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IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Direct Healthcare Professional Communication

09 06 2022

Ocaliva®▼ (obeticholic acid): New contraindication for the treatment of primary biliary cholangitis (PBC) in patients with decompensated liver cirrhosis or a history of prior hepatic decompensation

Dear Healthcare Professional,

Intercept, in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA), would like to inform you of the following:

Summary

Taking into consideration the inability to establish the safety and efficacy of obeticholic acid through clinical trials in patients with PBC with decompensated liver cirrhosis, or with a prior history of hepatic decompensation, as well as new safety information from post-marketing reports, the use of obeticholic acid is now contraindicated in patients with PBC with decompensated cirrhosis (including Child-Pugh Class B or C) or a prior decompensation event.

- **Treatment should be discontinued in patients with PBC with decompensated cirrhosis currently receiving obeticholic acid.**
- **Patients should be routinely monitored for progression of PBC and treatment with obeticholic acid should be permanently discontinued in patients with laboratory or clinical evidence of hepatic decompensation including progression to Child-Pugh class B or C.**
- **Treatment with obeticholic acid should not be started if the patient has decompensated cirrhosis or a history of a decompensation event prior to treatment initiation.**
- **The SmPC and the patient leaflet are being updated to reflect this new contraindication and additional warnings based on newly available safety data.**

Background information

Obeticholic acid is a farnesoid X receptor (FXR) agonist and a modified bile acid, approved under the commercial name Ocaliva. It received conditional marketing authorization in December 2016 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.

Interim analysis results from the studies intended to confirm efficacy and safety in patients with PBC with decompensated cirrhosis (moderate to severe hepatic impairment), i.e. study 747-401, and in a broader PBC population, i.e. study 747-302, were deemed highly likely to be futile by the trials' independent data monitoring committee. Given the difficulties completing the studies, the limited information available to further inform benefit/risk, and the medically more fragile nature of patients with PBC and decompensated cirrhosis, the SmPC is being updated to contraindicate the use of obeticholic acid in these patients. In addition, available safety data from post-marketing reports in patients with PBC with cirrhosis have also been considered, i.e. cases of hepatobiliary disorders, including hepatic failure and hepatic cirrhosis, for which there is a possibility of a causal association with obeticholic acid treatment.

As a consequence, section 4.3 ('Contraindications') of the SmPC is being updated to reflect the contraindication of obeticholic acid in patients with decompensated cirrhosis (e.g. Child-Pugh Class B or C) or a prior decompensation event, and section 4.4 ('Special warnings and precautions') will include new information about hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, occurring with obeticholic acid treatment in patients with PBC with cirrhosis, either compensated or decompensated. Section 4.8 ('Undesirable effects') is also being updated to include hepatobiliary disorders in the tabulated list of adverse reactions.

Additional changes in relation to the use of obeticholic acid in patients with concomitant hepatic disease and severe intercurrent illness will also be made throughout the SmPC.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to National Competent Authorities in accordance with the national spontaneous reporting system: www.hpra.ie.

▼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 +353 144 75 196 email medinfo@interceptpharma.com or at https://www.interceptmedinfo.com/ if you have any questions about the information contained in this letter or the safe and effective use of OCALIVA.
- Postal address: Two Pancras Square, Kings Cross, 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

Signature

Gail Cawkwell, MD, PhD

Senior Vice President Medical Affairs, Safety and Pharmacovigilance