The 2016 Hepatitis C Drug Approval Outlook

Here's what's in store this year for new hepatitis C therapies, as well as approvals for new uses of existing treatments.

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This promises to be another banner year for the expansion of treatment options for people living with hepatitis C virus (HCV). Numerous regimens are either awaiting U.S. Food and Drug Administration (FDA) approval, or in the case of already-approved treatments, for the green light for use by new populations of individuals.

Most imminently, the FDA is expected to issue a decision by January 28 about Merck's application for its once-daily fixed-dose combination tablet of the NS3/4A protease inhibitor grazoprevir and the NS5A replication complex inhibitor elbasvir to treat genotypes 1, 4 and 6 of the virus. The FDA granted breakthrough status to the combo tablet for the treatment of individuals with genotype 1 of the virus who have end-stage kidney disease and are on dialysis, and for those with genotype 4.

The FDA also granted the treatment priority review status. This designation is given to investigational treatments for serious conditions that would offer a significant improvement in safety or effectiveness over other treatments on the market. The status shortens the standard review period from 10 months to six months.

In the Phase II/III C-SURFER trial, grazoprevir/elbasvir cured 99 percent of those with genotype 1 and advanced chronic kidney disease. Also, in the various arms of the Phase III C-EDGE trial, the combo tablet, given with or without ribavirin, for the most part posted 90 percent or greater cure rates among various subgroups of people with hep C, including those with cirrhosis, people coinfected with HIV, and individuals receiving opioid agonist therapy for drug addiction. Lastly, Merck's treatment, plus ribavirin, cured 94 to 96 percent of people with genotype 1 who had failed a previous treatment in the Phase II C-SALVAGE study.

Gilead, meanwhile, is poised to continue its domination of the hep C field thanks to the company's upcoming fixed-dose, once-daily combination tablet that includes the already-approved Sovaldi (sofosbuvir) and the investigational pangenotypic (meaning it affects all genotypes) NS5A inhibitor velpatasvir. Gilead is seeking approval for the tablet to treat those with genotypes 1 through 6. Having granted the tablet priority review, the FDA is expected to issue a decision by June 28.

Gilead's current main offering, the blockbuster Harvoni (ledipasvir/sofosbuvir), is approved for all genotypes but 2 and 3. By effectively swapping the ledipasvir component with velpatasvir, the company's new combination tablet, if approved, will cover all of the main genotypes of hep C with a single pill. The treatment should prove especially vital in parts of the world where testing to determine an individual genotype poses a particular financial burden or unavailable—provided, of course, that the treatment itself is scalably priced for poorer nations.

The application for Sovaldi/velpatasvir is based on the four Phase III ASTRAL trials, which tested 12 weeks of the treatment among participants with genotypes 1 through 6, including those with compensated cirrhosis; those with decompensated cirrhosis also took ribavirin. By and large, cure rates were between 94 and 100 percent. It's likely that those with decompensated cirrhosis will need to take ribavirin to achieve such a high likelihood of treatment success.

As for new uses for existing hep C treatments, the first company in line is Bristol-Myers Squibb (BMS), which is seeking approval for the combination of Daklinza (daclatasvir) and Gilead's Sovaldi, with or without ribavirin, to treat individuals coinfected with HIV, those with advanced cirrhosis, including decompensated cirrhosis, and those whose hep C has recurred after receiving a liver transplant. The Sovaldi and Daklinza combination weas approved in July 2015 to treat genotype 3. Now that the FDA has granted priority review for BMS's application for these additional indications for the regimen, a decision is expected by late February.

BMS's new application is based in part on results from the Phase III ALLY-1 trial of 12 weeks of Sovaldi, Daklinza and ribavirin, which included participants who had all genotypes except 5. The regimen cured over 90 percent of those with Child-Pugh class A or B of cirrhosis, but only 56 percent of those with class C, or very advanced cirrhosis. BMS also submitted results from the Phase III ALLY-2 trial, in which 97 percent of HIV-coinfected participants with genotypes 1 through 4 of hep C were cured after 12 weeks of the regimen.

An early-July decision date is expected for a new indication for AbbVie's Viekira Pak (ombitasvir/paritaprevir/ritonavir; dasabuvir). The FDA has granted priority review for the company's application to expand the drug's approved uses to include those with genotype 1b and compensated cirrhosis, without the need for ribavirin.

Viekira Pak was approved in December 2014 to treat genotype 1 of hep C, including those with compensated cirrhosis. Currently, individuals with genotype 1b and compensated cirrhosis are advised to take 12 weeks of the regimen along with ribavirin. If the FDA gives the green light, the ribavirin indication would be dropped for this group.

AbbVie's new application is based on the Phase IIIb TURQUOISE-III trial, in which 100 percent of participants with genotype 1b and compensated cirrhosis were cured after 12 weeks of Viekira Pak alone.

The company has also applied for FDA approval of a new version of Viekira Pak that requires only once- instead of twice-daily dosing to treat those with genotype 1. A decision is expected in the

second half of the year.
