Original Effective Date: 11/29/2024
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Policy Number: C28551-A

Iqirvo (elafibranor)

PRODUCTS AFFECTED

Iqirvo (elafibranor)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Primary biliary cholangitis (PBC)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY BILIARY CHOLANGITIS (PBC):
   1. Documented diagnosis of primary biliary cholangitis (PBC)
      AND
   2. Documentation of TWO of the following that support the diagnosis [DOCUMENTATION REQUIRED]:
      i. Biochemical evidence of cholestasis based on ALP elevation

   ii. Presence of AMA or other PBC-specific autoantibodies (including sp100 or gp210, if AMA is negative)
   iii. Histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts

   AND

3. Documentation of the member's baseline (prior to treatment) alkaline phosphate (ALP) level [DOCUMENTATION REQUIRED]
   AND
4. Documentation member has been receiving ursodiol therapy (e.g., ursodiol generics, Urso250®, UrsoForte®, Actigall®) for ≥ 1 year at doses of 13-15 mg/kg/day and has had an inadequate response(alkaline phosphate level > 1.67 times the upper limit of normal); OR According to the prescribing physician the member is unable to tolerate ursodiol therapy
   AND
5. Prescriber attest to all the following:
   i. Iqirvo (elafibranor) will not be used in combination with Ocaliva (obeticholic acid)
      AND
   ii. Member does not have decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy)
      AND
   iii. Member has been evaluated for muscle pain or myopathy prior to treatment
      AND
   iv. For females of reproductive age, prescriber attests that member has been evaluated and is not pregnant prior to treatment and has been counselled on the use of effective non-hormonal contraception.

   AND
6. Prescriber attests they will monitor the member for hepatic adverse events, muscle pain or myopathy, and risk for bone fracture

CONTINUATION OF THERAPY:

A. PRIMARY BILIARY CHOLANGITIS:
   1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
      AND
   2. Documentation of positive response to therapy as indicated by alkaline phosphatase (ALP) decrease of at least 15% AND is less than 1.67-times the upper limit of normal (ULN) [DOCUMENTATION REQUIRED]
      AND
   3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   4. Prescriber attests that member does not have cirrhosis OR for a member that has cirrhosis, that the member has compensated cirrhosis with no evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia) and has not had a decompensation event. NOTE: Iqirvo is not recommended in members who have or who develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy).
      AND
   5. Documentation the member continues to receive ursodiol therapy OR According to the prescribing physician the member is unable to tolerate ursodiol therapy

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
80 mg once daily

Maximum Quantity Limits – 80 mg

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Peroxisome Proliferator-Activated Receptor Agonists

FDA-APPROVED USES:
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.
This indication 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).
Limitations of Use: Use of IQIRVO is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Primary Biliary Cholangitis (PBC) is a progressive autoimmune liver disease in which the small bile ducts of the liver become inflamed and damaged, leading to a build-up of bile acids. This damage results in liver cirrosis. The most common symptoms are fatigue and itching. However, patients with PCB may eventually require liver transplantation.

The criteria for diagnosis, based on the American Associan for the Study of Liver Diseases

(AASLD) guideline, is having met two of the three criteria below (see Reference 4):

- Biochemical evidence of cholestasis based on ALP elevation.
- Presence of AMA, or other PBC-specific autoantibodies, including sp100 or gp210, if AMA is negative.
- Histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts.

Guidelines support the utilization of ursodeoxycholic acid (UDCA) at a dose of 13 to 15 mg/kg as first line therapy for PBC. Typically response to therapy is assessed after 1 year of treament, looking for biochemical response (example, Alkaline Phosphate Levels (ALP) reduction)

Iquirvo (elafibranor) is a peroxisome proliferator-activated receptor (PPAR) agonist which exerts therapeutic effects by inhibiting bile acid synthesis through PPAR-alpha and PPAR-delta activation. The efficacy of Iquirvo (elafibranor) was studied in NCT04526665 which was a multi-center, randomized, double-blind placebo-controlled study in 161 adults with primary biliary cholangitis (PBC) who had an inadequate response to ursodeoxycholic acid (UDCA). The primary end point was a biochemical response at week 52. Biochemical response was defined as: an alkaline phosphatase level of <1.67 times the upper limit of the normal range, with a reduction of ≥15% from baseline, and normal total bilirubin level. Patients were included if they had:

- Definite or probable PBC
- ALP ≥ 1.67x upper limit of normal (ULN)
- Total bilirubin (TB) ≤ 2x ULN
- Taking ursodeoxycholic acid (UDCA) at least 12 months, with the dose stable for at lesat 3 months, prior to screening or they were unable to tolerate UDCA treatment.

Key exclusions included: a history of concomitant liver disease, clinically significant hepatic decompensation, significant renal disease. Patients were randomized to elafibranor 80 mg or placebo.

The primary endpoint of biochemical response was achieved in 51% of patients treated with Iqirvo, compated to 4% of patients in the placebo arm. Iqirvo received an accelerated FDA approval based on the reduction in ALP. Reductions in ALP are believed to clinically predict clinical benefit, including a reduction in progression to transplant. However, for continued approval, Iqirvo will have to show clinical benefit in confirmatory trials. The ongoing phase 3 trial, ELFIDENCE, is assessing all-cause mortality, hepatic decompensation and MELD score change, and liver transplantation.

The FDA labeling contains warnings regarding myalgia and myopathy, fracture risk, fetal harm, and liver injury. Additionally, Iqirvo should be avoided in patinets with a complete biliary obstruction, which would warrant interruption in treatment.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Iquirvo (elafibranor) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy.

OTHER SPECIAL CONSIDERATIONS:

Iquirvo (elafibranor) may cause fetal harm. Prescribers should verify that females of reproductive potential are not pregnant prior to initiating treatment and advise demale patients to of the protential risk to the fetus and to use effective contraception. Members should switch to an effective non-hormonal contraceptive or add a barrier method when using hormonal contraceptives for at least 3 weeks following the last dose of

elafibranor. Additionally, members should be advised not to breast feed during and up to 3 weeks following the last dose of elafibranor.

If administered with bile adic sequestrants, Iquirvo (elafibranor) should be adminsitered at least 4 hours before or 4 hours after administered the bile acid sequestrant.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Iqirvo TABS 80M

REFERENCES

1. Iqirvo (elafibranor) tablets [prescribing information]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc., June 2024
2. Kowdley, K. V., Bowlus, C. L., Levy, C., Akarca, U. S., Alvares-da-Silva, M. R., Andreone, P., Arrese, M., Corpechot, C., Francque, S. M., Heneghan, M. A., Invernizzi, P., Jones, D., Kruger, F. C., Lawitz, E., Mayo, M. J., Shiffman, M. L., Swain, M. G., Valera, J. M., Vargas, V., Vierling, J. M., … ELATIVE Study Investigators' Group (2024). Efficacy and Safety of Elafibranor in Primary Biliary Cholangitis. The New England journal of medicine, 390(9), 795–805. https://doi.org/10.1056/NEJMoa2306185
3. "Study of Elafibranor in Patients With Primary Biliary Cholangitis (PBC) (ELATIVE)", Clinical Trials.gov ID NCT04526665, https://clinicaltrials.gov/study/NCT04526665, accessed on August 13, 2024.
4. Lindor, K. D., Bowlus, C. L., Boyer, J., Levy, C., & Mayo, M. (2019). Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology (Baltimore, Md.)*, *69*(1), 394–419. https://doi.org/10.1002/hep.30145

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	P&T QUARTER 4 2024