*For your **PBC patients***

Unlock the IQIRVO EFFECT

A meaningful evolution in treatment for patients with inadequate response or intolerance to UDCA[1]

PBC=primary biliary cholangitis; UDCA=ursodeoxycholic acid.

Indication

IQIRVO® 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.

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).

Important Safety Information

Myalgia, Myopathy, and Rhabdomyolysis: Rhabdomyolysis resulting in acute kidney injury occurred in one IQIRVO-treated patient who had cirrhosis at baseline and was also taking a stable dose of an HMG-CoA reductase inhibitor (statin). Myalgia or myopathy, with or without CPK elevations, occurred in patients treated with IQIRVO alone or treated concomitantly with a stable dose of an HMG-CoA reductase inhibitor. Assess for myalgia and myopathy prior to IQIRVO initiation. Consider periodic assessment (clinical exam, CPK measurement) during treatment with IQIRVO, especially in those who have signs and symptoms of new onset or worsening of muscle pain or myopathy. Interrupt IQIRVO treatment if there is new onset or worsening of muscle pain, or myopathy, or rhabdomyolysis.

Please see additional Important Safety Information throughout and full Prescribing Information for IQIRVO.

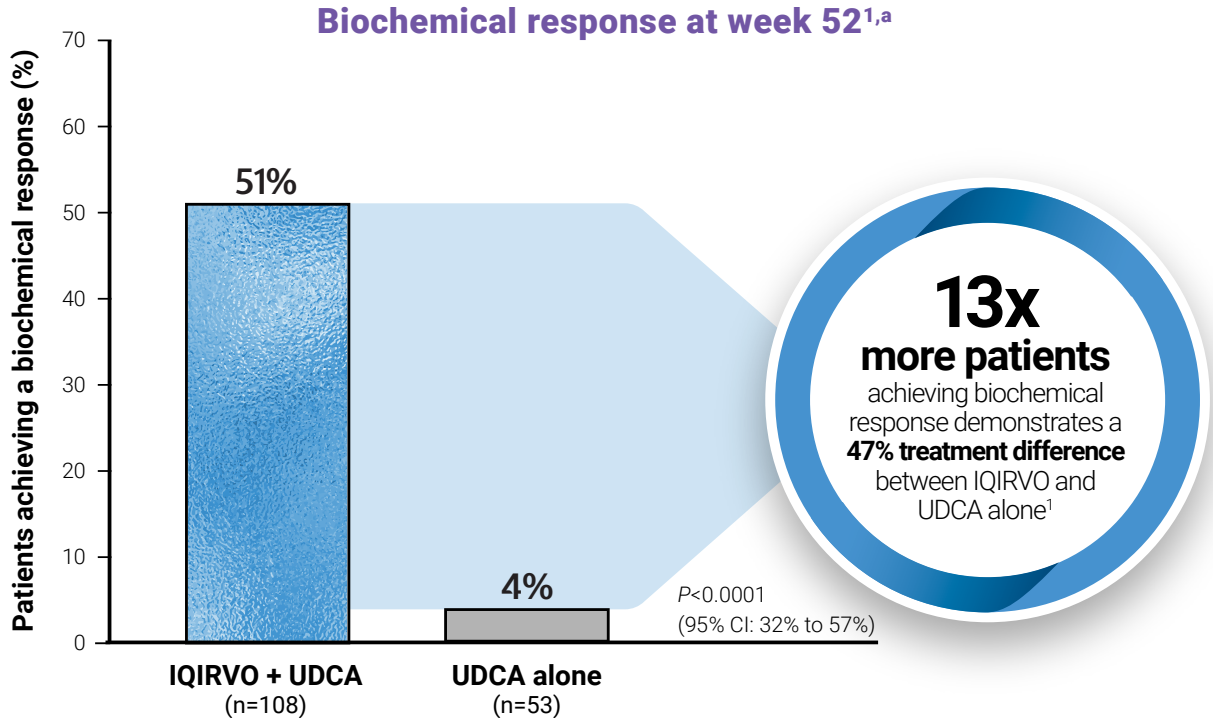
IQIRVO®
elafibranor 80 mg tablets

The ELATIVE® trial studied IQIRVO® (elafibranor) across patient types[2,3]

The ELATIVE trial was a double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of IQIRVO in patients with PBC and inadequate response or intolerance to UDCA[1]

- Eligible patients (n=161) between the ages of 18-75 years were randomly assigned (2:1) to receive either an 80-mg dose of elafibranor (n=108) or placebo (n=53) as an add-on to UDCA across 52 weeks[2]
  - No clinically relevant imbalances in baseline characteristics between treatment groups[3]
- Primary endpoint was biochemical response at 52 weeks, and select secondary endpoints were change in ALP and normalization, change in pruritus assessed by the WI-NRS, and change in pruritus-related patient-reported outcomes assessed by WI-NRS, PBC-40, and 5-D itch scale[2]
  - ULN for ALP was defined as 104 U/L for women and 129 U/L for men[1]

13x more patients achieved biochemical response vs UDCA alone[1]



Biochemical response at 52 weeks was defined as an ALP <1.67 x ULN, ALP decrease ≥15%, and total bilirubin ≤ ULN.[1]

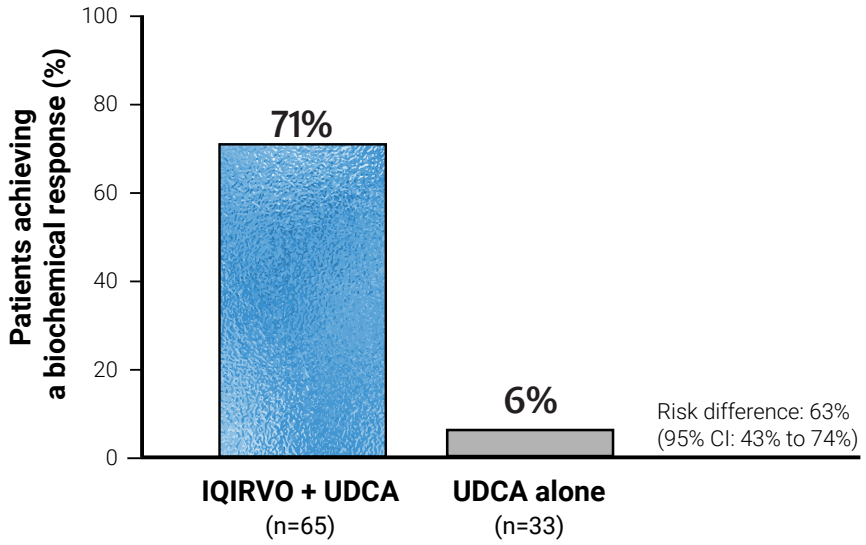
[a]Six patients in the IQIRVO group took IQIRVO alone, while 2 patients in the UDCA group took placebo alone.[1]

ALP=alkaline phosphatase; CI=confidence interval; ULN=upper limit of normal; WI-NRS=Worst Itch Numeric Rating Scale.

Please see Important Safety Information throughout and full Prescribing Information for IQIRVO.

71% of patients in a subgroup analysis saw biochemical response[3]

Biochemical response at week 52 in patients with ALP ≤3 x ULN at baseline[3]



ALP ≤3 x ULN

71% (n=46/65) of patients with baseline ALP ≤3 x ULN saw biochemical response[3]

Risk difference: 63% (95% CI: 43% to 74%)

ALP >3 x ULN

21% (n=9/43) of patients with baseline ALP >3 x ULN saw biochemical response[3]

Risk difference: 21% (95% CI: 2% to 35%)

Important Safety Information (continued)

Fractures: Fractures occurred in 6% of IQIRVO-treated patients compared to no placebo-treated patients. Consider the risk of fracture in the care of patients treated with IQIRVO and monitor bone health according to current standards of care.

Adverse Effects on Fetal and Newborn Development: IQIRVO may cause fetal harm when administered during pregnancy. For females of reproductive potential, verify that the patient is not pregnant prior to initiation of therapy. Advise females of reproductive potential to use effective non-hormonal contraceptives or add a barrier method when using systemic hormonal contraceptives during treatment with IQIRVO and for 3 weeks following the last dose of IQIRVO.

Please see additional Important Safety Information throughout and full Prescribing Information for IQIRVO.

IQIRVO® elafibranor 80 mg tablets

ALP normalization was achieved with IQIRVO[1]

15% of patients achieved ALP normalization when treated with IQIRVO® (elafibranor) vs 0% with UDCA alone[1]

Baseline ALP was[1]
321.9 U/L

ULN for ALP levels is[1]
104 U/L for women
—&—
129 U/L for men

Mean reduction to achieve ALP normalization with IQIRVO was[2]
216 U/L

Safety and tolerability established in the ELATIVE trial[1]

Common adverse reactions occurring in the ELATIVE trial[1,a]

Adverse Reaction[b]	UDCA alone (n=53) %	IQIRVO + UDCA (n=108) %
Weight gain[c]	21% (11)	23% (25)
Diarrhea	9% (5)	11% (12)
Abdominal pain[c]	6% (3)	11% (12)
Nausea	6% (3)	11% (12)
Vomiting	2% (1)	11% (12)
Arthralgia	4% (2)	8% (9)
Constipation	2% (1)	8% (9)
Muscle pain[c]	2% (1)	7% (8)
Fracture[c]	0	6% (7)
Gastroesophageal reflux disease	2% (1)	6% (7)
Dry mouth	2% (1)	5% (5)
Weight loss	0	5% (5)
Rash[c]	4% (2)	5% (5)

[a]Included 8 patients (5%) who were intolerant to UDCA and initiated treatment as monotherapy: 6 patients (5%) in the IQIRVO arm and 2 patients (4%) in the placebo arm.[1]
[b]Occurring in greater than or equal to 5% of patients in the IQIRVO treatment arm and at an incidence greater than or equal to 1% higher than in the placebo treatment arm.[1]
[c]Weight gain, abdominal pain, muscle pain, fracture, and rash include other related terms.[1]

Please see Important Safety Information throughout and full Prescribing Information for IQIRVO.

Dedicated support for your patients and their families

IPSEN CARES® patient support program helps patients get access to their IQIRVO® (elafibranor) prescription with the information and support they need

The IPSEN CARES patient support program provides patients and families with resources to help them better understand and manage their condition.

- Financial & Insurance Assistance[a]
- Dedicated, Individualized Support
- Continuity of Care
- Educational Materials & Programs

Visit IPSENCARES.COM or call (866) 435-5677
Monday-Friday, 8:00 AM – 8:00 PM ET
support@ipsencares.com

[a]Please see Patient Eligibility Terms and Conditions at ipsencares.com.

Important Safety Information (continued)

Drug-Induced Liver Injury: Drug-induced liver injury occurred in one patient who took IQIRVO 80 mg once daily and two patients who took IQIRVO at 1.5-times the recommended dosage, of which one presented with autoimmune-like hepatitis. The median time to onset of elevation in liver tests was 85 days. Obtain baseline clinical and laboratory assessments at treatment initiation with IQIRVO and monitor thereafter according to routine patient management. Interrupt IQIRVO treatment if 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 IQIRVO.

Hypersensitivity Reactions: Hypersensitivity reactions have occurred in a clinical trial with IQIRVO at 1.5-times the recommended dosage. Three patients (0.2%) had rash or unspecified allergic reaction that occurred 2 to 30 days after IQIRVO initiation. Hypersensitivity reactions resolved after discontinuation of IQIRVO and treatment with steroids and/or antihistamines. If a severe hypersensitivity reaction occurs, permanently discontinue IQIRVO. If a mild or moderate hypersensitivity reaction occurs, interrupt IQIRVO and treat promptly. Monitor the patient until signs and symptoms resolve. If a hypersensitivity reaction recurs after IQIRVO rechallenge, then permanently discontinue IQIRVO.

Biliary Obstruction: Avoid use of IQIRVO in patients with complete biliary obstruction. If biliary obstruction is suspected, interrupt IQIRVO and treat as clinically indicated.

Drug-Drug Interactions

IQIRVO 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. Switch to effective non-hormonal contraceptives or add a barrier method when using hormonal contraceptives during treatment with IQIRVO and for at least 3 weeks after last dose.

CPK elevation and/or myalgia occurred in patients on IQIRVO monotherapy. Co-administration of IQIRVO and HMG-CoA reductase inhibitors can increase the risk of myopathy. Monitor for signs and symptoms of muscle injury. Consider periodic assessment (clinical exam, CPK) during treatment. Interrupt IQIRVO treatment if there is new onset or worsening of muscle pain or myopathy.

Co-administration of IQIRVO with rifampin, an inducer of metabolizing enzymes, may reduce the systemic exposure of elafibranor resulting in delayed or suboptimal biochemical response. Monitor the biochemical response (e.g., ALP and bilirubin) when patients initiate rifampin during treatment with IQIRVO.

Bile acid sequestrants may interfere with IQIRVO absorption and systemic exposure, which may reduce efficacy. Administer IQIRVO at least 4 hours before or after a bile acid sequestrant , or at as great an interval as possible.

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IQIRVO®
elafibranor 80 mg tablets

UNLOCK THE IQIRVO EFFECT

A meaningful evolution in treatment for patients with inadequate response or intolerance to UDCA[1]

Adding IQIRVO® (elafibranor) to UDCA can offer efficacy with an established safety profile in a once-daily oral treatment[1]

13x more patients achieved biochemical response vs UDCA alone (51% vs 4% with UDCA alone)[1]

ALP normalization—only achieved with IQIRVO (15% vs 0% with UDCA alone)[1]

Established safety profile[1]

Move second-line treatment forward today and help patients achieve more, by learning about IQIRVO.[1] **Visit IQIRVOHCP.com**

Important Safety Information (continued)

Use in Special Populations

Pregnancy: Based on data from animal reproduction studies, IQIRVO may cause fetal harm when administered during pregnancy. There are insufficient data from human pregnancies exposed to IQIRVO to allow an assessment of a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Report pregnancies to Ipsen Biopharmaceuticals, Inc. adverse event reporting line at 1-855-463-5127 or https://www.ipsen.com/contact-us/.

Lactation: There are no data available on the presence of IQIRVO or its metabolites in human milk, or on effects of the drug on the breastfed infant or the effects on milk production. IQIRVO is not recommended during breastfeeding and for at least 3 weeks following last dose of IQIRVO because the risk to breastfed child cannot be excluded.

Females and Males of Reproductive Potential: IQIRVO may cause fetal harm when administered to pregnant women. Verify the pregnancy status of females of reproductive potential prior to initiating IQIRVO. Advise females of reproductive potential to use effective contraception during treatment with IQIRVO and for 3 weeks after the final dose.

The most common adverse events occurring in ≥10% of patients were weight gain (23%), abdominal pain (11%), nausea (11%), vomiting (11%), and diarrhea (11%).

You are encouraged to report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
You may also report side effects to Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127.

Please see additional Important Safety Information throughout and full Prescribing Information for IQIRVO.

References: 1. IQIRVO [package insert]. Ipsen Biopharmaceuticals, Inc. Cambridge, MA. **2.** Kowdley KV, Bowlus CL, Levy C, et al; ELATIVE Study Investigators' Group. Efficacy and safety of elafibranor in primary biliary cholangitis. *N Engl J Med*. 2024;390(9):795-805. **3.** Data on file. Ipsen Biopharmaceuticals, Inc.

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