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Obeticholic Acid

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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. 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

This policy supports medical necessity review for obeticholic acid (**Ocaliva**®) tablets.

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

Medical Necessity Criteria

Obeticholic acid (Ocaliva) tablets are considered medically necessary when the following are met:

1. **Primary Biliary Cholangitis.** Individual meets **ALL** of the following criteria:
   A. Age 18 years of age or older
   B. Has a diagnosis of primary biliary cholangitis as confirmed by **TWO** of the following:
      i. Alkaline phosphatase is elevated above the upper limit of normal as defined by normal laboratory reference values
      ii. Positive antimitochondrial antibodies or other primary biliary cholangitis-specific auto-antibodies (anti-sp100 and/or anti-gp210 and/or antibodies against the major M2

components [PDC-E2, 2-oxo-glutaric acid dehydrogenase complex]) if antimitochondrial antibodies are negative or in low titer (less than 1:80)
iii. Histologic evidence of primary biliary cholangitis from a liver biopsy

C. Has **ONE** of the following:
i. Inadequate response with ursodiol (ursodeoxycholic acid) despite at least 1 year of therapy
ii. Documented intolerance or contraindication with ursodiol (ursodeoxycholic acid)

D. Meets **ONE** of the following:
i. Does not have cirrhosis
ii. Has compensated cirrhosis without evidence of portal hypertension

E. Medication is prescribed by, or in consultation with, a gastroenterologist, hepatologist, or liver transplant physician.

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.

Reauthorization Criteria

Continuation of obeticholic acid (Ocaliva) tablets are considered medically necessary for primary biliary cholangitis when there is documentation of beneficial response and the individual meets **ONE** of the following:

1. Does not have cirrhosis

2. Has compensated cirrhosis without evidence of portal hypertension

Authorization Duration

Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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

Background

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.

References

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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.
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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.