Drug Coverage Policy

Effective Date 10/1/2025
Coverage Policy Number.....IP0304
Policy Title.....Ocaliva

Hepatology – Ocaliva

- Ocaliva® (obeticholic acid tablets – Intercept Pharmaceuticals)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Ocaliva, a farnesoid X receptor agonist, is indicated for the treatment of **primary biliary cholangitis** in adults without cirrhosis, or with compensated cirrhosis who do not have evidence of portal hypertension.[1] It is specifically indicated to be given either in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA.

Guidelines
The American Association for the Study of Liver Diseases (AASLD) guidelines for primary biliary cholangitis (2018) state that the diagnosis can be confirmed when patients meet two of the following criteria: 1) there is cholestasis as evidenced by alkaline phosphatase elevation; 2) anti-mitochondrial antibodies are present, or if negative for anti-mitochondrial antibodies, other primary biliary cholangitis-specific autoantibodies, including sp100 or gp210, are present; 3) there is histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts. It is specifically noted that diagnosis in a patient who is negative for anti-mitochondrial antibodies does not require a liver biopsy if other diagnostic criteria are met.[4] Treatment with UDCA (available in the US as ursodiol) is the recommended treatment for patients with primary biliary cholangitis who have abnormal liver enzyme values regardless of histologic stage.[3] Following 12 months of UDCA therapy, the patient should be evaluated to determine if second-line therapy is appropriate. It is estimated that up to 40% of patients have an inadequate response to UDCA; Ocaliva should be considered for these patients. An update to the 2018 AASLD guidelines for primary biliary cholangitis (2021) provide two updated recommendations:[9] 1) Fibrates can be considered as off-label alternatives for patients with primary biliary cholangitis and inadequate response to UDCA. However, fibrates are discouraged in patients with decompensated liver disease; and 2) Ocaliva is contraindicated in patients with advanced cirrhosis, defined as cirrhosis with current or prior evidence of liver decompensation (e.g., encephalopathy, coagulopathy) or portal hypertension (e.g., ascites, gastroesophageal varices, or persistent thrombocytopenia). In addition, the AASLD recommends careful monitoring of any patient with cirrhosis, even if not advanced, receiving Ocaliva.

The European Association for the Study of the Liver guidelines for diagnosis and management of patients with primary biliary cholangitis (2017) make similar recommendations.[7]

Safety
Ocaliva has a Boxed warning regarding hepatic decompensation and failure in patients with primary biliary cholangitis and cirrhosis.[1] Ocaliva is contraindicated in patients with primary biliary cholangitis with decompensated cirrhosis and patients with a prior decompensation event. It is also contraindicated in patients with compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, and persistent thrombocytopenia) as well as those with complete biliary obstruction.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Ocaliva. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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, approval requires Ocaliva to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Ocaliva is considered medically necessary when the following is met:

FDA-Approved Indication

1. **Primary Biliary Cholangitis.** Approve Ocaliva for the duration noted if the patient meets ONE of the following (A or B):
   Note: Primary Biliary Cholangitis is also known as Primary Biliary Cirrhosis.
   A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND

ii. According to the prescriber, the patient has a diagnosis of primary biliary cholangitis as defined by TWO of the following (TWO of a, b, or c):
- **a)** Alkaline phosphatase is elevated above the upper limit of normal as defined by normal laboratory reference values; OR
- **b)** Positive anti-mitochondrial antibodies or other primary biliary cholangitis-specific auto-antibodies, including sp100 or gp210, if anti-mitochondrial antibodies are negative; OR
- **c)** Histologic evidence of primary biliary cholangitis from a liver biopsy; AND

iii. Patient meets ONE of the following (a or b):
- **a)** According to the prescriber, the patient has been receiving ursodiol therapy for ≥ 1 year and has had an inadequate response; 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.

iv. 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.

v. The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician; OR

B) Patient is Currently Receiving Therapy. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. 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.

ii. Patient has responded to Ocaliva as determined by the prescriber.
Note: Examples of a response to Ocaliva therapy are improved biochemical markers of primary biliary cholangitis (e.g., alkaline phosphatase [ALP], bilirubin, gamma-glutamyl transpeptidase [GGT], aspartate aminotransferase [AST], alanine aminotransferase [ALT]).

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Ocaliva for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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 from AASLD (2019) do not make recommendations regarding therapy with Ocaliva.[1,8] Additional well-controlled studies are needed.

2. **Nonalcoholic Fatty Liver Disease (NAFLD), including Nonalcoholic Fatty Liver (NAFL) or Nonalcoholic Steatohepatitis (NASH).** Ocaliva is not FDA-approved for this indication and current NAFLD guidelines from AASLD (2023) do not recommend the off-label use of obeticholic acid to treat NASH until additional safety and efficacy data become available.[1,8]

References

1. Ocaliva® tablets [prescribing information]. Morristown, NJ: Intercept Pharmaceuticals; May 2022.
2. Nevens F, Andreone P, Mazzella G, et al. A placebo-controlled trial of obeticholic acid in primary biliary cholangitis. *N Engl J Med.* 2016;375(7):631-643.
3. Tsuneyama K, Baba H, Morimota Y, et al. Primary biliary cholangitis: its pathological characteristics and immunopathological mechanisms. *J Med Invest*. 2017;64(1.2):7-13.
4. Lindor KD, Bowlus CL, Boyer J, et al. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases (AASLD). *Hepatology*. 2019;69(1):394-419.
5. Trauner M, Nevens F, Shiffman ML, et al. Long-term efficacy and safety of obeticholic acid for patients with primary biliary cholangitis: 3-year results of an international open-label extension study. *Lancet Gastroenterol Hepatol*. 2019;4(6):445-453.
6. European Association for the Study of the Liver (EASL). EASL clinical practice guidelines: the diagnosis and management of patients with primary biliary cholangitis. *J Hepatol*. 2017;67:145-172.
7. Crabb DW, Im GY, Szabo G, et al. Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2020;71(1):306-333.
8. Rinella, M, Neuschwander B, Siddiqui, M, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 77(5):1797-1835, May 2023.
9. Lindor KD, Bowe CL, Boyer J, et al. Primary biliary cholangitis: 2021 practice guideline update from the American Association for the Study of Liver Diseases. *Hepatology.* 2022;75:1012-1013.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** policy title from "Obeticholic Acid" to "Hepatology – Ocaliva" **Primary Biliary Cholangitis.** **Updated** "Documented intolerance or contraindication with ursodiol (ursodeoxycholic acid)" to "According to the prescriber the patient is unable to tolerate ursodiol therapy; Note: Examples of ursodiol therapy include ursodiol generic tablets and capsules, Urso 250, Urso Forte, and Actigall." **Added** a note to: "Has compensated cirrhosis without evidence of portal hypertension" **Added** "Patient is Currently Receiving Therapy" criteria"	11/1/2024

Annual Revision	No criteria changes.	10/1/2025

The policy effective date is in force until updated or retired