VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Hepatology – Ocalvia Prior Authorization Policy
- Ocaliva® (obeticholic acid tablets – Intercept Pharmaceuticals)

REVIEW DATE: 07/22/2020

OVERVIEW

Ocaliva is indicated for the treatment of primary biliary cholangitis in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA.[1] Ocaliva was approved for this indication under accelerated approval based on reduction in alkaline phosphatase. An improvement in survival or primary biliary cholangitis-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.

Disease Overview

Primary biliary cholangitis is a chronic, progressive, cholestatic liver disease in which autoimmune destruction of small and medium intrahepatic bile ducts leads to cholestasis.[3,4] Cholestasis eventually progresses to advanced fibrosis, cirrhosis, and liver failure.[3-5] The serologic hallmark of primary biliary cholangitis is the finding of anti-mitochondrial antibodies in the serum.[3,4] In the 5% to 10% of patients in which anti-mitochondrial antibodies is absent or present only in low titer, nearly all will have primary biliary cholangitis-specific antinuclear antibodies, including sp100 and gp210, which are present in over 30% of patients who are negative for anti-mitochondrial antibodies by indirect immunofluorescence. The biochemical hallmark of primary biliary cholangitis is the finding of an elevated alkaline phosphatase level.[5]

Clinical Efficacy

The pivotal study evaluated Ocaliva in adult patients with primary biliary cholangitis who either had an inadequate response to UDCA (93% of patients) or were unable to tolerate UDCA (7% of patients).[2] The primary efficacy endpoint (composite of alkaline phosphatase level < 1.67 times the upper limit of normal, ≥ 15% reduction in alkaline phosphatase, and a total bilirubin ≤ upper limit of normal at Month 12) was met by 46% and 47% of patients treated with Ocaliva 5 mg and Ocaliva 10 mg, respectively. There were significant reductions in alkaline phosphatase with both Ocaliva groups early in treatment and sustained throughout the 12-month study. Through Year 3, Ocaliva therapy has resulted in a sustained reduction in alkaline phosphatase.[2,6]

Guidelines

The American Association for the Study of Liver Disease 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. Treatment with UDCA (available in the US as ursodiol) at a dose of 13 to 15 mg/kg/day orally 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 pateints. 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]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Ocaliva. 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. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ocaliva is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Primary Biliary Cholangitis (also known as Primary Biliary Cirrhosis).** Approve Ocaliva for the duration noted if the patient meets one of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (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 (a, b, c):
       - **a)** Alkaline phosphatase is elevated above the upper limit of normal as defined by normal laboratory reference values;
       - **b)** Positive anti-mitochondrial antibodies or other primary biliary cholangitis-specific auto-antibodies, including sp100 or gp210, if anti-mitochondrial antibodies are negative;
       - **c)** Histologic evidence of primary biliary cholangitis from a liver biopsy; AND
     - **iii.** Patient meets ONE of the following criteria (a or b):
       - **a)** Patient has been receiving ursodiol therapy for ≥ 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®.
     - **iv.** The agent is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician.
   - **B)** Patient is Currently Receiving Therapy. Approve for 1 year if the patient has responded to Ocaliva therapy 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, bilirubin, gamma-glutamyl transpeptidase [GGT], aspartate aminotransferase [AST], alanine aminotransferase [ALT]).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ocaliva is not recommended in the following situations:

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 (2010) 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 (2018) recommend against the off-label use of obeticholic acid to treat NASH until additional safety and efficacy data become available.[1,9]

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Ocaliva® tablets [prescribing information]. New York, NY: Intercept Pharmaceuticals Inc.; January 2018.
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. Pyrsopoulos NT. Primary Biliary Cirrhosis. Medscape Drugs, Diseases & Procedures Reference. Updated November 8, 2017. Available at: http://emedicine.medscape.com/article/171117-overview. Accessed on July 17, 2020.
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*. 2018;0:1-26.
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. 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.
7. 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.
8. 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.
9. 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 (AASLD). *Hepatology*. 2018;67(1):328-357.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual revision	No changes.	07/11/2018
Annual revision	• Primary Biliary Cholangitis: Wording in reference to "according to the prescribing physician" was changed to "according to the prescriber". For initial therapy approval, to confirm the diagnosis of primary biliary cholangitis, added that patients could be positive for anti-mitochondrial antibodies (AMAs) or other PBC-specific auto-antibodies including sp100 or gp210, if AMA is negative. Changed the approval duration for "Patients Currently Receiving Therapy" from 3 years to 1 year. Removed age requirement and specialist requirement from the criteria for "Patients Currently Receiving Therapy".	07/24/2019
Annual revision	No criteria changes.	07/22/2020