Pharmacy Policy Bulletin: J-0765 Primary Biliary Cholangitis – Commercial and Healthcare Reform	
Number: J-0765	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0765-009	**Original Date:** 09/07/2016
Effective Date: 10/28/2024	**Review Date:** 10/02/2024

Drugs Product(s):	• Iqirvo (elafibranor) • Livdelzi (seladelpar) • Ocaliva (obeticholic acid)

FDA-Approved Indication(s):	• Iqirvo
	  ○ Treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA.
	• Livdelzi
	  ○ Treatment of primary PBC in combination with UDCA in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA
	• Ocaliva
	  ○ Treatment of adult patients with primary PBC without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with UDCA with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

Background:	• PBC, formerly known as primary biliary cirrhosis, is a chronic autoimmune disease that results in the destruction of the bile ducts in the liver via inflammation. Bile is responsible for carrying waste products to the intestine and the destruction of the bile ducts results in waste products remaining in the liver leading to liver complications such as cirrhosis. • Ocaliva is a farnesoid X receptor agonist (FXR). Activation of the receptor leads to transport of bile acid out of the liver and decreases the formation of bile acids from cholesterol. • Iqirvo and Livdelzi is a peroxisome proliferator-activated receptor (PPAR) agonist. Therapeutic effects may include inhibition of bile acid synthesis through activation of PPAR-alpha and PPAR-delta for Iqirvo and PPAR-delta for Livdelzi. PPAR-delta signaling pathway includes Fibroblast Growth Factor 21 (FGF21)-dependent downregulation of CYP7A1, the key enzyme for the synthesis of bile

	acids from cholesterol. • UDCA, also known as ursodiol, possesses multiple proposed mechanisms of action for primary biliary cholangitis. UDCA replaces bile acid in the liver, stimulates the bile acid ducts in the liver, has anti-inflammatory effects, and reduces the hydrophobicity of the bile acid in the liver. Hydrophobicity of bile acid has been shown to be correlated to toxicity. • Alkaline phosphatase (ALP) and bilirubin are important biomarkers for the diagnosis of PBC along with antimicrobial antibody reactivity. ALP is also used to monitor for the progression of the disease. • Normal ALP ranges between 44 to 147 IU/L or 0.73 to 2.45 µkat/L. • Normal direct bilirubin ranges between from 0 to 0.4 mg/dL. Normal total bilirubin levels range from 0.2 to 1.2 mg/dL. • Treatment for primary biliary cholangitis is different than treatment for nonalcoholic steatohepatitis (NASH). Both diseases are associated with inflammation in the liver however the primary treatment for NASH based on clinical evidence is weight loss, avoiding alcohol consumption, and managing comorbidities. Ocaliva was studied in patients with NASH and did show some benefit in clinical trials with regards to improving the histology of the liver. However, the significance of the trial is limited because it was discontinued early and patients receiving Ocaliva were shown to have high cholesterol levels. • Prescribing Considerations: o Ocaliva, Iqirvo and Livdelzi should be prescribed by or in consultation with a hepatologist or a gastroenterologist. o Members who are initiated on therapy should be started on Ocaliva 5 mg tablets. Initiation on Ocaliva 10 mg tablets have led to an increased incidence of pruritus. o Ocaliva has a black box warning for hepatic decompensation and failure in PBC patients with cirrhosis. o Ocaliva is contraindicated in patients with decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event. o Iqirvo and Livdelzi is not recommended in patients with decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy)

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Iqirvo, Livdelzi or Ocaliva may be approved when all of the following criteria are met **(A. through D.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of primary biliary cholangitis (i.e., primary biliary cirrhosis) (ICD-10: K74.3).

C. The member meets one (1) of the following criteria **(1. or 2.):**

1. The member has experienced therapeutic failure to ursodiol monotherapy defined by one (1) of the following **(a. or b.):**

a. Alkaline phosphatase (ALP) level at least 1.67 times the upper limit of normal (ULN) after at least 12 months of ursodiol therapy

b. Total bilirubin level greater than 1 to 2 times the ULN after at least 12 months of ursodiol therapy

2. The member has experienced contraindication or intolerance to ursodiol monotherapy.

D. The member will be using Iqirvo, Livdelzi or Ocaliva in combination with ursodiol unless ursodiol is contraindicated or not tolerated.

II. Reauthorization

When a benefit, reauthorization of Iqirvo, Livdelzi or Ocaliva may be approved when all of the following criteria are met **(A., B. and C.)**:

A. The member has experienced positive clinical response defined by one (1) of the following **(1. or 2.):**
   1. ALP level less than 1.67 times the ULN
   2. Total bilirubin level less than the ULN
B. The member requires additional therapy with Iqirvo, Livdelzi or Ocaliva.
C. The member will be using Iqirvo, Livdelzi or Ocaliva in combination with ursodiol unless ursodiol is contraindicated or not tolerated.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Ocaliva should not be used in compensated cirrhosis with evidence of portal hypertension.
II. Iqirvo and Livdelzi should not be used in decompensated cirrhosis (e.g. ascites, variceal bleeding, hepatic encephalopathy).
III. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
IV. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization will be granted.

Automatic Approval Criteria

None

References:

1. Iqirvo [package insert]. Cambridge, MA: Ipsen Biopharmaceutical, Inc; June 2024.
2. Livdelzi [package insert]. Foster City, CA: Gilead Sciences, Inc.; August 2024.
3. Ocaliva [package insert]. Intercept Pharmaceuticals, Inc. New York, NY. May 2022.
4. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2022.
5. Combes, Burton, Robert L. Carithers, Willis C. Maddrey, Santiago Munoz, Guadalupe Garcia-Tsao, Gregory F. Bonner, James L. Boyer, Velimir A. Luketic, Mitchell L. Shiffman, Marion G. Peters, Heather White, Rowen K. Zetterman, Richard Risser, Stephen S. Rossi, and Alan F. Hofmann. "Biliary Bile Acids in Primary Biliary Cirrhosis: Effect of Ursodeoxycholic Acid." Hepatology (Baltimore, Md.). U.S. National Library of Medicine, 1999. Web. 28 July 2016.
6. Raoul Poupon. Clinical manifestations, diagnosis, and prognosis of primary biliary cholangitis (primary biliary cirrhosis). In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: May 12, 2019.
7. Sunil G Sheth, Sanjiv Chopra. Natural History and management of nonalcoholic fatty liver disease in adults In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: May 12, 2019.
8. Steven Flamm, Raoul Poupon. Trials of ursodeoxycholic acid for the treatment of primary biliary cholangitis (primary biliary cirrhosis) In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: May 12, 2019.