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First oral pan-genotypic HCV drugs approved for children as young as 3 years

November 1, 2021

from the Food and Drug Administration

Article type: FDA Update

Topics: Infectious Diseases , Pharmacology , Therapeutics , Urology

The Food and Drug Administration (FDA) has approved Epclusa (sofosbuvir and velpatasvir) and Mavyret (glecaprevir and pibrentasvir) for treatment of chronic hepatitis C virus (HCV) infection in pediatric patients as young as 3 years. These products are the first all-oral, pan-genotypic (genotypes 1-6) HCV treatment regimens for pediatric patients 3 years and older.

While HCV infection rates are lower in pediatric patients than in adults, antibodies to HCV are present in approximately 0.76% of children 2 to 13 years. Perinatal transmission is the most common source of HCV infection in children less than 12 years, with approximately 1,700 new cases per year in the United States (Ly KN, et al. *Ann Intern Med.* 2017;166:775-782).

Both products contain two direct-acting antiviral drugs that provide a complete regimen for treatment of chronic HCV infection. Epclusa is a fixed-dose combination of sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A

inhibitor. Mavyret is a fixed-dose combination of glecaprevir, an HCV NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor.

Both products are available as oral tablets and as newly approved oral pellets in dosing strengths suitable to accommodate the recommended weight-based dosing in pediatric patients.

Efficacy for both drugs was based on sustained virologic response (SVR12) defined as undetectable HCV RNA 12 weeks after the end of treatment. Virologic failure was rare among pediatric patients less than 12 years who completed treatment and follow-up. The overall SVR12 rate in pediatric patients 3 years to less than 12 years was 88% for Epclusa and 98% for Mavyret. Most of those who failed to achieve SVR12 had discontinued treatment due to adverse events or were lost to follow-up. The FDA did not require trials of these products in patients less than 3 years because chronicity of HCV infection is difficult to establish, and patients in this age group are unlikely to develop complications that necessitate treatment.

Gastrointestinal adverse events such as vomiting and upper abdominal pain were more common among younger pediatric patients for both drugs. In the Epclusa trials, vomiting and spitting up the drug led to treatment discontinuation in several patients younger than 6 years. In the Mavyret trials, rash occurred more frequently among pediatric patients less than 12 years compared to adolescents and adults and led to treatment discontinuation in one patient. Otherwise, the safety profile for both drugs was similar to that observed in adolescents and adults, with constitutional symptoms such as fatigue and headache being most common.

The FDA's Office of Pediatric Therapeutics (OPT), Division of Pediatric and Maternal Health (DPMH) and Division of Antivirals (DAV) contributed to this article. OPT resides in the Office of Clinical Policy and Programs in the Office of the Commissioner. DPMH and DAV reside, respectively, in the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine and Office of Infectious Diseases within the Office of New Drugs in the Center for Drug Evaluation and Research.

Resources

- Epclusa (sofosbuvir and velpatasvir) labeling
- Mavyret (glecaprevir and pibrentasvir) labeling