## Ocaliva® (obeticholic acid) – Safety update

- On May 26, 2021, the FDA announced that a new *Contraindication* will be added to the Ocaliva (obeticholic acid) drug label stating that it should not be used in primary biliary cholangitis (PBC) patients with advanced cirrhosis.
    - The *Boxed Warning* will also be revised to include this information along with related warnings about this risk.
- PBC is a rare, chronic disease affecting the ducts in the liver that carry bile, which helps with digestion. Some PBC patients with cirrhosis who took Ocaliva, especially those with evidence of advanced cirrhosis, developed liver failure, sometimes requiring liver transplant.
- Ocaliva was approved in May 2016 and is indicated for the treatment of PBC in combination with Ursodiol® (ursodeoxycholic acid) (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. The benefits of Ocaliva continue to outweigh the risks for its FDA approved indication.
- Patients with PBC who have cirrhosis and are taking Ocaliva should talk to their health care provider about these new warnings.
- Patients should immediately contact their health care provider if they develop signs or symptoms of worsening liver injury or development of advanced cirrhosis such as swollen/painful belly, yellowing of the eyes or skin, bloody/black stools, coughing or vomiting blood, metal status changes, nausea vomiting or diarrhea, loss of appetite, fever, tiredness, and less frequent urination.
- Before initiating Ocaliva, health care providers should determine whether a patient with PBC has advanced cirrhosis as the medicine is contraindicated in these patients. Patients should be routinely monitored for progression of PBC with laboratory and clinical assessments, and clinically significant adverse effects, to determine whether the medicine needs to be discontinued. Ocaliva should be permanently discontinued in patients with cirrhosis who progress to advanced cirrhosis.
- The safety update is based on information submitted to the FDA Adverse Event Reporting System and the medical literature.
    - In the five years since Ocaliva's approval, there were 25 cases of serious liver injury leading to liver decompensation or liver failure associated with Ocaliva in PBC patients with compensated or decompensated cirrhosis.
    - Many patients had advanced cirrhosis before starting Ocaliva and all were taking Ocaliva at recommended dosages.
    - After starting Ocaliva, the pace of the liver decompensation or failure reported suggested these adverse events, which resulted in liver transplant in a small number of cases, were related to the drug rather than progression of the underlying PBC.