Ocaliva® (obeticholic acid) – New boxed warning

- On February 1, 2018, the FDA announced the addition of a new *Boxed Warning* to the Ocaliva (obeticholic acid) drug label regarding hepatic decompensation and failure in incorrectly dosed primary biliary cholangitis (PBC) patients with Child-Pugh Class B or C decompensated cirrhosis.

- Ocaliva is indicated for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

- Ocaliva has been incorrectly dosed daily instead of weekly in patients with moderate to severe PBC, increasing the risk of serious liver injury.

    - In the 13 months after Ocaliva was approved in May 2016, the FDA has received reports of serious liver injury or death associated with Ocaliva.
    - A prior FDA Drug Safety announcement was published in September 2017.

- To ensure correct dosing and reduce the risk of liver problems, the FDA is clarifying the current recommendations for screening, dosing, monitoring, and managing PBC patients with moderate to severe liver disease taking Ocaliva. Refer to the drug label for more specific dosing information.

- Healthcare providers should follow the Ocaliva dosing regimen in the drug label, which is based on calculating a Child-Pugh score in PBC patients with suspected liver cirrhosis before treatment to determine their specific classification and starting dosage.

    - Dosing Ocaliva higher than recommended in the drug label can increase the risk for liver decompensation, liver failure, and sometimes death.
    - Patients should be routinely monitored for biochemical response, tolerability, and PBC progression, and re-evaluate Child-Pugh classification to determine if dosage adjustment is needed.
    - Close monitoring is recommended for patients at an increased risk of liver decompensation, including those with laboratory evidence of worsening liver function (eg, total bilirubin, INR, albumin) or progression to cirrhosis.
    - Temporarily stop Ocaliva in those with laboratory or clinical evidence of worsening liver function that may indicate decompensation and monitor the patient's liver function.
    - If a patient's condition returns to baseline, the risks and benefits of continuing Ocaliva therapy should be considered. Therapy may be re-initiated or discontinued depending upon the patients liver function status.

- Patients and caregivers should be educated on the specific signs and symptoms of worsening liver function, such as abdominal swelling, jaundice, bloody or black stools, coughing or vomiting up blood, or mental changes.

- Patients and caregivers should report general symptoms that are severe or do not subside such as stomach pain, nausea, vomiting or diarrhea, loss of appetite or weight loss, new or worsening fatigue, weakness, fever and chills, lightheadedness, and less frequent urination. Patients should also report any new or worsening severe skin itching to their healthcare provider.

- Similar safety information was also added to the patient Medication Guide.

- As a condition of approval, the FDA required the manufacturer of Ocaliva, Intercept Pharmaceuticals, to continue studying the medicine in patients with advanced PBC. These clinical trials are currently ongoing and the FDA expects to receive results in 2023.

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- The FDA will continue to monitor Ocaliva and will update the public if new information becomes available.