Ocaliva® (obeticholic acid) – FDA drug safety communication

- On December 12, 2024, the FDA announced that they have identified cases of serious liver injury among patients being treated for primary biliary cholangitis (PBC) with Intercept's Ocaliva (obeticholic acid) who did not have cirrhosis of the liver.

- The FDA had previously identified that PBC patients with advanced cirrhosis were at risk of serious liver injury when taking Ocaliva and updated the prescribing information to restrict its use in these patients. What is new is the identification of serious liver injury in individuals without cirrhosis.

- Ocaliva is approved via accelerated approval for the treatment of adult patients with PBC without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

- The new safety communication is based on the FDA's evaluation of liver safety in a postmarket clinical trial in patients who were appropriate for Ocaliva treatment based on the approved indication.

    — Among these patients, the risk of both liver transplant and death were higher in patients receiving Ocaliva compared with those receiving placebo. Specifically, among patients for whom Ocaliva was indicated, which were those with a lower risk of progression to liver transplant or death, 7 of 81 who received Ocaliva needed a liver transplant compared to 1 of 68 patients who received placebo.
    — An additional four patients receiving Ocaliva died, compared to one receiving placebo. Analyses evaluating the risk of liver transplant and death resulted in a hazard ratio of 4.77 (95% CI: 1.03, 22.09) for patients without advanced cirrhosis and not contraindicated from receiving the drug.

- Following the addition of the contraindication for PBC patients with advanced cirrhosis in May 2021, the FDA identified 20 cases (domestic, n = 13; foreign, n = 7) received by FDA between May 26, 2021, and September 18, 2024, reporting one or more of the following events in patients treated with Ocaliva: liver transplant (n = 7), evaluation or listing for liver transplant (n = 8), or liver-related death (n = 6).

    — Although the FDA was not able to assess the appropriateness of Ocaliva use for most of these cases because of limited information, they identified three U.S. cases of liver-related events that occurred in patients for whom Ocaliva should have been discontinued based on progression of their liver disease as indicated in the 2021 safety labeling changes. This shows the importance of ongoing monitoring of liver tests and prompt action to withdraw Ocaliva if there is evidence of progression towards cirrhosis.

- Health care professionals should monitor liver tests frequently in patients being treated with Ocaliva to detect and address worsening liver function early. Based on the current data, it is not clear if this monitoring will be sufficient to address the risk of serious liver injury.

    — Ocaliva treatment should be discontinued with any evidence of liver disease progression or if efficacy is not established.

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— The signs and symptoms of worsening liver injury should be explained to patients receiving Ocaliva and patients should be directed to contact health care professionals immediately if they develop any signs or symptoms of worsening liver injury.