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## **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](mailto:medicalinformation@advanzpharma.com)

DHPC COMMUNICATION PLAN	
<b>Medicinal product(s)/active substance(s)</b>	Ocaliva 5 mg and 10 mg film-coated tablets
<b>Marketing authorisation holder(s)</b>	ADVANZ PHARMA Limited Suite 17, Northwood House, Northwood Avenue, Santry, Dublin 9 Ireland
<b>Safety concern and purpose of the communication</b>	Recommendation on the revocation of the conditional marketing authorization of Ocaliva for primary biliary cholangitis (PBC)
<b>DHPC recipients</b>	All obeticholic acid prescribing hepatologists, prescribing gastroenterologists, prescribing internists and prescribing immunologists at their respective healthcare organizations.  The target group would be further defined at national level, in agreement with the respective national competent authority.
<b>Member States where the DHPC will be distributed</b>	Distribution in the EU/EEA Member States where Ocaliva is commercially available (France, Italy, Luxembourg, Germany, Spain, Netherlands, Austria, Belgium, Denmark, Ireland, Portugal, Sweden, Iceland, Finland, Greece, Cyprus, Hungary, Poland, Croatia, Czech Republic, Poland, Romania, Slovakia, Slovenia, Norway)
Timetable	
<b>DHPC and communication plan (in English) agreed by CHMP/CMDh</b>	27 June 2024
<b>Submission of translated DHPCs to the national competent authorities for review</b>	4 July 2024
<b>Agreement of translations by national competent authorities</b>	11 July 2024
<b>Dissemination of DHPC</b>	31 July 2024