Original Effective Date: 07/01/2019
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Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C16447-A

Ocaliva (obeticholic acid)

PRODUCTS AFFECTED

Ocaliva (obeticholic acid)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Primary biliary cholangitis (PBC)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY BILIARY CHOLANGITIS:
1. Documented diagnosis of primary biliary cholangitis (PBC)
   AND
2. Documentation of TWO of the following that support the diagnosis [DOCUMENTATION REQUIRED]:

i. Biochemical evidence of cholestasis based on alkaline phosphatase (ALP) elevation
ii. Presence of antimitochondrial antibody (AMA) or other PBC- specific autoantibodies (including sp100 or gp210, if AMA is negative)
iii. Histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts

AND

3. Documentation of the member's baseline (prior to treatment) alkaline phosphatase (ALP) level [DOCUMENTATION REQUIRED]
AND
4. Documentation member has been receiving ursodiol therapy (e.g., ursodiol generics, Urso250®, Urso Forte®, Actigall®) for ≥ 1 year at doses of 13-15 mg/kg/day and has had an inadequate response (alkaline phosphatase level > 1.67 times the upper limit of normal); OR According to the prescribing physician the member is unable to tolerate ursodiol therapy
AND
5. Member is not on concurrent treatment or will not be used in combination with Iqirvo (elafibranor) or Livdelzi (seladelpar) as verified by prescriber attestation, member medication fill history, or submitted documentation
AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Ocaliva (obeticholic acid) include: patients with complete biliary obstruction, patients with decompensated cirrhosis (e.g., Child- Pugh Class B or C) or a prior decompensation event, patients with compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia).]
AND
7. Prescriber attests they will monitor the member for hepatic adverse events
AND
8. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

CONTINUATION OF THERAPY:

A. PRIMARY BILIARY CHOLANGITIS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Documentation of positive response to therapy as indicated by alkaline phosphatase (ALP) decrease of at least 15% from pretreatment AND is less than 1.67-times the upper limit of normal (ULN) [DOCUMENTATION REQUIRED]
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
4. Prescriber attests that member does not have cirrhosis OR for a member that has cirrhosis, that the member has compensated cirrhosis with no evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia) and has not had a decompensation event. NOTE: Ocaliva should be permanently discontinued in patients who develop laboratory or clinical evidence of hepatic decompensation or who have compensated cirrhosis and develop evidence of portal hypertension.
AND
5. Documentation the member continues to receive ursodiol therapy OR According to the prescribing physician the member is unable to tolerate ursodiol therapy

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Recommended starting dosage is 5 mg orally once daily for 3 months
If an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of 5 mg once daily, and the member is tolerating Ocaliva, increase the dosage to 10 mg once daily.

Maximum Quantity Limits – Max dosage of 10mg once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Farnesoid X Receptor (FXR) Agonists

FDA-APPROVED USES:
Indicated for the treatment of adult patients with primary biliary cholangitis (PBC), without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

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 (6α-ethyl-CDCA), which makes it a 100-fold more potent 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.

In December 2024, the FDA issued a safety update for Ocaliva. Based on the review of postmarket clinical trial data, the FDA identified cases of serious liver injury among patients being treated for primary biliary cholangitis (PBC) with Ocaliva (obeticholic acid) who did not have cirrhosis of the liver. The FDA previously identified that PBC patients with advanced cirrhosis were at risk of serious liver injury when taking Ocaliva and updated the prescribing information to restrict its use in these patients. FDA's review of this required clinical trial found that some cases of liver injury in patients without cirrhosis resulted in liver transplant. This risk was notably higher for patients taking Ocaliva compared with a placebo. The FDA restricted the use of Ocaliva in patients who have PBC with advanced cirrhosis of the liver in 2021 because it can cause serious harm in those patients, adding a new contraindication to use of Ocaliva. However, the FDA's recent review of case reports submitted to them found that some patients with PBC and advanced cirrhosis were still taking the medicine despite these restrictions. The FDA recommends that frequent liver test monitoring is necessary to identify worsening liver function and ensure appropriate discontinuation of Ocaliva in light of this new safety information.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Ocaliva (obeticholic acid) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Ocaliva (obeticholic acid) include: Patients with complete biliary obstruction, decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event, or compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia).

OTHER SPECIAL CONSIDERATIONS:

Ocaliva has a Black Box Warning for Hepatic Decompensation and Failure in Primary Biliary Cholangitis Patients with cirrhosis. Per the package labeling:

- Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis.
- OCALIVA is contraindicated in PBC 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 evidence of hepatic decompensation, have compensated cirrhosis and develop evidence of portal hypertension, or experience clinically significant hepatic adverse reactions while on treatment.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina*

adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Ocaliva TABS 5MG, 10MG

REFERENCES

1. Ocaliva® tablets [prescribing information]. Morristown, NJ: Intercept Pharmaceuticals Inc.; May 2022.
2. 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.
3. Pyrsopoulos NT. Primary Biliary Cirrhosis. Medscape Drugs, Diseases & Procedures Reference. Updated June 25, 2015. Available at: http://emedicine.medscape.com/article/171117-overview.
4. 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.
5. 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.
6. 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.
7. Mousa H, Lleo A, Invernizzi P, et al. Advances in pharmacotherapy for primary biliary cirrhosis. Expert Opin Pharmacother. 2015;16(5):633-643.
8. 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 51st Annual Meeting of the European Association for the Study of Liver Disease (EASL); Barcelona, Spain; April 13-17, 2016.
9. 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 51st Annual Meeting of the European Association for the Study of Liver Disease (EASL); Barcelona, Spain; April 13-17, 2016.
10. European Association for the Study of the Liver (EASL) clinical practice guidelines: management of cholestatic liver diseases. J Hepatol. 2009;51(2):237-267.
11. 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.
12. Neuschwander-Tetri BA, Loomba R, Sanyal AJ, et al. Farnesoid X nuclear receptor ligand obeticholic acid for noncirrhotic, non-alcoholic steatohepatitis (FLINT): a multicenter, randomized, placebo-controlled trial. Lancet. 2015;385:956-965.
13. 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].
14. Lindor, K. D., Bowlus, C. L., Boyer, J., Levy, C., & Mayo, M. (2018). Primary biliary cholangitis: 2018 practice guidance from the American Association for the study of liver diseases. Hepatology.

doi:10.1002/hep.30145
15. Lindor, K. D., Bowlus, C. L., Boyer, J., Levy, C., & Mayo, M. (2021). Primary biliary cholangitis: 2021 practice guidance update from the American Association for the study of liver diseases. Hepatology, 75(4), 1012-1013. doi:10.1002/hep.32117

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Background	Q1 2025
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q1 2023
REVISION- Notable revisions: Prescriber Requirements Quantity	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file