Drug and Biologic Coverage Policy

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Obeticholic Acid

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Related Coverage Resources

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.

Coverage Policy

Obeticholic acid (Ocaliva®) is considered medically necessary when ALL of the following criteria are met:

- Age 18 years of age and older
- Documented diagnosis of primary biliary cholangitis (PBC; also known as primary biliary cirrhosis)
- Individual has at least two of the following:
  - History of elevated alkaline phosphatase (ALP) for at least 6 months
  - Presence of antimitochondrial antibody (AMA) OR PBC specific antibodies (anti-GP210 and/or anti-SP100 and/or antibodies against the major M2 components [PDC-E2, 2-oxo-glutaric acid dehydrogenase complex]) if AMA negative or in low titer (less than 1:80)
  - Evidence of PBC on liver biopsy
- Individual has either of the following:
  - Documented intolerance or contraindication per FDA label with Ursodiol (ursodeoxycholic acid [UDCA])
  - Both of the following:
    - Inadequate response with Ursodiol (ursodeoxycholic acid [UDCA]) despite at least 6 months of therapy (e.g., inadequate reduction of ALP [greater than or equal to 1.67 times the upper limit of normal] and/or total bilirubin [greater than the upper limit of normal but less than two times the upper limit of normal]; evidence of disease progression on biopsy)
    - Ocaliva will be used in combination with Ursodiol
Initial authorization and reauthorization is up to 12 months.

Obeticholic acid (Ocaliva) is considered medically necessary for continued use when the following is met:

- Documentation of beneficial clinical response

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.

Obeticholic acid (Ocaliva) is considered experimental, investigational or unproven for ANY other use including the following:

- Non-alcoholic steatohepatitis (NASH)

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

FDA Approved Indications

FDA Approved Indication
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.

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.1

Recommended Dosing

FDA Recommended Dosing
Starting Dosage
The recommended starting dosage of Ocaliva is 5 mg orally once daily in adult patients who have not achieved an adequate biochemical response to an appropriate dosage of UDCA for at least 1 year or are intolerant to UDCA is dependent upon disease stage.

- Non-cirrhotic patients or compensated cirrhotic patients with no or mild hepatic impairment (Child-Pugh Class A) are dosed once daily.
- Cirrhotic patients with moderate or severe hepatic impairment (Child-Pugh Class B or C) or patients who have previously experienced a decompensation event are dosed initially once weekly and not more than twice weekly.

Maximum Dosage
The maximum recommended dosage of Ocaliva is 10 mg once daily.

Other FDA Information
On September 21, 2017, the FDA issued a drug safety communication warning about serious liver injury with obeticholic acid being incorrectly dosed in some patients with moderate to severe decreases in liver function resulting in an increased risk of serious liver injury and death. (FDA, 2017)

General Background

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
The serologic hallmark of primary biliary cholangitis is the finding of anti-mitochondrial antibodies in the serum. 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.

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). 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.

Professional Societies/Organizations
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. 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. The European Association for the Study of the Liver guidelines for diagnosis and management of patients with primary biliary cholangitis (2017) make similar recommendations.

Experimental, Investigational, Unproven Uses
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. Additional well-controlled studies are needed.

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.

Coding/ Billing Information

Note: Obeticholic acid is typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

References

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