

FDA Drug Safety Communication

FDA warns about serious liver injury with Ocaliva (obeticholic acid) for rare chronic liver disease

Safety Announcement

[09-21-2017] The Food and Drug Administration (FDA) is warning that the liver disease medicine Ocaliva (obeticholic acid) is being incorrectly dosed in some patients with moderate to severe decreases in liver function, resulting in an increased risk of serious liver injury and death. These patients are receiving excessive dosing, particularly a higher frequency of dosing than is recommended in the drug label for them. Ocaliva may also be associated with liver injury in some patients with mild disease who are receiving the correct dose. The recommended dosing and monitoring for patients on Ocaliva are described in the current drug label. We are working with the drug manufacturer, Intercept Pharmaceuticals, to address these safety concerns.

Ocaliva is used to treat a rare, chronic liver disease known as primary biliary cholangitis (PBC). PBC causes the bile ducts in the liver to become inflamed, damaged and destroyed. This causes bile, a fluid that helps in digestion, to build up in the liver. This build-up damages the liver over time, eventually causing it to lose its ability to function. Ocaliva has been shown to improve a certain blood test that measures liver problems.

Health care professionals should determine the patient's baseline liver function prior to starting Ocaliva. Patients with moderate to severe liver impairment (Child-Pugh B and C) should be started on the approved dosing schedule of 5 mg once weekly, rather than the 5 mg daily dosing used for other PBC patients, and if needed, can be increased up to a maximum approved dose of 10 mg twice weekly. Health care professionals should monitor patients frequently for disease progression, and reduce the dosing frequency to once- or twice-weekly for patients who progress to moderate or severe liver impairment. In all patients treated with Ocaliva, monitor frequently for liver injury (e.g., worsened liver blood tests and adverse liver-related reactions that may be inconsistent with the patient's extent of disease). If liver injury is suspected, discontinue Ocaliva. After the patient has stabilized, weigh the benefits against the risks when deciding whether to re-initiate treatment. Educate patients on the symptoms of potential liver injury.

Patients should contact your health care professional if you have questions or concerns about taking Ocaliva. Report new or worsening severe skin itching to your health care professional. Also contact them immediately if you develop any of the following symptoms that may be signs of liver injury:

- New or worsening fatigue
- Diarrhea
- Weight loss
- Abdominal pain
- Decreased appetite
- Nausea and vomiting

- Change in behavior or confusion
- Vague symptoms such as anxiety or unease
- Abdominal swelling
- Yellow eyes or skin
- Bloody stools

In the 13 months after Ocaliva was approved in May 2016, FDA received reports of serious liver injury or death associated with Ocaliva.* The FDA's Adverse Event Reporting System (FAERS) includes only reports submitted to FDA, so there may be additional cases about which we are unaware.

Nineteen cases of death were identified, of which eight provided information about the patient's cause of death. The cause of death was reported to be worsening of PBC disease in seven cases, with cardiovascular disease cited in the other case. Seven of these eight cases described patients with moderate to severe decreased liver function who received Ocaliva 5 mg daily, instead of a dose no greater than 10 mg twice weekly as recommended in the label prescribing information for patients with this extent of decreased liver function.

FDA also identified 11 cases of serious liver injury with Ocaliva use. Six of the patients who had moderate or severe decreases in liver function at baseline and developed serious liver injury were receiving Ocaliva 5 mg daily, instead of a dose no greater than 10 mg twice weekly as recommended by FDA in the drug label. Three of these six patients died, which were included in the 19 death cases mentioned previously. Ocaliva was discontinued in four of six cases, which resulted in one patient experiencing symptom resolution and an improvement in a liver blood test. The remaining three cases did not report the response after discontinuation. The other five cases of serious liver injury were reported in patients with no or mild decreases in liver function prior to initiating Ocaliva. Four of these five patients received Ocaliva 5 mg daily, and one did not report the dose. Ocaliva was discontinued in all five cases, which resulted in one patient experiencing symptom resolution and one patient experiencing improved liver blood tests and symptom resolution. The remaining three cases did not report the response after discontinuation.

We urge health care professionals and patients to report side effects involving Ocaliva and other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

*The cases were reported to the FDA Adverse Event Reporting System (FAERS).

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