Drug Coverage Policy

Effective Date.....02/01/2025
Coverage Policy Number.....IP0711
Policy Title.....Livdelzi

Hepatology – Livdelzi

- Livdelzi™ (seladelpar capsules – Gilead)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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).

Medical Necessity Criteria

Livdelzi is considered medically necessary when the following are met:

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, v, and vi):
      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.

vi. Preferred product criteria is met for the product(s) as listed in the below table(s)

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 history 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]).

Employer Plans:

Product	Criteria
Livdelzi capsules	**ONE** of the following: 1. Patient has tried, and according to the prescriber has experienced inadequate efficacy OR significant intolerance with Iqirvo 2. Patient has significant pruritus

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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.

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

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	02/01/2025

The policy effective date is in force until updated or retired.