30 August 2024
EMA/294368/2024

Update as of 12 September 2024:

By his order of 4 September 2024 in Case T-455/24 R, the President of the General Court of the European Union has temporarily suspended the Commission Implementing Decision of 30 August 2024 that had revoked the conditional marketing authorisation for Ocaliva. By virtue of this order, the marketing authorisation for Ocaliva remains valid for the time being.
EMA will provide further updates as needed.

EMA recommends revoking conditional marketing authorisation for Ocaliva

Benefits of Ocaliva no longer considered to outweigh its risks

On 27 June 2024, EMA's human medicines committee (CHMP) concluded its review of the medicine Ocaliva (obeticholic acid) and recommended that the medicine's marketing authorisation be revoked, because its benefits are no longer considered to outweigh its risks. Ocaliva is used to treat adults with primary biliary cholangitis (PBC), an autoimmune condition that causes gradual destruction of the bile ducts in the liver, which can lead to liver failure and increase the risk of liver cancer.

At the time of its conditional marketing authorisation in 2016, Ocaliva was shown to reduce the blood levels of alkaline phosphatase (ALP) and bilirubin (markers of liver damage) in patients with PBC, and this was considered indicative of an improvement in the condition of the liver. However, the clinical benefits of Ocaliva needed to be demonstrated in further studies, which were requested by EMA as part of the conditions to the marketing authorisation of the medicine. In particular, study 747-302 was a randomised clinical trial aimed at confirming the clinical benefits and safety of Ocaliva in patients for whom ursodeoxycholic acid (UDCA, another medicine for PBC) does not work well enough, or who cannot take UDCA.

The CHMP reviewed the findings from this study, alongside other available data including real-world data and data from supportive studies submitted by the company that markets Ocaliva, and information submitted by healthcare professional and patient associations. In addition, the CHMP took into account the feedback from a group of experts in liver disease, which provided their views on specific questions posed by the CHMP, and views from people with experience living with PBC.

After reviewing the available evidence, the committee concluded that the clinical benefits of Ocaliva have not been confirmed. In particular, study 747-302 failed to show that Ocaliva was more effective

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

than placebo (a dummy treatment) in terms of the number of patients whose disease worsened or who died, both in the overall population and in a group of patients with early stage PBC.

The committee also considered that the data from supportive studies and real-world data were not sufficient to confirm the benefits of Ocaliva and could not counterbalance the negative results of study 747-302. The CHMP therefore concluded that the benefits of Ocaliva do not outweigh its risks and recommended that its marketing authorisation be revoked in the European Union (EU).

The CHMP opinion was sent to the European Commission, which issued a legally binding decision applicable in all EU Member States on 30 August 2024.

Information for patients

- A recent study failed to confirm that the medicine Ocaliva (obeticholic acid) is effective at treating primary biliary cholangitis (PBC, an autoimmune condition that causes gradual destruction of the small bile ducts in the liver).
- Study 747-302 failed to show that Ocaliva was more effective than placebo (a dummy treatment) in terms of the number of patients whose disease worsened or who died, both in the overall population and in a group of patients with early stage PBC.
- EMA's human medicines committee (CHMP) therefore recommended that Ocaliva is taken off the market in the European Union, because its benefits are no longer considered to outweigh its risks. However, the company may still supply the medicine through compassionate use or named-patient programmes to patients already receiving Ocaliva.
- If you are taking Ocaliva, you should speak to your doctor about this decision and what it means for you and your treatment.

Information for healthcare professionals

- A review of available data concluded that the clinical benefits of Ocaliva (obeticholic acid), used to treat primary biliary cholangitis (PBC), have not been confirmed.
- In particular, study 747-302 failed to show any differences between Ocaliva and placebo for the primary composite endpoint of death, liver transplant, or hepatic decompensation in the overall population of PBC patients who are either unresponsive or intolerant to ursodeoxycholic acid (HR 1.01 [95%CI: 0.68, 1.51], p-value: 0.954).
- EMA therefore recommended that the marketing authorisation for Ocaliva be revoked in the European Union, because its benefits are no longer considered to outweigh its risks. However, the company may still supply the medicine through compassionate use or named-patient programmes to existing patients.
- Healthcare professionals should not start any new patients on Ocaliva outside of a clinical trial. For patients currently on treatment with Ocaliva, available treatment options should be considered.

A direct healthcare professional communication (DHPC) has been sent to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC has also been published on a dedicated page on the EMA website.

More about the medicine

Ocaliva (obeticholic acid) is used to treat adults with primary biliary cholangitis (PBC), an autoimmune condition in which there is gradual destruction of the bile ducts in the liver. As a result of the damage to the biliary ducts, bile builds up in the liver causing damage to the liver tissue. This may lead to scarring and liver failure, and may increase the risk of liver cancer. Ocaliva is used together with another medicine, ursodeoxycholic acid (UDCA), in patients who do not respond sufficiently to UDCA alone, and on its own in patients who cannot take UDCA.

PBC is rare, and Ocaliva was designated an 'orphan medicine' (a medicine used in rare diseases) on 27 July 2010.

Ocaliva was granted a conditional marketing authorisation in December 2016. Conditional authorisation is granted on the basis of less comprehensive data than are normally required. It is granted for medicines that fulfil an unmet medical need to treat serious diseases and when the benefits of having them available earlier outweigh any risks associated with using the medicines while waiting for further evidence.

At the time of approval, the main study showed that Ocaliva reduced the blood levels of the substances ALP and bilirubin (markers of liver damage) in patients with PBC, including those who could not be treated with UDCA. Reductions in ALP and bilirubin were considered to be indicators for future improvements in the condition of the liver. However, the benefits of Ocaliva needed to be confirmed in further studies.

The medicine was therefore granted a marketing authorisation on condition that the company provided further data on its benefits and safety from two additional studies (study 747-302 and study 747-401).

More information about the medicine can be found on the EMA website.

More about the procedure

The review of Ocaliva was initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a legally binding decision applicable in all EU Member States on 30 August 2024.