31 July 2024

Ocaliva▼ (obeticholic acid): recommendation for revocation of the marketing authorisation in the European Union due to unconfirmed clinical benefit

Dear Healthcare professional,

ADVANZ PHARMA, in agreement with the European Medicines Agency and <National Competent Authority> would like to inform you of the following:

Summary

- **The phase 3 confirmatory Study 747-302 (COBALT) of Ocaliva in primary biliary cholangitis (PBC) patients did not confirm the clinical benefit of Ocaliva.**
- **As a consequence, the benefit-risk balance of Ocaliva is no longer favourable and its marketing authorisation in the EU has been recommended for revocation.**
- **No new patients should be started on Ocaliva outside of a clinical trial. For patients currently on treatment with Ocaliva, available treatment options should be considered.**

Background

Obeticholic acid (OCA) was authorised in the European Union (EU) in December 2016 for the treatment of adult patients with primary biliary cholangitis (PBC), in combination with ursodeoxycholic acid (UDCA), who have an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

This initial authorisation was based on results from a phase 3, randomized, double-blind, placebo-controlled study (POISE), which demonstrated a statistically significant sustained reduction in the biomarker alkaline phosphatase (ALP). At the time of approval, uncertainty remained as to the extent to which the observed changes in those laboratory parameters correlated with clinical liver outcomes.

The medicine was therefore granted a marketing authorisation on condition that the company provided additional data from the COBALT study in order to confirm the efficacy and safety of the medicine. COBALT, was a confirmatory double-blind, randomised, placebo-controlled multicentre study investigating the clinical benefit associated with Ocaliva treatment in patients with PBC who are either unresponsive or intolerant to UDCA treatment based on clinical endpoints.

EMA's human medicines committee (CHMP) has concluded a review of Ocaliva, taking into account the results from the COBALT study, in the context of all available data.

COBALT with 67% of the planned events (a non-negligible portion), failed to show any differences between treatments for the primary composite endpoint of death, liver transplant, or hepatic decompensation for the ITT population: HR 1.01 (95%CI: 0.68, 1.51), p-value: 0.954. In the

subgroup of compensated PBC patients, currently included in the authorised indication, results were nearly identical in both treatment arms (21.3% vs 21.7% OCA and placebo, respectively, HR 0.98 [95% CI: 0.58, 1.64]).

Thus, the study has failed to demonstrate any efficacy of Ocaliva treatment in relevant clinical outcomes and across the spectrum of PBC patients, including an early stage PBC subpopulation and was therefore not able to confirm the clinical benefit of Ocaliva.

Supportive real-world outcomes data were not considered sufficient to overcome the negative results of COBALT.

In conclusion, as the clinical benefit was not confirmed, the CHMP concluded that the benefit-risk balance of Ocaliva is no longer favourable and recommended the revocation of the conditional marketing authorisation in the EU. If this recommendation is confirmed by the European Commission, Ocaliva will no longer be authorised in the EU.

No new patients should be started on Ocaliva outside of a clinical trial. For patients currently on treatment with Ocaliva, available treatment options should be considered.

Call for reporting

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

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/

Company contacts point

You also may contact our Medical Information department via email medicalinformation@advanzpharma.com