OCALIVA®
obeticholic acid

ADHERENCE

Optimizing Patient Adherence to OCALIVA

The importance of personalized patient support and motivation

Patients with primary biliary cholangitis (PBC) live with a complex, progressive condition.[1] PBC can best be managed with daily adherence to a treatment regimen.

Medication adherence can be optimized when patients' beliefs concerning their illness and its treatment are understood.

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.

SELECTED 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.**

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

Medication Adherence: A Complex Problem With Costly Consequences

In order for OCALIVA, or any medication, to work effectively—in this case, lowering alkaline phosphatase (ALP) and preventing the toxic buildup of bile acids in the liver[2]—patients must be adherent to their treatment regimen.

> ***"Drugs don't work in patients who don't take them."***
>
> –Former Surgeon General C. Everett Koop, MD

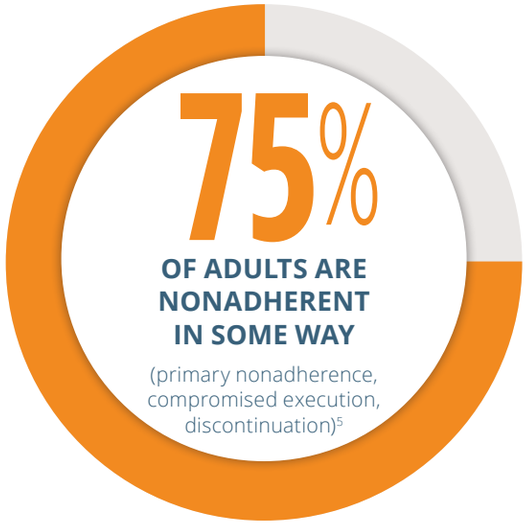
The direct and indirect costs of nonadherence

Approximately half of all prescriptions dispensed for chronic illnesses are not taken as prescribed.[3] Nonadherence accounts for enormous costs and consequences:

$337 BILLION
in preventable healthcare costs[4]

Approximately
125,000
deaths annually[3]

Estimated
1 patient death every
4.2 MINUTES[3]



Understanding Your Patients' Motivations and Beliefs Can Help Address Nonadherence

Patients are nonadherent to their medications for many different reasons, ranging from practical barriers to psychological beliefs.

Drivers of nonadherence	Examples
PRACTICAL	***"My medicine is too expensive."***
ENVIRONMENTAL/ SOCIAL	***"I feel alone in managing my condition."***
BELIEFS ABOUT CONDITION	***"It's not serious; the symptoms come and go."***
BELIEFS ABOUT TREATMENT	***"I'm worried about side effects."***

Support programs and resources that address the personal drivers of nonadherence can empower patients to take a more active role in their health.

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Beliefs and Barriers Affecting Patient Adherence to OCALIVA

Utilizing thematic analysis,[6-9] customized research identified patient beliefs and perceptions that affect treatment for PBC.[a]

Key insights and patient voices are shown in the table below, along with recommendations for what you can do to address these potential barriers with your patients to support adherence to treatment.

Key finding	What you can do
"My experience with PBC is different from what I hear from others. I don't have the same symptoms, and their negativity really scares me."	• Convey to patients that one person's experience with PBC may differ from another's • Encourage patients to learn all they can about PBC and provide educational tools and resources
"People tell me I must not be sick because I look healthy." **-and-** **"I have other conditions with similar side effects to PBC. It's hard to tell what's causing my symptoms."**	• Spend time talking about the individual patient's symptoms • Encourage patients to keep track of their symptoms between appointments and share them with you • Ask patients what they would like to achieve from treatment and discuss how this aligns with clinical goals
"I don't understand what's happening to me. I'm afraid that I'll die from PBC."	• Reinforce with patients the key hallmarks of PBC and the need for ongoing monitoring, including blood tests and disease state markers
"I've been told that OCALIVA is filled through a specialty pharmacy. How does that work, and who can I call when I need a refill or have a question about OCALIVA?"	• Explain how specialty pharmacies differ from other pharmacies • Share the contact information for the point person in your practice

[a]Combination of insight mining, literature review of published papers, social listening assessment, and in-depth interview of patients, healthcare providers, and advocacy group representatives.

Interconnect® Support Services: Personalized Treatment Support for Patients Prescribed OCALIVA

When you choose OCALIVA for your patients, Interconnect® Support Services is available to provide comprehensive, personalized support to assist you and help your patients start and stay on therapy. Interconnect® Support Services:

- **EMPOWERS** patients to better manage their condition through customized resources received by mail or email
- **ENGAGES** patients on a personal level by connecting them with dedicated Care Coordinators
- **EDUCATES** patients about utilizing specialty pharmacies
- **ENABLES** access to OCALIVA through benefit investigation and co-pay assistance

Our Commitment to Adherence

Interconnect® patient support can help. This unique service offers comprehensive, personalized support to help your patients start and stay on therapy.

Interconnect® SUPPORT SERVICES

To learn more:

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

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IMPORTANT SAFETY INFORMATION

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

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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.

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.

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.

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. 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.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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 click here for **Full Prescribing Information, including Boxed WARNING,** for OCALIVA.

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

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References:

1. Sclair SN, Little E, Levy C. Current concepts in primary biliary cirrhosis and primary sclerosing cholangitis. *Clin Transl Gastroenterol*. 2015;6(8):e109. doi:10.1038/ctg.2015.33 **2.** OCALIVA full prescribing information. New York, NY: Intercept Pharmaceuticals, Inc; 2021. **3.** U.S. Food and Drug Administration. Why you need to take your medications as prescribed or instructed. https://www.fda.gov/drugs/resourcesforyou/specialfeatures/ucm485545.htm. Accessed May 2, 2017. **4.** The Express Scripts Lab. The 2013 drug trend report. April 14, 2014. http://lab.express-scripts.com/lab/drug-trend-report. Accessed May 6, 2016. **5.** PhRMA. Improving prescription medicine adherence is key to better healthcare: taking medicines as prescribed can lower costs and improve health outcomes. http://phrma.org/sites/default/files/pdf/PhRMA_Improving%20Medication%20Adherence_Issue%20Brief.pdf. Accessed May 2, 2017. **6.** Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101. **7.** Petrie KJ, Jago LA, Devcich DA. The role of illness perceptions in patients with medical conditions. *Curr Opin Psychiatry*. 2007;20(2):163-167. **8.** Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res.* 2006;60(6):631-637. **9.** Zolnierek KB, DiMatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care.* 2009;47(8):826-834.

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

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