Direct Acting Antivirals – Safety Updates

- On February 14, 2017, the FDA announced 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™ (daclatasvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), Olysio® (simeprevir), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir/paritaprevir/ritonavir), Viekira Pak™ (dasabuvir; ombitasvir/paritaprevir/ritonavir), Viekira XR™ (dasabuvir/ ombitasvir/paritaprevir/ritonavir), and Zepatier™ (elbasvir/grazoprevir).
- As requested by the FDA in October 2016, 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.