



FDA Drug Safety Communication: FDA warns of serious liver injury risk with hepatitis C treatments Viekira Pak and Technivie

Safety Announcement

[10-22-2015] The U.S. Food and Drug Administration (FDA) is warning that hepatitis C treatments Viekira Pak and Technivie can cause serious liver injury mostly in patients with underlying advanced liver disease. As a result, we are requiring the manufacturer to add new information about this safety risk to the drug labels.

Patients taking these medicines should contact their health care professional immediately if they develop fatigue, weakness, loss of appetite, nausea and vomiting, yellow eyes or skin, or light-colored stools, as these may be signs of liver injury. Patients should not stop taking these medicines without first talking to their health care professionals. Stopping treatment early could result in drug resistance to other hepatitis C medicines. Health care professionals should closely monitor for signs and symptoms of worsening liver disease, such as ascites, hepatic encephalopathy, variceal hemorrhage, and/or increases in direct bilirubin in the blood.

Viekira Pak and Technivie are used to treat chronic hepatitis C, a viral infection that can last a lifetime and lead to serious liver and other health problems, including cirrhosis, liver cancer, and death. These medicines reduce the amount of hepatitis C virus in the body by preventing it from multiplying and may slow down the disease.

Our review of adverse events reported to the FDA Adverse Event Reporting System (FAERS) database and to the manufacturer of these medicines, AbbVie, identified cases of hepatic decompensation and liver failure in patients with underlying liver cirrhosis who were taking these medicines. Some of these events resulted in liver transplantation or death. These serious outcomes were reported mostly in patients taking Viekira Pak who had evidence of advanced cirrhosis even before starting treatment with it.

Since the approvals of Viekira Pak in December 2014 and Technivie in July 2015, at least 26 worldwide cases submitted to FAERS were considered to be possibly or probably related to Viekira Pak or Technivie. In most of the cases, liver injury occurred within 1 to 4 weeks of starting treatment. Some of the cases occurred in patients for whom these medicines were contraindicated or not recommended (see Data Summary). FAERS includes only reports submitted to FDA, so there are likely additional cases about which we are unaware.

We are requiring AbbVie to include information about serious liver injury adverse events to the *Contraindications, Warnings and Precautions, Postmarketing Experience, and Hepatic Impairment* sections of the Viekira Pak and Technivie drug labels.

We urge health care professionals and patients to report side effects involving Viekira Pak or Technivie to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Facts about Viekira Pak and Technivie

- Viekira Pak is a fixed-dose combination of dasabuvir, ombitasvir, paritaprevir, and ritonavir used with or without ribavirin, another hepatitis C medicine. Viekira Pak is FDA-approved for use in patients with *genotype 1* chronic hepatitis C infection *including* those with compensated cirrhosis.
- Technivie is a fixed-dose combination of ombitasvir, paritaprevir, and ritonavir, used in combination with ribavirin. It is FDA-approved for use in patients with *genotype 4* chronic hepatitis C virus infection *without* cirrhosis.
- Viekira Pak and Technivie are antiviral medicines that reduce the amount of hepatitis C virus in the body by preventing the virus from multiplying and may slow down the disease.
- Before starting to take Viekira Pak or Technivie, patients should tell their health care professionals if they:
 - Have liver problems other than hepatitis C infection
 - Have HIV infection
 - Are taking birth control medicine containing ethinyl estradiol
- Common side effects include, nausea, itching, and sleep problems.
- From approval in December 2014 through August 2015, the nationally estimated number of patients dispensed a Viekira Pak prescription from U.S. outpatient retail and mail order pharmacy settings is 10,104 patients.¹
- Due to Technivie’s recent approval in July 2015, accurate data on the number of prescriptions dispensed is not available at this time.

Additional Information for Patients and Caregivers

- Viekira Pak and Technivie may cause serious liver injury, including life-threatening liver failure, mainly in patients with underlying advanced liver disease.
- Do not stop taking these medicines without first talking to your health care professional. Stopping treatment early could result in drug resistance to other hepatitis C medicines.
- Contact your health care professional right away if you take Viekira Pak or Technivie and experience any of these signs and symptoms of liver problems:
 - Fatigue
 - Weakness
 - Loss of appetite
 - Nausea and vomiting
 - Yellow eyes or skin
 - Light-colored stools
- Discuss any questions or concerns about Viekira Pak or Technivie with your health care professional.
- Carefully read the patient Medication Guide that comes with your [Viekira Pak](#) or [Technivie](#) prescriptions.

- Report any side effects from Viekira Pak or Technivie to your health care professional and the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

Additional Information for Health Care Professionals

- Hepatic decompensation and hepatic failure, including liver transplantation or death, in patients with cirrhosis have been associated with the use of Viekira Pak and Technivie.
- Viekira Pak is contraindicated in patients with moderate and severe hepatic impairment (Child-Pugh Class B & C).
- Technivie is not indicated for use in patients with cirrhosis, and should not be used in patients with moderate and severe hepatic impairment (Child-Pugh Class B & C).
- Hepatic laboratory testing should be performed at baseline, during the first 4 weeks of starting treatment, and as clinically indicated.
 - If alanine aminotransferase (ALT), bilirubin, or both are elevated above baseline levels, repeat the test and monitor closely.
 - Advise patients to contact you or another health care professional immediately if they experience signs and symptoms of hepatic injury or toxicity while taking Viekira Pak or Technivie, such as:
 - Fatigue
 - Weakness
 - Lack of appetite
 - Nausea and vomiting
 - Jaundice or discolored feces
 - Monitor for increasing bilirubin values and for clinical signs and symptoms of hepatic decompensation such as ascites, hepatic encephalopathy, and variceal hemorrhage.
 - Viekira Pak and Technivie should be discontinued in the presence of decompensated cirrhosis with or without increased levels of bilirubin and/or transaminase.
 - Consider discontinuing Viekira Pak or Technivie if ALT levels remain persistently greater than 10 times the upper limit of normal (ULN).
 - Discontinue Viekira Pak or Technivie if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalized ration (INR).
- Health care professionals who have initiated treatment with Viekira Pak or Technivie in patients with cirrhosis should discuss with the patients the risks of hepatic decompensation and hepatic failure and should closely monitor them.
- Female patients must discontinue ethinyl estradiol-containing birth control products prior to starting treatment with Viekira Pak or Technivie.
 - Alternative methods of contraception during Viekira Pak or Technivie treatment are recommended.
 - Ethinyl estradiol-containing products can be restarted approximately 2 weeks following completion of treatment with Viekira Pak or Technivie.
- Encourage patients to read the patient Medication Guide that comes with their [Viekira Pak](#) and [Technivie](#) prescriptions.

- Report adverse events involving Viekira Pak or Technivie to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

Data Summary

FDA evaluated worldwide postmarketing cases of hepatic decompensation and hepatic failure submitted to the FDA Adverse Event Reporting System (FAERS) database, and submitted by the manufacturer AbbVie, since approval of Viekira Pak in December 2014 and of Technivie in July 2015. Of the 26 assessable cases in which causality to components of Viekira Pak or Technivie was attributed to be possible or probable, 10 patients experienced hepatic failure resulting in transplantation or death, and 16 patients experienced various degrees of liver dysfunction.

The postmarketing cases of hepatic decompensation and liver failure are difficult to interpret because they occurred mostly in patients with underlying advanced chronic liver disease. However, temporal association from starting Viekira Pak or Technivie and resolution of symptoms in some patients after the medicine was stopped suggest a potential causal association.

The presentation of liver injury in patients with advanced liver disease who receive treatment with Viekira Pak or Technivie may differ from patients with less-advanced disease. Transaminase elevations did not appear to be a predominant presentation in the cases with advanced liver disease, in contrast to what has been observed in patients with less-advanced liver disease as described in the current prescriber’s information.

FDA emphasizes that Viekira Pak and Technivie are contraindicated in moderate and severe hepatic impairment (Child-Pugh Class B & C). Technivie is not indicated for use in patients with cirrhosis. Some of the postmarketing cases of hepatic failure occurred in patients for whom Viekira Pak and Technivie are contraindicated or not recommended. Some cases provided insufficient data to definitively assess baseline liver status.

Resources

1. Source: PHAST Patient Monthly, Dec 2014-Aug 2015, Extracted Oct 2015.
2. Centers for Disease Control and Prevention: Information on hepatitis C virus. <http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1>
3. National Institute of Diabetes and Digestive and Kidney Disease: Information on hepatitis C virus. <http://www.niddk.nih.gov/health-information/health-topics/liver-disease/hepatitis-c/Pages/ez.aspx>