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# Subject: Primary Biliary Cholangitis

**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.**


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## 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) is an additional therapeutic option 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.

The FDA approved elafibranor (Iqirvo) on June 10, 2024 and seladelpar (Livdelzi) on August 14, 2024 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. These agents were approved for the PBC indication 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). Elafibranor (Iqirvo) and seladelpar (Livdelzi) are peroxisome proliferator-activated receptor (PPAR) agonists, both of which activate PPAR-alpha, PPAR-gamma, and PPAR-delta in vitro. However, the mechanism by which they exert their therapeutic effect in patients with PBC is not well understood. Pharmacological activity that is potentially relevant to therapeutic effects includes inhibition of bile acid synthesis through activation of PPAR-alpha and PPAR-delta. The signaling pathway for PPAR-delta was reported to include Fibroblast Growth Factor

21 (FGF21)-dependent downregulation of CYP7A1, the key enzyme for the synthesis of bile acids from cholesterol.

Elafibranor (Iqirvo)

The safety and efficacy of elafibranor (Iqirvo) was evaluated in a multi-center, randomized, double-blind, placebo-controlled study, which included 161 adults with PBC with an inadequate response or intolerance to UDCA. Patients were randomized to receive elafibranor (Iqirvo) 80 mg (n=108) or placebo (n=53) once daily for at least 52 weeks. When applicable, patients continued their pre-study dose of UDCA throughout the study. Patients were included in the study 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 liver disease or in case of decompensated cirrhosis. The mean age of patients was 57 years (range: 36 – 76 years), and the mean weight was 70.8 kg (range: 43 – 134 kg). The population was predominately female (96%) and Caucasian (91%). The baseline mean ALP concentration was 321.9 U/L (range: 151 – 1398 U/L), and 39% of patients had a baseline ALP concentration greater than 3-times the ULN. The mean baseline TB concentration was 0.56 mg/dL (range: 0.15 - 1.76 mg/dL), and 96% of patients had a baseline TB concentration less than or equal to ULN. The baseline mean concentration of ALT was 50 U/L (range: 11 - 188 U/L) and mean baseline concentration for AST was 46 U/L (range: 14 - 203 U/L). Most patients (95%) received study treatment (elafibranor or placebo) in combination with UDCA. There were 6 (6%) in the elafibranor-treated patients and 2 (4%) in the placebo-treated patients who were unable to tolerate UDCA and received elafibranor (Iqirvo) as monotherapy. At baseline, 12 (11%) of the elafibranor-treated patients and 8 (15%) of the placebo-treated patients met at least one of the following criteria: serum albumin < 3.5g/dL, INR >1.3, TB > 1-time ULN, Fibroscan >16.9 kPa, or historical biopsy suggestive of cirrhosis. The primary endpoint was biochemical response at Week 52, where biochemical response was defined as achieving ALP less than 1.67-times ULN, TB less than or equal to ULN, and ALP decrease greater than or equal to 15% from baseline. The ULN for ALP was defined as 129 U/L for males and 104 U/L for females. The ULN for TB was defined as 1.20 mg/dL. ALP normalization (i.e., ALP less than or equal to ULN) at Week 52 was a key secondary endpoint. Table 1 provides the results at Week 52 for the percentage of patients who achieved biochemical response, achieved each component of biochemical response, and achieved ALP normalization.

**Table 1: Percentage of Patients with PBC Achieving Biochemical Response and ALP Normalization at Week 52[a]**

| | Elafibranor (Iqirvo) 80mg Once Daily (N=108) | Placebo (N=53) | Treatment Difference, % (95% CI)[e] |
|---|---|---|---|
| Biochemical response rate, n (%)[b] | 55 (51) | 2 (4) | 47 (32, 57) |
| | | | |
| Components of biochemical response | | | |
| ALP less than 1.67-times ULN, n (%) | 56 (52) | 5 (9) | 42 (27, 53) |
| Decrease in ALP of at least 15%, n (%) | 81 (75) | 9 (17) | 58 (43, 69) |
| TB less than or equal to ULN, n (%)[c] | 92 (85) | 44 (83) | 2 (-9, 16) |
| | | | |
| ALP normalization, n (%)[d] | 16 (15) | 0 (0) | 15 (6, 23) |

[a] Patients who prematurely stopped the study treatment or used rescue therapy for PBC prior to the week 52 assessment were considered non-responders. For two other patients with missing data at Week 52, the closest non-missing assessment from the double-blind treatment period was used.

[b] Biochemical response is defined as ALP <1.67-times ULN and TB ≤ULN and ALP decrease from baseline ≥ 15% at Week 52. The p-value from the exact Cochran–Mantel–Haenszel (CMH) test was < 0.0001.

[c] The mean baseline total bilirubin was 0.56 mg/dL and was less than or equal to the ULN in 96% of the enrolled patients.

[d] Normalization of ALP at week 52 is defined as ALP ≤1-time ULN. The p-value from the exact CMH test was 0.0019.

[e] For biochemical response and its components: calculated using the Newcombe method stratified by (1) ALP > 3-times ULN or TB > ULN (Yes/No) and (2) 14-day baseline average PBC Worst Itch Numeric Rating Scale score ≥ 4 (Yes/No). For ALP normalization: calculated using unstratified Newcombe method.

The most common adverse reactions with elafibranor (Iqirvo) (reported in ≥ 5% and higher compared to placebo) are weight gain, diarrhea, abdominal pain, nausea, vomiting, arthralgia, constipation, muscle injury, fracture, gastroesophageal reflux disease, dry mouth, weight loss, and rash.

Seladelpar (Livdelzi)

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/µL 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 2 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 2: 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 ≤ULN and ALP decrease from baseline ≥ 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 ≥ 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.

**Elafibranor (Iqirvo)**

Initiation of elafibranor (Iqirvo) **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. Elafibranor (Iqirvo) will be used in combination with ursodiol treatment
    b. Elafibranor (Iqirvo) 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 seladelpar (Livdelzi)
6. Elafibranor (Iqirvo) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
7. The dosage does not exceed 80 mg once daily

**Approval duration**: 6 months

Continuation of elafibranor (Iqirvo) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria ("1" to "7"):

1. Authorization or reauthorization for elafibranor (Iqirvo) 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 elafibranor (Iqirvo) 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 elafibranor (Iqirvo) in combination with ursodiol treatment, unless elafibranor (Iqirvo) 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 seladelpar (Livdelzi)
6. Elafibranor (Iqirvo) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
7. The dosage does not exceed 80 mg once daily

**Approval duration**: 1 year

Elafibranor (Iqirvo) 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.

**Seladelpar (Livdelzi)**

Initiation of seladelpar (Livdelzi) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria ("1" to "8"):

1. The member has a diagnosis of primary biliary cholangitis (PBC)
2. The member has tried elafibranor (Iqirvo) and has a documented intolerance or inadequate response (e.g., no reduction in ALP level as compared to baseline) to therapy – documentation must be submitted
3. 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
4. The member's baseline ALP level is elevated
5. **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

6. **NOT** being administered in combination with obeticholic acid (Ocaliva) or elafibranor (Iqirvo)
7. Seladelpar (Livdelzi) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
8. 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 "8"):

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 tried elafibranor (Iqirvo) and has a documented intolerance or inadequate response (e.g., no reduction in ALP level as compared to baseline) to therapy – documentation must be submitted
3. The member has had a positive biochemical response to treatment (e.g., a reduction in ALP level as compared to baseline)
4. 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
5. 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
6. **NOT** being administered in combination with obeticholic acid (Ocaliva) or elafibranor (Iqirvo)
7. Seladelpar (Livdelzi) is prescribed by, or in consultation with, a gastroenterologist or hepatologist
8. 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

Elafibranor (Iqirvo)

- Elafibranor (Iqirvo) is a peroxisome proliferator-activated receptor (PPAR) 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.
- Elafibranor (Iqirvo) 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 elafibranor (Iqirvo) is 80 mg orally once daily with or without food. If patient is taking bile acid sequestrants, administer elafibranor (Iqirvo) at least 4 hours before or 4 hours after taking the bile acid binding sequestrant, or at as great an interval as possible.
- Before treatment, verify that females of reproductive potential are not pregnant. Elafibranor (Iqirvo) is a weak CYP3A4 inducer and may reduce the systemic exposure of progestin and ethinyl estradiol (CYP3A4 substrates), which may lead to contraceptive failure and/or an increase in breakthrough bleeding. Hormonal contraceptives should be switched to effective non-hormonal contraceptives or add a barrier method when using hormonal contraceptives while on elafibranor (Iqirvo) therapy and for at least 3 weeks after the last dose. Additionally, advise lactating patients not to breastfeed during elafibranor (Iqirvo) treatment and for 3 weeks after the last dose.
- Monitor for signs and symptoms of muscle injury in patient taking elafibranor (Iqirvo) and HMG-CoA reductase inhibitors, and monitor the biochemical response (e.g., ALP and bilirubin) when patients initiate rifampin during elafibranor (Iqirvo) treatment. Rifampin, an inducer of metabolizing enzymes, may reduce the systemic exposure of elafibranor and its active metabolite via increased metabolism and may result in delayed or suboptimal biochemical response.

Seladelpar (Livdelzi)

- 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

Elafibranor (Iqirvo)

- No dosage adjustment of elafibranor (Iqirvo) is needed for patients with mild, moderate, or severe renal impairment.
- No dosage adjustment of elafibranor (Iqirvo) is recommended for patients with mild hepatic impairment (Child-Pugh A). The safety and efficacy of elafibranor (Iqirvo) in patients with decompensated cirrhosis have not been established. Use of elafibranor (Iqirvo) 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 elafibranor (Iqirvo) if the patient progresses to moderate or severe hepatic impairment (Child-Pugh B or C).

Seladelpar (Livdelzi)

- 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**

Elafibranor (Iqirvo)

- Elafibranor (Iqirvo) tablets are available as 80 mg, round, orange, film-coated tablets, debossed with ‘ELA 80’ on one side and plain on the other side and is supplied in a child-resistant 30-count bottle (NDC 15054-0080-1).

Seladelpar (Livdelzi)

- 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**

Elafibranor (Iqirvo)

- None

Seladelpar (Livdelzi)

- None

**Contraindications**

Elafibranor (Iqirvo)

- None

Seladelpar (Livdelzi)

- None

**Precautions/Warnings**

Elafibranor (Iqirvo)

- **Myalgia, Myopathy, and Rhabdomyolysis:** Assess for muscle pain and myopathy prior to elafibranor (Iqirvo) initiation. Consider periodic assessment (clinical exam, CPK measurement). Interrupt elafibranor (Iqirvo) if there is new onset or worsening of muscle injury, or muscle pain.
- **Fractures:** The risk of fracture should be considered in the care of patients treated with elafibranor (Iqirvo). Apply current standards of care for assessing and maintaining bone health.
- **Adverse Effects on Fetal and Newborn Development:** May cause fetal harm. Verify that a female of reproductive potential is not pregnant prior to initiating elafibranor (Iqirvo). Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- **Drug-Induced Liver Injury:** Obtain clinical and laboratory assessments at treatment initiation and monitor thereafter according to routine patient management. Interrupt the treatment if liver tests worsen, or patients develop signs and symptoms consistent with clinical hepatitis. Consider permanent discontinuation if liver tests worsen after restarting elafibranor (Iqirvo).
- **Hypersensitivity Reactions:** If severe hypersensitivity reactions occur, permanently discontinue elafibranor (Iqirvo). If a mild or moderate hypersensitivity reaction occurs, interrupt elafibranor (Iqirvo) and treat promptly. Monitor until signs and symptoms resolve.
- **Biliary Obstruction:** Avoid use in patients with complete biliary obstruction. If biliary obstruction is suspected, interrupt elafibranor (Iqirvo) and treat as clinically indicated.

Seladelpar (Livdelzi)

- **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 |

**Note:** HCPCS code for elafibranor (Iqirvo) and seladelpar (Livdelzi)

### ICD-10 Diagnosis Codes That Support Medical Necessity for elafibranor (Iqirvo) and seladelpar (Livdelzi)

| | |
|---|---|
| K74.3 | Primary biliary cholangitis |

## 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.<br>Child-Pugh Class A: 5 to 6 points<br>Child-Pugh Class B: 7 to 9 points<br>Child-Pugh Class C: 10 to 15 points | | | |

## REFERENCES:


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4. Elafibranor (Iqirvo) [package insert]. Cambridge, MA: Intercept Pharmaceuticals, Inc.; June 2024.
5. Livdelzi (seladelpar) [package insert]. Foster City, CA: Gilead Sciences, Inc., August 2024.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2025 June 26]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.


## COMMITTEE APPROVAL:

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

## GUIDELINE UPDATE INFORMATION:

| | |
|---|---|
| 04/01/26 | New Medical Coverage Guideline: Merger of 09-J5000-02, Seladelpar (Livdelzi) Capsule and 09-J4000-93, Elafibranor (Iqirvo) Tablet to create the Primary Biliary Cholangitis MCG and updating the seladelpar (Livdelzi) position statement to require a step through elafibranor (Iqirvo). |