FDA Approves Gilead's Vosevi Combo Pill for Hepatitis C Re-treatment

Tuesday, 18 July 2017
Written by Liz Highleyman

On July 18, the U.S. Food and Drug Administration(FDA) approved Gilead Sciences' Vosevi, a new once-daily combination pill containing sofosbuvir, velpatasvir, and voxilaprevir. Vosevi was approved as "salvage therapy" for people with all hepatitis C virus (HCV) genotypes who were not previously cured with prior direct-acting antiviral therapy.

Vosevi is a single-tablet regimen taken without ribavirin for 12 weeks. It contains the nucleotide HCV NS5B polymerase inhibitor sofosbuvir (sold separately as Sovaldi), the pangenotypic NS5A inhibitor velpatasvir (combined with sofosbuvir in the Epclusa coformulation), and the NS3/4A protease inhibitor voxilaprevir (approved for the first time). Pangenotypic regimens that work against all HCV genotypes have the potential to be used anywhere in the world without the need for prior genotypic testing.

The advent of direct-acting antivirals (DAAs) has made hepatitis C treatment shorter, more tolerable, and much more effective. Cure rates in clinical trials exceed 95% for most patient groups, including those who were previously treated unsuccessfully with interferon-based therapy.

Vosevi fills an unmet need for people who were previously treated unsuccessfully with DAA regimens, including those who received an NS5A inhibitor. Re-treatment for this population is challenging because HCV can develop resistance to DAAs, reducing the effectiveness of other drugs in the same class.

"Direct-acting antiviral drugs prevent the virus from multiplying and often cure HCV," Edward Cox of the FDA's Center for Drug Evaluation and Research said in an FDA press release. "Vosevi provides a treatment option for some patients who were not successfully treated with other HCV drugs in the past."

Vosevi is now approved for re-treatment of adult chronic hepatitis C patients with HCV genotypes 1 through 6 who were previously treated with a NS5A inhibitor, and for those with genotypes 1a or 3 who were previously treated with a sofosbuvir-containing regimen without a NS5A inhibitor. Vosevi is indicated for people without cirrhosis or with compensated cirrhosis, but it is not approved for people with severe decompensated cirrhosis.

Vosevi was approved based on clinical trials showing that it produces high rates of sustained virological response, or continued undetectable HCV at 12 weeks post-treatment (SVR12), which is considered a cure.

In the Phase 3 POLARIS trials, Vosevi taken for 12 weeks cured 96% to 97% of patients with all HCV genotypes who were previously treated with DAAs, while an 8-week regimen produced an overall SVR12 rate of 95% for people who had not used DAAs before.

POLARIS-4 looked at people who had received prior DAA therapy, but without a NS5A inhibitor. Cure rates were 97% for 12 weeks of Vosevi and 90% for 12 weeks of Epclusa (sofosbuvir/velpatasvir), showing that the former was statistically superior. The difference was larger among patients with cirrhosis (96% vs 86%, respectively). In POLARIS-1, 96% of patients

who had previously taken NS5A inhibitors were cured with 12 weeks of Vosevi, while no one in a placebo control group was cured.

Looking at people who had not used DAAs, 8 weeks of Vosevi did not statistically measure up to 12 weeks of Epclusa in the POLARIS-2 trial, with SVR12 rates of 98% vs 95%, respectively. The difference was largely driven by a lower Vosevi response rate (92%) among people with genotypes 1a or 4. However, in POLARIS-3, Vosevi taken for either 8 or 12 weeks cured 96% of patients with genotype 3 and compensated cirrhosis, considered one of the most difficult groups to treat.

"Treatment with Vosevi resulted in high cure rates in clinical studies of patients who were not previously cured with several widely-prescribed DAA regimens and will provide physicians with an important new therapeutic option that could offer hope for their hardest-to-treat patients," Ira Jacobson of Mount Sinai Beth Israel Medical Center, who was a principle investigator for Vosevi clinical trials, said in a Gilead press release.

Vosevi was generally safe and well-tolerated in clinical trials. The most common adverse events associated with Vosevi were headache, fatigue, diarrhea, and nausea. Less than 1% of study participants stopped treatment early due to adverse events.

The drugs in Vosevi can interact with certain other medications, which could lead to sub-therapeutic drug levels or worse side effects. Vosevi should not be used with several other drugs including rifampin, amiodarone, St. John’s wort, and carbamazepine. It can also interact with some antiretrovirals used to treat HIV, including atazanavir (Reyataz), efavirenz (Sustiva), lopinavir/ritonavir (Kaletra), and tipranavir (Aptivus). Complete safety information is available in the Vosevi prescribing information.
As is the case with all DAAs, curing hepatitis C can trigger hepatitis B virus (HBV) reactivation, which can lead to severe liver injury. Anyone considering treatment with Vosevi should be screened for HBV, and those with active HBV should receive hepatitis B antiviral therapy.

To assist eligible people in the U.S., Gilead's Support Path program provides information about access and reimbursement coverage options.Gilead will also offer a Vosevi Co-pay Coupon Program for people with private insurance who need assistance paying for out-of-pocket medication costs.

7/18/17

Sources

Food and Drug Administration. FDA approves Vosevi for Hepatitis C. Press release. July 18, 2017.
Gilead Sciences. U.S. Food and Drug Administration Approves Gilead’s Vosevi (Sofosbuvir/Velpatasvir/Voxilaprevir) for Re-Treatment of Adults with Chronic Hepatitis C Virus. Press release. July 18, 2017.