obeticholic acid (Ocaliva®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO141

Description

Obeticholic acid (Ocaliva) is a Farnesoid X Receptor (FXR) agonist that works by suppressing bile acid synthesis and increasing bile acid transport out of the hepatocytes, thus reducing overall hepatic exposure to toxic levels of bile acids.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
obeticholic acid (Ocaliva)	5 mg tablets	Primary Biliary Cholangitis (PBC)	30 tablets/30 days
	10 mg tablets		

Initial Evaluation

I. Obeticholic acid (Ocaliva) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a gastroenterologist or hepatologist; **AND**
   B. A diagnosis of **Primary Biliary Cholangitis (PBC)** [i.e. primary biliary cirrhosis]; **AND**
      1. Diagnosis confirmed by **TWO** of the following:
         i. Alkalaine phosphate (e.g. ALP) level at least 1.5 times the upper limit of normal
         ii. Positive antimitochondrial antibodies (AMA) test
         iii. Histopathologic evidence (i.e. nonsuppurative cholangitis and destruction of small or medium-sized bile ducts); **AND**
      2. Treatment with ursodeoxycholic acid (e.g. Urso, Ursodiol) has been ineffective, contraindicated, or not tolerated; **AND**
         i. Inadequate response is defined as an alkaline phosphate level greater than 1.67 times the upper limit of normal after one year of treatment with ursodeoxycholic acid; **AND**
      3. Member has compensated liver disease (Child-Pugh A).

II. Obeticholic acid (Ocaliva) is considered investigational when used for all other conditions, including but not limited to:

A. Non-alcoholic steatohepatitis (NASH)
B. Non-alcoholic fatty liver disease (NAFLD)
C. Familial partial lipodystrophy
D. Obesity

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has a diagnosis of **Primary Biliary Cholangitis (PBC)** [i.e. primary biliary cirrhosis]; **AND**
    A. Member has compensated liver disease (Child-Pugh A); **AND**
IV. Member has exhibited improvement or stability of disease symptoms (e.g. reduction of pruritus, reduced fatigue, or decrease in alkaline phosphate levels)

Supporting Evidence

I. Obeticholic acid (Ocaliva) is FDA-approved for the treatment of primary biliary cholangitis (PBC) when used in combination with ursodeoxycholic acid (UDCA) in adults with inadequate response to UDCA; or, as monotherapy in adults unable to tolerate UDCA.
II. Per the American Association for the Study of Liver Diseases (AASLD) guidelines, UDCA at a dose of 13 to 15 mg/kg/day is the first-line therapy for PBC.
III. Treatment response in PBC is monitored using liver biochemical values - specifically, serum ALP and total bilirubin. Improvements in liver tests are typically seen within a few weeks, with the majority of liver test improvements occurring within 6 to 9 months. About 20% of patients will have normalization of liver biochemistries after two years.
IV. Per guidelines, the benefit of obeticholic acid (Ocaliva) in patients with decompensated liver disease is unestablished. In September 2017, the FDA issued a warning regarding inappropriate dosing of obeticholic acid (Ocaliva) in patients with moderate to severe liver impairment (Child-Pugh-Turcotte B and C), which was associated with worsening PBC and death. Therefore, the use of obeticholic acid (Ocaliva) in patients with decompensated PBC is not recommended.

Investigational or Not Medically Necessary Uses

I. Obeticholic acid (Ocaliva) has not been sufficiently evaluated in the following settings:
    A. Non-alcoholic steatohepatitis (NASH)
        1. Obeticholic acid (Ocaliva) is being studied in an ongoing clinical trial that enrolled 2,480 participants. A total of 931 patients with stage F2–F3 fibrosis were included

in the primary analysis [311 in the placebo group, 312 in the obeticholic acid (Ocaliva) 10 mg group, and 308 in the obeticholic acid (Ocaliva) 25 mg group]. An interim analysis was done after a minimum of 750 randomized patients with fibrosis stages F2 or F3 reached their actual or planned month-18 visit.

- The primary endpoint of fibrosis improvement by at least one stage with no worsening of NASH was met by 37 (12%) patients in the placebo group, 55 (18%) patients in the obeticholic acid (Ocaliva) 10 mg group (p=0.045 vs placebo), and 71 (23%) patients in the obeticholic acid (Ocaliva) 25 mg group (p=0.0002 vs placebo).
- The primary endpoint of NASH resolution (based on no hepatocellular ballooning and no residual lobular inflammation) with no worsening of fibrosis **did not** meet statistical significance in the intent-to-treat population (25 [8%] patients in the placebo group vs 35 [11%] in the obeticholic acid (Ocaliva) 10 mg group [p=0·18] or 36 [12%] in the obeticholic acid (Ocaliva) 25 mg group [p=0·13]).
- Treatment-emergent adverse events occurred in 548 (83%) patients in the placebo group, 579 (89%) in the obeticholic acid (Ocaliva) 10 mg group, and 601 (91%) in the obeticholic acid (Ocaliva) 25 mg group.
- Pruritus was the most common adverse event and was seen in 123 (19%) patients in placebo group, 183 (28%) patients in the obeticholic acid (Ocaliva) 10mg group, and 336 (51%) patients in the obeticholic acid (Ocaliva) 25mg group.
- The end-of-study analysis will evaluate the effect of obeticholic acid (Ocaliva) on clinical outcomes (including progression to cirrhosis and all-cause mortality) and the long-term safety of obeticholic acid and will be completed once approximately 291 adjudicated clinical outcome events occur. Patients are expected to have a minimum follow-up time of approximately 4 years.

2. According to the practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association first line treatment for NASH is weight loss as it generally reduces hepatic steatosis, achieved either by hypocaloric diet alone or in conjunction with increased physical activity. Loss of at least 3-5% of body weight appears necessary to improve steatosis, but a greater weight loss (up to 10%) may be needed to improve necroinflammation.
3. Based on the data reviewed to date, the predicted benefit of obeticholic acid (Ocaliva) based on a surrogate histopathologic endpoint remains uncertain and does not sufficiently outweigh the potential risks for the treatment of patients

with liver fibrosis due to NASH. Additional efficacy and safety data are needed to support its use in NASH.

B. Non-alcoholic fatty liver disease (NAFLD)
C. Familial partial lipodystrophy
D. Obesity

References

1. Ocaliva [Prescribing Information]. New York, NY: Intercept Pharmaceuticals, Inc. January 2018.
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4. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. Hepatology. 2019;69(1):394-419.
5. Zobair M Younossi MD, Vlad Ratziu MD, Rohit Loomba MD, Mary Rinella MD, et al. Obeticholic acid for the treatment of non-alcoholic steatohepatitis: interim analysis from a multicentre, randomised, placebo-controlled phase 3 trial. The Lancet. December 2019. 394(10215): 2184–2196. doi: https://doi.org/10.1016/S0140-6736(19)33041-7
6. Chalasani N, Younossi 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, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012;55(6):2005-2023. https://www.ncbi.nlm.nih.gov/books/NBK548806/

Policy Implementation/Update:

Action and Summary of Changes	Date
Added supporting evidence for the investigational use in NASH	07/2020
Prior authorization criteria transitioned to policy format. Updated initial and renewal durations. Addition of specialist requirements. Addition of confirmed diagnosis and Child Pugh A classification. Further clarification of characteristics of inadequate response to ursodeoxycholic acid. Addition of renewal criteria.	12/2019
Policy created	06/2016