Ocaliva

(obeticholic acid)

New Product Slideshow

MPR

Introduction

- **Brand name:** Ocaliva
- **Generic name:** Obeticholic acid
- **Pharmacological class:** Farnesoid X receptor (FXR) agonist
- **Strength and Formulation:** 5mg, 10mg; tablets
- **Manufacturer:** Intercept
- **How supplied:** Bottle—30
- **Legal Classification:** Rx

OCALIVA


Rx only
OCALIVA™
(obeticholic acid) tablets
10 mg
30 tablets
Intercept

Indications

- Treatment of **primary biliary cholangitis** (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA

Dosage & Administration

- Initially 5mg once daily
- Increase to 10mg once daily if inadequate reduction in ALP and/or total bilirubin after 3 months and tolerated the drug; max 10mg once daily
- **Moderate or severe hepatic impairment:** initially 5mg once weekly; increase to 5mg twice weekly (≥3 days apart) then to 10mg twice weekly (≥3 days apart) if inadequate reduction in ALP and/or total bilirubin after 3 months and tolerated the drug

Dosage & Administration

- **Intolerable pruritus:** consider adding an antihistamine or bile acid binding resin; or reducing dose to 5mg every other day (if intolerant to 5mg daily) or 5mg once daily (if intolerant to 10mg daily); or temporarily interrupt for up to 2 weeks then restart at lower dose
- Increase dose to 10mg once daily as tolerated for optimal response

Considerations for Special Populations

- **Pregnancy:** Limited data to inform a drug-associated risk
- **Nursing mothers:** Consider benefits and adverse effects
- **Pediatric:** Not established
- **Geriatric:** No differences in safety or efficacy
- **Hepatic impairment:** See Adults

Contraindications

- Complete biliary obstruction

Warnings/Precautions

- **Discontinue** if intolerable pruritus persists or complete biliary obstruction develops
- **Monitor** for elevations in liver biochemical tests and liver-related adverse effects
- **Monitor** for changes in serum lipid levels
- If unresponsive after 1 year of treatment at max tolerable dose (10mg once daily) and experienced HDL-C reduction, reevaluate

Interactions

- Separate by ≥4hrs or at greatest possible interval with bile acid binding resins (eg, cholestyramine, colestipol, colesevelam)
- **Concomitant warfarin:** monitor INR and adjust dose as needed
- **Concomitant CYP1A2 substrates** with narrow therapeutic index (eg, theophylline, tizanidine); monitor

Adverse Reactions

- Pruritus
- Fatigue
- Abdominal pain/discomfort
- Rash
- Oropharyngeal pain
- Dizziness
- Constipation
- Arthralgia
- Thyroid function abnormality
- Eczema
- Liver-related effects
- HDL-C reduction

Mechanism of Action

- The farnesoid X receptor is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways
- Its activation **decreases** the intracellular hepatocyte concentrations of bile acids by suppressing *de novo* synthesis from cholesterol and by increased transport of bile acids out of the hepatocytes
- This limits the overall size of the circulating bile acid pool while promoting choleresis, reducing hepatic exposure to bile acids

Pharmacokinetics

- **Distribution:** Highly protein bound (>99%) in human plasma
- **Metabolism:** Conjugated with glycine or taurine in the liver
- **Elimination:** Fecal

Clinical Trials

- **Trial 1** was a randomized, double-blind, placebo-controlled, 12-month trial (N=216) that evaluated the safety and efficacy of Ocaliva in patients with PBC who were taking UDCA for ≥12 months or who were unable to tolerate UDCA and did not receive for ≥3 months

Clinical Trials

- Patients were randomized (1:1:1) to receive either Ocaliva 10mg once daily for 12 months, Ocaliva titration, or placebo
- The **primary endpoint** was a responder analysis at Month 12, defined as a composite of ALP <1.67×ULN, total bilirubin ≤ULN, and an ALP decrease ≥15%

Clinical Trials

- Study data showed that **48%** (95% CI: 36, 60) of patients in the Ocaliva 10mg arm and **46%** (95% CI: 34, 58) in the Ocaliva titration arm achieved a response to the primary composite endpoint at Month 12, vs. **10%** (95% CI: 4, 19) of patients in the placebo arm

Clinical Trials

- In a pooled analysis, 51 PBC patients with baseline ALP ≥1.67×ULN and/or total bilirubin >ULN were evaluated for a biochemical response to Ocaliva as monotherapy
- At Month 3, **38%** of Ocaliva-treated patients achieved a response to the composite endpoint vs. **4%** of placebo-treated patients
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/ocaliva/drug/34568/