Pharmacy Policy Bulletin

Title:	Obeticholic acid (Ocaliva®)
Policy #:	Rx.01.186

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for Obeticholic acid (Ocaliva®) as provided under the member's prescription drug benefit.

Description:

Primary biliary cholangitis (PBC; previously referred to as primary biliary cirrhosis) is a chronic, progressive autoimmune cholestatic liver disease. PBC is characterized by a T-lymphocyte-mediated attack on small intralobular bile ducts. A continuous assault on the bile duct epithelial cells leads to their gradual destruction and eventual disappearance. The sustained loss of intralobular bile ducts causes the signs and symptoms of cholestasis. Ursodeoxycholic acid (UDCA), a naturally occurring hydrophilic bile acid, was the first therapy approved for the treatment of PBC. In individual trials and meta-analyses, UDCA has been associated with improved liver biochemistries as well as long-term outcomes (eg, reduction in the likelihood of liver transplantation or death); however, up to 40% of UDCA-treated patients have a suboptimal or absent response to UDCA. Although most patients with PBC are not cirrhotic, cirrhosis is the end stage of the disease and patients are at risk for all of the complications of cirrhosis. This includes hepatocellular carcinoma (HCC), portal hypertension, variceal bleeding, and the need for liver transplant. Other complications related to chronic cholestasis include osteopenia/osteoporosis, dyslipidemia, and vitamin deficiencies.

Obeticholic acid is an agonist for Farnesoid X Receptor (FXR), a nuclear receptor expressed in the liver and intestine. FXR is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. FXR activation decreases the intracellular hepatocyte concentrations of bile acids by suppressing *de novo* synthesis from cholesterol as well as by increased transport of bile acids out of the hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.

Obeticholic acid (Ocaliva®) is indicated for the treatment of adult patients with primary biliary cholangitis (PBC) without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

Policy:

INITIAL CRITERIA: Obeticholic acid (Ocaliva®) is approved when ALL of the following are met:

1. Diagnosis of primary biliary cholangitis (also known as primary biliary cirrhosis); and
2. Member is 18 years of age or older; and
3. One of the following:
    a. Used in combination with ursodeoxycholic acid and patient had suboptimal response to at least 12 consecutive months of treatment with ursodeoxycholic acid (e.g., Actigal, Urso, Urso Forte, ursodiol); or
    b. Inability to tolerate ursodeoxycholic acid; and
4. Prescribed by or in consultation with hepatologist or gastroenterologist; and
5. Member does not have evidence of advanced cirrhosis (i.e., cirrhosis with current or prior evidence of hepatic decompensation including encephalopathy or coagulopathy); and

6. Member does not have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Obeticholic acid (Ocaliva®) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Member does not have evidence of advanced cirrhosis (i.e., cirrhosis with current or prior evidence of hepatic decompensation including encephalopathy or coagulopathy); and
3. Member does not have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)

Reauthorization duration**:** 2 years

Black Box Warning as shown in the drug Prescribing Information:

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis. OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension. Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation; have compensated cirrhosis and develop evidence of portal hypertension; or experience clinically significant hepatic adverse reactions while on treatment.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Boonstra K, Beuers U, Ponsioen CY. Epidemiology of primary sclerosing cholangitis and primary biliary cirrhosis: a systematic review. *J Hepatol*. 2012;56(5):1181-8. Accessed January 06, 2023.

Carey EJ, Ali AH, Lindor KD. Primary biliary cirrhosis. *Lancet*. 2015;386(10003):1565-75. Accessed January 06, 2023.

Lindor KD, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote EJ; American Association for Study of Liver Diseases. Primary biliary cirrhosis. *Hepatology*. 2009;50(1):291-308. Accessed January 06, 2023.

Ocaliva® (obeticholic acid) [package insert]. New York, NY. Intercept Pharmaceuticals, Inc. May 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=cdfbe0cd-eb15-45a1-ac17-531bcda21aec&type=display. Accessed January 06, 2023.

Obeticholic acid. Lexi-drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at online.lexi.com.proxy1.lib.tju.ed. Accessed January 06, 2023.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Ocaliva®	Obeticholic acid

Cross References:

Off-Label Use Rx. 01.33

Policy Version Number:	8.00
P&T Approval Date:	December 08, 2022
Policy Effective Date:	April 01, 2023
Next Required Review Date:	December 08, 2023