8th February 2018

OCALIVA®▼ (obeticholic acid) Important Prescriber Information.

Reinforced differential dosing recommendations for OCALIVA in primary biliary cholangitis (PBC) patients with moderate and severe hepatic impairment.

Dear Healthcare Professional,

Intercept, in agreement with the European Medicines Agency and the National Competent Authority, is reminding prescribers about OCALIVA dosing in patients with moderate to severe hepatic impairment.

Summary

Due to the risk of serious liver injury in patients with moderate to severe liver impairment, doctors are reminded:

- that prior to initiation of treatment with obeticholic acid the patient's hepatic status must be known
- to adjust doses of OCALIVA in patients with moderate to severe hepatic impairment (see Table 1 below)
- to monitor all patients for progression of PBC disease with laboratory and clinical assessment to determine whether dosage adjustment is needed
- to monitor patients at an increased risk of hepatic decompensation more closely, including those with laboratory evidence of worsening liver function or progression to cirrhosis
- to reduce dosing frequency in patients who progress to advanced disease (i.e. from Child-Pugh Class A to Child-Pugh Class B or C).

Background on the safety concern

OCALIVA is a farnesoid X receptor (FXR) agonist and a modified bile acid approved for the treatment of PBC, in combination with ursodeoxycholic acid (UDCA), in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

In the post-marketing setting, serious liver injury and death have been reported with more frequent dosing of obeticholic acid than recommended in patients with moderate to severe decreases in liver function. Liver-related adverse events have occurred both early in treatment and after months of treatment.

Hepatically impaired PBC patients with cirrhosis or elevated bilirubin are most at risk of liver related complications.

Section 4.2 of the SmPC has been updated with the following specific dosing recommendations for patients with **hepatic impairment (Child Pugh Classes A, B and C):**

Table 1: Dosage Regimen by PBC Patient Population

Staging/Classification	**Non-Cirrhotic or** **Child-Pugh Class A**	**Child-Pugh Class B or C or** **Decompensated Cirrhotic**
Starting Dosage	**5 mg once daily**	**5 mg once weekly**
Dosage Titration	For patients who have not achieved an adequate reduction in alkaline phosphatase (ALP) and/or total bilirubin after **6 months** of treatment and the patient is tolerating obeticholic acid, titrate up to **10 mg once daily**	For patients who have not achieved an adequate reduction in ALP and/or total bilirubin after **3 months** of treatment and the patient is tolerating obeticholic acid, titrate up to **5 mg twice weekly** (at least 3 days apart) and subsequently to **10 mg twice weekly** (at least 3 days apart) based on response and tolerability
Maximum Dosage	**10 mg once daily**	**10 mg twice weekly** (at least 3 days apart)

Call for reporting

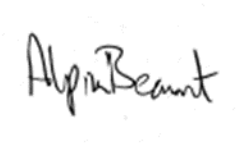
Please continue to report suspected adverse drug reactions (ADRs) to National Competent Authorities in accordance with the national spontaneous reporting system, see section 4.8 of the SmPC for how to report adverse reactions.

▼This medicinal product is subject to additional monitoring, allowing quick identification of new safety information.

Company contact point

- You also may contact our Medical Information department via phone Tel No 03301003694 email medinfo@interceptpharma.com or at https://interceptpharma.com/about/medical-information-requests/ if you have any questions about the information contained in this letter or the safe and effective use of OCALIVA.
- Intercept Pharma UK and Ireland 6th Floor, 2 Pancras Square, London, N1C 4AG UK
- Contact point details for further information are given in the product information of the medicinal product (SmPC and PIL) at http://www.ema.europa.eu/ema/.

Yours faithfully



Alpna Beaumont
Qualified Person for Pharmacovigilance
Intercept Pharma Ltd.