Intercept

PrOCALIVA® (obeticholic acid), 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, has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization.

OCALIVA: Dose guide

PAAB

OCALIVA®
obeticholic acid

CA-PP-PB-0141

OCALIVA: Taken orally

OCALIVA is available in 2 dosage strengths:

- 5 mg 

- 10 mg 

Pill is not actual size.

Treatment with OCALIVA in patients with moderate and severe hepatic impairment should be initiated and monitored by a healthcare provider with experience managing PBC.

Prior to the initiation of OCALIVA in patients with suspected cirrhosis, assess the patient's Child-Pugh classification (A, B or C) and determine the appropriate starting dosage, as follows:

For non-cirrhotic or compensated Child-Pugh Class A patients

Recommended starting dose:
5 mg once daily

Assess efficacy and tolerability

If tolerable, increase to a maximum dose of **10 mg once daily*** if inadequate reduction in ALP and/or total bilirubin levels after first 6 months of treatment

Adapted from OCALIVA Product Monograph.

- Routinely monitor patients during OCALIVA treatment for progression of PBC disease with laboratory and clinical assessments to determine whether dosage adjustment is required
  - Reduce the dosing frequency for patients who progress from Child-Pugh Class A to Child-Pugh Class B or C
- Close monitoring is recommended for patients at an increased risk of hepatic decompensation, including those with laboratory evidence of worsening liver function (i.e. total bilirubin, INR, albumin) and/or progression to cirrhosis
  - Interrupt OCALIVA treatment in patients with laboratory or clinical evidence of worsening liver function indicating risk of decompensation, and monitor the patient's liver function
  - If the patient's condition returns to baseline, weigh the potential benefits of restarting OCALIVA treatment
  - If OCALIVA is re-initiated, use the recommended starting dosage with adjustment for Child-Pugh classification
- Consider discontinuing OCALIVA in patients who have experienced clinically significant liver-related adverse reactions

OCALIVA administration

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.

For patients taking a bile acid binding resin, OCALIVA should be taken at least 4 hours before or 4 hours after taking the bile acid resin, or at as great an interval as possible.

OCALIVA should be taken orally and 30 minutes before breakfast

For Child-Pugh Class B or C or patients with a prior decompensation event†

Recommended starting dose:
5 mg once weekly

At 3 months

Assess efficacy and tolerability

If tolerable, titrate up to **5 mg twice weekly (at least 3 days apart)*** if inadequate reduction in ALP and/or total bilirubin levels

Subsequent doses

Titrate to a maximum dose of
10 mg twice weekly (at least 3 days apart)
based on response and tolerability

Adapted from OCALIVA Product Monograph.

OCALIVA is indicated for the treatment of PBC in combination with UDCA in adults with inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA

* Prior to dosage adjustment, re-calculate the Child-Pugh classification.

† Gastroesophageal variceal bleeding, new or worsening jaundice, spontaneous bacterial peritonitis, etc.

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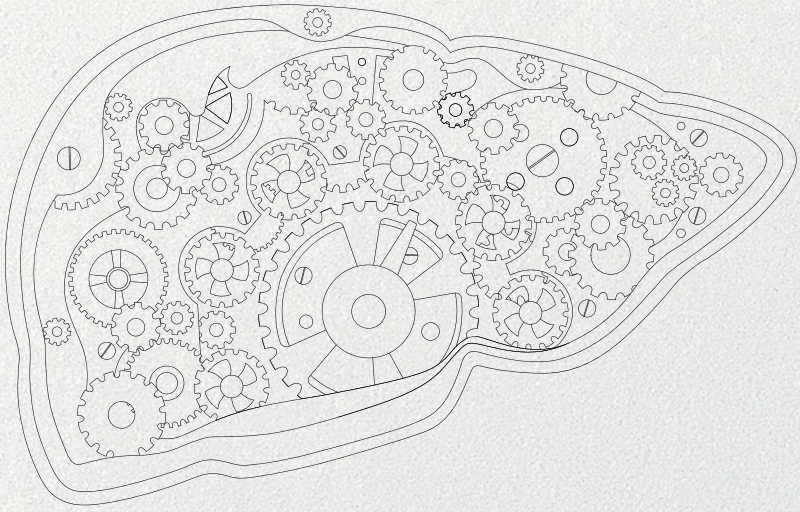
OCALIVA: Pruritus management guide



REFERENCE: OCALIVA Product Monograph, Intercept Pharmaceuticals, Inc. October 5, 2018.

OCALIVA®
obeticholic acid

Setting patient expectations about pruritus from the start

In the POISE trial, pruritus was the most common adverse event reported (OCALIVA titration + UDCA: 56%)*

- **Approximately 60% of patients had a history of pruritus upon enrollment in POISE**
- **62% (24/39) of patients with pruritus in the titration arm required an intervention (e.g. dose adjustment, treatment interruption or initiation of bile acid binding resin or antihistamine)**

1% of patients in the OCALIVA titration arm discontinued treatment due to pruritus

- Pruritus was mostly mild to moderate in severity and generally started within the first month following the initiation of treatment with OCALIVA and decreased in severity over time with continued dosing
- Severe pruritus was reported in 19% of patients in the OCALIVA titration arm, and 7% of patients in the placebo arm of the POISE trial
  - 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
- For patients in the OCALIVA treatment arm who increased their dosage from 5 mg once daily to 10 mg once daily after 6 months of treatment (n=33), the incidence of severe pruritus was 0% from months 0 to 6 and 15% from months 6 to 12

* POISE was a phase III, randomized, double-blind, placebo-controlled, 12-month trial in patients with PBC (n=216) who were taking UDCA for at least 12 months (on a stable dosage for at least 3 months), or who were unable to tolerate UDCA and did not receive UDCA for at least 3 months. Patients were randomly assigned 1:1:1 to receive either OCALIVA 10 mg once daily for the entire 12 months (n=73), OCALIVA titration (5 mg once daily for the initial 6 months, with the option to increase to 10 mg dosage once daily for the last 6 months if the patient was tolerating OCALIVA but had ALP ≥1.67 x ULN and/or bilirubin >ULN or less than 15% ALP reduction) (n=70) or placebo (n=73). OCALIVA or placebo was administered in combination with UDCA in 93% of patients during the trial and as monotherapy in 7% of patients who were unable to tolerate UDCA. Initiation of therapy with a starting dosage of OCALIVA 10 mg once daily is not recommended due to an increased risk of pruritus.

Considerations for managing intolerable pruritus

For patients with intolerable pruritus on OCALIVA, consider one or more of the following:

ADD an antihistamine or bile acid binding resin

REDUCE THE DOSAGE of OCALIVA to:

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

- 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

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

- 5 mg once weekly, for patients intolerant to 5 mg twice weekly
- 10 mg once weekly, for patients intolerant to 10 mg twice weekly

TEMPORARILY INTERRUPT OCALIVA dosing

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

- for up to 2 weeks followed by restarting at a reduced dosage
  - Increase the dosage to 10 mg once daily, as tolerated, to achieve optimal response

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

- for up to 2 weeks followed by restarting at a reduced dosage, if applicable
  - Increase the dosage to 10 mg twice weekly, as tolerated, to achieve optimal response

Consider discontinuing OCALIVA treatment in patients who continue to experience persistent, intolerable pruritus

Clinical use:

Marketing authorization with conditions for this indication is based on a randomized, placebo-controlled, phase 3 study that assessed alkaline phosphatase (ALP) and bilirubin as a composite endpoint.
Marketing authorization with conditions for the indication for use as monotherapy is based on data from a pooled analysis from a randomized, phase III placebo-controlled study, of 12-month duration, and a randomized, double-blind, phase II placebo-controlled study, of 3-month duration.
Pediatrics (<16 years of age): The safety and efficacy of OCALIVA in pediatric patients have not been established.
Geriatrics (≥65 years of age): Efficacy and safety data in subjects over 65 years of age are limited. Although no overall differences in safety or efficacy were observed between subjects greater than 65 and those less than 65 years of age. The safety and efficacy of OCALIVA as monotherapy in subjects over 65 years of age have not been established.

Contraindications:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container
- Patients with complete biliary obstruction

Most serious warnings and precautions:

Hepatic decompensation and failure in incorrectly dosed PBC patients with Child-Pugh Class B or C or decompensated cirrhosis

- In post-marketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with 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
- Treatment with OCALIVA in patients with moderate to severe hepatic impairment should be initiated and monitored by a healthcare provider with experience managing PBC

Other relevant warnings and precautions:

- Liver-related adverse reactions
- Severe pruritus
- Use in pregnant and/or nursing women
- Patients with hepatic impairment
- Reduction in high density lipoprotein-cholesterol (HDL-C)

For more information:

Please consult the Product Monograph at **https://www.interceptpharma.com/wp-content/uploads/2018/10/OCALIVA_CA_PM_E.pdf** for important information relating to adverse reactions, interactions and dosing information which has not been discussed in this piece.

The Product Monograph is also available by calling our medical department at: 1-844-782-4278.