

# Drug Policy

<b>Policy:</b>	<b>Ocaliva (obeticholic acid)</b>	<b>Annual Review Date:</b> <b>05/16/2024</b>
		<b>Last Revised Date:</b> <b>05/16/2024</b>

## OVERVIEW

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. Ocaliva was approved for this indication under accelerated approval based on reduction in alkaline phosphatase (ALP). An improvement in survival or PBC-related symptoms has not been established. The prescribing information notes that continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Description/Mechanism of Action: Ocaliva is structurally similar to an endogenous bile acid, with the addition of an ethyl group in the 6-alpha position (6 $\alpha$ -ethyl-CDCA), which makes it a 100-fold more potent agonist at the 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. Activation of FXR reduces the intracellular concentrations of bile acids in hepatocytes by suppressing de novo synthesis from cholesterol and by increased transport of bile acids out of the hepatocytes. In general, these mechanisms limit the amount of circulating bile acid, while promoting choleresis, and therefore reduce hepatic exposure to bile acids.

## POLICY STATEMENT

This policy involves the use of Ocaliva. Prior authorization is recommended for pharmacy benefit coverage of Ocaliva. 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 Ocaliva as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Ocaliva 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 Ocaliva is recommended in those who meet the following criteria:

- 1. Primary Biliary Cholangitis (PBC), also known as Primary Biliary Cirrhosis, Initial Therapy**  
**Criteria.** *Patient must meet the following criteria*

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- A. Patient is 18 years of age or older; AND
- B. Ocaliva is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician; AND
- C. The patient has a diagnosis of PBC as defined by TWO of the following according to the prescribing physician:
  - a. Alkaline phosphatase (ALP) elevated above the upper limit of normal (ULN) 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
- D. Patient meets ONE of the following criteria:
  - a. Patient has been receiving ursodiol therapy for  $\geq 1$  year and has had an inadequate response according to the prescriber; OR
  - b. According to the prescriber the patient is unable to tolerate ursodiol therapy; AND  
Note: Examples of ursodiol therapy include ursodiol generic tablets and capsules, Urso 250, Urso Forte, and Actigall.
- E. Patient meets one of the following (a or b):
  - a) Patient does not have cirrhosis; OR
  - b) Patient has compensated cirrhosis without evidence of portal hypertension; AND  
Note: Examples of evidence of portal hypertension include ascites, gastroesophageal varices, and persistent thrombocytopenia. Ocaliva is contraindicated in these patients.
- F. Ocaliva will be used in combination with ursodeoxycholic acid, unless the patient is intolerant

## 2. PBC, Patients Currently Receiving Therapy

**Criteria.** Patient must meet the following criteria

- A. Patient is 18 years of age or older; AND
- B. Ocaliva is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician; AND
- C. Patient meets one of the following (a or b):
  - a. Patient does not have cirrhosis; OR
  - b. Patient has compensated cirrhosis without evidence of portal hypertension; AND  
Note: Examples of evidence of portal hypertension include ascites, gastroesophageal varices, and persistent thrombocytopenia. Ocaliva is contraindicated in these patients.
- D. The patient has responded to Ocaliva therapy as determined by the prescriber (e.g. improved biochemical markers of PBC [e.g., alkaline phosphatase, bilirubin, gamma-glutamyl transpeptidase [GGT], aspartate aminotransferase [AST], alanine aminotransferase [ALT]); AND
- E. Ocaliva will be used in combination with ursodeoxycholic acid, unless the patient is intolerant

### Initial Approval/ Extended Approval.

A) Initial Approval: 180 days

B) Extended Approval: 365 days

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### CONDITIONS NOT RECOMMENDED FOR APPROVAL

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Ocaliva 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. Alcoholic Liver Disease.** There are no data available to support the use of Ocaliva in patients with alcoholic hepatitis. Ocaliva is not FDA-approved for this indication and current alcoholic liver disease guidelines do not make recommendations regarding therapy with Ocaliva. Additional well-controlled studies are needed.
- 2. Nonalcoholic Fatty Liver Disease (NAFLD), including Nonalcoholic Fatty Liver (NAFL) or Nonalcoholic Steatohepatitis (NASH).** There are limited data available evaluating the efficacy of Ocaliva in patients with NAFLD and NASH. Ocaliva is not FDA-approved for this indication and current NAFLD guidelines do not make recommendations regarding therapy with Ocaliva. Additional well-controlled studies are needed.
- 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

- Ocaliva® tablets [prescribing information]. San Diego, CA: Intercept Pharmaceuticals Inc.; May 2016.
- Intercept Pharmaceuticals. Obeticholic Acid. Briefing document for the Food and Drug Administration Gastrointestinal Drugs Advisory Committee. Meeting Date: April 7, 2016. Available at: <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/GastrointestinalDrugsAdvisoryCommittee/UCM494110.pdf>. Accessed on April 21, 2016.
- Pyrsoopoulos NT. Primary Biliary Cirrhosis. Medscape Drugs, Diseases & Procedures Reference. Updated June 25, 2015. Available at: <http://emedicine.medscape.com/article/171117-overview>. Accessed on May 9, 2016.
- Lindor KD, Gershwin ME, Poupon R, et al. American Association for the Study of Liver Diseases (AASLD) practice guidelines: primary biliary cirrhosis. *Hepatology*. 2009;50(1):291-308.
- Silveira MG, Brunt EM, Heathcote J, et al. American Association for the Study of Liver Diseases Endpoints Conference: design and endpoints for clinical trials in primary biliary cirrhosis. *Hepatology*. 2010;52(1):349-359.
- Hirschfield GM, Mason A, Luketic V, et al. Efficacy of obeticholic acid in patients with primary biliary cirrhosis and inadequate response to ursodeoxycholic acid. *Gastroenterol*. 2015;148:751-761.
- Urso 250® tablets and Urso Forte® tablets [prescribing information]. Bridgewater, NJ: Aptalis Pharma US, Inc.; June 2013.

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8. Mousa H, Lleo A, Invernizzi P, et al. Advances in pharmacotherapy for primary biliary cirrhosis. *Expert Opin Pharmacother*. 2015;16(5):633-643.
9. Harms MH, Lammers WJ, Marmon T, et al. Improvement in estimated survival after 1 year of obeticholic acid treatment in primary biliary cholangitis [poster 352]. Presented at: the International Liver Congress 2016, the 51<sup>st</sup> Annual Meeting of the European Association for the Study of Liver Disease (EASL); Barcelona, Spain; April 13-17, 2016.
10. Mayo MJ, Kremer AE, Beuers U, et al. Mitigation of pruritus during obeticholic acid treatment in patients with PBC: strategies and successes [poster 357]. Presented at: the International Liver Congress 2016, the 51<sup>st</sup> Annual Meeting of the European Association for the Study of Liver Disease (EASL); Barcelona, Spain; April 13-17, 2016.
11. European Association for the Study of the Liver (EASL) clinical practice guidelines: management of cholestatic liver diseases. *J Hepatol*. 2009;51(2):237-267.
12. O'Shea RS, Dasarathy S, McCullough AJ, et al. Alcoholic liver disease: practice guideline by the American Association for the Study of Liver Diseases and the American College of Gastroenterology. *Hepatology*. 2010;51(1):307-328.
13. Neuschwander-Tetri BA, Loomba R, Sanyal AJ, et al. Farnesoid X nuclear receptor ligand obeticholic acid for non-cirrhotic, non-alcoholic steatohepatitis (FLINT): a multicenter, randomized, placebo-controlled trial. *Lancet*. 2015;385:956-965.
14. Ratziu V, Sanyal AJ, MacConell L, et al. REGENERATE: a phase 3, double-blind, randomized, long-term, placebo-controlled, multicenter study evaluating the safety and efficacy of obeticholic acid in subjects with nonalcoholic steatohepatitis [poster 488]. Presented at: the International Liver Congress 2016, the 51<sup>st</sup> Annual Meeting of the European Association for the Study of Liver Disease (EASL); Barcelona, Spain; April 13-17, 2016.
15. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2016 May 17]. Available from: [https://clinicaltrials.gov/ct2/results?term=obeticholic acid&Search=Search](https://clinicaltrials.gov/ct2/results?term=obeticholic+acid&Search=Search). Search term: obeticholic acid.
16. Chalasani N, Younassi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology*. 2012;55(6):2005-2023
17. Obeticholic acid. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 14 Feb 2018. Accessed on 13 June 2018.