Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Ocaliva (obeticholic acid)

- **Prime Therapeutics will review Prior Authorization requests**
  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6453KS-OCVA.pdf

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional
Original Effective Date: June 5, 2016
Revision Date(s): June 5, 2016; October 1, 2016; October 15, 2017; October 1, 2018
Current Effective Date: October 1, 2018

Institutional
Original Effective Date: June 5, 2016
Revision Date(s): June 5, 2016; October 1, 2016; October 15, 2017; October 1, 2018
Current Effective Date: October 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Ocaliva Prior Authorization (PA) program is to ensure that patients prescribed therapy meet the selection requirements defined in product labeling and/or clinical guidelines and/or clinical studies. The PA defines appropriate use as the Food and Drug Administration (FDA) labeled indication or as supported by guidelines and/or clinical evidence.

Target Agent

- **Ocaliva** (obeticholic acid)

FDA Approved Indications and Dosage[4]

Agent	Indication	Dosing
Ocaliva® (obeticholic acid) Tablets	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	Initial dose: 5 mg once daily for first 3 months Maintenance dose: 10 mg once daily, for patients who have not achieved an adequate reduction in ALP and/or total bilirubin and who are tolerating Ocaliva Maximum dose: 10 mg once daily

POLICY

Prior Authorization Criteria and Quantity Limits for Approval

Initial Evaluation

Ocaliva (obeticholic acid) will be approved when following are met:

1. The patient has the diagnosis of Primary Biliary Cholangitis (PBC) confirmed by TWO of the following:
    a. There is biochemical evidence of cholestasis with an alkaline phosphatase elevation of at least 1.5 times the upper limit of normal
    b. Presence of antimitochondrial antibody (AMA): a titer of 1:40 or higher OR a level that is above the testing laboratory's upper limit of normal range
    c. Histologic evidence of nonsuppurative destruction cholangitis and destruction of interlobular bile ducts

    AND
2. The prescriber has documented the patient's baseline alkaline phosphatase (ALP) level and total bilirubin level

    AND

3. ONE of the following:
   a. BOTH of the following:
      i. The patient has tried and had an inadequate response to ursodeoxycholic acid (UDCA) for at least 1 year
      AND
      ii. The patient will continue treatment with ursodeoxycholic acid (UDCA) with the requested agent
   OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ursodeoxycholic acid (UDCA)

   AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
5. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
   OR
   b. ALL of the following
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

Length of Approval: 12 months

Renewal Evaluation

Ocaliva (obeticholic acid) will be approved when the following are met:

1. The patient has been previously approved for the requested agent through Prime Therapeutics Prior Authorization Review process
   AND
2. ONE of the following:
   a. The patient is currently on AND will continue treatment with ursodeoxycholic acid (UDCA) with the requested agent
   OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ursodeoxycholic acid (UDCA)

   AND
3. The patient has had an alkaline phosphatase (ALP) decrease of at least 15% from baseline 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)
   AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
6. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
      OR
   b. ALL of the following
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
         AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

Length of Approval: 12 months

Agent	FDA Labeled Contraindication(s)
Ocaliva (obeticholic acid)	Patients with complete biliary obstruction

Brand (generic)	Quantity Per Day Limit
Ocaliva (obeticholic acid)	
5 mg tablet	1 tablet
10 mg tablet	1 tablet

RATIONALE

Primary biliary cholangitis (PBC), also formerly known as primary biliary cirrhosis, involves an immunologic attack on the intrahepatic bile ducts ultimately leading to cirrhosis and liver failure.[2,3] Patients with PBC may be asymptomatic, or they may present with symptoms such as fatigue, pruritic, jaundice, cholestatic liver enzymes, antimitochondrial antibodies, and signs and symptoms of cirrhosis. Common laboratory test abnormalities in patients with PBC include elevated alkaline phosphatase, antimitochondrial antibodies (AMA), antinuclear antibodies (ANA), and hyperlipidemia.[3]

A diagnosis of PBC is established if there are no extrahepatic biliary obstruction, no comorbidity affecting the liver, and at least two of the following are present:

1. There is biochemical evidence of cholestasis based on mainly an alkaline phosphatase elevation (at least 1.5 times the upper limit of normal)
2. Presence of AMA (with a titer of 1:40 or higher)
3. Histologic evidence of PBC (nonsuppurative destruction cholangitis and destruction of interlobular bile ducts)[2,3]

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.[2,4] UDCA delays the progression to end-stage liver disease, enhance survival, and its good tolerability by patients.[2] An inadequate response to UDCA is defined as alkaline phosphatase levels > 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. Patients taking UDCA or obeticholic acid are monitored with liver biochemical tests. Improvement (assessed on liver biochemical tests) on UDCA typically occurs by 6-9 months with 20% of patients achieving normalization of liver biochemical tests by year 2. A liver biopsy is typically done when there is a suboptimal response to assess disease activity (defined as transaminase persistently above 5 times the upper limit of normal after at least 6 months of UDCA plus obeticholic acid). Beyond cirrhosis and liver failure, there are many other complications of PBC that need treatment. Complications include: pruritus, metabolic bone disease, hypercholesterolemia, xanthomas, malabsorption, vitamin deficiencies, hypothyroidism, and anemia.[2,4]

Obeticholic acid was approved based on randomized, double-blind, placebo controlled, 12-month trial in patients with PBC who were taking UDCA for at least 12 months, or who were unable to tolerate UDCA and did not receive UDCA for at least 3 months. Patient inclusion was ALP 1.67 times upper limit of normal (ULN) or greater and/or if total bilirubin was greater than 1 times ULN but less than 2 times ULN. Patients were excluded from the trial if they had other liver disease, presence of clinically significant hepatic decompensation events (i.e., portal hypertension and its complications, cirrhosis with complications or hepato-renal syndrome), severe pruritic, or Model for End Stage Liver Disease (MELD) score of 15 or greater. Prime end points 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]

REVISIONS

06-05-2016	Ocaliva (obeticholic acid) added to New to Market Drug medical policy effective 06-05-2016.
10-01-2016	Stand-alone policy effective 10-01-2016.
10-15-2017	In Policy section: Initial Evaluation ▪ In Item 2 b added "OR a level that is above the testing laboratory's upper limit of normal range" to read "Presence of antimitochondrial antibody (AMA): a titer of 1:40 or higher OR a level that is above the testing laboratory's upper limit of normal range" ▪ In Item 3 added "and total bilirubin level" to read "The prescriber has documented the patient's baseline (prior to treatment) phosphatase (ALP) level and total bilirubin level" Renewal Evaluation ▪ In Item 4 added "AND the total bilirubin is less than or equal to the upper limit of normal (ULN)" to read "The patient has had an alkaline phosphatase (ALP) decrease of at least 15% AND is less than 1.67-times the upper limit of normal (ULN) AND the total bilirubin is less than or equal to the upper limit of normal (ULN)"
	Rationale section updated
	References updated
10-01-2018	In Description section: ▪ Converted FDA Approved Indication and Dosage information into a chart for more clarity

	In Policy section: Summary of revisions: • Simplified requirement of diagnostic parameters language in initial evaluation • Renewal - clarified ALP decrease from baseline Initial Evaluation ▪ In Item 1 removed "as evidenced" and added" confirmed" and "three criteria a the time of diagnosis" to read "The patient has the diagnosis of Primary Biliary Cholangitis (PBC) confirmed by TWO of the following:" ▪ In Item 2 removed "(prior to treatment)" and added "alkaline" to read "The prescriber has documented the patient's baseline alkaline phosphatase (ALP) level and total bilirubin level" Renewal Evaluation ▪ Added "Ocaliva (obeticholic acid) will be approved when the following are met:" ▪ In Item 3 added "from basline" and "ALP" to read "The patient has had an alkaline phosphatase (ALP) decrease of at least 15% from baseline AND ALP is less than 1.67-times the upper limit of normal (ULN)"
	Rationale section updated
	References updated

REFERENCES

1. Ocaliva prescribing information. Intercept Pharmaceuticals, Inc. March 2018.
2. Lindor, Keith D., et al. Primary Biliary Cirrhosis. American Association for the Study of Liver Diseases (AASLD) Practice Guidelines. *Hepatology* 2009; 50 (1): 291-307.
3. Poupon, Raoul, MD., et al. Clinical Manifestations, Diagnosis, and Prognosis of Primary Biliary Cholangitis (primary biliary cirrhosis). UpToDate. Last updated January 2017. Literature current through April 2018.
4. UpToDate. Overview of the treatment of primary biliary cholangitis (primary biliary cirrhosis).