DOSING GUIDE

OCALIVA®
obeticholic acid

INDICATION

OCALIVA 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 a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN INCORRECTLY DOSED PBC PATIENTS WITH CHILD-PUGH CLASS B OR C OR DECOMPENSATED CIRRHOSIS

- **In postmarketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with Primary Biliary Cholangitis (PBC) with decompensated cirrhosis or Child-Pugh Class B or C hepatic impairment when OCALIVA was dosed more frequently than recommended.**
- **The recommended starting dosage of OCALIVA is 5 mg once weekly for patients with Child-Pugh Class B or C hepatic impairment or a prior decompensation event.**

Contraindications

OCALIVA is contraindicated in patients with complete biliary obstruction.

Please see additional Important Safety Information throughout and accompanying Full Prescribing Information, including Boxed WARNING, for OCALIVA. **Rx only.**

DOSAGE AND ADMINISTRATION FOR OCALIVA

For non-cirrhotic or compensated Child-Pugh Class A patients[1]:

- Starting dose: **5 mg once daily**
- Titration dose: **10 mg once daily**

Not actual size.

For patients with Child-Pugh Class B or C or with a prior decompensation event[1]:

- Starting dose: **5 mg once WEEKLY**
- Titration dose and schedule: *See next page*

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Hepatic Decompensation and Failure in Incorrectly Dosed PBC Patients with Child-Pugh Class B or C or Decompensated Cirrhosis

In postmarketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with decompensated cirrhosis or Child-Pugh B or C hepatic impairment when OCALIVA was dosed more frequently than the recommended starting dosage of 5 mg once weekly. Reported cases typically occurred within 2 to 5 weeks after starting OCALIVA and were characterized by an acute increase in total bilirubin and/or ALP concentrations in association with clinical signs and symptoms of hepatic decompensation (e.g., ascites, jaundice, gastrointestinal bleeding, worsening of hepatic encephalopathy). Patients who died due to liver-related complications generally had decompensated cirrhosis prior to treatment and were started on OCALIVA 5 mg once daily, which is 7-fold greater than the once-weekly starting regimen in this population.

Routinely monitor patients for progression of PBC disease, including liver-related complications, with laboratory and clinical assessments. Dosage adjustment, interruption or discontinuation may be required. Close monitoring is recommended for patients at an increased risk of hepatic decompensation. Severe intercurrent illnesses that may worsen renal function or cause dehydration

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Dosage adjustment for patients with Child-Pugh Class B or C or with a prior decompensation event[1]

START OF TREATMENT	3 MONTHS	SUBSEQUENTLY
5 mg once WEEKLY for moderate or severe hepatic impairment (Child-Pugh Class B or C), or if a prior decompensation event[a]	**5 mg twice WEEKLY (at least 3 days apart)** if an adequate reduction in ALP and/or total bilirubin has not been achieved after 3 months and the patient is tolerating OCALIVA	**10 mg twice WEEKLY (at least 3 days apart)** depending on response and tolerability

[a]Eg, gastroesophageal variceal bleeding, new or worsening jaundice, spontaneous bacterial peritonitis.

Routinely monitor patients during treatment with OCALIVA for disease progression and the occurrence of liver-related adverse reactions[1]

Treatment management for pruritus

For patients with severe/intolerable pruritus on OCALIVA, consider one or more of the following[1]:

Add an antihistamine or bile acid binding resin

Reduce the dosage of OCALIVA *(only if patient is non-cirrhotic or compensated Child-Pugh Class A)*

- **5 mg every other day**, for patients intolerant to 5 mg once daily
- **5 mg once daily**, for patients intolerant to 10 mg once daily

Temporarily interrupt OCALIVA dosing for up to 2 weeks

- Restart at a reduced dosage if applicable
- Up-titrate based on biochemical response, tolerability, and Child-Pugh classification

Consider discontinuing OCALIVA treatment in patients who continue to experience persistent, intolerable pruritus despite management strategies.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

(e.g., gastroenteritis), may exacerbate the risk of hepatic decompensation. Interrupt treatment with OCALIVA in patients with laboratory or clinical evidence of worsening liver function indicating risk of decompensation, and monitor the patient's liver function. Consider discontinuing OCALIVA in patients who have experienced clinically significant liver-related adverse reactions. Discontinue OCALIVA in patients who develop complete biliary obstruction.

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Important instructions

Prior to initiation of OCALIVA in patients with suspected cirrhosis: Use the information in the accompanying Full Prescribing Information to determine the patient's Child-Pugh classification, then determine appropriate starting dosage

- Routinely monitor patients taking OCALIVA for biochemical response, tolerability, and disease progression. Re-evaluate Child-Pugh classification and adjust dosage if needed. **Reduce dosing frequency to once weekly for patients who progress to Child-Pugh Class B or C**

How supplied/storage[1]

5 mg

5 mg OCALIVA is available as an off-white to yellow, round tablet debossed with "INT" on one side and "5" on the other side

— 30 tablets (NDC 69516-005-30)

10 mg

10 mg OCALIVA is available as an off-white to yellow, triangular tablet debossed with "INT" on one side and "10" on the other side

— 30 tablets (NDC 69516-010-30)

- OCALIVA tablets should be stored at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-86°F)

IMPORTANT SAFETY INFORMATION

Liver-Related Adverse Reactions

Dose-related, liver-related adverse reactions including jaundice, worsening ascites and primary biliary cholangitis flare have been observed in clinical trials, as early as one month after starting treatment with OCALIVA 10 mg once daily up to 50 mg once daily (up to 5-times the highest recommended dosage). Monitor patients during treatment with OCALIVA for elevations in liver biochemical tests and for the development of liver-related adverse reactions.

Severe Pruritus

Severe pruritus was reported in 23% of patients in the OCALIVA 10 mg arm, 19% of patients in the OCALIVA titration arm, and 7% of patients in the placebo arm in a 12-month double-blind randomized controlled trial of 216 patients. Severe pruritus was defined as intense or widespread itching, interfering with activities of daily living, or causing severe sleep disturbance, or intolerable discomfort, and typically requiring medical interventions. Consider clinical evaluation of patients with new onset or worsening severe pruritus. Management strategies include the addition of bile acid resins or antihistamines, OCALIVA dosage reduction, and/or temporary interruption of OCALIVA dosing.

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Interconnect® SUPPORT SERVICES **Your Patients. Our Commitment.**

When you prescribe OCALIVA for your patients, Interconnect® provides them with comprehensive support.

Your patients can expect comprehensive, personalized support—right from the start

Your dedicated Care Coordinator will call you after you enroll and provide ongoing personalized support. Communications from Interconnect® can be tailored to your needs and preferences.

Financial assistance

Help navigating insurance coverage to provide treatment access for **as little as a $0 co-pay**[a]

Personalized support

Ongoing personalized support and check-ins, tailored to individual preferences

Education

Informational resources for your patients, including refill reminders and answers to questions about OCALIVA

[a]Except where prohibited by state law. Some people will not qualify for certain offerings. Intercept reserves the right to rescind, revoke, or amend this offer without notice.

For full terms and conditions, please visit ocalivahcp.com/downloadtermsandconditions.

For more information contact Interconnect® Support Services

- In an independent study, both patients and providers rated the Interconnect® support services very highly, outranking similar programs

1-844-622-ICPT **interconnectsupport.com**

IMPORTANT SAFETY INFORMATION

Reduction in HDL-C

Patients with PBC generally exhibit hyperlipidemia characterized by a significant elevation in total cholesterol primarily due to increased levels of high-density lipoprotein-cholesterol (HDL-C). Dose-dependent reductions from baseline in mean HDL-C levels were observed at 2 weeks in OCALIVA-treated patients, 20% and 9% in the 10 mg and titration arms, respectively, compared to 2% in the placebo arm. Monitor patients for changes in serum lipid levels during treatment. For patients who do not respond to OCALIVA after 1 year at the highest recommended dosage that can be tolerated (maximum of 10 mg once daily), and who experience a reduction in HDL-C, weigh the potential risks against the benefits of continuing treatment.

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IMPORTANT SAFETY INFORMATION

Adverse Reactions

The most common adverse reactions occurring in ≥5% of subjects taking OCALIVA were pruritus, fatigue, abdominal pain and discomfort, rash, oropharyngeal pain, dizziness, constipation, arthralgia, thyroid function abnormality, and eczema.

Drug Interactions

- **Bile Acid Binding Resins:** Bile acid binding resins such as cholestyramine, colestipol, or colesevelam adsorb and reduce bile acid absorption and may reduce the absorption, systemic exposure, and efficacy of OCALIVA. If taking a bile acid binding resin, take OCALIVA at least 4 hours before or 4 hours after taking the bile acid binding resin, or at as great an interval as possible.
- **Warfarin:** The International Normalized Ratio (INR) decreased following coadministration of warfarin and OCALIVA. Monitor INR and adjust the dose of warfarin, as needed, to maintain the target INR range when coadministering OCALIVA and warfarin.
- **CYP1A2 Substrates with Narrow Therapeutic Index:** Obeticholic acid, the active ingredient in OCALIVA, may increase the exposure to concomitant drugs that are CYP1A2 substrates. Therapeutic monitoring of CYP1A2 substrates with a narrow therapeutic index (e.g., theophylline and tizanidine) is recommended when coadministered with OCALIVA.
- **Inhibitors of Bile Salt Efflux Pump:** Avoid concomitant use of inhibitors of the bile salt efflux pump (BSEP) such as cyclosporine. Concomitant medications that inhibit canalicular membrane bile acid transporters such as the BSEP may exacerbate accumulation of conjugated bile salts including taurine conjugate of obeticholic acid in the liver and result in clinical symptoms. If concomitant use is deemed necessary, monitor serum transaminases and bilirubin.

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To report SUSPECTED ADVERSE REACTIONS, contact Intercept Pharmaceuticals, Inc. at 1-844-782-ICPT or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Reference: 1. OCALIVA [package insert]. New York, NY: Intercept Pharmaceuticals, Inc.; 2020.

To learn more about OCALIVA, please visit ocalivahcp.com.

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For more information about Intercept Pharmaceuticals, Inc., please visit interceptpharma.com.

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