

## Direct Acting Antivirals – Safety Updates

- On February 14, 2017, the <u>FDA announced</u> class labeling revisions for all direct acting antivirals (DAAs) regarding the risk of hepatitis B virus reactivation in patients co-infected with hepatitis C virus (HCV) and hepatitis B virus (HBV).
  - DAAs include: Daklinza<sup>™</sup> (daclatasvir), Epclusa<sup>®</sup> (sofosbuvir/velpatasvir), Harvoni<sup>®</sup> (ledipasvir/sofosbuvir), Olysio<sup>®</sup> (simeprevir), Sovaldi<sup>®</sup> (sofosbuvir), Technivie<sup>™</sup> (ombitasvir/paritaprevir/ritonavir), Viekira Pak<sup>™</sup> (dasabuvir; ombitasvir/paritaprevir/ritonavir), Viekira XR<sup>™</sup> (dasabuvir/ ombitasvir/paritaprevir/ritonavir), and Zepatier<sup>™</sup> (elbasvir/grazoprevir).
- As requested by the <u>FDA in October 2016</u>, a *Boxed Warning*, risk of hepatitis B virus reactivation in patients co-infected with HCV and HBV, was added to the DAA drug labels.
- A new Warning discusses the risk of HBV reactivation that has been reported in HCV/HBV co-infected
  patients who were undergoing or had completed treatment with HCV DAAs, and who were not receiving
  HBV antiviral therapy.
  - Some cases have resulted in fulminant hepatitis, hepatic failure, and death.
  - Cases have been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in patients with serologic evidence of resolved HBV infection [ie, HBsAg negative and hepatitis B core antibody (anti-HBc) positive].
  - HBV reactivation has also been reported in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV DAAs may be increased in these patients.
  - HBV reactivation is characterized as an abrupt increase in HBV replication manifesting as a rapid increase in serum HBV DNA level.
  - In patients with resolved HBV infection, reappearance of HBsAg can occur.
  - Reactivation of HBV replication may be accompanied by hepatitis, ie, increases in aminotransferase levels and, in severe cases, increases in bilirubin levels, liver failure, and death can occur.
- In the Dosage and Administration section, information has been added about testing all patients for evidence of current or prior HBV infection by measuring HBsAg and anti-HBc before initiating HCV treatment.
- Similar information about the risks has been added to the *Patient Counseling* section.
- The class labeling revisions are to ensure the following:
  - Test all patients for evidence of current or prior HBV infection by measuring HBsAg and anti-HBc before initiating treatment with HCV DAAs.
  - In patients with serologic evidence of HBV infection, monitor for clinical and laboratory signs of hepatitis flare or HBV reactivation during HCV treatment and during post-treatment follow-up.
  - Initiate appropriate patient management for HBV infection as clinically indicated.



OptumRx® specializes in the delivery, clinical management and affordability of prescription medications and consumer health products. We are an Optum® company — a leading provider of integrated health services. Learn more at **optum.com**.

All Optum® trademarks and logos are owned by Optum, Inc. All other brand or product names are trademarks or registered marks of their respective owners.

This document contains information that is considered proprietary to OptumRx and should not be reproduced without the express written consent of OptumRx.

RxNews® is published by the OptumRx Clinical Services Department.

©2017 Optum, Inc. All rights reserved.