SOVALDI AND THE HEPATITIS C VIRUS: A CASE FOR A CARVE-OUT
CALIFORNIA ASSOCIATION OF HEALTH PLANS
FEBRUARY 2014

Overview

In December of 2013, the pharmaceutical manufacturer Gilead Sciences Inc. received approval from the U.S. Food and Drug Administration (FDA) for the release of sofosbuvir, a new drug to treat the hepatitis C virus (HCV). Sofosbuvir (brand name Sovaldi) is estimated to cost $1,000 per tablet with a typical course of treatment of 12 weeks. This high price point means a single treatment regimen for one patient will, at a minimum, cost approximately $84,000, plus the cost of necessary companion drugs. Longer treatment regimens may be necessary for some patients, doubling the cost of an individual's treatment. This drug is only one of an estimated 25 potential HCV drugs in the pipeline for approval.

Sovaldi represents a significant advance in therapy for HCV as it provides a higher cure rate, allows for a shorter duration of treatment, has fewer adverse effects and opens up treatment options for individuals with comorbid conditions for which traditional treatments are contraindicated. The traditional treatment regimen for HCV includes at least two drugs, pegylated interferon and ribavirin, for a treatment duration of 12 to 72 weeks. Previously, a third drug was added for some individuals (protease inhibitor Incivek (telaprevir) or Victrelis (boceprevir)). Interferon is a protein that interferes with viral reproduction. The amount administered for the treatment of HCV is well above natural levels in the body leading to adverse and often serious side effects. As a result, for individuals with certain conditions, including but not limited to HIV and advanced liver disease, the traditional treatment for HCV is contraindicated.

Prior to Sovaldi, cure rates were lower and the first wave of protease inhibitors were not indicated for use in co-infection such as HIV. According to the Centers for Disease Control (CDC), approximately a quarter of individuals with HIV also have HCV[1]. In addition, individuals with decompensated cirrhosis and those awaiting liver transplant for hepatocellular carcinoma (HCC) are also eligible for treatment. For individuals where a contraindication exists, medicine has focused on management of the HCV as a chronic condition and staving off liver failure.

The introduction of Sovaldi has resulted in a marked expansion of those eligible for HCV treatment. Sovaldi is approved to treat HCV infection genotypes 1, 2, 3 and 4, including those with HCC (liver cancer) meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection[2] and provides a high potential to cure these individuals. The universe of treatable HCV patients is moving well beyond those individuals previously eligible or seeking treatment in the plans.

Moreover, the less severe side effects make treatment more palatable overall. Traditional HCV treatment resulted in almost universal negative side effects including, but not limited to fatigue, flu-

[1] http://www.cdc.gov/hepatitis/Populations/hiv.htm
[2] http://www.gilead.com/news/press-releases/2013/12/us-food-and-drug-administration-approves-gileads-sovaldi-sofosbuvir-for-the-treatment-of-chronic-hepatitis-c

like symptoms, mild anxiety, skin rash, depression, nausea, and diarrhea.[3] Sovaldi, which can be taken independent of interferon, has significantly fewer side effects with patients primarily reporting fatigue and headaches[4]. Since HCV can be managed as a chronic condition and not all patients advance to severe stages of liver disease, not everyone diagnosed with HCV seeks treatment. The new, less detrimental treatment regimen presents an opportunity for patients who would have otherwise not sought care or have refused treatment with interferon due to the side effects.

Sovaldi also presents an opportunity for physicians that have been previously unable to offer a treatment option for HCV patients or were who were unwilling to treat patients using treatment including interferon. On January 29, 2014, the American Association for the Study of Liver Disease (AASLD) and Infectious Disease Society of America (IDSA) jointly released new recommendations for HCV therapy, recommending Sovaldi as first line therapy for all genotypes and as an integral part of the regimen for most patients being re-treated for HCV. Older drugs, such as the "newer" protease inhibitors Incivek and Victrelis, have been made obsolete by the same guidelines as they are specifically not recommended for treatment.

In addition, some of the regimens recommended by the AASLD and IDSA are not evidence based. They have also recommended some interferon free oral drug regimens which have not yet received FDA approval. The recommendations and cost of treatment are summarized in the table below. All oral (interferon free regimen) have been increasingly requested by the physicians, doubling the cost of therapy (see column 5).

Genotype	Recommended Regimen	Cost (AWP)	Interferon Free Recommended Regimen	Cost (AWP)
1	Sovaldi +RBV+ PEG 12 weeks	$ 111,403	Sovaldi+ Olysio +RBV 12 weeks	$180,887
2	Sovaldi+RBV x12 weeks	$ 101,249	Sovaldi+RBV x12 weeks	$ 101,249
3	Sovaldi+RBV x24 weeks	$ 202,498	Sovaldi+RBV x24 weeks	$ 202,498
4	Sovaldi +RBV+ PEG 12 weeks	$ 111,403	Sovaldi+RBV x24 weeks	$ 202,498

RBV=ribavirin PEG= pegylated interferon alfa

Population Prevalence

Currently, it is not possible to determine the full impact of the release of Sovaldi or other upcoming HCV treatments on each Medi-Cal Managed Care Plan as many HCV individuals were previously not eligible for treatment or failed to seek treatment due to the side effects. However, the potentially

[3] http://www.hepatitis.va.gov/provider/reviews/treatment-side-effects.asp
[4] http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_patient_pi.pdf

eligible population across the state is extensive. The California Hepatitis Alliance estimates that approximately 600,000 persons in California have been exposed to HCV with at least 475,000 chronically ill, excluding people incarcerated or homeless. The CDC believes the actual number is much larger as 75 percent of infected persons do not know they have the disease with 17,000 new infections reported each year.

In addition, in 2013 the CDC recommended all Baby Boomers (born 1945-1965) receive testing for HCV. California is home to approximately 9.8 million Baby Boomers. The new Optional Adult expansion population includes a large number of individuals falling within this age bracket who have not previously been insured. As a result, this population will likely include large number of individuals with HCV not receiving treatment and not identified by the state as needing treatment for HCV. The Medi-Cal population also includes many homeless individuals as well as those in the corrections system. Overall prevalence rates do not account for these two high risk populations.

Initial Trends

Currently, Sovaldi therapy costs $84,000 for 12 weeks of treatment for HCV genotypes 1 and and $168,000 for the 24-week treatment required for genotype 3[5]. Based on a general calculation, if we assume that 475,000 individuals have HCV statewide and a 26% of the state's population is in Medi-Cal, then Medi-Cal has approximately 123,5000 individuals with HCV on its rolls. As a result, the total cost for treatment using Sovaldi is approximately $10,374,000,000 to $20,748,000,000. This population assumption is likely an underestimation of the actual Medi-Cal population impacted by the disease as the population estimate for HCV does not include the homeless or prison populations.

Based on initial feedback from the plans, the requests for Sovaldi are increasing at a faster rate than other pharmaceutical treatments. Plans' experiences included:

- A small health plan received 14 requests in only one week.
- A similarly situated plan received 12 in the 2 months since Sovaldi was released compared to an average of 2 requests per month.
- A COHS plan reported 13 requests since January.
- Another mid-sized plan received at least 10 requests in the last two weeks of January alone, with one regional specialist telling the plan that the provider had as many as 50-75 of the plan's members that needed treatment as well.
- One of our largest member plans has received 15 to 20 cases per week.

We expect these numbers to grow as more patients and physicians learn about the new treatment option for HCV.

[5] The Wholesaler Acquisition Cost (WAC) of a 28-tablet bottle of Sovaldi in the United States is $28,000. - See more at: http://www.gilead.com/news/press-releases/2013/12/us-food-and-drug-administration-approves-gileads-sovaldi-sofosbuvir-for-the-treatment-of-chronic-hepatitis-c#sthash.pjjiIBEa.dpuf

Areas of Concern

The Medi-Cal Managed Care Plans have identified several specific areas of concern regarding the introduction of Sovaldi as well as the upcoming release of new HCV treatments onto the market. These concerns will result in increased financial risk to the plans and include, but are not limited to:

1. Potentially significant increase in the number of HCV patients in treatment due to the effectiveness and low level of side effects.

    a. Some Sovaldi regimens are interferon free. Hepatologists have indicated that they have hundreds of patients they have been holding back from treatment, waiting for new drugs, as interferon is extremely difficult to tolerate, and is contraindicated for many patients. Subsequently, there is a backlog of patients unable or unwilling to take interferon waiting for this new drug and interferon-free regimens.

    b. Sovaldi has a higher cure rate than previous regimens as well as lower pill burden, lower adverse effect profile, fewer drug interactions, shorter duration of treatment and is recommended by clinical guidelines as the first line treatment nearly universally. These factors significantly inhibit the plans ability to manage HCV with a less expensive alternative.

    c. Although national guidelines have encouraged universal testing of baby boomers, many doctors have resisted testing patients, especially ones known or suspected of not being able to tolerate treatment. Large increases in screening and, therefore, diagnosis large are likely leading to further demand for treatment.

2. Difficulty managing the treatment regimen given the wide population for which the drug is recommended.

    a. Many health plans were restricting treatment to those with advancing (stage 3 or 4) liver disease, since HCV can be managed as a chronic illness and is not necessarily fatal. Treatment regimens are moving towards interferon-free regimens, reducing adverse effects but increasing costs significantly which makes the treatment more appealing to patients with early HCV infections.

    b. Many patients who have failed treatment years before or have been denied treatment for some of the HCV genotypes because of lower efficacy will now be eligible and seek out treatment.

    c. Many hepatologists are advocating for the treatment of <u>all</u> HCV patients, even if they have no signs of disease, are injecting drugs and are at high risk of re-infection. Many hepatologists view it as a public health issue which is difficult to agree against as the treatment does no harm. However, more than half of people with Hepatitis C never develop clinically significant liver disease – meaning, they are not being harmed by HCV and are not going to be harmed in their lifetime. The provision of a

$100,000 treatment to prevent an unknown possibility of future liver is not a cost-effective use of resources and is not manageable by health plans.

3. Multiple high potential drugs and drug combinations are in clinical trials, the first of which are likely to be available to patients in early 2015.

    a. Future regimens will contain multiple direct-acting antivirals, such as Sovaldi and Olysio (another recent approval similar to Incivek and Victrelis, which costs $68,000 per treatment course), greatly increasing the cost of therapy while offering improved cure rates and lower incidence of adverse effects.

    b. Two or three direct acting antiviral regimens currently in clinical trials could cost $200,000 - $300,000 per course in the next few years.

    c. Because of relatively low volume of patients and definitive and clear treatment guidelines, health plans will be unable to manage the costs of these regimens or negotiate with manufacturers on a plan-level basis, very similar to treatment of hemophilia with blood factor.

4. Effectiveness of the treatment may lead to patients being treated repeatedly.

    a. The treatment does not prevent re-infection. If people continue to lead a high-risk lifestyle, they will be re-infected. We will likely see some demand for re-treatment with re-infection.

5. Geographic variation.

    a. There are large variations in the prevalence of HCV across the state. Urban environments and those areas with certain ethnicities have much higher incidence of HCV. As a result, the financial impact on the plans may vary greatly and make rate development difficult. Requests for this treatment option will hit some plans much more heavily than others.

6. Increased patient awareness.

    a. Because of the toxicity of previous treatments, plans have had relatively low numbers of requests for HCV treatment. However, now that there is a regimen available with fewer side effects, plans are starting to see increasing numbers of requests which will only grow as information spreads.

    b. HCV patients have a strong advocacy network due to support groups and patient activist organizations. As a result, information on the effectiveness of the new treatment option will spread quickly among the patient population and result in large increases in requests.

Recommendation:

CAHP and our member plans believe Sovaldi and other HCV drugs should be carved out of the Medi-Cal managed care contracts in order to prevent undue financial risk to the health plans. The treatment cost for one patient on Sovaldi ($100,000 or more) far exceeds the capitation payments for that member and several more members, leading costs to quickly surpass the 1% of revenue benchmark that requires early rate-adjustment for plans. In the immediate term, these costs were not taken into account in the current actuarially-based rate methodology and, thus, will result in significant and undue financial risk for the plans. Given the likely pent up demand, neither DHCS nor the plans can accurately estimate utilization and, therefore, annualized cost of the HCV treatment for each health plan. As a result, plans are left exposed to untenable, long-term financial risk.

Because of the clear advantages of Sovaldi over other treatment regimens and clinical treatment guidelines that advocate Sovaldi therapy over all other regimens, plans will not be able to manage HCV treatment with cost saving therapeutic alternatives similar to treatment of hemophilia. Therefore, health plans would be unable to mitigate the cost of HCV therapy by driving utilization toward equally effective, formulary equivalent drugs.

Treatment of HCV will see future cost savings from avoidance of chronic liver disease and liver cancers. However, due to the migratory/transient nature of the Medi-Cal population, the individual health plans themselves are unlikely to cover the patient long enough to realize the long-term savings. Consequently, the plans will experience the full cost burden of the HCV therapy, while only the State will experience the cost benefits of treatment.

Finally, a carve-out will lower Medi-Cal costs due to the potential rebates DHCS could negotiate on single source, brand name HCV drugs like Sovaldi; savings which would not be experienced by plans individually. The HCV population in comparison to the Medi-Cal population as a whole is small while the cost of treatment is extremely high. Individual health plans' HCV populations will be smaller still and vary significantly by geography. This small size prevents plans from using their Pharmacy Benefits Manager (PBMs) to reduce the cost of these drugs as they do today with other drugs on their formularies. By carving out HCV drugs, DHCS has the ability to leverage its statewide purchasing power to increase the affordability of these high-cost medications.