Ocaliva (obeticholic acid) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
9/1/2023	10/1/2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Ocaliva® (obeticholic acid) Tablet	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 UDC		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Primary Biliary Cholangitis	Primary biliary cholangitis (PBC), formerly known as primary biliary cirrhosis, is an autoimmune chronic progressive cholestatic liver disease that predominantly affects women. PBC is characterized by a T-lymphocyte-mediated attack on small intralobular bile ducts eventually leading to their gradual destruction and disappearance, ultimately leading to cirrhosis and liver failure. Patients with PBC may be asymptomatic, or they may present with symptoms such as fatigue, pruritus, jaundice, cholestatic liver enzymes, and signs and symptoms of cirrhosis. Common laboratory test abnormalities in patients with PBC include elevated alkaline phosphatase (ALP), antimitochondrial antibodies (AMA), antinuclear antibodies (ANA), and hyperlipidemia.(2-5) According to the American Association for the Study of Liver Diseases (AASLD) 2018 Practice Guidance on Primary Biliary Cholangitis, the diagnosis of PBC is generally based on the presence of at least two of the following criteria:(2) 1. Biochemical evidence of cholestasis based on alkaline phosphatase (ALP) elevation 2. Presence of AMA (with a titer greater than 1:80), OR if AMA is negative (or present only in low titer [less than or equal to 1:80]), other PBC-specific auto antibodies including sp100 or gp210 3. Histologic evidence of PBC (nonsuppurative destruction cholangitis and destruction of interlobular bile ducts) Management of PBC includes treatment of symptoms and complications that result from chronic cholestasis and suppression of the underlying pathogenic process (destruction of small intralobular hepatic bile ducts). Ursodeoxycholic acid (ursodiol, UDCA) is first-line therapy for PBC.(2,3) UDCA improves biochemical indices and

	delays histologic progression, ultimately enhancing survival. UDCA has minimal side effects and is generally well tolerated. An inadequate response to UDCA, as defined by the Toronto criteria, is an alkaline phosphatase level greater than 1.67 times the upper limit of normal after one year of UDCA. In patients with an inadequate response to UDCA, obeticholic acid can be used in combination with UDCA or it can be used as monotherapy in patients who are unable to tolerate UDCA.(2) Fibrates can be considered as an off-label alternative for patients with PBC and an inadequate response to UDCA, but are discouraged in patients with decompensated liver disease.(7) Treatment response is monitored using liver biochemical tests. Specifically, serum ALP and total bilirubin predict outcomes in this context. Improvement is typically observed within a few weeks, and 90% of the improvement usually occurs by 6-9 months; about 20% of patients achieve normalization of liver biochemistries after two years.(2,3)
Efficacy	Ocaliva (obeticholic acid) is a farnesoid X receptor (FXR) agonist. FXR is 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 hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting choleresis, thus reducing hepatic exposure to bile acids.(1) Obeticholic acid was approved based on a randomized, double-blind, placebo controlled, 12-month trial in patients with PBC (POISE – NCT01473524). Inclusion criteria included an intolerance to UDCA or a suboptimal biochemical response to UDCA after 12 months of UDCA. Suboptimal biochemical response (treatment failure) was defined as ALP 1.67 times the upper limit of normal (ULN) or greater, and/or total bilirubin greater than the ULN but less than 2 times ULN.(1,6) Of note, the suboptimal biochemical response, defined for the study inclusion, was based on a modification of the Toronto criteria.(5,6) Primary endpoints for responders were defined as 3 criteria: ALP less than 1.67 times the ULN, total bilirubin less than or equal to ULN, and an ALP decrease of at least 15%.(1)
Safety(1)	Ocaliva has a boxed warning of hepatic decompensation and failure in incorrectly dosed PBC patients with Child-Pugh class B or C or decompensated cirrhosis. In post-marketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with PBC with decompensated cirrhosis or Child-Pugh Class B or C hepatic impairment when Ocaliva was dosed more frequently than recommended. Ocaliva is contraindicated in patients with complete biliary obstruction.

REFERENCES

Number	Reference
1	Ocaliva prescribing information. Intercept Pharmaceuticals, Inc. February 2022.
2	Lindor KD, Bowlus CL, Boyer J, et al. Primary Biliary Cholangitis: 2021 Practice Guidance Updated from the American Association for the Study of Liver Diseases (AASLD). Hepatology 75(4):p 1012-1013, April 2022. | DOI: 10.1002/hep.32117
3	Laschtowitz A, de Veer RC, Van der Meer AJ, Schramm C. Diagnosis and treatment of primary biliary cholangitis. United European Gastroenterol J. 2020 Jul;8(6):667-674. doi: 10.1177/2050640620919585. Epub 2020 Apr 16. PMID: 32299307; PMCID: PMC7437077.
4	Tanaka A. Current understanding of primary biliary cholangitis. Clin Mol Hepatol. 2021 Jan;27(1):1-21. doi: 10.3350/cmh.2020.0028. Epub 2020 Dec 3. PMID: 33264835; PMCID: PMC7820210.
5	European Association for the Study of the Liver (EASL) 2017 Clinical Practice Guidelines: The Diagnosis and Management of Patients with Primary Biliary Cholangitis.
6	Corpechot C, Poupon R, Chazouilleres O. New Treatments/Targets for Primary Biliary Cholangitis. J Hepatol Reports. 2019;1(3):203-213.

Number	Reference
7	Lindor KD, Bowlus CL, Boyer J, et al. Primary Biliary Cholangitis: 2021 Practice Guidance Update from the American Association for the Study of Liver Diseases (AASLD).

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Ocaliva	Obeticholic Acid Tab 10 MG	10 MG	M ; N ; O ; Y	N		
Ocaliva	Obeticholic Acid Tab 5 MG	5 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Ocaliva	Obeticholic Acid Tab 10 MG	10 MG	30	Tablets	30	DAYS			
Ocaliva	Obeticholic Acid Tab 5 MG	5 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Ocaliva	Obeticholic Acid Tab 10 MG	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ocaliva	Obeticholic Acid Tab 5 MG	5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of primary biliary cholangitis (PBC) and ALL of the following: 1. Diagnosis was confirmed by at least TWO of the following: A. There is biochemical evidence of cholestasis with an alkaline phosphatase (ALP) elevation B. Presence of antimitochondrial antibody (AMA): a titer greater than 1:80 C. If the AMA is negative or present only in low titer (less than or equal to 1:80), presence of other PBC-specific autoantibodies, including sp100 or gp210 D. Histologic evidence of nonsuppurative destruction cholangitis and destruction of interlobular bile ducts **AND** 2. The prescriber has measured the patient's baseline alkaline phosphatase (ALP) level and total bilirubin level (prior to therapy with the requested agent) **AND** 3. ONE of the following: A. The patient does NOT have cirrhosis **OR** B. The patient has compensated cirrhosis with NO evidence of portal hypertension **AND** 4. ONE of the following: A. BOTH of the following: 1. The patient has tried and had an inadequate response after at least 1 year of therapy with ursodeoxycholic acid (UDCA) (inadequate response defined as ALP greater than or equal to 1.67-times the upper limit of normal [ULN], and/or total bilirubin greater than the ULN but less than 2x ULN, after 1 year of treatment with UDCA) **AND** 2. The patient will continue treatment with ursodeoxycholic acid (UDCA) with the requested agent **OR** B. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ursodeoxycholic acid (UDCA) **OR** B. The patient has another FDA approved indication for the requested agent **OR** C. The patient has another indication that is supported in compendia for the requested agent **AND** 2. If the patient has an FDA approved indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist, hepatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence (for oncology also include NCCN: NCCN 1 or 2a recommended use) **Length of Approval**: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met:

Module	Clinical Criteria for Approval
	1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. ONE of the following: A. For primary biliary cholangitis (PBC), ALL of the following: 1. ONE of the following: A. The patient does NOT have cirrhosis **OR** B. The patient has compensated cirrhosis with NO evidence of portal hypertension **AND** 2. ONE of the following: A. The requested agent will be used in combination with ursodeoxycholic acid (UDCA) **OR** B. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ursodeoxycholic acid (UDCA) **AND** 3. The patient has had an alkaline phosphatase (ALP) decrease of greater than or equal to 15% from baseline (prior to therapy with the requested agent) AND ALP is less than 1.67-times the upper limit of normal (ULN) **AND** 4. The patient's total bilirubin is less than or equal to the upper limit of normal (ULN) **OR** B. For another FDA approved indication or another compendia supported indication, the patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist, hepatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Length of Approval**: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: 12 months