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Federal Employee Program

HEPATITIS C AGENTS

Epclusa (sofosbuvir & velpatasvir), **Harvoni** (ledipasvir & sofosbuvir), **Mavyret** (glecaprevir and pibrentasvir), **Sovaldi** (sofosbuvir), **Vosevi** (sofosbuvir, velpatasvir, & voxilaprevir), Zepatier (elbasvir, grazoprevir)

Preferred Hepatitis C products: Epclusa, Harvoni, Mavyret, Sovaldi and Vosevi

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections, or liver cancer (1).

Regulatory Status

FDA-approved indications:

1. **Epclusa** is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult and pediatric patients 3 years of age and older with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infections (2):
    a. Without cirrhosis or with compensated cirrhosis
    b. With decompensated cirrhosis for use in combination with ribavirin
2. **Harvoni** is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of chronic hepatitis C virus (HCV) in adults and pediatric patients 3 years of age and older (3):
    a. Genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
    b. Genotype 1 infection with decompensated cirrhosis, in combination with ribavirin
    c. Genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin
3. **Mavyret** is a fixed-dose combination of glecaprevir, a hepatitis C virus (HCV) NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult and pediatric patients 3 years and older with chronic HCV genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).

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Mavyret is also indicated for the treatment of adult and pediatric patients 3 years and older with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both (4).

4. **Sovaldi** is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of (5):
    a. Adult patients with genotype 1, 2, 3 or 4 chronic hepatitis C infection without cirrhosis or with compensated cirrhosis as a component of a combination antiviral treatment regimen
    b. Pediatric patients 3 years of age and older with genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin
5. **Vosevi** is a fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, velpatasvir, an HCV NS5A inhibitor, and voxilaprevir, an HCV NS3/4A protease inhibitor, and is indicated for the treatment of adult patients with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have (6):
    a. Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor
    b. Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor
        i. Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5 or 6 infection previously treated with sofosbuvir without an NS5A inhibitor
6. **Zepatier** is a fixed-dose combination containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, and is indicated for treatment of chronic HCV genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg. Zepatier is indicated for use with ribavirin in certain patient populations (7).

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7. **Ribavirin** is a nucleoside analogue indicated in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age or older with compensated liver disease (8).

No dose adjustment in direct-acting antivirals (DAAs) dosing is required in patients with renal impairment when using the recommended regimens (2-8).

Mavyret and Zepatier are contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C) due to potential toxicity. Mavyret is also contraindicated in patients with any history of prior hepatic decompensation (4,7).

Ribavirin has boxed warnings regarding embryo-fetal toxicity, hemolytic anemia, and monotherapy not recommended. Ribavirin therapy is contraindicated in women who are pregnant and in men whose female partners are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in both female patients and in female partners of male patients who are taking ribavirin therapy. At least two reliable forms of effective contraception must be utilized during treatment and during the 6-month post-treatment follow-up period (8).

If a Hepatitis C medication is administered with ribavirin, the contraindications to ribavirin also apply to the combination regimen. The primary toxicity of ribavirin is hemolytic anemia. The boxed warning explains that the anemia associated with ribavirin therapy may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin (8).

Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi and Zepatier have a boxed warning for Hepatitis B virus reactivation, occasionally fulminant, during or after Hepatitis C virus (HCV) therapy which have been reported in HBV/HCV coinfected patients who were not already on HBV suppressive therapy. In light of these observations, all patients initiating HCV therapy should be assessed for

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HBV coinfection with testing for HBsAg, anti-HBs, and anti-HBc (2-7).

The safety and effectiveness of Vosevi in pediatric patients less than 18 years of age have not been established (6). The safety and effectiveness of Zepatier in pediatric patients less than 12 years old or weighing less than 30 kg have not been established (7). The safety and effectiveness of Epclusa, Harvoni, Mavyret, and Sovaldi in pediatric patients less than 3 years of age have not been established (2-5).

Summary

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people infected with hepatitis C virus (HCV) have no symptoms of the disease until liver damage becomes apparent, which may take several years. Safety and effectiveness of Vosevi in pediatric patients less than 18 years of age have not been established. The safety and effectiveness of Zepatier in patients less than 12 years of age or weighing less than 30kg have not been established. The safety and effectiveness of Epclusa, Harvoni, Mavyret and Sovaldi in pediatric patients less than 3 years of age have not been established (1-8).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Epclusa, Harvoni, Mavyret, Sovaldi, Vosevi, and Zepatier while maintaining optimal therapeutic outcomes.

References

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