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### IN BRIEF

## Hepatitis B Reactivation with Direct-Acting Antiviral Drugs for Hepatitis C

The FDA recently announced that it will require the labeling of all direct-acting antiviral drugs used for treatment of hepatitis C virus (HCV) infection to include a boxed warning about a risk of hepatitis B virus (HBV) reactivation associated with their use.<sup>1</sup>

Table 1. Direct-Acting Antiviral Drugs for HCV in the US

Drug	FDA-Approved Indication
<i>Daklinza</i> – daclatasvir (BMS)	Genotypes 1, 3
<i>Epclusa</i> – sofosbuvir/velpatasvir (Gilead)	Genotypes 1-6
<i>Harvoni</i> – sofosbuvir/ledipasvir (Gilead)	Genotypes 1, 4, 5, 6
<i>Olysio</i> – simeprevir (Janssen)	Genotypes 1, 4
<i>Sovaldi</i> – sofosbuvir (Gilead)	Genotypes 1-4
<i>Technivie</i> – ombitasvir/paritaprevir/ritonavir (Abbvie)	Genotype 4
<i>Viekira Pak</i> , <i>Viekira XR</i> – dasabuvir/ombitasvir/paritaprevir/ritonavir (Abbvie)	Genotype 1
<i>Zepatier</i> – elbasvir/grazoprevir (Merck)	Genotypes 1, 4

Twenty-four cases of HBV reactivation occurring during treatment with direct-acting antiviral drugs for HCV were identified from the FDA Adverse Event Reporting System and the medical literature.<sup>2-5</sup> Before starting direct-acting antiviral treatment for HCV, some of these patients were hepatitis B surface antigen (HbsAG) positive and others showed evidence of resolved HBV infection. HBV reactivation generally occurred within 4-8 weeks of starting treatment. Reactivation of HBV can cause increases in bilirubin and aminotransferase levels, fulminant hepatitis, hepatic failure, and death. Of the 24 patients, two died and one required a liver transplant.

HBV reactivation was not identified before FDA approval of these drugs because the clinical trials used to support their approval excluded patients with HBV co-infection. The mechanism by which HBV reactivation occurs during treatment with direct-acting antiviral drugs for HCV is unknown. Patients should be screened for current or past HBV infection before starting treatment with a direct-acting antiviral and monitored for HBV reactivation during and following treatment with these drugs. ■

1. FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. Available at: [www.fda.gov/Drugs/DrugSafety/ucm522932.htm](http://www.fda.gov/Drugs/DrugSafety/ucm522932.htm). Accessed October 13, 2016.
2. JM Collins et al. Hepatitis B virus reactivation during successful treatment of hepatitis C virus with sofosbuvir and simeprevir. *Clin Infect Dis* 2015; 61:1304.

3. A De Monte et al. Direct-acting antiviral treatment in adults infected with hepatitis C virus: reactivation of hepatitis B virus coinfection as a further challenge. *J Clin Virol* 2016; 78:27.
4. AR Ende et al. Fulminant hepatitis B reactivation leading to liver transplantation in a patient with chronic hepatitis C treated with simeprevir and sofosbuvir: a case report. *J Med Case Rep* 2015; 9:164.
5. C Wang et al. Hepatitis due to reactivation of hepatitis B virus in endemic areas among patients with hepatitis C treated with direct-acting antiviral agents. *Clin Gastroenterol Hepatol* 2016 July 5 (epub).

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