Important Drug Safety Notice

TO ALL PARTICIPATING PHARMACIES

Circular Letter MC24-050-CG
December 16, 2024

Based on its review of postmarket clinical trial data, the U.S. Food and Drug Administration (FDA) identified cases of serious liver injury among patients being treated for primary biliary cholangitis (PBC) with Ocaliva (obeticholic acid) who did not have cirrhosis of the liver.

The FDA restricted the use of Ocaliva in patients who have PBC with advanced cirrhosis of the liver in 2021 because it can cause serious harm in those patients, adding a new Contraindication to the Ocaliva prescribing information and patient Medication Guide. However, recent review of case reports submitted to FDA* found that some patients with PBC and advanced cirrhosis were still taking the medicine despite these restrictions.

RECOMMENDATIONS

1. FDA is notifying health care professionals and patients of this new safety information, and that frequent liver test monitoring is necessary to identify worsening liver function and ensure appropriate discontinuation of Ocaliva. FDA will continue to monitor the medicine's safety and will follow up if additional information becomes available.

2. **RECOMMENDATIONS:**

   a. **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.
   - Discontinue Ocaliva treatment with any evidence of liver disease progression or if efficacy is not established.
   - Explain the signs and symptoms of worsening liver injury to patients receiving Ocaliva and direct them to contact you immediately if they develop any signs or symptoms of worsening liver injury.

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507
T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726
MC-Rx.com

b. **Patients:**

- Should talk to your health care professional about this safety risk and the benefits of continuing treatment with Ocaliva.
- Discuss any concerns you may have, including about possible alternative treatments. Contact your health care professional immediately if you develop any symptoms, which may indicate worsening liver injury.
- Contact your health care professional immediately if you develop any of the following symptoms which may indicate worsening liver injury.
- Any of these specific symptoms:
  - ❖ Swollen belly
  - ❖ Yellow eyes or skin
  - ❖ Bloody or black stools
  - ❖ Coughing up or vomiting blood
  - ❖ Mental status changes such as confusion, slurred speech, mood swings, changes in personality, or increased sleepiness or difficulty waking up
- Any of these general symptoms if they are severe or do not go away after a few days:
  - ❖ Belly pain
  - ❖ Nausea, vomiting, or diarrhea
  - ❖ Loss of appetite or weight loss
  - ❖ New or worsening tiredness
  - ❖ Weakness
  - ❖ Fever and chills
  - ❖ Lightheadedness
  - ❖ Less frequent urination

3. Expect patients to visit your pharmacy asking for information on this safety issue and prepare your pharmacy staff on how to handle the situation.

MC-Rx Pharmacy Services Department

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507
T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726
MC-Rx.com

FDA U.S. FOOD & DRUG ADMINISTRATION

Ocaliva (obeticholic acid) by Intercept Pharmaceuticals: Drug Safety Communication - Serious Liver Injury Being Observed in Patients without Cirrhosis

[12/12/2024]

AUDIENCE: Gastroenterology, Hepatology, Patient, Health Care Professional, Pharmacy

ISSUE: The FDA identified cases of serious liver injury among patients being treated for primary biliary cholangitis (PBC) with Ocaliva (obeticholic acid) who did not have cirrhosis of the liver.

The original clinical trial showed a decrease in alkaline phosphatase (ALP) that supported FDA accelerated approval. FDA required the additional postmarket clinical trial to verify the clinical benefit of Ocaliva. FDA evaluated liver safety in the postmarket clinical trial in patients who were appropriate for Ocaliva treatment based on the approved indication in the prescribing information. 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. (Note: The liver transplant case in the placebo group occurred after the patient switched to commercially available Ocaliva and was dosed with Ocaliva for two years prior to liver transplant; this case may also be related to Ocaliva treatment.) 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% confidence interval: 1.03, 22.09) for patients without advanced cirrhosis and not contraindicated from receiving the drug.

FDA is notifying health care professionals and patients of this new safety information, and that frequent liver test monitoring is necessary to identify worsening liver function and ensure appropriate discontinuation of Ocaliva. FDA will continue to monitor the medicine's safety and will follow up if additional information becomes available.

BACKGROUND: Ocaliva is a prescription medicine approved in May 2016 that has been shown to improve a certain liver test called ALP in patients with PBC who have not responded well enough to another medicine called ursodeoxycholic acid.

The FDA previously communicated about the risk of serious liver injury associated with Ocaliva in May 2021 (restriction of Ocaliva use in PBC patients with advanced cirrhosis). Additional communications about related safety issues for Ocaliva occurred in February 2018 (addition of

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507
T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726
MC-Rx.com

FDA U.S. FOOD & DRUG ADMINISTRATION

Boxed Warning to highlight correct dosing of Ocaliva) and September 2017 (warning about serious liver injury with incorrect dosing).

RECOMMENDATIONS:

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.
- Discontinue Ocaliva treatment with any evidence of liver disease progression or if efficacy is not established.
- Explain the signs and symptoms of worsening liver injury to patients receiving Ocaliva and direct them to contact you immediately if they develop any signs or symptoms of worsening liver injury.

Patients:

- Should talk to your health care professional about this safety risk and the benefits of continuing treatment with Ocaliva.
- Discuss any concerns you may have, including about possible alternative treatments. Contact your health care professional immediately if you develop any symptoms, which may indicate worsening liver injury.
- Contact your health care professional immediately if you develop any of the following symptoms which may indicate worsening liver injury.
- Any of these specific symptoms
  - Swollen belly
  - Yellow eyes or skin
  - Bloody or black stools
  - Coughing up or vomiting blood
  - Mental status changes such as confusion, slurred speech, mood swings, changes in personality, or increased sleepiness or difficulty waking up
- Any of these general symptoms if they are severe or do not go away after a few days
  - Belly pain
  - Nausea, vomiting, or diarrhea
  - Loss of appetite or weight loss
  - New or worsening tiredness
  - Weakness
  - Fever and chills

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507
T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726
MC-Rx.com

- Lightheadedness
- Less frequent urination

Health care professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report online.
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on form, or submit by fax to 1-800-FDA-0178.

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507

T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726

MC-Rx.com