mg (1 tablet) per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Primary Biliary Cholangitis (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Initial reauthorization: reduction in alkaline phosphatase (ALP) level from pretreatment level;
   b. Subsequent reauthorization: continued reduction or maintenance of initial reduction in ALP level;
3. If request is for a dose increase, new dose does not exceed 10 mg (1 tablet) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AASLD: American Association for the Study of Liver Diseases
NASH: Non-alcoholic steatohepatitis
PBC: Primary biliary cholangitis
ALP: Alkaline phosphatase
UDCA: Ursodeoxycholic acid
FDA: Food and Drug Administration
ULN: Upper limit of normal
FXR: Farnesoid X receptor
ICER: Institute for Clinical and Economic Review

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
ursodiol (Urso®, Urso Forte®)	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/Boxed Warnings
- Contraindication(s):
  - Complete biliary obstruction.

- Boxed Warning(s):
  - Hepatic decompensation and failure in incorrectly dosed PBC patients with Child-Pugh class B or C or decompensated cirrhosis.

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 2018 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.
- In 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.

References

1. Ocaliva® Prescribing Information. New York, NY: Intercept Pharmaceuticals, Inc.; February 2020. Available at https://www.interceptpharma.com/wp-content/uploads/2020/02/US-Package_Insert-07Feb2020_VV-REG-030820.pdf. Accessed April 22, 2021.
2. Lindor, KD, Bowlus CL, Boyer J et al. Primary Biliary Cholangitis: 2018 Pracitice Guidance from the American Association for the Study of Liver Diseases (AASLD). Hepatology. 2018; 0(0): 1-26. Available at: https://www.aasld.org/sites/default/files/guideline_documents/PracticeGuidelines-PBCNovember2018.pdf. Accessed April 22, 2021.
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. Accessed April 22, 2021.
4. Obeticholic Acid for the Treatment of Nonalcoholic Steatohepatitis: Comparative Clinical Effectiveness and Value. Institute for Clinical and Economic Review (ICER). July 26, 2016. Available at: https://icerreview.org/wpcontent/uploads/2016/07/NECEPAC_OCA_NASH_Evidence_Report_FINAL.pdf. Accessed April 22, 2021.
5. Younossi ZM, Bernstein D, Shiffman ML, Kwo P, Kim WR, Kowdley KV, Jacobson IM. Diagnosis and Management of Primary Biliary Cholangitis. Am J Gastroenterol. 2019 Jan;114(1):48-63. doi: 10.1038/s41395-018-0390-3. PMID: 30429590. Accessed April 22, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1) Policy title was updated.	06/16/2020	09/14/2020

2) Approval duration for Medicaid was added. 3) Continued Therapy Approval criteria II.A.1 was rephrased. 4) References were updated.		
Policy was reviewed: 1. Policy title table updated. 2. Clinical policy section standard verbiage was updated to include "The provision of prescriber samples…". 3. Continued therapy II.A.1 criteria was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Appendix B for therapeutic alternatives standard verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance...". Updated also to remove brand Actigall® due to discontinuation. 5. References were updated.	04/22/2021	06/10/2021