The Hepatitis C Blockbuster Season Has Begun

With the FDA approval of Sovaldi (sofosbuvir) and Olysio (simeprevir), many people with hepatitis C, including those coinfected with HIV, will likely line up for long-stalled treatment. Sovaldi in particular has the potential to reap billions in sales.

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It's here, and it's expensive.

On December 6, the U.S. Food and Drug Administration (FDA) approved Gilead Sciences' hotly anticipated Sovaldi (sofosbuvir), granting a broad indication for its use to treat people with genotypes 1 through 4 of hepatitis C virus (HCV), including those coinfected with HIV and those who have liver cancer and are waiting for a transplant.

"This is a very significant advance," says Steven L. Flamm, MD, the chief of the liver transplant program at the Northwestern University Feinberg School of Medicine in Chicago, who has been conducting ongoing trials of Sovaldi in partnership with Gilead.

For the past two and a half years, the standard treatment for hep C has been a regimen of one out of two protease inhibitors—Incivek (boceprevir) and Victrelis (telaprevir)—paired with interferon and ribavirin. Now the nucleotide analog polymerase inhibitor Sovaldi promises to cut standard treatment time from the previous range of 24 to 48 weeks down to 12 to 24 weeks, in addition to lessening side effects and raising cure rates from about 70 percent to the 80 to 90 percent range in many cases.

Most groundbreakingly, Sovaldi is the backbone of the first-ever interferon-free, all-oral hep C drug regimen. While the once-daily pill must still be taken in combination with ribavirin, those with genotypes 2 and 3 of the virus can now avoid the weekly injection of interferon and its onerous, flu-like side effects. And to the surprise of many in the hep C community, the FDA has given clinicians the option of considering interferon-free treatment for people with genotype 1 who are interferon ineligible. This could provide the option of interferon-free treatment to vast swaths of Americans, because 70 percent of U.S. cases of hep C are genotype 1 and many physicians believe that simply not wanting to take interferon qualifies someone as ineligible for interferon. (Opting for this treatment route would be a gamble, however, because cutting interferon for treatment of genotype 1 also lowers the likelihood of a cure.)

The cost of this miracle drug? $1,000 a day.

Granted, Sovaldi's price tag is still in the same general stratosphere as the therapies it will most likely eclipse, but physicians and advocacy groups such as the AIDS Healthcare Foundation and the Fair Pricing Coalition have expressed outrage at what they see as a brazen and greedy move on Gilead's part.

The pharmaceutical giant stands to reap a colossal reward for its investment in hep C therapeutics. Analysts with BMO Capital Markets expect Sovaldi's 2014 revenue to come in at around $1.9 billion. Matthew Roden, an analyst at UBS, has said that the drug's annual sales could eventually climb higher than the $13 billion brought in by Pfizer's cholesterol-lowering Lipitor (atorvastatin) in its biggest year.

Outside of how Sovaldi's exorbitant cost may tax the U.S. health care system, the overriding concern among hep C advocates is over access to treatment for those without robust insurance coverage.

"I think it's a potentially dangerous bar that will hopefully not be the floor for subsequent drugs that are going to be approved in the coming years," Michael Ninburg, executive director of Hepatitis Education Project in Seattle, says of Sovaldi's price tag.

Receiving the FDA nod two weeks before Sovaldi, Janssen Therapeutics' NS3/4A protease inhibitor Olysio (simeprevir) costs 21 percent less: $66,360 for 12 weeks of treatment, compared with $84,000 for Sovaldi's 12-week regimen. (Because 24 weeks of Sovaldi are recommended for treating genotype 3 and for treating genotype 1 without interferon, the cost would double in these cases.) Olysio is only approved for use among those with genotype 1 of the virus, with a recommended treatment regimen of 12 weeks combined with either 24 or 48 weeks of pegylated interferon and ribavirin, depending on past treatment experience.

In pooled results from the Phase III QUEST-1 and QUEST-2 trials, Olysio's sustained virologic response (SVR, considered a cure) rates ranged from a high of about 80 percent for treatment-naive study participants and for those who had relapsed on a previous treatment, down to 65 percent for prior partial-responders to treatment and 53 percent for prior null-responders.

A major factor weighing against Olysio's potential for widespread use is the fact that, among those with genotype 1a who have what's known as a Q80K polymorphism, just 58 percent achieved a cure in Phase III trials. Nearly half of Americans with genotype 1a have the polymorphism.

Meanwhile, in the NEUTRINO Phase III trial, 12 weeks of Sovaldi in combination with interferon and ribavirin boasted a cure rate of 89 percent among genotype 1 participants—and that was without the need for the extended "tail" of the latter two drugs, as with Olysio. (Breaking the results down by subtype, the cure rate for genotype 1a was 92 percent and for 1b it was 82 percent.) In the PHOTON-1 study of an interferon-free 24-week regimen of Sovaldi and ribavirin, 76 percent of treatment-naive study participants with genotype 1 achieved an SVR.

Kris Kowdley, MD, a clinical professor of medicine at the University of Washington in Seattle, argues that Olysio's lower cost is unlikely to play much in the drug's favor, while both the Q80K polymorphism concern and Olysio's longer period of treatment with interferon and ribavirin will weigh against the drug.

Meanwhile, pharmaceutical companies such as AbbVie, Bristol-Myers Squibb and Boehringer Ingelheim are all racing to get their own hep C drugs to market over the next two years, with a wave of advanced clinical trials researching combination therapies that have been pushing average SVR rates ever-closer to 100 percent. Gilead is also gunning for FDA approval, likely to come at the end of 2014, for a coformulated pill of Sovaldi along with the company's investigatory NS5A inhibitor ledipasvir. Thus far, cure results in trials of the two drugs have been near perfect.

While the price of Incivek and Victrelis steadily rose after they were released, a cost war could lower prices of the new crop of drugs in the coming years. Express Scripts, the nation's largest pharmacy benefits manager, has indicated that the company may exclude pricier hep C therapies from formularies down the road if these drug regimens offer no greater benefit in outcome over their cheaper competition. So even if Gilead's once-a-day pill offered unique convenience, it still might get nixed for coverage in favor of a more cheaply priced multi-pill regimen from AbbVie, should the two companies' regimens promise comparable cure rates.

As for now, both Sovaldi and Olysio are available and insurers are weighing their options. While this process can take three to six months, there is still the possibility of receiving coverage before the ultimate say-so is issued. Lorren Sandt, the Fair Pricing Coalition's HCV co-chair, says she is particularly concerned about how the high cost of treatment may restrict access to those receiving medical coverage through Medicare and state Medicaid programs, AIDS Drug Assistance Programs (ADAP), the Veterans Administration and in correctional facilities. Another worry among some hep C advocates is that individual insurers may opt not to cover the newer treatments unless someone has already failed treatment with the older drugs.

Sandt says that those concerned about access because of lack of insurance, high deductibles or even co-pays should take heart in the particularly generous patient assistance programs (PAPs) that Janssen and Gilead have set up to ease the sticker shock.

"I don't want patients to see the price and think that they can't afford it," Sandt says. "Follow up with your doctor, find out if you're a candidate for therapy. And if you are and you can't afford it, make sure that you access the drug assistance programs."

Gilead, for one, will provide financial assistance for Sovaldi to those who have no insurance and who have a maximum household income of $100,000 for a family of three and 500 percent of federal poverty level for larger households. There is assistance to bring co-pays down to no more than $5 in most cases, and financial aid for as much as $16,000 is available to go toward prescription deductibles and coinsurance obligations. Gilead is also partnering with an independent non-profit, the Patient Access Network (PAN) Foundation, which assists both federally- and privately-insured people who need assistance with out-of-pocket medication

expenses. For more information on financial aid for Sovaldi, click here, and for Olysio, click here.

When it comes to deciding who should receive treatment now as opposed to waiting for greater developments in treatment, Northwestern's Steven Flamm says elements to weigh include how advanced a patient's liver disease may be and what kind of other symptoms, such as overwhelming fatigue, may add urgency to a particular case. Then there is simply the matter of highly motivated patients, those who are eager to rid themselves of the virus for any number of reasons and should be given the option to do so.

Considering Sovaldi treatment, the University of Washington's Kris Kowdley says, "There's no question that for genotype 2, there is more or less very little room to improve," when Phase III trials of a 12-week regimen of the drug with ribavirin brought in SVR rates greater than 90 percent for those without cirrhosis.

For people with genotype 3, "especially in the commonly encountered genotype 3 patient that is treatment experienced and has cirrhosis," Kowdley says that the prescribed 24 weeks of treatment with Sovaldi "is a very reasonable approach, given 60 percent SVR. But we still have opportunities to improve that further."

The results Kowdley refers to come from the Phase III VALENCE trial, in which cure rates ranged between 85 and 93 percent for treatment-naïve participants either with or without cirrhosis and for treatment-experienced participants without cirrhosis.

And for treatment-naive people with genotypes 1, 4, 5 and 6, Kowdley describes the 12-week regimen of Sovaldi, ribavirin and interferon as "very attractive," considering its 90 percent SVR rate in the NEUTRINO Phase III trial. (Sovaldi is only approved for genotypes 1 through 4, but clinicians may still prescribe the drug off label to treat genotypes 5 and 6, using this trial as a guide.)

Reflecting on these same genotypes, Kowdley says, "I think there is clearly evidence from Phase II data from smaller studies that, in the absence of interferon, there may also be a role for [Sovaldi's use in] treatment-experienced patients, and there may be a role for prior [protease inhibitor]-treated patients."

Physicians may also opt to prescribe Sovaldi and Olysio together off label. Phase II research of the pair given for 12 weeks demonstrated 93 to 100 percent cure rates among genotype 1 null responders who had mild to moderate fibrosis.

"Now, whether insurance is going to cover this—when we say 'that's the million dollar question' facetiously, that's not that far from the truth," Flamm says, "because it's going to be very costly to use those two medications together. I think there will be a significant impetus for third-party payers to try to adhere to the approved regimen and not cover these drugs. But people are going to try."