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

This program applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE
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 DRUGS
Ocaliva (obeticholic acid)

QUANTITY LIMIT TARGET DRUG- RECOMMENDED LIMIT

Brand (generic)	GPI	Multisource Code	Quantity per Day Limit
Ocaliva (obeticholic acid)			
5 mg tablet	52750060000320	M, N, O, Y	1 tablet
10 mg tablet	52750060000330	M, N, O, Y	1 tablet

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Ocaliva (obeticholic acid) will be approved when the following criteria are met:

Initial Evaluation
Obeticholic acid will be approved when following are met:

1. The patient does NOT have any FDA labeled contraindications to therapy with the requested agent
   AND
2. The patient has the diagnosis of Primary Biliary Cholangitis (PBC) as evidenced by TWO of the following three criteria at the time of diagnosis:
   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
3. The prescriber has documented the patient's baseline (prior to treatment) alkaline phosphatase (ALP) level and total bilirubin level
   AND
4. ONE of the following:
   a. BOTH of the following:
      i. The patient has tried treatment with ursodeoxycholic acid (UDCA) for at least 1 year and had an inadequate response
         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

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

1. The patient has been previously approved for therapy through Prime Therapeutics Prior Authorization Review process
AND
2. The patient does NOT have any FDA labeled contraindications to therapy with the requested agent
AND
3. 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

4. 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)
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

including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[4]

FDA Indication: For 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.

Dosing: The recommended starting dosage 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.

If an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months of 5 mg once daily, and the patient is tolerating Ocaliva, increase the dosage to 10 mg once daily.

CLINICAL RATIONALE[1-5]

Primary biliary cholangitis (PBC; also formerly known as primary biliary cirrhosis) is a female dominated (75-90%) progressive autoimmune disease of unknown etiology. However, it is believed to be due to both genetic predisposition and environmental triggers (e.g. infection with organisms of the family Enterobacteriaceae). Although not studied systemically, PBC has a published overall prevalence of 40.2 cases per 100,000 population (age- and sex-adjusted) and an overall incidence of 2.7 cases per 100,000 population (age-adjusted) in the United States. PBC involves an immunologic attack on the intrahepatic bile ducts ultimately leading to cirrhosis and liver failure. The majority of patients with PBC (90-95%) have the characteristic serologic signature AMA (antimitochondrial antibody), which has a 98% specificity for the disease.

The American Association for the Study of Liver Diseases (AASLD) recommends the following for PBC diagnosis: Two of the following three criteria must be met:

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 (a titer of 1:40 or higher)
3. Histologic evidence of nonsuppurative destruction cholangitis and destruction of interlobular bile ducts

Historically, ursodeoxycholic acid (ursodiol, UDCA) was the only FDA approved treatment for PBC and is advocated as first-line therapy due to its ability to delay progression to end-stage liver disease, enhance survival, and its good tolerability by patients. 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. After 5 years, another 15-35% will have normalization. A liver biopsy is typically done when there is a suboptimal response to assess disease activity. 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.

Ocaliva's indication was approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. The primary endpoint in trial 1 was a responder analysis at Month 12, where response was defined as a composite of three 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%. The FDA medical review of Ocaliva indicates that uncertainty remains whether ALP can predict outcomes in advanced stage disease; published literature currently supports total bilirubin to be a surrogate that predicts clinical outcomes in advanced disease. A knowledge gap exists in the literature about whether ALP reduction in advanced stage disease can be predictive of clinical outcomes similar to what was observed in the Ocaliva trials for early stage disease. It

is not known if ALP remains elevated in patients in advanced disease or whether it starts to trend downward or whether ALP normalizes. There is adequate evidence to support that a reduction of ALP is reasonably likely to predict clinical benefit; however until the phase 4, confirmatory trial is completed the validity of the ALP as a surrogate is unknown.[5]

REFERENCES

1. UpToDate. Overview of the treatment of primary biliary cholangitis (primary biliary cirrhosis). http://www.uptodate.com/contents/overview-of-the-treatment-of-primary-biliary-cholangitis-primary-biliary-cirrhosis?source=search_result&search=primary+biliary+cirrhosis&selectedTitle=1%7E132. Accessed 05/04/2017.
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3. Medscape. Primary Biliary Cirrhosis. http://emedicine.medscape.com/article/171117-overview. Accessed 05/05/2017.
4. Ocaliva prescribing information. Intercept. May 2016.
5. US FDA Ocaliva Medical Review. Created 07/8/16.