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Subject: Seladelpar (Livdelzi) Capsule

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Primary biliary cholangitis (PBC) is a chronic, progressive autoimmune cholestatic liver disease that slowly destroys the intrahepatic bile ducts within the liver. This causes bile to accumulate in the liver resulting in gradual injury to liver cells and ultimately cirrhosis. Women account for about 90% of PBC cases, and it is most commonly diagnosed between the ages of 35 and 60 years. Patients are often initially asymptomatic, and the first sign of disease is often abnormal liver tests [e.g., alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST)]. Common symptoms of PBC prior to the onset of cirrhosis include fatigue, pruritus, and dry eyes and mouth. Once symptoms develop, the median duration of survival is 5 to 8 years. The serological hallmark of PBC is the presence of anti-mitochondrial antibody (AMA), a highly disease-specific antibody identified in about 95% of patients with PBC. There is no cure for PBC; however, the use of ursodiol (a.k.a., ursodeoxycholic acid, UDCA) can help improve liver function and may help slow disease progression (i.e., onset of cirrhosis). However, up to 30 to 40% of UDCA-treated patients have an inadequate biochemical response. Obeticholic acid (Ocaliva) and elafibranor (Iqirvo) are additional therapeutic options used either as monotherapy or in combination with UDCA. Obeticholic acid is a semi-synthetic bile acid analogue and farnesoid X receptor (FXR) agonist. FXR is expressed in the liver and intestine, and is responsible for regulating bile acid, inflammatory, fibrotic, and metabolic pathways. When obeticholic acid activates FXR, bile acid synthesis by the liver is suppressed and transport of bile acids out of hepatocytes is increased, thereby decreasing intracellular bile acid concentrations in hepatocytes. Elafibranor (Iqirvo) and its main active metabolite GFT1007 are peroxisome proliferator-activated receptor (PPAR) agonists, both of which activate PPAR-alpha, PPAR-gamma, and PPAR-delta in vitro and are thought to inhibit bile acid synthesis through activation of PPAR-alpha and PPAR-delta.

On August 14, 2024, the FDA approved a second PPAR agonist, seladelpar (Livdelzi), for the treatment of PBC in combination with UDCA in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver

decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). Seladelpar (Livdelzi) inhibits bile acid synthesis through activation of PPAR-delta, which is a nuclear receptor expressed in most tissues, including the liver and reduces bile acid synthesis through Fibroblast Growth Factor 21 (FGF21)-dependent downregulation of CYP7A1, the key enzyme for the synthesis of bile acids from cholesterol.

The safety and efficacy of seladelpar (Livdelzi) was evaluated in a randomized, double-blind, placebo-controlled trial. The study included 193 adult patients with PBC with an inadequate response or intolerance to UDCA. Patients were included in the trial if their ALP was greater than or equal to 1.67-times the ULN and total bilirubin (TB) was less than or equal to 2-times the ULN. Patients were excluded if they had other chronic liver diseases, clinically important hepatic decompensation including portal hypertension with complications, or cirrhosis with complications (e.g., Model for End Stage Liver Disease [MELD] score of 12 or greater, known esophageal varices or history of variceal bleeds, history of hepatorenal syndrome). Enrolled patients were randomized 2:1 to either seladelpar (Livdelzi) 10 mg (N=128) or placebo (N=65) once daily for 12 months; treatment with seladelpar (Livdelzi) and placebo was administered in combination with UDCA in 181 patients (94%) or as monotherapy in 12 patients (6%) who were unable to tolerate UDCA. The mean age of patients was 57 years (Range: 28 -75 years); 95% were female; 88% were Caucasian, 6% Asian, 2% African American, and 3% American Indian or Alaska Native. Twenty-nine percent of the patients identified as Hispanic/Latino. At baseline, 18 (14%) of the seladelpar-treated patients and 9 (14%) of the placebo-treated patients met at least one of the following criteria: Fibroscan >16.9kPa; historical biopsy or radiological evidence suggestive of cirrhosis; platelet count < 140,000/ μ L with at least one additional laboratory finding including serum albumin < 3.5 g/dL, INR > 1.3, or TB > 1-time ULN; or clinical determination of cirrhosis by the investigator. The mean baseline ALP concentration was 314 U/L (range: 161-786 U/L), corresponding to 2.7-times ULN. The mean baseline TB concentration was 0.8 mg/dL (range: 0.3-1.9 mg/dL) and was less than or equal to the ULN in 87% of the patients. Other mean baseline liver biochemistries were 48 U/L for ALT (range: 9-115 U/L) and 40 U/L for AST (range: 16-94 U/L). The primary endpoint was biochemical response at Month 12, where biochemical response was defined as achieving ALP less than 1.67-times ULN, an ALP decrease of greater than or equal to 15% from baseline, and TB less than or equal to ULN. ALP normalization (i.e., ALP less than or equal to ULN) at Month 12 was a key secondary endpoint. The ULN for ALP was defined as 116 U/L. The ULN for TB was defined as 1.1 mg/dL. Table 1 presents results at Month 12 for the percentage of patients who achieved biochemical response, achieved each component of biochemical response, and achieved ALP normalization. Seladelpar (Livdelzi) demonstrated greater improvement on biochemical response and ALP normalization at Month 12 compared to placebo.

Table 1: Percentage of Patients with PBC Achieving Biochemical Response and ALP Normalization at Month 12^a

	Seladelpar (Livdelzi) 10mg Once Daily (N=128)	Placebo (N=65)	Treatment Difference, % (95% CI) ^d
Biochemical response rate, n (%) ^{a,c}	79 (62)	13 (20)	42 (28, 53)
Components of biochemical response			
ALP less than 1.67-times ULN, n (%)	84 (66)	17 (26)	39 (25, 52)
Decrease in ALP of at least 15%, n (%)	107 (84)	21 (32)	51 (37, 63)
TB less than or equal to ULN, n (%) ^c	104 (81)	50 (77)	4 (-7, 17)
ALP normalization, n (%) ^{b,c}	32 (25)	0 (0)	25 (18, 33)

^a Biochemical response is defined as ALP <1.67-times ULN and TB \leq ULN and ALP decrease from baseline \geq 15%.

^b ALP normalization is defined as ALP less than or equal to ULN.

^c $p < 0.0001$ for seladelpar (Livdelzi) 10 mg versus placebo. P-values were obtained using the Cochran–Mantel–Haenszel test stratified by baseline ALP level (< 350 U/L versus ≥ 350 U/L) and baseline pruritus NRS (< 4 versus ≥ 4).

^d 95% unstratified Miettinen and Nurminen confidence intervals (CIs) are provided. Patients who discontinued treatment prior to Month 12 or who had missing data were considered as non-responders.

The most common adverse reactions with seladelpar (Livdelzi) (reported in $\geq 5\%$ and higher compared to placebo) are headache, abdominal pain, nausea, abdominal distension, and dizziness.

POSITION STATEMENT:

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of seladelpar (Livdelzi) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria (“1” to “7”):

1. The member has a diagnosis of primary biliary cholangitis (PBC)
2. The member does **NOT** have **ANY** of the following for use:
 - Decompensated cirrhosis (e.g., Child-Pugh Class B or C)
 - A prior decompensation event (e.g., ascites, jaundice, variceal bleeding, hepatic encephalopathy)
 - Compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)
 - Complete biliary obstruction
3. The member’s baseline ALP level is elevated
4. **EITHER** of the following (“a” or “b”):
 - a. Seladelpar (Livdelzi) will be used in combination with ursodiol treatment
 - b. Seladelpar (Livdelzi) will be used as monotherapy because of **ONE** of the following (“i” or “ii”):
 - i. The member has not achieved an adequate biochemical response to ursodiol
 - ii. The member has experienced persistent and intolerable adverse effects with the use of ursodiol, despite dosage reduction and other management interventions, that necessitates the complete discontinuation of ursodiol treatment
5. **NOT** being administered in combination with obeticholic acid (Ocaliva) or elafibranor (Iqirvo)
6. Seladelpar (Livdelzi) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
7. The dosage does not exceed 10 mg once daily

Duration of approval: 6 months

Continuation of seladelpar (Livdelzi) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria (“1” to “7”):

1. Authorization or reauthorization for seladelpar (Livdelzi) has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of PBC (if another health plan, documentation of a health plan-paid claim for seladelpar (Livdelzi) during the 90 days immediately

before the authorization request must be submitted); **OR** the member previously met **ALL** indication-specific initiation criteria (with the exception of the baseline ALP requirement).

2. The member has had a positive biochemical response to treatment (e.g., a reduction in ALP level as compared to baseline)
3. Member is taking seladelpar (Livdelzi) in combination with ursodiol treatment, unless seladelpar (Livdelzi) was initiated as monotherapy due to prior intolerance to or ineffectiveness of ursodiol
4. The member does **NOT** have **ANY** of the following for use:
 - Decompensated cirrhosis (e.g., Child-Pugh Class B or C)
 - A prior decompensation event (e.g., ascites, jaundice, variceal bleeding, hepatic encephalopathy)
 - Compensated cirrhosis with evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)
 - Complete biliary obstruction
5. **NOT** being administered in combination with obeticholic acid (Ocaliva) or elafibranor (Iqirvo)
6. Seladelpar (Livdelzi) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
7. The dosage does not exceed 10 mg once daily

Duration of approval: 1 year

Seladelpar (Livdelzi) is considered **experimental or investigational** for the treatment of confirmed noncirrhotic nonalcoholic steatohepatitis (NASH)/noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), nonalcoholic fatty liver disease (NAFLD)/metabolic dysfunction-associated steatotic liver disease (MASLD), and all other off-label indications. There is insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcomes.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Seladelpar (Livdelzi) is a peroxisome proliferator-activated receptor (PPAR)-delta agonist indicated for the 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.
- Seladelpar (Livdelzi) is approved under accelerated approval based on reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
- The recommended dosage for seladelpar (Livdelzi) is 10 mg orally once daily with or without food. If a patient is taking bile acid sequestrants, administer seladelpar (Livdelzi) at least 4 hours before or 4 hours after taking the bile acid binding sequestrant, or at as great an interval as possible.
- Seladelpar (Livdelzi) is a substrate of CYP2C9, CYP2C8, CYP3A4, and the transporters BCRP, P-gp, and OAT3. Therefore, monitor CYP2C9 poor metabolizers who receive a concomitant moderate to strong CYP3A4 inhibitor more frequently for adverse reactions. Increased seladelpar AUC is expected in patients who are CYP2C9 poor metabolizers with concomitant use of a moderate to

strong CYP3A4 inhibitor. Additionally, avoid use with strong CYP2C9 inhibitors as well as OAT3 and BCRP inhibitors. Also monitor biochemical response (e.g., ALP and bilirubin) when patients initiate rifampin.

Dose Adjustments

- No dosage adjustment of seladelpar (Livdelzi) is needed for patients with mild, moderate, or severe renal impairment.
- No dosage adjustment of seladelpar (Livdelzi) is recommended for patients with mild hepatic impairment (Child-Pugh A). The safety and efficacy of seladelpar (Livdelzi) in patients with decompensated cirrhosis have not been established. Use of seladelpar (Livdelzi) is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy). Monitor patients with cirrhosis for evidence of decompensation. Consider discontinuing seladelpar (Livdelzi) if the patient progresses to moderate or severe hepatic impairment (Child-Pugh B or C).

Drug Availability

- Seladelpar (Livdelzi) is available as 10 mg capsules, which have a light gray opaque body, and a dark blue opaque cap with "CBAY" imprinted on the cap and "10" on the body. It is package in a 30-count bottle (NDC 61958-3301-1).

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- **Fractures:** Fractures occurred in 4% of seladelpar-treated patients compared to no placebo-treated patients. Consider the risk of fracture in the care of patients treated with seladelpar (Livdelzi) and monitor bone health according to current standards of care.
- **Liver Test Abnormalities:** Seladelpar (Livdelzi) has been associated with dose-related increases in serum transaminase (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) levels greater than 3-times upper limit of normal (ULN) in PBC patients receiving 50 mg once daily (5-times higher than the recommended dosage) and 200 mg (20-times higher than the recommended dosage) once daily. Transaminase levels returned to pretreatment levels upon seladelpar (Livdelzi) discontinuation. Seladelpar (Livdelzi) 10 mg once daily did not show a similar pattern for increases in transaminase levels. Obtain baseline clinical and laboratory assessments at treatment initiation with seladelpar (Livdelzi) and monitor thereafter according to routine patient management. Interrupt seladelpar (Livdelzi) treatment if the liver tests (ALT, AST, total bilirubin [TB], and/or alkaline phosphatase [ALP]) worsen, or the patient develops signs and symptoms consistent with clinical hepatitis (e.g., jaundice, right upper quadrant pain, eosinophilia). Consider permanent discontinuation if liver tests worsen after restarting seladelpar (Livdelzi).
- **Biliary Obstruction:** Avoid use of seladelpar (Livdelzi) in patients with complete biliary obstruction. If biliary obstruction is suspected, interrupt seladelpar (Livdelzi) and treat as clinically indicated.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified
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ICD-10 Diagnosis Codes That Support Medical Necessity

K74.3	Primary biliary cholangitis
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REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at [Coverage Protocol Exemption Request](#).

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

Child-Pugh Nomogram

Parameter	Points Scored for Observed Findings		
	1 point	2 points	3 points
Encephalopathy grade	None	1 or 2	3 or 4
Ascites	Absent	Slight	Moderate
Serum bilirubin (mg/dL)	<2	2 to 3	>3
Serum albumin (g/dL)	>3.5	2.8 to 3.5	<2.8
International Normalized Ratio (INR)	<1.7	1.7 to 2.2	>2.2

Child-Pugh Class is obtained by adding the points from all 5 parameters to derive a total score, which can range from 5 to 15 points.
Child-Pugh Class A: 5 to 6 points

Child-Pugh Class B: 7 to 9 points Child-Pugh Class C: 10 to 15 points
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REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/11/26.

GUIDELINE UPDATE INFORMATION:

01/01/25	New Medical Coverage Guideline: Seladelpar (Livdelzi) for the 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.
03/15/25	Review and revision to the guideline consisting of updating the position statement to remove documentation requirements and allow prescribing in consultation with a gastroenterologist or hepatologist.
08/15/25	Review and revision to guideline consisting of updating the references.
04/01/26	Retire MCG. Seladelpar (Livdelzi) added to the 09-J5000-42, Primary Biliary Cholangitis MCG.