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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	July 5, 2024
Subject:	Iqirvo	**Page:**	1 of 5

Last Review Date: September 6, 2024

Iqirvo

Description

Iqirvo (elafibranor)

Background
Iqirvo (elafibranor) 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. However, the mechanism by which Iqirvo exerts its therapeutic effects in patients with primary biliary cholangitis (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 (1).

Regulatory Status
FDA-approved indication: 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 (1).

Limitations of Use: Use of Iqirvo is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy) (1).

Iqirvo has been associated with myalgia, myopathy, and rhabdomyolysis. Patients should be assessed for muscle pain and myopathy prior to Iqirvo initiation. Patients with signs or symptoms of new onset or worsening of muscle pain or myopathy should consider periodic assessment (clinical exam, CPK measurement) (1).

Iqirvo use may result in fractures, drug-induced liver injury, and biliary obstruction. Consider risk of fractures and monitor bone health according to current standards of care. Baseline liver function tests should be obtained at treatment initiation with Iqirvo and monitored thereafter. Treatment should be interrupted if liver tests worsen, or if the patient develops signs and symptoms consistent with clinical hepatitis. Consider discontinuation if liver tests worsen after restarting Iqirvo. Avoid use of Iqirvo in patients with complete biliary obstruction. If biliary obstruction is suspected, interrupt Iqirvo and treat as clinically indicated (1).

Iqirvo may cause fetal harm when administered during pregnancy. Advise females of reproductive potential to use effective non-hormonal contraceptives or add a barrier method when using hormonal contraceptives during treatment with Iqirvo and for 3 weeks following the last dose of Igirvo (1).

The safety and effectiveness of Iqirvo in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Iqirvo may be considered **medically necessary** if the conditions indicated below are met.

Iqirvo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Primary biliary cholangitis (PBC)

AND submission of medical records (e.g., chart notes, laboratory values) documenting **ONE** of the following:

a. An inadequate response to ursodeoxycholic acid (UDCA) **AND** Iqirvo will be used in combination with UDCA
b. An intolerance to ursodeoxycholic acid (UDCA)

AND submission of medical records (e.g., chart notes, laboratory values) documenting **ONE** of the following:

a. Confirmation of diagnosis with elevated serum alkaline phosphatase level **AND ONE** of the following tests:
   i. Positive antimitochondrial antibody test
   ii. Liver biopsy
   iii. Ultrasound scan of liver
b. **NO** decompensated cirrhosis
c. **NO** preliminary biliary obstruction prior to initiation of therapy and agreement to discontinue therapy if complete biliary obstruction develops

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Primary biliary cholangitis (PBC)

AND submission of medical records (e.g., chart notes, laboratory values) documenting **ALL** of the following:

a. Confirmation of patient improvement with **ALL** of the following:
   i. Serum alkaline phosphatase (ALP) decrease of at least 15%
   ii. Total bilirubin level of ≤ 1.1 mg/dL for females and ≤ 1.5 mg/dL for males
b. **NO** decompensated cirrhosis

c. **NO** evidence of complete biliary obstruction

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Quantity 90 tablets per 90 days

Duration 6 months

Prior – Approval *Renewal* Limits

Quantity 90 tablets per 90 days

Duration 12 months

Rationale

Summary
Iqirvo (elafibranor) is a PPAR agonist indicated for the treatment of PBC. Iqirvo is not recommended in patients who have or develop decompensated cirrhosis. Iqirvo has been associated with myalgia, myopathy, rhabdomyolysis, fractures, potential risk to a fetus, drug-induced liver injury, and biliary obstruction. The safety and effectiveness of Iqirvo in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Iqirvo while maintaining optimal therapeutic outcomes.

References
1. Iqirvo [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; June 2024.

Policy History

Date	Action
July 2024	Addition to PA
September 2024	Annual review. Per FEP, added managed PA verbiage to requirements

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.