PRIOR AUTHORIZATION POLICY

POLICY: Hepatology – Livdelzi Prior Authorization Policy

- Livdelzi™ (seladelpar capsules – Gilead)

REVIEW DATE: 08/15/2024

OVERVIEW

Livdelzi, a peroxisome proliferator-activated receptor (PPAR)-delta agonist, is indicated for the 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.[1]

Livdelzi was approved under accelerated approval based on reduction in alkaline phosphatase (ALP).[1] An improvement in survival or liver decompensation events has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitation of use:
Livdelzi is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy).

Guidelines

The American Association for the Study of Liver Diseases (AASLD) guidelines for primary biliary cholangitis (2018) state that the diagnosis can be confirmed when patients meet two of the following criteria: 1) there is cholestasis as evidenced by alkaline phosphatase elevation; 2) anti-mitochondrial antibodies are present, or if negative for anti-mitochondrial antibodies, other primary biliary cholangitis-specific autoantibodies, including sp100 or gp210, are present; 3) there is histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts. It is specifically noted that diagnosis in a patient who is negative for anti-mitochondrial antibodies does not require a liver biopsy if other diagnostic criteria are met.[2] Treatment with UDCA (available in the US as ursodiol) is the recommended treatment for patients with primary biliary cholangitis who have abnormal liver enzyme values regardless of histologic stage. Following 12 months of UDCA therapy, the patient should be evaluated to determine if second-line therapy is appropriate. It is estimated that up to 40% of patients have an inadequate response to UDCA; Ocaliva® (obeticholic acid tablets), a faresoid X receptor agonist, should be considered for these patients. An update to the 2018 AASLD guidelines for primary biliary cholangitis (2021) provide two updated recommendations:[3] 1) Fibrates can be considered as off-label alternatives for patients with primary biliary cholangitis and inadequate response to UDCA. However, fibrates are discouraged in patients with decompensated liver disease; and 2) Ocaliva is contraindicated in patients with advanced cirrhosis, defined as cirrhosis with current or prior evidence of liver decompensation (e.g., encephalopathy, coagulopathy) or portal hypertension (e.g., ascites, gastroesophageal varices, or persistent thrombocytopenia). In addition, the AASLD recommends careful monitoring of any patient with cirrhosis, even if not advanced, receiving Ocaliva.

Safety

The safety and efficacy of Livdelzi in patients with decompensated cirrhosis have not been established.[1] Use of Livdelzi is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy). Patients with cirrhosis should be monitored for evidence of decompensation. Consider discontinuing Livdelzi if the patient progresses to moderate or severe hepatic impairment (Child-Pugh B or C).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Livdelzi. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Livdelzi as well as the monitoring required for adverse events and long-term efficacy, approval requires Livdelzi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Livdelzi is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Primary Biliary Cholangitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   Note: Primary Biliary Cholangitis is also known as Primary Biliary Cirrhosis.
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, the patient has a diagnosis of primary biliary cholangitis as defined by TWO of the following (a, b, or c):
       - **a)** Alkaline phosphatase is elevated above the upper limit of normal as defined by normal laboratory reference values; OR
       - **b)** Positive anti-mitochondrial antibodies or other primary biliary cholangitis-specific auto-antibodies, including sp100 or gp210, if anti-mitochondrial antibodies are negative; OR
       - **c)** Histologic evidence of primary biliary cholangitis from a liver biopsy; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has been receiving ursodiol therapy for ≥ 1 year and has had an inadequate response according to the prescriber; OR
       - **b)** According to the prescriber the patient is unable to tolerate ursodiol therapy; AND
         Note: Examples of ursodiol therapy include ursodiol generic tablets and capsules, Urso 250, Urso Forte, and Actigall.
     - **iv.** Patient does not currently have, or have a history of, a hepatic decompensation event; AND
       Note: Examples of hepatic decompensation include ascites, gastroesophageal varices, variceal bleeding, hepatic encephalopathy, and coagulopathy.
     - **v.** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician.
   - **B)** Patient is Currently Receiving Therapy. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient does not currently have, or have a of, a hepatic decompensation event.
       Note: Examples of hepatic decompensation include ascites, gastroesophageal varices, variceal bleeding, hepatic encephalopathy, and coagulopathy.
     - **ii.** Patient has demonstrated a response to therapy as determined by the prescriber.
       Note: Examples of a response to therapy are improved biochemical markers of primary biliary cholangitis (e.g., alkaline phosphatase [ALP], bilirubin, gamma-glutamyl transpeptidase [GGT], aspartate aminotransferase [AST], alanine aminotransferase [ALT]).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Livdelzi is not recommended in the following situations:

1. **Alcoholic Liver Disease**. There are no data available to support the use of Livdelzi in patients with alcoholic hepatitis.

2. **Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)/Nonalcoholic Fatty Liver Disease (NAFLD), including Metabolic Dysfunction-Associated Steatohepatitis (MASH)/Non-Alcoholic Steatohepatitis (NASH).** There is not sufficient data available to support the use of Livdelzi in patients with MASLD/NAFLD. Clinical development of Livdelzi for MASH was halted after liver biopsies of some patients had shown evidence of interface hepatitis.[4] Although an independent panel of hepatologists and pathologists concluded there was no chemical, biochemical, or histological evidence this was attributed to active treatment, resumption of the clinical program was not pursued.

3. **Concomitant use with Ocaliva (obeticholic acid tablets) or Iqirvo (elafibranor tablets)**. There are no data available to support the use of Livdelzi in combination with Ocaliva or Iqirvo in patients with PBC.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Livdelzi™ capsules [prescribing information]. Foster City, CA: Gilead; August 2024.
2. Lindor KD, Bowlus CL, Boyer J, et al. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases (AASLD). *Hepatology*. 2019;69(1):394-419.
3. Lindor KD, Bowe CL, Boyer J, et al. Primary biliary cholangitis: 2021 practice guideline update from the American Association for the Study of Liver Diseases. *Hepatology*. 2022;75:1012-1013.
4. US National Institutes of Health. A Study to Evaluate Seladelpar in Subjects With Nonalcoholic Steatohepatitis (NASH). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2024 Aug 15]. Available at: https://clinicaltrials.gov/study/NCT03551522. NLM Identifier: NCT03551522