Vosevi™ (sofosbuvir/velpatasvir/voxilaprevir) – New drug approval

- On July 18, 2017, Gilead announced the FDA approval of Vosevi (sofosbuvir/velpatasvir/voxilaprevir), for the treatment of adult patients with chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor, or genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.
    - Additional benefit of Vosevi over Epclusa® (sofosbuvir/velpatasvir) was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor.
- There are an estimated 2.7 to 3.9 million Americans who have chronic HCV. Approximately 75% of Americans with HCV have genotype 1; 20 – 25% have genotypes 2 or 3; and a small number of patients are infected with genotypes 4, 5 or 6.
- Vosevi is a single tablet, fixed-dose direct-acting antiviral (DAA) combination product containing an NS5B polymerase inhibitor (sofosbuvir), an NS5A inhibitor (velpatasvir), and an NS3/4 protease inhibitor (voxilaprevir).
    - Other products containing one or more of the active ingredients in Vosevi include Sovaldi® (sofosbuvir), Harvoni® (ledipasvir/ sofosbuvir), and Epclusa (sofosbuvir/velpatasvir).
- The approval of Vosevi is supported by data from the POLARIS-1 study evaluating 12 weeks of treatment among adults with HCV genotype 1, 2, 3, 4, 5 or 6 with or without compensated cirrhosis who had failed prior treatment with an NS5A inhibitor-containing regimen, as well as data from the POLARIS-4 study evaluating 12 weeks of treatment among adults with HCV genotypes 1, 2, 3, or 4 with or without compensated cirrhosis who had failed prior treatment with a sofosbuvir-containing regimen that did not include an NS5A inhibitor.
    - Across the two studies, 96% – 97% of patients treated with Vosevi achieved the primary endpoint of sustained virologic response, defined as maintaining undetectable viral load 12 weeks after completing therapy.
- Similar to other DAA products, Vosevi carries a boxed warning regarding the risk of hepatitis B virus (HBV) reactivation in patients co-infected with HCV and HBV.
- Vosevi is contraindicated with rifampin.
- Other warnings and precautions of Vosevi include serious symptomatic bradycardia when coadministered with amiodarone and risk of reduced therapeutic effect due to concomitant use of Vosevi with P-gp inducers and/or moderate to potent inducers of cytochrome.
- The most common adverse events (≥10%, all grades) with Vosevi use were headache, fatigue, diarrhea and nausea.
    - The proportion of patients who permanently discontinued treatment due to adverse events was 0.2% for those who received Vosevi for 12 weeks.
- The recommended dose of Vosevi is 1 tablet orally once daily for 12 weeks. See table below for details.

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Genotype	Patients previously treated with an HCV regimen containing:	Duration of treatment
1, 2, 3, 4, 5, or 6	NS5A inhibitor	12 weeks
1a or 3	sofosbuvir without an NS5A inhibitor	12 weeks

  - All patients should be tested for evidence of current or prior HBV infection by measuring hepatitis B surface antigen and hepatitis B core antibody before initiating HCV treatment with Vosevi.
  - No dosage recommendation can be given for patients with severe renal impairment (estimated glomerular filtration rate < 30 mL/min/1.73 m^2) or with end stage renal disease, due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite.
  - Vosevi is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to higher exposures of voxilaprevir in these patients.

- To support patients and their families, Gilead's U.S. Support Path® program provides information regarding access and reimbursement coverage options to U.S. patients who need assistance with coverage for their Gilead HCV medications, including Vosevi.

  - Support Path conducts benefits investigations and provides patients with information regarding their insurance options.
  - In addition, the Vosevi Co-pay Coupon Program offers co-pay assistance for eligible patients with private insurance who need assistance paying for out-of-pocket medication costs.

- Gilead plans to launch Vosevi by next week. Vosevi will be available as a single combination tablet containing sofosbuvir 400 mg/velpatasvir 100 mg/voxilaprevir 100 mg.

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