Real patients

Help your patients get their best experience with OCALIVA

A guide for dosing and pruritus management

INDICATION

OCALIVA, a farnesoid X receptor (FXR) agonist, is indicated for the treatment of adult patients with primary biliary cholangitis (PBC)

- without cirrhosis or
- with compensated cirrhosis who do not have evidence of portal hypertension,

either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients 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 PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

- **Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis.**
- **OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension.**
- **Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation; have compensated cirrhosis and develop evidence of portal hypertension; or experience clinically significant hepatic adverse reactions while on treatment.**

Contraindications

OCALIVA is contraindicated in patients with:

- decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event.
- compensated cirrhosis who have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia).
- complete biliary obstruction.

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

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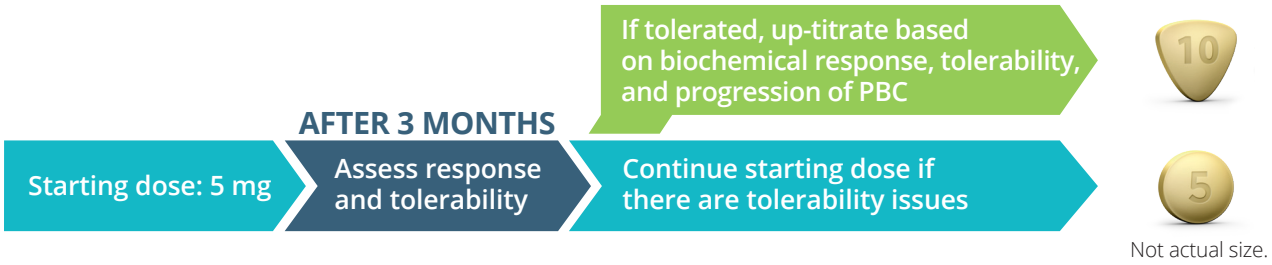
DOSAGE AND ADMINISTRATION FOR OCALIVA

For patients without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension[1]

Prior to the initiation of OCALIVA, healthcare providers should determine whether the patient has decompensated cirrhosis (eg, Child-Pugh Class B or C), has had a prior decompensation event, or has compensated cirrhosis with evidence of portal hypertension (eg, ascites, gastroesophageal varices, persistent thrombocytopenia) because OCALIVA is contraindicated in these patients.

- Starting dose: **5 mg once daily**
- Titration dose: **10 mg once daily**
  - — After the first 3 months, for patients who have not achieved an adequate reduction in ALP and/or total bilirubin and who are tolerating OCALIVA, increase to a maximum dosage of 10 mg once daily



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Patient management[1]

- Continue to closely monitor patients with compensated cirrhosis, concomitant hepatic disease (eg, autoimmune hepatitis, alcoholic liver disease), and/or severe intercurrent illness for new evidence of portal hypertension[a] or increases above the upper limit of normal in total bilirubin, direct bilirubin, or prothrombin time to determine whether drug discontinuation is needed
- Permanently discontinue OCALIVA in patients who:
  - — develop laboratory or clinical evidence of hepatic decompensation (eg, ascites, jaundice, variceal bleeding, hepatic encephalopathy)
  - — have compensated cirrhosis and develop evidence of portal hypertension[a]
  - — experience clinically significant hepatic adverse reactions, or
  - — develop complete biliary obstruction

[a]Eg, ascites, gastroesophageal varices, persistent thrombocytopenia.
ALP, alkaline phosphatase; PBC, primary biliary cholangitis.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

Hepatic Decompensation and Failure in PBC Patients with Cirrhosis

Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in PBC patients with cirrhosis, either compensated or decompensated. Among postmarketing cases reporting it, median time to hepatic decompensation (e.g., new onset ascites) was 4 months for patients with compensated cirrhosis; median time to a new decompensation event (e.g., hepatic encephalopathy) was 2.5 months for patients with decompensated cirrhosis. Some of these cases occurred in patients with decompensated cirrhosis when they were treated with higher than the recommended dosage for that patient population; however, cases of hepatic decompensation and failure have continued to be reported in patients with decompensated cirrhosis even when they received the recommended dosage.

TITRATION SCHEDULE FOR MANAGING PRURITUS

In a roundtable of 11 leading experts in the fields of gastroenterology, hepatology, and psychiatry, recommendations related to pruritus management were suggested.[2]

When administering OCALIVA, ask your patients about pruritus and re-evaluate 2–4 weeks after the initial dose to ensure that pruritus symptoms are managed and not left untreated.[2]

Consider titrating OCALIVA dosage to help patients experiencing pruritus due to treatment.

Assess pruritus[a] at current daily OCALIVA dosage[1,2]

	IF AT 5 MG ONCE DAILY	IF AT 10 MG ONCE DAILY
NONE OR MILD	Up-titrate to 10 mg[b] once daily	Stay at 10 mg
MODERATE	Up-titrate to 10 mg[b] once daily OR stay at 5 mg[c]	Stay at 10 mg
SEVERE	Reduce to 5 mg every other day[c] OR temporarily pause treatment for up to 2 weeks[d]	Reduce to 5 mg once daily[c]

Consider the following management strategies when evaluating patients with new onset or worsening severe pruritus[1]:

- Add an antihistamine or bile acid binding resin
- Reduce the dosage of OCALIVA to:
  - —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 and titrate the dosage based on biochemical response and tolerability
- Consider discontinuing OCALIVA treatment in patients who continue to experience persistent, intolerable pruritus despite management strategies

[a]Pruritus severity can be assessed using objective measurement tools, such as the Visual Analogue Scale (VAS), 5-D Itch Scale, PBC-40 tool, or PBC-27 tool.[2]
[b]After the first 3 months, for patients who have not achieved an adequate reduction in ALP and/or total bilirubin and who are tolerating OCALIVA, increase to maximum of 10 mg once daily.[1]
[c]Based on clinical judgment and patient feedback, which may include factors other than pruritus severity and should reflect patient choice and comfort.[2]
[d]If treatment is paused for 2 weeks, restart at 5 mg every other day, then gradually up-titrate to 5 mg daily and, if tolerated, to 10 mg daily.[2]

IMPORTANT SAFETY INFORMATION (cont'd)

Hepatic Decompensation and Failure in PBC Patients with Cirrhosis (cont'd)

Hepatotoxicity was observed in the OCALIVA clinical trials. A dose-response relationship was observed for the occurrence of hepatic adverse reactions including jaundice, worsening ascites, and primary biliary cholangitis flare with dosages of OCALIVA of 10 mg once daily to 50 mg once daily (up to 5-times the highest recommended dosage), as early as one month after starting treatment with OCALIVA in two 3-month, placebo-controlled clinical trials in patients with primarily early stage PBC.

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

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MONITORING PATIENTS FOR TREATMENT SUCCESS ON OCALIVA

Help patients get the best experience on OCALIVA by evaluating response and managing pruritus throughout PBC treatment.

The recommended pruritus management strategies include titration of OCALIVA dosing, close follow-up with patients, and offering pharmacological and nonpharmacological treatments.[2]

Monitoring schedule[1,2]

START OF TREATMENT	**INITIATE** OCALIVA at 5 mg once daily. **MANAGE** patient expectations regarding when they may see a response to treatment (ie, some patients may see reductions in ALP as early as the first 2 weeks) and the possibility of pruritus. **DISCUSS** the importance of preventative pruritus management and the Intercept Pruritus Kit.[a]
2 WEEKS	**ASSESS** for pruritus, as it may present within the first 2 weeks of treatment, and remind patients that OCALIVA may still be lowering their ALP.
1 MONTH	**EVALUATE** for pruritus and review management strategies, intensifying management as needed. **ENSURE** adherence to OCALIVA by reminding patients of the importance of ALP reductions.
3 MONTHS	**CONTINUE** to evaluate pruritus to determine if the patient is appropriate for up-titration to 10 mg.[b]
3-6 MONTHS	**PERFORM** liver monitoring every 3 to 6 months per AASLD guidelines[3] and your clinical judgment. In addition, continue monitoring for pruritus and other side effects.

[a]The Intercept Pruritus Kit is available in the US only, and is not provided outside of the US.[2]
[b]After the first 3 months, for patients who have not achieved an adequate reduction in ALP and/or total bilirubin and who are tolerating OCALIVA, increase to maximum of 10 mg once daily.[1]

Routinely monitor patients for biochemical response, tolerability, and progression of PBC, including hepatic adverse reactions, during treatment[1]

Consider discontinuing OCALIVA treatment in patients who continue to experience persistent, intolerable pruritus despite management strategies[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Hepatic Decompensation and Failure in PBC Patients with Cirrhosis (cont'd)

Routinely monitor patients for progression of PBC, including hepatic adverse reactions, with laboratory and clinical assessments to determine whether drug discontinuation is needed. Closely monitor patients with compensated cirrhosis, concomitant hepatic disease (e.g., autoimmune hepatitis, alcoholic liver disease), and/or with severe intercurrent illness for new evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia) or increases above the upper limit of normal in total bilirubin, direct bilirubin, or prothrombin time to determine whether drug discontinuation is needed. *(cont'd)*

PROACTIVE MANAGEMENT STRATEGIES CAN HELP YOUR PATIENTS WHO ARE EXPERIENCING PRURITUS

Patients can incorporate these suggestions into their daily routine to help manage pruritus[2]:

- Advise patients to take cooler showers; if a patient prefers warmer showers, recommend showering in the morning to avoid escalation of symptoms near bedtime
- Recommend switching to mild or unscented soap and laundry detergents
- Encourage the application of moisturizers that can help prevent dry skin
- Advise patients to avoid clothing made from materials that can irritate the skin
- Recommend the elimination of tobacco smoking

The Intercept Pruritus Kit for your patients

This Intercept-provided pruritus kit contains samples to soothe pruritus symptoms, including but not limited to aloe gel, lidocaine spray, an oatmeal bath, and hydrocortisone ointment.[2]

AASLD, American Association for the Study of Liver Diseases; ALP, alkaline phosphatase; PBC, primary biliary cholangitis.

References: 1. OCALIVA full prescribing information. New York, NY: Intercept Pharmaceuticals, Inc; 2021. **2.** Pate J, Gutierrez JA, Frenette CT, et al. Practical strategies for pruritus management in the obeticholic acid-treated patient with PBC: proceedings from the 2018 expert panel. *BMJ Open Gastroenterol.* 2019;6(1):e000256. doi:10.1136/bmjgast-2018-000256 **3.** Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases. *Hepatology.* 2019;69(1):394-419.

IMPORTANT SAFETY INFORMATION (cont'd)

Hepatic Decompensation and Failure in PBC Patients with Cirrhosis (cont'd)

Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation (e.g., ascites, jaundice, variceal bleeding, hepatic encephalopathy), have compensated cirrhosis and develop evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia), experience clinically significant hepatic adverse reactions, or develop complete biliary obstruction. If severe intercurrent illness occurs, interrupt treatment with OCALIVA and monitor the patient's liver function. After resolution of the intercurrent illness, consider the potential risks and benefits of restarting OCALIVA treatment.

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 clinical 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 binding resins or antihistamines, OCALIVA dosage reduction, and/or temporary interruption of OCALIVA dosing.

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ACCESS TO OCALIVA PATIENT ASSISTANCE

Ensure your patients have access to the support they need throughout their treatment journey by enrolling them in Interconnect® Support Services.

For more information about Interconnect® Support Services, visit interconnectsupport.com or call 1-844-622-4278.

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IMPORTANT SAFETY INFORMATION (cont'd)

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.

Adverse Reactions

The most common adverse reactions (≥5%) are: 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 co-administering OCALIVA and warfarin.
- CYP1A2 Substrates with Narrow Therapeutic Index
  Obeticholic acid 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 co-administered 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.

Please see additional Important Safety Information on previous pages and accompanying **Full Prescribing Information, including Boxed WARNING,** for OCALIVA or visit www.ocalivahcp.com.

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.

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