OPTUMRx®

Mavyret™ (glecaprevir/pibrentasvir), Zepatier® (elbasvir/grazoprevir), and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) – Safety update

- On August 28, 2019, the FDA announced that the use of Mavyret™ (glecaprevir/pibrentasvir), Zepatier® (elbasvir/grazoprevir), or Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) to treat chronic hepatitis C (CHC) in patients with moderate to severe liver impairment has resulted in rare cases of worsening liver function or liver failure.

- Mavyret, Zepatier, and Vosevi are FDA-approved to treat CHC in patients without liver impairment or with mild liver impairment (Child-Pugh A).

- Each of these medicines contain a hepatitis C virus (HCV) protease inhibitor and are not indicated for use in patients with moderate to severe liver impairment.

- FDA recommendations for healthcare providers:

    - Mavyret, Zepatier, or Vosevi should be prescribed as indicated in the prescribing information.
    - The severity of liver disease should be assessed at baseline and patients should be closely monitored for signs and symptoms of worsening liver function such as increases in liver enzymes, jaundice, ascites, encephalopathy, and variceal hemorrhage.
    - Close monitoring is especially warranted in those with pre-existing significant liver problems or risk factors, such as hepatocellular carcinoma or alcohol abuse, which can also contribute to clinical worsening of liver function or liver failure during treatment.
    - Mavyret, Zepatier, and Vosevi therapy should be discontinued if patients develop signs and symptoms of liver decompensation or as clinically indicated.
    - Mavyret and Zepatier should not be prescribed in patients with any history of prior hepatic decompensation.
    - Vosevi is indicated for patients who have previously failed certain other HCV treatments and is not recommended in patients with any history of hepatic decompensation unless the benefits outweigh the risk of liver injury, liver failure or death.

- FDA recommendations for patients:

    - Be aware that the risk of serious liver injury is rare.
    - Contact a healthcare provider immediately if signs of liver injury occur such as fatigue, weakness, loss of appetite, nausea and vomiting, yellow eyes or skin, or light-colored stools.
    - Discuss the benefits and risks of taking Mavyret, Zepatier, or Vosevi with a healthcare provider.
    - Do not stop taking these medicines without first talking with your healthcare provider because stopping treatment early can lead to inadequate treatment, which may cause HCV to come back.

- The FDA safety alert is based on 63 cases of liver decompensation associated with Mavyret, Zepatier, and Vosevi from the FDA Adverse Event Reporting System. Some cases led to liver failure and there were 8 deaths.

    - Ten cases reported isolated hyperbilirubinemia and jaundice without concomitant evidence of increased transaminase levels or other hepatic decompensation events.
    - Of the 63 cases, 13 were in patients without cirrhosis, 18 with compensated cirrhosis (Child-Pugh A), 21 with decompensated cirrhosis, and 11 with unknown liver function status at baseline.

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    - More than half of the cases that reported no cirrhosis or compensated cirrhosis at baseline were incorrectly classified and had evidence of advanced liver disease or pre-existing risk factors impacting the liver prior to receiving treatment that may have signified or directly contributed to the development of hepatic decompensation or liver failure.
    - The median time to onset of a liver-related event or liver decompensation after initiating treatment was 22 days (range: 2 days to 16 weeks).
    - Treatment discontinuation resulted in resolution of symptoms or reduced liver biochemical values in 39 of the 63 cases, and there were two cases of recurrence of symptoms upon re-initiating treatment.

- The FDA we will continue to monitor this safety concern and will communicate any new information if it becomes available.