Economics of Biotechnology and Medical Innovations
Details: Hepatitis-C
Vivek Ghosal: Fall 2024

** I am pasting multiple materials on Hep-C in this 'details' file. There is some overlap between various articles and writings.*

*** You should go through this entire document. I have highlighted a few parts for class lecture discussions. There will be some non-highlighted portions we will discuss in class.*

**** Some of the articles are older and many of the posted links in those pages don't work. The main point here is what is written below, and not the links.*
++

A. Medications to Treat Hepatitis C – A Timeline

Source:
https://www.hepatitiscentral.com/medications-to-treat-hepatitis-c-a-timeline/

The Hepatitis C virus was discovered in 1989. Since then significant research, testing and public health awareness has led to a decrease in HCV transmission as well as treatments leading to a cure. Since 1989 interferon has been the main component of treatment options, however new medications have been made available in recent years showing higher sustained virologic response (SVR) rates, especially for genotype 1, the most predominant genotype in the world.

Below is a timeline summarizing the history of HCV and treatment options in the United States. For treatment protocols, please see Hepatitis C Treatments By Genotype.

2019

Generic versions of sofosbuvir/velpatasvir (trade name **Epclusa**) and (ledipasvir/sofosbuvir) (trade name **Harvoni**) announced.

In June, **Rebetol was discontinued** due to business reasons unrelated to any safety, efficacy or quality issues.

Also in June, **all versions of Daklinza were discontinued**.

2018

Olysio was discontinued May 25, 2019 due to obsolescence.

December 31, 2018 **Viekira XR and Technivie were discontinued** for business reasons unrelated to safety or effectiveness. Viekira Pak is still available.

2017

Mavyret (glecaprevir and pibrentasvir), was approved in August as the first 8 week treatment for all HCV genotypes without cirrhosis who have not been previously treated. Results of the trials demonstrated that **92-100 percent of patients who received Mavyret for eight, 12 or 16 weeks duration had no virus detected in the blood 12 weeks after finishing treatment, suggesting that patients' infection had been cured**.

July 18, 2017, FDA approves Gilead's **Vosevi (sofosbuvir, velpatasvir and voxilaprevir)** as the first once-daily, single-table regimen approved for patients with genotypes 1-6 who have been previously treated with the direct-acting antiviral drug sofosbuvir or other drugs for HCV that inhibit a protein called NS5A. Trials demonstrated that **96-97 percent of patients who received Vosevi had no virus detected in the blood 12 weeks after finishing treatment, suggesting that patients' infection had been cured**.

2016

On January 28th **Zepatier, a combination of elbasvir and grazoprevir**, with or without ribavirin earned FDA approval. Trials demonstrated sustained virologic response **(SVR) rates of up to 97 percent in genotype 1 patients and up to 100 percent in patients with genotype 4**.

Epclusa (sofosbuvir/velpatasvir) was approved on June 28th as the first all-oral, single tablet regimen for the treatment of adults with genotype 1-6 chronic hepatitis C virus infection. Epclusa is also the first single tablet regimen approved for the treatment of patients with HCV genotype 2 and 3, without the need for ribavirin. **After 12 weeks, 98 percent of patients taking Epclusa achieved SVR and 94 percent of patients with decompensated cirrhosis taking Epclusa with ribavirin achieved SVR**.

2015

Daklinza (daclatasvir), was approved in July for use with sofosbuvir as the **first 12-week, all-oral treatment option for patients with chronic hepatitis C virus genotype 3**. SVR rates are reduced in HCV genotype 3 infected patients with cirrhosis.

Also approved in July, **Technivie (ombitasvir, paritaprevir and ritonavir)** is used in combination with ribavirin for the treatment of HCV genotype 4 infections in patients that do not have scarring and poor liver function (cirrhosis). **Technivie is the first drug approved to treat genotype 4 HCV infection without interferon**.

2014

The FIRST once-daily pill that doesn't require interferon or ribavirin, Harvoni (ledipasvir/sofosbuvir) tablets are approved by the FDA in October. This medication is indicated for the treatment of hepatitis c, genotype 1 infections.

Two months later, the FDA approves Viekira Pak (ombitasvir/paritaprevir/ritonavir and dasabuvir) oral combination therapy for the treatment of patients with genotype 1 HCV infection including those with compensated cirrhosis. Limitations of use include those with decompensated liver disease.

2013

In November, the FDA approves Olysio (simeprevir) capsules to be used in combination with peginterferon alfa and ribavirin or in combination with sofosbuvir. Its efficacy is established in patients with hepatitis c genotype 1. In addition to other limitations, simeprevir isn't recommended for those that have failed previous treatment regimens that included simeprevir or other HCV protease inhibitors.

The following month, the FDA approves Sovaldi (sofosbuvir) tablets to be used in combination with ribavirin or with pegylated interferon and ribavirin. Its efficacy is established in patients with hepatitis c genotypes 1, 2, 3 or 4, including those with hepatocellular carcinoma awaying liver transplant and those with hepatitis c/HIV co-infection. Duration of treatment is usually 12-24 weeks.

2011

On May 13th, the FDA approves Victrelis (boceprevir) for the treatment of chronic hepatitis C genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy, including prior null responders, partial responders, and relapsers.

Ten days later, on May 23rd, Incivek (telaprevir) is approved by the FDA for use in combination with peginterferon alfa and ribavirin for the treatment of genotype 1 HCV infection in adults with compensated liver disease, including cirrhosis, who are treatment-naïve or who have been previously treated with interferon-based treatment, including prior null responders, partial responders, and relapsers.

2002

Pegasys (peginterferon alfa-2a) produced by Genentech, Inc. is approved by the FDA in October for the treatment of chronic HCV as part of a combination therapy.

In December, Genentech, Inc. gets FDA approval for its version of ribavirin, Copegasus. Copegasus is indicated for the treatment of chronic hepatitis C virus infection in combination with Pegasys in patients 5 years of age and older with compensated liver disease that were not previously treated with interferon alpha as well as in adults coinfected with HIV.

2001

Merck's Pegintron (peginterferon alfa-2b) injections are approved by the FDA and is indicated for the treatment of chronic HCV patients with compensated liver disease. For certain patients peginterferon alfa-2b may be administered with ribavirin.

1998

FDA approves Merck's Rebetol (ribavirin) to be used in combination with interferon alfa-2b (both pegylated and non-pegylated) injections for the treatment of chronic hepatitis c in patients 3 years of age and older with compensated liver disease. Additionally, Schering-Plough announces that the FDA has approved the combination use of Rebetol and Intron to be marketed as Rebetron for the treatment of chronic hepatitis C in patients with compensated liver disease who have relapsed following interferon therapy.

1997

FDA approves Infergen (interferon alfacon-1) injection sometimes taken in combination with ribavirin for the treatment of chronic HCV in patients 18 years of age and older with compensated liver disease.

1992

The United States blood supply is tested for HCV. Although routine testing for Hepatitis C began in 1990, more sensitive testing of the U.S. Blood supply virtually eliminated the HCV from all its blood banks.

1991

The first Hepatitis C treatment is approved by the FDA. The Food & Drug Administration (FDA) approves the first treatment for Hepatitis C – Schering-Plough's Intron A. Unfortunately, the initial treatment resulted in very few people actually clearing the virus.

1989

Hepatitis C Virus is identified!

1970's

Non-A, non-B hepatitis was recognized in the mid-1970's. While non-A, non-B hepatitis was originally thought to be insignificant, it was later realized that it was a disease that often advanced silently to cirrhosis and even cancer. Efforts were directed at identifying its cause and seeking out drug treatments that might impede its advance.

B. Gilead to Buy Pharmasset for $11 Billion

Source:
https://dealbook.nytimes.com/2011/11/21/gilead-to-buy-pharmasset-for-11-billion/
By Andrew Pollack and Michael J. de la Merced
November 21, 2011 8:05 am

David Paul Morris/Bloomberg News
Test samples in a Gilead Sciences laboratory in Foster City, Calif.

Gilead Sciences made a bold move on Monday to capture the lead in developing the next generation of hepatitis C drugs, agreeing to pay $11 billion in cash for Pharmasset.

The treatment of hepatitis C has undergone a revolution this year, with new pills from Vertex Pharmaceuticals and Merck sharply increasing the cure rates and also often cutting the required duration of treatment. But those new drugs still must be used with alpha interferon, a type of drug injected once a week that can cause severe flulike symptoms and other side effects.

Pharmasset, based in Princeton, N.J., is pushing to develop the first all-oral treatment regimen, doing away with the need for interferon. Its drug candidate, PSI-7977, has just entered the final phase of clinical testing and could be on the market by 2014, Gilead said.

Pharmasset is "way ahead of everybody else," Norbert W. Bischofberger, Gilead's executive vice president for research and development, told analysts in a Monday morning conference call.

But Gilead's bid to dominate the market comes at a high price. It will pay $137 a share in cash, nearly 89 percent above Pharmasset's closing price on Friday. Even before the deal, shares of Pharmasset had risen more than 240 percent over the last year on expectations for PSI-7977.

Investors balked at the deal on Monday, with shares of Gilead falling 9 percent on the announcement.

"For Gilead to give up effectively one-third of their value for an unproven asset still subject to significant ongoing clinical risk seems remarkable," Geoffrey Porges, biotechnology analyst at Sanford C. Bernstein & Company, wrote in a note Monday.

Thomas Wei of Jefferies & Company estimated that Gilead's sales of hepatitis C drugs would have to reach $4 billion a year — difficult, but not impossible — to justify the purchase price.

Competition to acquire Pharmasset and a setback for one of its own hepatitis C drug candidates contributed to Gilead's willingness to pay up, according to remarks by Gilead executives in the call with analysts.

Some analysts applauded the move. Geoffrey Meacham, an analyst at JPMorgan, called it "a bold and strategically positive deal" for Gilead.

Major drug makers have been on an acquisition spree in the last few years, driven by the need to refill their product pipelines. Gilead, based near San Francisco, has made 10 deals since 2006, although the one for Pharmasset is the biggest in its 24-year history.

While Gilead's deal-making record is mixed — particularly those aimed at moving the company into cardiovascular medicine — Pharmasset's lineup is a better fit for the portfolio. Gilead is a leader in developing and selling drugs to treat H.I.V. infection and AIDS, and also sells medicines for hepatitis B, but it has not distinguished itself in the hepatitis C area.

Between Pharmasset's drugs and Gilead's own experimental hepatitis C products, "we have all the ingredients in hand now" to explore various combinations of oral drugs, Dr. Bischofberger said. Eventually, he said, Gilead hopes to combine two or three hepatitis C drugs into a single pill, a strategy that has been very successful with its drug Atripla for AIDS.

An estimated three million to four million Americans — and as many as 170 million people worldwide — have chronic infections of hepatitis C. Many of those infected in the United States are baby boomers who injected drugs using contaminated needles decades ago and might not even know they have the disease. The infection can cause liver cirrhosis and liver cancer, but often not for decades.

Until recently, treatment of genotype 1 of the disease, which accounts for about 70 percent of the infections in the United States and is one of the most resistant strains, involved an almost yearlong regimen of interferon and ribavirin, an oral medicine.

The new drugs, Incivek from Vertex and Victrelis from Merck, when combined with the existing two drugs, increase the cure rate for genotype 1 to 60 to 80 percent. And in some cases, they require only 24 weeks of treatment.

Pharmasset's PSI-7977 has been tested mostly for genotypes 2 and 3, which generally require only 24 weeks of treatment with the older drugs. In one small test, 10 of 10 patients treated with the drug and ribavirin were considered cured after only 12 weeks of treatment, a result that astounded researchers. It is less clear how well PSI-7977 will do against the tougher and more common genotype 1.

As with H.I.V., a combination of two or three drugs might be needed, so drug makers will either have to cooperate with each other or make deals to buy up the various ingredients.

Roche, for instance, has made acquisitions and licensing deals. It owns rights to one of Pharmasset's drugs, called mericitabine. Pharmasset has been testing PSI-7977 in combination

with drugs from Bristol-Myers Squibb and Johnson & Johnson. Those arrangements are expected to continue despite the takeover.

Shares of Inhibitex, which is developing what is also considered a promising hepatitis C drug, rose 19 percent on Monday to $10.61 on speculation that it might be the next takeover target.

Pharmasset's board unanimously approved the deal, which will be carried out through a tender offer, according to the companies. The takeover is expected to dilute Gilead's earnings through 2014 and then begin adding to them in 2015.

Gilead plans to pay for the deal with cash on hand, bank loans and new bonds, with financing from Bank of America Merrill Lynch and Barclays Capital. Gilead said on Monday that it would suspend its share repurchase program for now.

Besides Barclays and Bank of America, Gilead was advised by the law firm Skadden, Arps, Slate, Meagher & Flom. Pharmasset was advised by Morgan Stanley and the law firm Sullivan & Cromwell.

C. CVS: One In 12 Hepatitis C Patients Not Adhering To $1,000/Day Pill

Source:
https://www.forbes.com/sites/davidkroll/2014/09/17/one-in-12-hepatitis-c-patients-not-adhering-to-1000day-pill/?sh=43b9be283957

Sep 17, 2014, 10:22pm EDT

David Kroll Former Contributor
Pharma & Healthcare

Over 8 percent of hepatitis C patients taking Sovaldi (sofosbuvir; Gilead) are failing to complete their full, 12-week course of drug therapy, a dropout rate roughly four times that observed in clinical trials.

By discontinuing the drug, shown to have a 90+% cure rate, these patients (and their insurance providers) are incurring health care costs of $28,000 or $56,000, without knowing if they are rid of the virus.

Whether such patients will have to restart a complete 12-week course of the $1,000 per day pill remains a question for medicine and pharmacy experts. (The lowest, discounted retail price I could find in my neighborhood is $1,056/pill, via GoodRx.)

This real-world data comes from an analysis released this morning by CVS Health Research Institute, led by Troyen Brennan, MD, MPH, executive vice president and chief medical officer of CVS Health.

Dr. Brennan and William Shrank, MD, the company's chief scientific officer, published a viewpoint article in *JAMA* last month, offering perspective on the high price but remarkable benefits of Sovaldi. Previous interferon-based therapies offered a 40% cure rate.

Sovaldi is the first of several drugs specifically targeted to the hepatitis C machinery that replicates its RNA genome (the NS5B polymerase, in this case).

The costs of the drug are amplified by the patient population itself. In the U.S., hepatitis C infects between 3.4 to 4.4 million people, with another 0.5 to 1 million among the homeless and incarcerated, according to NHANES data. According to Gilead's security filings, only about 80,000 patients in the U.S. and Europe have started on the drug, reports Jaimy Lee at Modern Healthcare.

Much attention has been paid to the costs of treating this large population with Sovaldi and the potential for it to increase individual health care coverage by $200 to $300 per year.

But less attention has been spent discussing the cost savings from precluding the need to manage the cirrhosis and liver cancer caused by the virus, as well as the costs of liver transplants.

I asked Dr. Brennan why they chose to post today's report as a white paper on the CVS Health site rather than run it through peer-review for *JAMA* or another medical or pharmacotherapy journal.

"It's fairly straightforward and represents analytics of our utilization data that are looked at all the time," said Brennan. "The other thing is that it's very topical right now and if we waited six weeks to six months for review and publication by a leading journal, it might not be as topical anymore."

In addition, the study is freely-available here as a PDF, as opposed to behind a paywall as with their August *JAMA* article.

Far less aversive than interferon

Together with Alan M. Lotvin, MD, executive vice president of the CVS Health's specialty pharmacy arm, the team sought to determine Sovaldi's adherence and completion patterns in patients, now that the drug has been released for use in the general hepatitis C population for about nine months.

They also assessed the factors that might influence discontinuation of Sovaldi and what type of pharmacy services the patients were provided.

For example, a known risk factor for discontinuation of drugs prior to Sovaldi is being new to therapy. Those treated previously and not cured are likely to be sicker and more motivated to complete the full course of the new drug.

In the web excerpt of his book, *The Upside of Irrationality*, Duke University behavioral economist Dan Ariely wrote of his personal experiences with interferon. Ariely had contracted hepatitis C from infected blood transfusions he received while being treated for severe burns after a military training accident.

> The initial protocol called for self-injections of interferon three times a week. The doctors advised me that after each injection I would experience flu-like symptoms, including fever, nausea, headaches and vomiting. But I was determined to kick the disease, so every Monday, Wednesday, and Friday evening for 18 months I plunged the needle deep into my thigh. About an hour later the nausea, shivering and headache would set in.
>
> Every injection day was miserable. I had to face giving myself a shot followed by a 16-hour bout of sickness in the hope that the treatment would cure me in the long run. I had to endure what psychologists call a “negative immediate effect” for the sake of a “positive long-term effect”.

And that was for a drug that, with ribavirin, had no more than a 40 percent cure rate, even for an 18-*month* course. After such an experience, an oral, once-daily medicine for 12 week with a 95 percent cure rate would be far more welcomed by a patient undergoing this experience relative to a treatment-naive patient.

So why do patients stop taking the drug?

Since Sovaldi was approved last December, the CVS/caremark pharmacy benefits management service has filled 16,560 prescriptions for the drug. More than 65 percent of these patients received the new drug without interferon. Forty-three percent took Sovaldi and ribavirin while 23% took Sovaldi plus Olysio.

The team pulled out the data for 1,965 hepatitis C patients with at least 44 months of drug therapy information for analysis. Those who had received previous therapies could then be compared with those receiving Sovaldi as their first drug for the disease. As with previous drugs, 8.7 percent of treatment naive-patients discontinued Sovaldi while only 5.3 percent of the previously-treated patients stopped the drug prematurely.

For patients taking Sovaldi with other medications, the discontinuation rates were up to four-fold higher than those observed in clinical trials (2.0 to 3.6 percent. Those taking Sovaldi with peg-interferon and ribavirin discontinued at a rate of 10.2 percent while 9.0 percent of those taking Sovaldi and ribavirin did not complete the full course.

The best adherence, a 4.3 percent discontinuation rate, was observed in patients taking Sovaldi with Olysio (simeprevir), the Janssen/Johnson & Johnson NS3/4A protease inhibitor approved in November 2013.

Specialty pharmacy services

Because CVS/caremark is the nation's second largest pharmacy benefits manager, they have access to information for patients using non-CVS pharmacies. The team was able to show that discontinuation was higher in patients using non-CVS pharmacy services (8.5 percent) than CVS specialty pharmacy services (5.9 percent).

The reason underlying the difference is a bit of a mystery because other pharmacy chains offer specialty pharmacy services for patients like those with hepatitis C. For example, CVS Specialty Pharmacy offers 24/7 telephone access to trained staff, including pharmacists, that provide disease education and drug counseling as well as help in navigating insurance issues.

But even when broken out, non-CVS speciality pharmacies faired only slightly better than standard, non-CVS retail pharmacies (8.3 percent discontinuation vs. 8.8 percent).

Brennan didn't really trumpet this result as much as I might have expected, but did make a general point about the economic value of specialty pharmacy services and how CVS deploys their program.

"It's a matter of expert pharmacists keeping up with the patients, making sure that they've refilled the medicine, as well as automated adherence signaling. It's a high-touch approach, and that's what specialty pharmacies do. We've also integrated this specialty expertise into our retail settings so they can still enroll in the specialty pharmacy program."

"With these drugs, even low levels of adherence are extremely expensive," says Brennan.

That holds for the cost of the ineffective drug stopped prematurely plus the likelihood that it or another expensive drugs will have to be prescribed in the future.

The main takehome point of the CVS Health study is that we need to look more closely at drug adherence in the community setting, not just for disease management, but for cost containment as well.

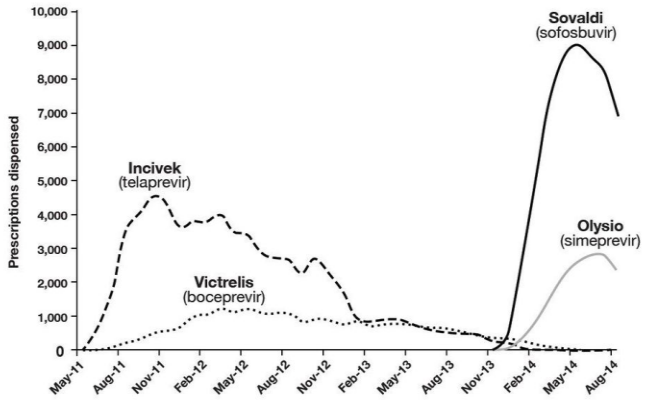
As Dr. Brennan says, "In the clinical trials, the discontinuation rates were in the 2 to 3 percent range, but things are never like that in the real world."

The clinical trial process is tightly controlled, has more intensive participant follow-up, and patients are generally more motivated.

Waiting for "The Next Big Thing"

Already, prescriptions for Sovaldi have plateaued and are decreasing in what appears a pharmaceutical version of the Apple effect: doctors may be holding out prescribing Sovaldi until an even more effective combination product is expected to be approved later next year.

Figure 1: Utilization Trends of Hepatitis C Treatments (May 2011 – Aug 2014)



Beginning December 2013, when Sovaldi first became available, there was a massive rush to use the medication, with increasing numbers of patients beginning treatment each month. This was due to the fact that in the months leading up to the FDA approval of Sovaldi, many patients with hepatitis C who were not experiencing symptoms or adverse health effects had delayed pursuing any treatment until the new, highly effective drug became available. In contrast to the rapid uptake observed initially, CVS Health data show a plateau and then a downward trend in the number of new starters of Sovaldi during May – August 2014. Vertex has announced that Incivek sales will cease in the U.S. in October 2014.

Dr. Brennan calls this the "warehousing" of patients. When patients are hepatitis C-positive but aren't yet showing severe symptoms, the slow-moving nature of the disease causes some hepatologists to hold off beginning expensive drug treatments.

"Hepatologists will tell these patients, 'Wait, you're not progressing. we're not going to treat you now, we're going to wait until these better medications are out,'" says Brennan.

Most are awaiting Gilead's fixed-dose combination drug: sofosbuvir from Sovaldi and a newer agent, ledipasvir, that targets the NS5A protein involved in hepatitis C viral replication. This

combination will only be for patients with the genotype 1 version of the viral infection, but it represents 75 percent of all hepatitis C patients. The drug course will only be for eight weeks and phase 3 trials suggest cure rates of over 95 percent.

Gilead hasn't offered a specific price yet but Reuters is reporting a $95,000 price for the eight-week course. The FDA action data on Gilead's filing is October 10.

D. Harvoni, a Hepatitis C Drug from Gilead, Wins F.D.A. Approval

Source:

https://www.nytimes.com/2014/10/11/business/harvoni-a-hepatitis-c-drug-from-gilead-wins-fda-approval.html

By Andrew Pollack

Oct. 10, 2014

The first complete treatment for hepatitis C that requires taking only a once-a-day pill won approval Friday from the Food and Drug Administration.

The drug, called Harvoni from Gilead Sciences, could shorten the duration of treatment and provide the first all-oral regimen for many patients. The new drug also appears to be a bit less expensive for some patients than Gilead's existing blockbuster hepatitis C drug, Sovaldi, which has become the poster child for those complaining that the cost of medicines is out of control.

Sovaldi costs $1,000 a pill, or $84,000 for a typical 12-week course of treatment, but it must be used with other drugs. Harvoni is even more expensive at $1,125 a pill, or $94,500 for a 12-week course of treatment. But that is roughly in line with the total cost for Sovaldi and the drugs used with it. Many patients will be able to take Harvoni for only eight weeks, at a cost of about $63,000.

This will probably not mollify insurance companies and Medicaid programs, many of which are restricting the use of Sovaldi to the most seriously ill patients.

"They are not prepared to cover the cost even at $63,000," said Dr. Steven Miller, the chief medical officer of Express Scripts, which manages pharmacy benefits for employers and insurance companies. "Their budgets just are not going to be able to tolerate it."

He said the patients eligible for the shorter regimen are also the ones least in need of treatment.

But some patient advocates hope the pricing will persuade payers to relax their restrictions.

"We're talking about a much lower cost to Medicaid for a substantial number of people, and to me that's a game changer," said Ryan Clary, executive director of the National Viral Hepatitis Roundtable, a coalition of organizations that receives some funding from drug companies.

Gilead defended the price. "We believe the price of Harvoni reflects the value of the medicine," it said in a statement. "Unlike long-term or indefinite treatments for other chronic diseases, Harvoni offers a cure at a price that will significantly reduce hepatitis C treatment costs now and deliver significant health care savings to the health care system over the long term."

Harvoni is a combination of sofosbuvir, the ingredient in Sovaldi, and a new medicine from Gilead called ledipasvir, which is not available as a stand-alone product. The two drugs attack the virus in different ways.

By combining drugs into a single pill, Gilead is repeating the strategy it used to become the leading supplier of drugs for H.I.V. Its drug Atripla, which combines three medicines, was the first once-a-day complete treatment for that disease.

Gilead estimates that over the long run as many as half of the patients might be able to receive only eight weeks of treatment.

Three million to four million Americans are infected with hepatitis C, which can gradually damage the liver. Harvoni's approval is only for the main subtype of hepatitis, called genotype 1, which accounts for about 70 percent of the cases in the United States.

In clinical trials, more than 90 percent of the patients treated with Harvoni had no detectable virus in their blood 12 weeks after treatment ended. Doctors say that is considered an effective cure.

Harvoni may shorten treatment for hepatitis C.
Gilead Sciences

Sovaldi, which was approved in December, has already made a huge difference for patients, reducing the duration of treatment to 12 weeks from 24 or 48 weeks, increasing the cure rate and reducing side effects.

But Sovaldi is not supposed to be used by itself. Patients with genotype 1 are supposed to also take the older hepatitis C drugs, alpha interferon and ribavirin. Interferon in particular, which is given as a weekly injection, can have debilitating side effects such as flulike symptoms and depression.

In practice, many doctors this year have been avoiding the use of interferon by prescribing Sovaldi with another new pill, Johnson & Johnson's Olysio. That combination has not been approved by the F.D.A. and costs about $150,000.

Compared with that off-label combination, Harvoni is far less expensive, which could mean lower sales for Johnson & Johnson's drug.

It is not so much the price per patient of Sovaldi but the total cost that has insurers and Medicaid programs worried. Sales of Sovaldi in the first half of the year were nearly $6 billion, almost all of it in the United States, shattering the record for first-year sales of any drug.

“Ironically, if this drug were not a breakthrough drug, people would not object to it because so many people would not be standing in line,” said Ed Schoonveld, a principal at ZS Associates, a consultant to drug companies.

Caught off guard by the surge in demand, many insurers and state Medicaid programs have started to restrict the use of Sovaldi to patients who have more advanced liver disease. Some are requiring patients to demonstrate they have not abused alcohol or illicit drugs in a number of months.

Some advocacy groups, led by the National Viral Hepatitis Roundtable, sent a letter last month to Sylvia Mathews Burwell, the secretary of health and human services, saying that such restrictions were “discriminatory and violate the spirit and the intent of the Affordable Care Act.”

It can take 20 years or more for hepatitis C to cause noticeable cirrhosis or liver cancer. Many people infected with the virus never suffer noticeable liver damage.

That is why in many cases it can be acceptable for patients without advanced liver damage to delay treatment. Many patients, on advice from their doctors, have been delaying treatment until Harvoni became available.

Gilead and some doctors make the case that even if liver damage is not serious, people with a chronic virus infection can have various other health problems, including an increased risk of heart attack. Treating the disease early is better, they argue, because it avoids liver damage to begin with.

“The sooner you cure them, the more likely you are to have better long-term outcomes for these patients,” John F. Milligan, president and chief operating officer of Gilead, said at the Morgan Stanley health care conference last month.

Gilead recently agreed to allow several generic drug manufacturers in India to make and sell much less expensive copies of Sovaldi in about 90 poorer countries. That agreement also applies to Harvoni.

Analysts think the introduction of Harvoni will keep Gilead in the lead in the market for hepatitis C treatments. Just this week, Bristol-Myers Squibb said it would essentially give up for now on fielding its own combination treatment, a tacit acknowledgment that its regimen would not be competitive.

The competition for Gilead is expected from AbbVie, which could receive F.D.A. approval for its combination regimen by the end of this year. Insurers hope to play Gilead and AbbVie against each other to obtain lower prices, but it is not clear that will work.

E. Inside the $100 million ad blitz for a $1,100-a-pill drug for hepatitis C

Source:

https://www.statnews.com/2016/03/08/harvoni-hepatitisc-ads/

By Rebecca Robbins

March 8, 2016

Alex Hogan/STAT

A $100 million ad blitz has whipped up patient demand for Harvoni, the $1,100-a-pill hepatitis C treatment, even as the drug's price has drawn a barrage of lawsuits, state investigations, and sharp condemnation from members of Congress.

STAT analyzed data from media research firms for the most detailed look to date at the aggressive consumer marketing strategy for Harvoni, made by Gilead Sciences of Foster City, Calif.

At a time when some insurers have been reluctant to cover — and some physicians have been reluctant to prescribe — such an expensive drug, Gilead has pushed Harvoni in front of potential patients at every opportunity: as they read celebrity gossip, watch science fiction shows, follow the news, and more. As a result, doctors say patients are coming in asking for the drug by name, apparently not deterred by the cost or by the heavy political and legal fire aimed at Harvoni's price tag.

Patients "have Harvoni on the mind because of these TV commercials," said Mount Sinai Hospital hepatologist Dr. Douglas Dieterich.

Indeed, the Harvoni marketing push, which launched last spring, has been one of the year's most expensive prescription drug ad campaigns.

Just a handful of prescription drugs were advertised more widely, and most of those treat conditions — such as erectile dysfunction and psoriasis — that afflict far more patients in the United States than hepatitis C. About 3.5 million Americans have the viral infection, which usually lies dormant for years but can eventually cause liver failure and liver cancer.

Related: Massachusetts threat to sue Gilead over prices is an uncertain gambit

More than 11,000 ads for Harvoni have aired on TV channels from FOX to Animal Planet to the Game Show Network to Syfy. The total value of the time slots is estimated at $60 million to upwards of $80 million, according to the data from media research firms iSpot.tv and Kantar Media.

And the TV ads were just the start: Last year Gilead bought more than $30 million worth of ad space to tout Harvoni in magazines from People to Popular Mechanics to Better Homes and Gardens, as well as more than $5 million worth of ads online. (The iSpot and Kantar data reflect the list price of TV, magazine, and digital ad space, and don't take into account any discounts Gilead may have negotiated.)

Last year Gilead bought more than $30 million worth of Harvoni ads in magazines like this one (far right). *STAT*

On top of all that, Gilead has run other ads that don't mention its hep C drugs by name — but do find a way to get them in front of patients. The unbranded magazine and TV spots tell patients they "haven't been forgotten" and urge them to go to a website for more information about hep C. Patients who click to learn about treatment options end up at the Harvoni website. The cost of these unbranded ads is not included in the $100 million estimate for the Harvoni campaign.

Gilead spokeswoman Cara Miller declined a request for an interview about the company's advertising strategy for Harvoni.

Harvoni and an earlier version of the drug, sold as Sovaldi, have been in the headlines lately because of an intense backlash over their costs. Before discounts, a full course of Harvoni is priced at $94,500 and a course of Sovaldi costs $84,000.

In Massachusetts, the attorney general has threatened to sue Gilead over those prices, suggesting that they may constitute unfair trade practices. The New York state attorney general, meanwhile, is investigating insurers that have denied patients coverage for Harvoni.

And a Senate committee in December excoriated Gilead for putting profits over patients when it set the prices of its two drugs. "If Gilead's approach is the future of how blockbuster drugs are launched in America, it's going to cost billions and billions of dollars to treat just a fraction of patients in America," Senator Ron Wyden, a Democrat from Oregon, said at the time.

Related: Gilead pricing for Sovaldi hepatitis C drug slammed by senators

Amid all this negative publicity, US sales of Harvoni slowed down in the fourth quarter of last year — but the drug remains a blockbuster. It's generated $12 billion in US sales since its approval in late 2014. Sovaldi, which is still used for some patients, has generated $11 billion in US sales since being approved in late 2013.

Sales have been brisk partly because the drugs work. In the vast majority of patients, they can cure hepatitis C with few side effects in a matter of weeks, eliminating the potential need for grueling (and expensive) treatments like liver transplants later in life.

Harvoni's strong sales numbers likely also reflect Gilead's aggressive advertising, which has targeted patients who have been living with the condition for years.

Increased screening in recent years has helped create a sizable population of patients who know they have hepatitis C but who haven't yet addressed it. Others may know they're at risk because of past behavior, such as intravenous drug use, but haven't yet been tested.

To spur those groups into action, Gilead has heavily pushed a TV spot called "I am Ready," which features graying men and women declaring that they're finally prepared to confront, and overcome, hepatitis C. As rain melts into sunshine, off-screen narrators declare, "I am ready to put hep C behind me" and "I am ready to be cured."

Like most drug advertisers, Gilead last year devoted the majority of its TV ad dollars for Harvoni to the big broadcast networks ABC, NBC, CBS, and FOX — which draw increasingly aging viewers, including baby boomers between the ages of about 50 to 70, who are five times more likely than other adults to have hepatitis C.

Harvoni ads also target more niche audiences. Consider the $600,000 worth of Harvoni ads last year in the magazine of the American Association of Retired Persons. Or the $3 million Gilead spent advertising on Black Entertainment Television and in Ebony magazine — which makes sense given that African-American baby boomers are twice as likely as others in that age group to have hepatitis C.

Men are also disproportionately likely to have hep C, which may explain Gilead's investment last year in a collective $13 million worth of ads on ESPN and the Golf Channel and in Sports Illustrated and Men's Journal.

Gilead is wooing patients directly at a time when both private insurers and Medicaid programs are balking at the high price of Harvoni. In some cases, they're only agreeing to pay for treatment for the sickest patients, leaving those with relatively healthy livers unable to get treated. Other insurers will only pay for a competitor's lower-priced drug.

Doctors, too, have proved a barrier; some are encouraging patients to hold out for cheaper therapies.

“A lot of physicians are taking a wait-and-see attitude,” said John Mack, who publishes Pharma Marketing News. As a result, he said, Gilead is going directly to patients, trying to “push them” into talking with their doctors and requesting the medication by name.

Dieterich, of Mount Sinai Hospital, said that physicians sometimes have to “do a little fast-talking” to reassure patients that other medications can work just as well as the brand-name drug they’ve seen so often on TV. Competing hepatitis C drugs Viekira Pak and Zepatier aren’t being advertised, so Gilead has the field to itself.

“We’re battling their successful direct-to-consumer advertising,” Dieterich said.

Gilead has said it’s expecting sales from Sovaldi and Harvoni to flatten this year, but the ads may well continue.

The company is already eyeing new markets: It got new approvals last month to market Harvoni for a new segment of patients with hepatitis C, those with advanced liver disease.

F. Sovaldi leads Medicare spending; See how much other drugs cost in 2014 Part D claims

Source:
https://www.healthcarefinancenews.com/news/soldadi-leads-medicare-spend-see-how-much-other-drugs-cost-part-d-claims

Aug 18, 2016

Overall, CMS said the amount it spent on drugs in 2014 grew by 17 percent year over year, driven by rising pharmaceutical costs.
Henry Powderly

The Centers for Medicare and Medicaid Services paid out $3.1 billion in claims for hepatitis drug Sovaldi, the agency showed on Thursday, making it the top drug by Medicare spending for the entire year.

What's striking, though, is only 33,000 Medicare beneficiaries received the pricey drug.

By contrast, Nexium, an acid reflux drug that topped Medicare Part D spending in 2013, was second on the list with nearly $2.7 billion in Medicare payments. However, more than 1.4 million Medicare beneficiaries received that medication.

Overall, CMS said the amount it spent on drugs in 2014 grew by 17 percent year over year, driven by rising pharmaceutical costs.

The table below shows individual Medicare spending for every drug billed to the federal health insurer in 2014. It is sortable by total spend, beneficiaries and the number of claims.

Drug	Generic Name	Beneficiaries	Prescribers	Total claims	Total cost
SOVALDI	SOFOSBUVIR	33,028	7,323	109,543	$3,106,589,192.32
NEXIUM	ESOMEPRAZOLE MAGNESIUM	1,405,570	286,927	7,537,736	$2,660,052,054.25
CRESTOR	ROSUVASTATIN CALCIUM	1,752,423	266,499	9,072,799	$2,543,475,141.92
ABILIFY	ARIPIPRAZOLE	405,048	130,933	2,963,457	$2,526,731,476.43
ADVAIR DISKUS	FLUTICASONE/SALMETEROL	1,420,515	281,775	6,093,354	$2,276,060,160.95
SPIRIVA	TIOTROPIUM BROMIDE	1,211,919	253,277	5,852,258	$2,158,219,163.39
LANTUS SOLOSTAR	INSULIN GLARGINE,HUM.REC.ANLOG	972,882	224,710	4,441,782	$2,016,728,436.29
JANUVIA	SITAGLIPTIN PHOSPHATE	789,828	190,741	4,495,964	$1,775,094,282.42
LANTUS	INSULIN GLARGINE,HUM.REC.ANLOG	787,077	223,502	4,284,173	$1,725,391,907.14
REVLIMID	LENALIDOMIDE	27,142	9,337	178,373	$1,671,610,361.68

I have listed the top-10. The url link on top of page provides a longer list of pharma.

G. This is the most expensive drug in America

Source:
https://www.marketwatch.com/story/this-is-the-most-expensive-drug-in-america-2016-04-09

By Emma Court

Published: Apr 14, 2016 5:45 p.m. ET

It costs $84,000 per treatment -- but was originally only supposed to cost $36,000.

MarketWatch photo illustration/Shutterstock

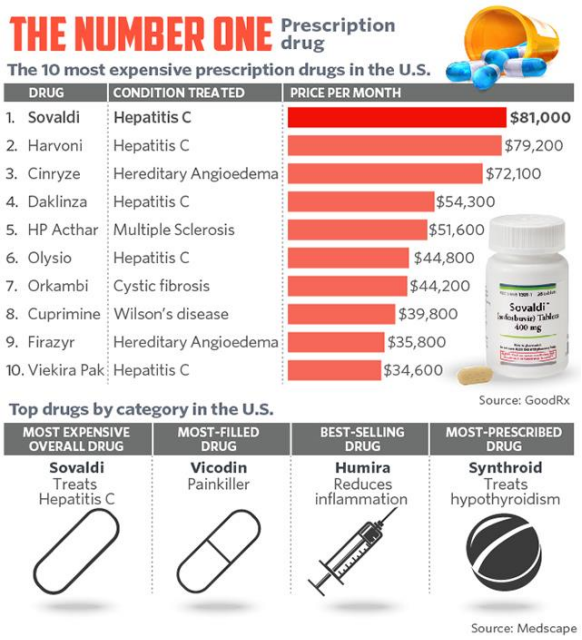
In 2014, a new hepatitis C drug came to market, an innovative treatment offering a cure for a disease that desperately needed one. The price tag: about $84,000 for a 12-week course of treatment, enough to make it the most expensive prescription drug in America.

In the medical world, the halls of insurance offices nationwide and even our nation's Capitol, all hell broke loose.

The drug, Gilead Sciences Inc.'s Sovaldi GILD, +0.28% remains the most expensive drug in America today, topping a list compiled by drug price comparison website GoodRx. Second on the list is its sister drug Harvoni, which combines Sovaldi with another drug.

Insurer trade groups, activists and politicians alike have denounced Sovaldi's price tag as far too expensive, especially considering the size of the patient population: currently about 3.5 million people in the U.S. are estimated to have hepatitis C. Gilead maintains that the innovation of the treatment justifies its price.

Sovaldi triggered debates about too-high drug prices that continue to this day, intensifying last year when Martin Shkreli, who was CEO of Turing Pharmaceuticals at the time, hiked prices on the cancer drug Daraprim by 5,000%.



For all the attention it received, Daraprim doesn't actually make GoodRx's top 10 list of most expensive drugs in the U.S., though Elizabeth Davis, GoodRx's head of data and content, said she believes Daraprim could get pushed into the top 10 this quarter.

By and large, the top 10 costly drugs are new ones, with all but three emerging in the last five years. The list is also dominated by hepatitis C drugs, with most advances in curing the disease only happening in recent years (all of the hepatitis C drugs on the top 10 list were approved in 2013 or later).

Why is Sovaldi so expensive?

The ire spurred by Sovaldi's cost was at least in part motivated by another -- much lower -- number quoted by the drug's initial developer Pharmasset Inc.

'We all pay the cost of Sovaldi.' *Clare Krusing, a spokeswoman for the insurers' trade group America's Health Insurance Plans*

In a 2011 SEC filing, Pharmasset projected "a U.S. base rate of $36,000 per course of treatment," which typically runs 12 weeks. Pharmasset was bought by Gilead before Sovaldi went to market at a price tag of more than twice that initial number.

Critics point to the $36,000 figure in the SEC filing as proof that Sovaldi's high price tag cannot be justified in terms of expenses -- and is motivated by profit alone.

But others say it's fair for a drug's price to take into account how innovative the product is.

"It's a cost-effective drug, by most metrics," said Craig Garthwaite, a health economist who teaches at Northwestern University's Kellogg School of Management. "We always wanted a treatment for Hep C. We got one, now we have to pay for it."

The U.S. Senate Finance Committee launched an investigation into Sovaldi and Harvoni that concluded in late 2015, finding that "Gilead's own documents and correspondence show its pricing strategy was focused on maximizing revenue — even as the company's analysis showed a lower price would allow more patients to be treated."

"Review of company documents reveals that the return on investment for acquiring Pharmasset and additional research and development were not key considerations in determining the pricing of these drugs," the report said, though it noted that Gilead spent billions of dollars acquiring the drug's developer and hundreds of millions in the clinical trial and FDA approval process.

Gilead said in a statement that the prices of its two list-topping drugs "reflect the innovation of the medicines," because by curing hepatitis C, they realize "significant savings to the health-care system over the long-term."

"The one-time cost of Harvoni or Sovaldi pales in comparison to the lifetime costs associated with treating [hepatitis C]," the company said, adding that more than 770,000 people world-wide have been treated with the drugs, a substantial improvement on earlier hepatitis C treatments, which offered "cure rates of only 50% to 60%" to the new drugs' rates of more than 90%.

How much of that $84,000 is paid by the patient?

As is the case with prescription drugs, the gross price — $81,000 for a 30-day supply of the most common dosage and quantity — is rarely the price patients, or even insurers, pay.

Since Sovaldi was approved, several other competing hepatitis C drugs have been released, negotiating power that helped drive down Sovaldi's price for the insurer, said John Rother, president and chief executive officer of National Coalition on Health Care.

So while $81,000 is the most that could be paid for a 30-day supply of Sovaldi, GoodRx has recorded insurers and/or customers paying anywhere from $24,455 to $75,600 over the last month.

Gilead said it works to ensure "broad patient access to our hepatitis C cures" through a patient assistance program, which it said gives eligible uninsured people the drugs at no cost.

"Most payers receive substantial discounts on Sovaldi and Harvoni -- with the steepest discounts (in excess of 50% for Harvoni) going to Medicaid and the [Veteran Affairs health system]," it said. "In addition, 96% of insured individuals in the U.S. have formulary coverage for one of Gilead's [hepatitis C] therapies."

But make no mistake about it, NCHC's Rother said, "it's still hugely expensive, even with that, given the number of people taking it. Even half-priced, it's priced more than the original price" disclosed by Pharmasset in 2011.

How much patients actually pay out-of-pocket for the drug depends on whether they have insurance, and what kind. Those with high-deductible plans and on Medicare likely pay large amounts of their own money, about $8,000 to $10,000, Rother said, while those with insurance would pay less.

But even if insurance covers the drug, its costs are still getting passed on in the form of higher premiums and out-of-pocket costs, said Clare Krusing, a spokeswoman for the insurers' trade group America's Health Insurance Plans. "So we all pay the cost of Sovaldi."

The drug also took a bite out of state Medicaid budgets, costing more than $1 billion to treat just 2.4% of those with hepatitis C in 2014, according to the finance committee report. (Since 2014, discounts for the drug have been made more available.)

In Massachusetts, the burden the two drugs placed on Medicaid and prison health care programs prompted an investigation by the state attorney general's office, The Wall Street Journal reported earlier this year.

The 'poster child' for expensive drugs?

Beyond the debate over Sovaldi's price tag, there's also the question of whether Sovaldi actually deserves the title of most expensive drug.

More expensive than Sovaldi and Harvoni are certain cancer-fighting biological therapies, which are administered by a doctor or in the hospital and therefore not technically considered prescription drugs, Rother noted.

There are also prescription drugs that are more expensive if a longer-term perspective is taken on cost. Sovaldi and Harvoni, as Gilead noted in a statement, cure hepatitis C, so the price tag is a one-time price, assuming the patient isn't reinfected.

For instance, there's an expensive class of new cholesterol drugs, PCSK9 inhibitors that "can add up and far exceed" the costs of Sovaldi and Harvoni, possibly requiring a lifelong dosage, Krusing said. These include Praluent, made by Sanofi S.A. SAN, +0.57% and Regeneron Pharmaceuticals Inc.'s REGN, +0.10% and Amgen Inc.'s AMGN, +0.96% Repatha.

Ivonne Cameron, the president and chief executive officer of the nonprofit Hepatitis Foundation International, worries that Sovaldi and Harvoni have become the "poster child for high-cost medication."

"It's scaring away patients," she said, noting that "hard to reach, hard to treat" populations such as intravenous drug users are more likely to be intimidated by the price tag.

Her organization educates worried callers about resources that can alleviate that price burden and about organizations that help with access to care, she said.

“You essentially have something that can all but cure a disease. And for our patients they’re essentially hearing the message ‘there’s a cure but you can’t access it,’ ” she said. “That’s a major concern.”

H. Will Hepatitis C Virus Medication Costs Drop in the Years Ahead?

FEBRUARY 08, 2017

Source:
https://www.pharmacytimes.com/view/will-hepatitis-c-virus-medicaton-costs-drop-in-the-years-ahead

Laurie Toich, Assistant Editor

The high cost of hepatitis C virus (HCV) drugs has caused significant financial strain for patients and the health care system. These drugs cost as much as $95,000 for a 12-week treatment, but carry a 90% or better cure rate, which many believe justifies the cost.

While some insurers have implemented cost containment strategies to prevent early stage patients from receiving the treatment, lawsuits have been filed challenging the ethics of these practices.

Lawmakers are now struggling to create legislation that will provide these patients with the treatments they need, but a majority of proposals do not gain traction, according to a report published by *Mediware*.

Sofosbuvir (Sovaldi) received FDA approval in 2013, and was the first drug deemed safe and effective without interferon. It was also the first approved curative treatment for HCV.

No previous treatments resulted in a sustained virologic response, which made sofosbuvir a highly sought-after drug. Gilead Sciences priced the treatment at $1000 per pill, making the total cost of the treatment $84,000.

Gilead then combined sofosbuvir with a new drug, ledipasvir, to create the even more effective combination treatment, Harvoni. Harvoni's total treatment cost is $94,500 for a 12-week regimen.

If CDC estimates are correct and 3.5 million Americans have HCV, then treatment with Harvoni would cost payers $331 billion, which was more than total drug spending in 2013, according to the report.

Although most other specialty drugs only treat a small number of patients, HCV drugs treat a large patient population, and provide manufacturers with opportunities to generate significant revenue.

Interestingly, sofosbuvir only costs $900 in Egypt, and $55,000 in Canada, substantially less than the cost in the United States. This has caused some lawmakers to accuse Gilead of price gouging, and limiting access to effective treatments, according to the report.

In some states, Medicaid beneficiaries may not have equal access to the drugs. US Senators have reported that some states cover 9.1% of enrollees for HCV treatment, while others only cover

less than 1%.

Medicaid is unable to cover treatment for all enrollees, since covering 1 treatment with Harvoni costs the same as the annual health care costs for 29 enrollees, which highlights the need for lower costs, according to the study.

Both private and public insurers have had to create eligibility requirements that prioritize patients with liver damage, and those who have failed to respond to less costly treatments due to the high price of newer drugs. However, the Department of Veterans Affairs recently announced they would cover HCV treatment costs for all veterans as a result of increased funding and decreased drug costs, according to the report.

With President Donald Trump advocating for lower drug costs, patients with HCV may gain expanded access to treatment.

Proposals such as allowing Medicare price negotiation, capping out-of-pocket drug costs, importing drugs, and limiting manufacturer' spending on patient marketing could all result in lower HCV drug costs, the authors wrote.

Competition has also been seen to impact HCV drug pricing, and will likely continue to do so in the future as more drugs receive regulatory approval.

The FDA's approval of Viekira Pak (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets) in 2014 impacted the pricing of Harvoni. The new approval elicited support from Express Scripts, who then dropped Harvoni and sofosbuvir for patients with HCV genotype 1.

This resulted in Gilead's stocks taking a 20% hit, prompting them to offer discounts for Harvoni to certain payers. If manufacturers take similar actions, drug costs may be reduced even further.

The most recent approval of Merck's Zepatier (elbasvir and grazoprevir) caused waves for many reasons. First, the drug's cure rate was 97% to 100% in patients with HCV genotype 4, and 94% to 97% in patients with genotype 1, which is higher compared with other drugs.

Notably, the price for the drug was only $54,600 for 12-weeks of treatment, which improves access to affordable drugs, according to the report.

A pipeline drug, odalasvir, being developed by Achillion Pharmaceuticals and Johnson & Johnson, also has the potential to reduce drug costs. The drug has shown a 100% cure rate in as little as 6 weeks in combination with sofosbuvir. Shorter treatment spans will likely result in less costly drugs, the authors noted.

Despite treatment for HCV being medically necessary, payers still do not think the high costs for the drugs warrant widespread treatment. However, critics may counter that in the long run, payers are costing themselves more money.

Patients who do not receive treatment for HCV are more likely to develop liver cancer and type 2 diabetes, experience plaque build-up in the arteries, and have an increased risk of stroke, according to the report.

While Gilead's drugs remain some of the highest priced on the market, the entrance of new, lower cost drugs will likely drive down the cost of HCV treatment over time.

Until that happens, specialty pharmacies and their pharmacists should focus on directing patients to copay assistance programs, and help patients adhere to treatments, the report concluded.

I. Why Egypt Is at the Forefront of Hepatitis C Treatment

Source:

https://www.theatlantic.com/health/archive/2018/05/why-egypt-is-at-the-forefront-of-hepatitis-c-treatment/561305/

Despite the availability of revolutionary new drugs, countries with more resources haven't made as much progress against the disease.

Ted Alcorn
May 29, 2018

Egyptian workers line up near a van for an examination check-up for Hepatitis CAFP Contributor / Getty

Just five years ago, with the best medical therapies available, the odds of curing a person infected with hepatitis C were no better than a coin toss. Eliminating the disease from a whole country was unthinkable.

But today, Egypt is wiping the disease from its population at an unprecedented pace. The effort was made possible by revolutionary new drugs—but no country, including the United States, has come close to deploying them at equivalent scale. Egypt has shown that dramatic improvements in public health are possible when drugs are priced affordably—and a government makes an effort to systematically deploy them. But Egypt is also the exception that proves the rule that while modern society has proven capable of developing transformative medical innovations, it's far less proficient at maximizing their use.

The hepatitis C epidemic in Egypt—the country with the highest prevalence of the disease in the world—started around 50 years ago, when the government was attempting to get rid of one plague and ended up substituting it for another. For millennia the Nile Delta has been an ideal breeding ground for schistosomiasis, a parasite spread to humans by freshwater snails. In the mid-20th century, the Egyptian government conducted multiple mass-treatment campaigns using an injectable emetic—and needles were repeatedly reused. Hepatitis C virus, not yet known but transmitted efficiently by blood, was inadvertently spread to many citizens. By 2008, one in 10 Egyptians had chronic hepatitis C.

The virus causes progressive liver damage that only becomes apparent over a decade or more, when it culminates in cancer or liver failure. By 2015 hepatitis C accounted for 40,000 deaths per

year in Egypt—7.6 percent of all deaths there—and depressed national GDP growth by 1.5 percent.

While infection is more common in rural and poor areas, few segments of Egyptian society are untouched by it. John Ward, who led the CDC's division of viral hepatitis for more than 13 years and is now a director at the nonprofit Task Force for Global Health, says he sees its impact even among Egyptian expatriates he meets by chance in Washington, D.C. "I'll be in a cab, I'll say I work on hepatitis C, and that starts the whole conversation going about family, friends, in-laws, fathers lost to hepatitis C. So it's a very big problem."

The outlook for the disease changed in late 2013 with the advent of effective but expensive new cures. Whereas prior treatments induced fatigue and other side effects and cleared the infection in fewer than half of patients, the new therapies were painless and cured the disease over 90 percent of the time. Gilead Sciences introduced the first such drug to the U.S. market at $84,000 per patient. At that price, treating the entire infected Egyptian population would have cost half a trillion dollars, nearly double the country's gross domestic product.

The circumstances recalled the introduction of AIDS drugs two decades ago, when drug makers set high prices that countries in the greatest need were least able to afford. The Egyptian government wanted to make hepatitis C treatment available to every citizen who needed it. But that would require a sufficiently low price to purchase the huge volume necessary, a system to deliver the drugs to those already diagnosed, and a campaign to screen everyone else for the disease.

As the Egyptian government began price negotiations with Gilead, the country was also scrutinizing the drug company's application for a patent. (They did not issue one, allowing generic manufacturers to enter the Egyptian market.) "I'd call the conversations friendly but they are good negotiators," recalled Gregg Alton, an executive vice president at Gilead who represented the company in the meetings.

Gilead ultimately agreed to license the drugs for sale in Egypt and a number of other countries at $300 per one-month supply, or $900 for the whole 12-week course of treatment. Generic manufacturers eventually drove the price in Egypt to $84 per patient.

Wahid Doss, the chairman of Egypt's National Committee for Control of Viral Hepatitis, says that the country's determination to provide treatment at a massive scale helped them make their case. "Part of the success story and why Gilead agreed was that they saw that we really wanted to have an impact in our country." Gilead ultimately sold their hepatitis C drugs to over 160,000 Egyptian patients, according to Alton. "They made some money as well," Doss points out. "It wasn't an act of charity."

With affordable drugs secured, the country set out to distribute them at a scale never before attempted. In 2014, they debuted an online portal for those with the disease to register for treatment; within three days, 200,000 people had signed up. Over the next three years, more than 1.6 million Egyptians received hepatitis C treatment, according to data from the World Bank.

That is more than all the patients treated during that time in the United States and Europe combined.

But that first flood of Egyptians seeking a cure were largely those already diagnosed with hepatitis C, and over time the challenge has shifted from making the drugs available to identifying additional people who need them. “The people going to those treatment centers tend to dry up,” explains Ward. “Obviously if you’re not testing, you’re not diagnosing, and you don't have anyone to treat.”

So in 2017, the Ministry of Health initiated a nationwide screening program. More than 260 teams of community-health workers are proceeding village by village. By late 2017, they’d screened 1,200 communities. Still, treatment has slowed from a high-point in 2016. According to the CDA Foundation, which compiles epidemiological data on viral hepatitis, the number of Egyptians treated in 2017 fell by roughly 30 percent compared to 2016, despite an estimated 4 million people still infected in the country.

With the promise of free drugs from the government for those diagnosed, civil-society organizations from factories to churches to mosques have gotten involved in screening, too. The prevalence of hepatitis C is around twice as high in the poorest quintile of the population compared to the wealthiest, but J. Stephen Morrison, the senior vice president of the Center for Strategic and International Studies, says the epidemic cuts across society in a way that has benefited the elimination efforts. “[Hepatitis C] may carry a stigma but there are few families in Egypt who haven’t had some loved one who has struggled with this.”

Last year, in the upscale neighborhood of Katameya Heights in New Cairo, a chapter of the Rotary Club arranged a hepatitis C screening for the neighborhood residents and their household staff. One of the organizers was Mohamed Ziwar, who had recently retired from a leadership role at the drug company Bayer. He says the club contracted nurses from a local lab that does genetic analysis to spend three days in the neighborhood, where they screened about 1,000 people, and then arranged treatment for the 30 who tested positive. “After we finished this, we got other requests from relatives of these people, that they would love to go through the investigation,” Ziwar said.

Ziwar estimated that the club ended up spending about $5,000. It could have been much higher but since it was a charitable effort, the lab did the blood analysis nearly at cost. But screening the whole group was significantly more expensive than the price of the drugs needed to treat the 30 infected residents. This is proving to be true at the national level as well. While the diagnostics are inexpensive, as many as 20 people must be screened to identify one new person who is infected, and it adds up. To ensure all the residents of a given community get tested, screening teams must sometimes return multiple times.

How fast Egypt eliminates the disease hinges on how swiftly it diagnoses the people infected, and authorities there are still determining the scale of their screening program and gathering the resources to pay for it. At the rate the country is currently screening and treating patients it would cut disease prevalence in half by 2023; if it substantially scales up the program, at an additional cost of $530 million, it could essentially eliminate the disease by then.

The magnitude of Egypt's efforts may make it easier for other countries to follow. Amr Elshalakani, a health specialist at the World Bank, points out that bulk purchases of screening kits used for diagnosis may drive up worldwide production capacity and reduce their cost. "There's an Egypt-specific benefit but also a global public-health good," he said. "Those changes in prices can have global implications for other countries that are looking to address hepatitis C."

And while the new drugs revolutionized the treatment of individual patients, luring the epidemic out of the shadows is now the central challenge worldwide. In 2016, only one in five people globally with chronic hepatitis C has been diagnosed, according to the World Health Organization, and in low-income countries, it is fewer than one in 10. Until those tens of millions of people are screened and diagnosed, they will never benefit from the latest medications. "What is happening in Egypt is just a preview of what every other country is going to face," says Homie Razavi, the CDA Foundation's managing director.

Only a handful of countries are charting a similar path towards elimination of hepatitis C. Many countries with far more resources at their disposal are nowhere close to treating their entire population. For example, of people with hepatitis C in the United States, fewer than 20 percent have received treatment.

In the long-term, the benefits of eliminating hepatitis C are unambiguous—Egypt's campaign will avert tens of thousands of deaths and reduce overall health-care expenditures—but the costs of screening must be paid up-front. "Economically, it makes absolute sense to treat versus not to treat, but the governments hold off. They say 'We're only in office four years, we'll never see the benefit,'" says Razavi. "What is different in Egypt is there was a political commitment to action, and they took that information and ran with it."

It wouldn't have been possible without affordable drugs, either, and for a country to obtain a price within reach, wealth might actually be a disadvantage. In poorer countries like Egypt, pharmaceutical companies have been more willing to offer drugs at or near the cost of manufacturing, to reflect the countries' ability to pay. In another example, last summer Pfizer announced that it would drastically discount a number of its patented chemotherapies in the six sub-Saharan countries where 44 percent of Africa's cancer cases occur.

But in upper middle–income countries, pharmaceutical companies see an opportunity for profit and are not showing the same flexibility. In China and Brazil, where drugmakers have priced their hepatitis C therapies well above the marginal cost of production, the governments are considering whether to pay—or to deny or legally skirt their patents so generic competition can drive prices down. Experts say that conflicts over drug prices in such markets may only increase as the burden of disease in those countries continues to shift from infectious diseases to those like cancer or diabetes that have effective but costly therapies.

How countries will muster funding to address hepatitis C—and how much—are still open questions. According to the World Health Organization, by the end of 2017 more than 80 countries had developed national plans to eliminate hepatitis C, an almost fivefold increase over 2012, but fewer than half attached a financial commitment. Without resources, few people infected with hepatitis C will be diagnosed and still fewer treated.

In contrast with the past two decades' efforts to address other infectious diseases like HIV, tuberculosis, and malaria, in which international donors made significant contributions and also managed much of how the campaigns were run, countries increasingly have to go it alone. Robert Hecht, the president of Pharos Global Health Advisors, says this represents a shift in global health. "I think the era of these large donor funds for diseases where the money helps pay for the drugs and delivery of care, I think we're seeing the end of that era."

On the whole, it seems easier for global society to develop efficacious drugs than to effectively deploy them. Much of the potential benefit of new therapies often goes unrealized, because high prices render them unaffordable or because governments forgo the effort necessary to deploy them at scale. The monumental impacts that are possible depend as much on willpower, funding, and detailed policy strategy—the nuts and bolts of public health—as on the cures themselves.

J. Gilead forecasts steep slide in 2018 hepatitis C revenues

Source:
https://www.biopharmadive.com/news/gilead-hepatitis-c-revenues-slide-fourth-quarter-earnings/516494/

Author
Ned Pagliarulo @NedPagliarulo
Published
Feb. 6, 2018

Dive Brief:

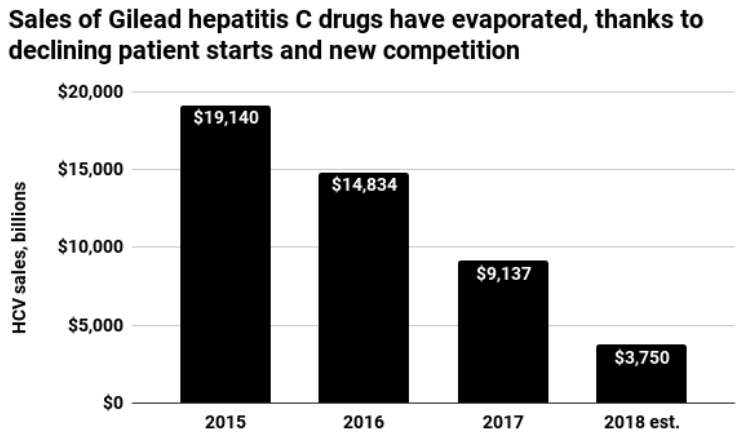
- Gilead Sciences Inc. will continue to feel the financial sting this year of declining revenues from its hepatitis C business, forecasting combined 2018 sales of the drugs reaching only a fifth of what the biotech recorded at the height of its commercial success three years ago.
- Altogether, sales of Harvoni, Sovaldi, Epclusa and Vosevi are expected to bring in between $3.5 billion and $4 billion this year — about 60% less than 2017's total of $9.1 billion. Overall 2017 revenues, meanwhile, fell 14% year over year to just over $23 billion.
- Company executives anticipate the hepatitis C market will begin to stabilize by the middle of this year, potentially positioning Gilead to rebound. Yet a return to growth remains uncertain, dependent on strengthening performance in HIV and advances in newer therapeutic areas like NASH and cell therapy.

Dive Insight:

Over the past two years, Gilead has watched sales of its once dominant hepatitis C drugs rapidly erode, due in part to the drug's efficacy in essentially curing most patients of the liver disease.

After Gilead's Sovaldi (sofosbuvir) and Harvoni (ledipasvir/sofosbuvir) were first launched, tens of thousands of new patients began treatment — pushing annual revenues from the drugs to nearly $20 billion in 2015. That bolus of patients has ebbed considerably, while new competition both stole market share and brought down net prices.

Even though investors had expected a downward slide, many were taken by surprise last year at the steepness of the drugs' decline. Gilead predicts between just $3.5 billion and $4 billion in hepatitis C revenues in 2018.



*2018 estimate shown at midpoint of $3.5B to $4B range
Credit: Ned Pagliarulo / BioPharma Dive, data from company

On a conference call Tuesday, company executives sought to turn the page on the past few years and look ahead to an eventual return to growth.

"Gilead's HCV revenue should be a more predictable, albeit smaller, piece of our financial story," said company CEO John Milligan on a Feb. 6 investor call.

"By removing most of the overhang of declining HCV revenues going forward, we can focus on the positive financial trends driven by the continued uptake of TAF-containing regimens and short-term and long-term growth through Yescarta, selonsertib and filgotinib."

Analysts appeared optimistic about Gilead's prospects for rebounding.

Jefferies analyst Michael Yee, for example, wrote a Feb. 6 note entitled "The early turnaround is beginning." Yee anticipates higher revenues from the company's HIV drugs, as well as potential launches of several experimental medicines, will fuel an "early growth cycle."

That narrative will look a lot more solid if the Food and Drug Administration approves Gilead's triple combination treatment for HIV next week, with a decision expected by Feb. 12. The drug, referred to as BIC/FTC/TAF, pairs a novel compound called bictegravir with two already approved drugs. Four late-stage studies demonstrated the combo's viral suppression capabilities matched that of current treatment regimens containing GlaxoSmithKline plc's Tivicay (dolutegravir).

Gilead expects the combo, taken as a single pill, will prompt some patients to switch treatments and anticipates a strong launch.

Yet challenges still stand in the way of Gilead's comeback story. In HIV, GSK recently won approval of a two-drug combo and looks set to continue to compete. Other opportunities, such as Gilead's JAK inhibitor filgotinib and efforts in non-alcoholic steatohepatitis (NASH), face either entrenched rivals or unproven commercial markets.

Key clinical data will come this year for filgotinib, and Gilead thinks it could launch a treatment for NASH by 2020 if all goes according to plan.

Cell therapy, where Gilead made a $11.9 billion bet on Kite Pharma and its pipeline of CAR-T treatments, could eventually become a major business for the biotech. With approval of Yescarta (axicabtagene ciloleucel) in lymphoma, Gilead is an unquestioned leader in the space.

But what is still in question is whether CAR-T will turn out to be a commercial success. Given Yescarta's complexity, Gilead has rolled the treatment out to new centers with deliberate care. By mid year, however, the biotech hopes to have enough centers certified in administering Yescarta to cover 80% of the estimated 7,500 patients eligible to receive the therapy in the U.S.

Sales of the complex therapy in the fourth quarter totaled $7 million, implying less than 20 patients had received the $373,000 treatment during the three month period. Even if Yescarta grows as fast as analysts expect, it won't move the needle financially for some time.

In the nearer term, Gilead still has the resources to be an active acquirer. At the end of 2017, Gilead held $36.7 billion in cash and equivalents. Guidance from the company suggests about $28 billion of that will be repatriated to the U.S. due to the recent changes in the tax code.

Executive comments mostly focused on acquiring new technology around cell therapy, such as gene editing capabilities, but other areas might be in reach as well.

K. Take a Bow, Pharma, for the Hepatitis C Drugs

The direct-acting virals revolutionized the treatment of hepatitis C. They also ushered turbocharged pricing. At least patients—and society—got a major health benefit in return.

March 28, 2018

It may be time to take a break, for just a moment, from criticizing drug manufacturers for their price gouging and other sins and allow them to take a victory lap for some good work they have done.

In less than four years, the treatment of hepatitis C has gone from failure rates as high as 70% to success rates as high as 99%. A whole new class of medications, direct-acting antivirals (DAAs), have defeated hepatitis C and completely replaced the only available treatment, inept pegylated interferon-alfa plus ribavirin therapy with miracle cures. It's like the glory days of the vaccines that wiped out polio, measles, and chicken pox.

HCV affects 2.7 to 3.9 million people in the U.S., primarily baby boomers who received contaminated blood transfusions or needles or unsafe hemodialysis before the current safety practices were implemented. Now the at-risk populations are intravenous drug users and people with HIV.

As recent as 2014, the standard treatment for HCV was 48 weeks of peginterferon plus ribavirin, a miserable regimen characterized by failure to respond, depression, anemia, and other sickening side effects. Patients who needed treatment the most, those with progressing liver failure, were the most likely to fail treatment.

Successive waves of increasingly elegant direct-acting antivirals have transformed treatment. The first generation appeared in 2011 when Merck and Vertex Pharmaceuticals (in partnership with Janssen) debuted Victrelis (boceprevir) and Incivek (telaprevir). This generation also includes the 2013 direct-acting antivirals, Olysio (simeprevir) from Janssen and Sovaldi (sofosbuvir) from Gilead. They are oral single agent protease or polymerase inhibitors that tipped outcomes in favor of patients. Olysio and Sovaldi drove the sustained viral response—no detectable virus after 12 weeks of therapy—to 80% and 90% of patients, respectively. These two medications also cut treatment down to 12 weeks for most patients. However, the drawback for all four of the first-generation direct-acting antivirals was that they still required most patients to be treated with interferon and ribavirin.

Hail Harvoni

Harvoni from Gilead, approved in October 2014, is the true landmark HCV medication and the first of the second-generation products. It combines a polymerase inhibitor with a protease inhibitor, a combination that ushered in complete freedom from interferon injections. In its clinical trials, its sustained viral response was 94% of patients.

Harvoni particularly was instrumental in the demise of the very first DAAs. Incivek was pulled from the market in October 2014 and Victrellis shortly thereafter.

In August 2015, the American Association for the Study of Liver Disease and the Infectious Diseases Society of America issued clinical guidelines for hepatitis C that validated what was taking place in clinician's offices—nasty pegylated interferon was disappearing. In those guidelines, all of the recommended treatments for healthier patients were direct-acting antivirals, and the word "interferon" appeared only twice in passing in the 23-page document.

But the direct-acting antivirals also ushered in an era of high-priced drugs and huge increases in what patients and payers are paying for medications. Sovaldi was dubbed "the $1,000 pill" because of its $84,000 price tag for complete treatment. Gilead launched Harvoni a few months later at a price of $94,500 per treatment.

Despite those prices, the world was ready and willing for Sovaldi and Harvoni. Many clinicians and patients had postponed treatment in anticipation of them, so there was pent-up demand. Gilead's revenues skyrocketed. In 2014, sales of the two drugs totaled $12.4 billion. In 2015, sales increased to $19.2 billion before the tide started to turn. Several additional direct-acting antivirals were approved in 2014 through 2016 including Viekira Pak and Viekira Pak XR from AbbVie, Zepatier from Merck, and Daklinza from Bristol-Myers Squibb. Gilead's revenue from its hepatitis C drugs plummeted to $14.8 billion in 2016 and to $9.1 billion in 2017. Increased competition from the other hepatitis C drugs and a falloff in new starts contributed to the decline.

One more time

Even though a sea change had already occurred, innovation continued. The newest hepatitis C medications, Epclusa and Vosevi from Gilead and Mavyret from AbbVie, mark the third time that this therapy has been reinvented. The innovation this time around is that all three are pangenotypic medications, meaning that they are approved to treat all six genetic variations of the hepatitis C virus. The preceding direct-acting antivirals were approved for only some of the variations, and genetic testing was required to help determine the proper choice of therapy. Epclusa was approved in June 2016 and Vosevi in July 2017. Both are from Gilead, giving it four hepatitis C medications. Gilead has been successful in creating more effective treatments by mixing and matching from its earlier hepatitis C drugs. Epclusa, for example, takes Sovaldi and combines it with a new active ingredient, velpatasvir, and Vosevi is a combination of Sovaldi, velpatasvir, and a third drug, voxilaprevir.

A month after Vosevi's approval, the FDA approved Mavyret, which has disrupted the hepatitis C market in a couple of ways. Most importantly, it is priced at $26,400 for a complete course of treatment, a fraction of Epclusa's $74,760 price before discounts and rebates. Some reports say Mavyret has already captured a third of the hepatitis C market.

The new era of direct-acting antivirals means patients don't have to suffer through interferon treatment and its bad side effects, says Andrew Muir, MD, chair of the American Association for the Study of Liver Diseases and the Infectious Disease Society of America.

The breakneck pace of change has made it difficult for early hepatitis C leader Janssen to keep up. In September 2017 it announced it was tossing in the towel on further development of hepatitis C treatments and would switch to hepatitis B.

The change in hepatitis C treatment is undeniably phenomenal. "Taking out interferon was a huge deal from a side effect perspective," says Andrew Muir, MD, the gastroenterology chief at Duke, and chair of AASLD's hepatitis C interest group.

Other benefits include having several treatment choices to pick from, he says, in contrast to when the interferon and ribavirin combination was the only option. Patients with hepatitis C tend to have a wide range of liver, renal, and cardiac comorbidities. Many were ineligible for interferon therapy, so they were, in effect, forced to live with hepatitis C. "Now, it is gratifying to be able take it off their plate," Muir says.

Muir adds that another major change in the works focuses on who gets treated. When the protease/polymerase inhibitors first appeared, payers' utilization management practices often tried to limit treatment to individuals with the highest liver fibrosis scores. Gradually though, he says, that has evolved to a point where more payers allow treatment for all stages of hepatitis C. A combination of lower prices, the efficacy of the new drugs, and the goal of preventing costly advanced liver disease is driving the change.

This change, though, did not come easily in Medicaid. From 2014 through 2016, many state Medicaid programs limited treatment to the sickest individuals because of the high cost of the direct-acting antivirals. State officials said their limited budgets made many of the drugs unaffordable. In Washington State, a federal judge ordered access, and CMS also took action to enforce its regulations about the availability of medicines. Muir says that Medicaid programs are expanding access as the costs of hepatitis C drugs come down.

Drug companies may deserve laurels but they can't rest on them. There is still a huge unmet need. An estimated 170 million people worldwide have hepatitis C. It is time for AbbVie and Gilead to seriously consider an additional price break for their products. With that number of people needing treatment for hepatitis C, there's more than enough revenue in their wonderful medicines.

Source: https://www.managedcaremag.com

L. The biggest drug launches–Hep C dominates but Tecfidera stands out

Source:
http://www.evaluate.com/vantage/articles/data-insights/biggest-drug-launches-hep-c-dominates-tecfidera-stands-out

Vantage
February 21, 2018

Amy Brown

Not all blockbusters make a big splash from the start – but initial demand is a pretty good indicator of future success. A look at which novel drugs hit the ground running the fastest over the past 20 years throws up a list dominated by more recent launches, namely the hepatitis C antivirals.

The record holder is Harvoni, which pulled in an eye-watering $10.1bn in its first four quarters on the US market. Hepatitis C therapies occupy the four top places, though a handful of older products also put in impressive debut performances (see tables below).

This analysis was conducted using historical quarterly sales data from *EvaluatePharma*, with the first full four quarters on the US market summed to create the ranking tables. Excluded were generics and vaccines, as their purchasing patterns tend to look very different from novel acute or chronic therapies.

Hitting the ground running – top 10 launches

Product	Company	Drug type	US launch	US sales over 1st full four qtrs ($bn)
Harvoni	Gilead Sciences	Hepatitis C antiviral	2014	10.09
Sovaldi	Gilead Sciences	Hepatitis C antiviral	2013	8.51
Epclusa	Gilead Sciences	Hepatitis C antiviral	2016	3.13
Olysio	Johnson & Johnson	Hepatitis C antiviral	2013	1.94
Tecfidera	Biogen	MS therapy	2013	1.72
Incivek	Vertex	Hepatitis C antiviral	2011	1.56
Celebrex	Pharmacia	Cox-2 inhibitor – pain	1999	1.55
Genvoya	Gilead Sciences	HIV antiviral	2015	1.30
Ibrance	Pfizer	CDK 4 & 6 inhibitor – breast cancer	2015	1.10
Vioxx	Merck & Co	Cox-2 inhibitor – pain	1999	1.01

Source: EvaluatePharma.

The analysis shows how unique the relatively short-lived hepatitis C revolution was. The highly successful launches of these agents demonstrated how swiftly healthcare systems – at least in wealthy countries – will embrace a curative therapy.

Holding the crown outside hep C is Biogen's multiple sclerosis therapy Tecfidera. The oral pill not only offered patients convenience and efficacy, its safety profile was comparatively benign compared with existing therapies, driving huge interest from the start.

It will be interesting to see whether Tecfidera's biggest competitive threat will rob it of this accolade; Roche's Ocrevus, approved last year, has achieved sales of $686m in its first two full US quarters, pointing to a performance that could match the Biogen pill if all continues to plan.

Elsewhere in the analysis, the Cox-2 inhibitors too were stand-out successes, until the real safety profile of Vioxx emerged. That drug was ultimately withdrawn after around five years on the market, though Celebrex remains available, albeit capturing only a third of its original revenues.

More recent success stories include Pfizer's Ibrance, the first CDK4/6 inhibitor to reach the market and whose mechanism has swiftly become the first-line option in Her2-negative, HR-positive breast cancer.

The true top 10?

The success of drugs like Tecfidera, Ibrance and the Cox-2 inhibitors is even more notable when considering that they were the first of their kind on the market.

Products like Harvoni and Epclusa represented real treatment advancements, but they arguably did not have as much work to do as the first to launch in this field, Incivek. The same is true for Gilead's HIV therapy Genvoya, a quad therapy that rode the wave of the company's existing HIV franchise.

Looking at the top 10 products outside the combination antivirals brings in Lipitor, the most commercially successful drug to date, which was also a hit from the start.

Outside the antivirals – biggest drug launches

Product	Company	Drug type	US launch	US sales over 1st full four qtrs ($m)
Tecfidera	Biogen	MS therapy	2013	1,719
Celebrex	Pharmacia	Cox-2 inhibitor – pain	1999	1,553
Ibrance	Pfizer	CDK 4 & 6 inhibitor – breast cancer	2015	1,102
Vioxx	Merck & Co	Cox-2 inhibitor – pain	1999	1,008
Lipitor	Pfizer	Statin – high cholesterol	1997	990
Neulasta	Amgen	Neutropaenia therapy	2002	897
Eylea	Regeneron	VEGFr kinase inhibitor – eye disease	2011	838
Opdivo	Bristol-Myers Squibb	Anti-PD1 antibody – cancer	2014	823
Lucentis	Roche	Anti-VEGF antibody – eye disease	2006	790
Avastin	Roche	Anti-VEGF antibody – cancer	2004	714

Source: EvaluatePharma.

This analysis also illustrates how successful VEGF-targeting agents have become, commercially and medically, spanning cancer and eye diseases. As essentially the same asset, Roche's victories with Avastin and Lucentis are particularly notable. The inclusion of these as separate entities knocks Merck & Co's Januvia from the table, putting it in 11th place; this would have provided the league table with its only diabetes treatment.

Finally, the recent immuno-therapy wave gets an entrant in Opdivo, launched in the US in the last few days of 2014. Bristol-Myers Squibb's product was actually beaten to the market by Merck & Co's rival PD-1 antibody Keytruda by three months, but still managed to engineer a much more successful launch. An already established I-O presence with Yervoy presumably gave Bristol an advantage in the early days, an edge that it is struggling to maintain.

With several closely watched and very highly valued assets nearing pivotal readouts in immunotherapy, many hope that this field will yield further big launches. For the hepatitis C records to be broken, however, another special case will surely have to emerge.

M. Lessons From Biggest Pharma Drug Launches Of All Time

Source:
https://www.forbes.com/sites/johnlamattina/2018/12/11/lessons-from-the-biggest-pharma-drug-launches-of-all-time/?sh=55722da94316

Dec 11, 2018, 07:23am EST

John LaMattina Contributor
Healthcare
I cover news on drugs and R&D in the pharma industry

One way to measure the importance of a new drug is how fast the drug is taken up by the market. Furthermore, this is a key metric as a strong commercial launch usually predicts that the drug will become a major revenue generator. Recently, Lisa Urquhart of *EP Vantage* put together a list of the top 16 commercial launches of all time and it is striking not just in terms of the past but also what to expect going forward in terms of major drug successes.

Lesson #1 – The Era of Drugs for the Masses Is Over

There was a time when the success of a drug launch was based not just on the quality of the new medicine but also on the market size of the treated disease. Drugs to treat heart disease, depression, diabetes, or arthritis historically dominated market sales. These drugs were relatively cheap ($2 – 5/pill) and were prescribed to millions of patients. In addition, drug companies created huge sales forces to get these new medicines to prescribers. The more successful the launch, the more likely the drug will be a major revenue generator during its years of patent exclusivity.

An example of this type of successful launch was Pfizer's Lipitor. Although it was the fifth statin approved, Lipitor's superior efficacy, combined with the broad acceptance of the importance of statins for millions of heart patients, enabled it to generate U.S. sales of $1.54 billion (inflation adjusted) in its first 12 months on the market. While a record at the time, this was outdone a mere 24 months later with Pfizer's launch of the arthritis drug, Celebrex, with an inflation adjusted $2.30 billion in first year sales.

However, in the almost 20 years since the launch of Celebrex, we haven't seen a billion dollar first year start for a drug that is intended for broad disease populations. Instead, we have witnessed the rise of the small market high priced drugs.

Lesson #2 – Small Market High Priced Drugs Are the Future

The top three entries on Urquhart's list are Gilead's hepatitis C drugs: Harvoni at a whopping $10.67 billion, Sovaldi at $9.02 billion and Epclusa with $3.22 billion. Their dominance is due to a number of factors. First, there was a pent-up demand for hepatitis C cures and these drugs delivered. Second, the initial high price for these drugs with initial LIST prices of $94,000 for Harvoni and $84,000 for Sovaldi, helped drive revenues. It must be noted, however, that these were list prices and that ensuing competition has dropped the price to under $30,000 depending on the deals struck by payers with drug manufacturers.

But the hepatitis C drugs are not unique. The sixth and eighth most successful launches are the high priced multiple sclerosis drugs Tecfidera (Biogen) and Ocrevus (Roche) with 12 month sales of $1.84 billion and $1.68 billion, respectively. Again, these are cases were that mirror the hepatitis C situation: high drug prices coupled with a patient population of only a few million. The same can be said for the new wave of cancer drugs. Pfizer's Ibrance for breast cancer is number 13 all time at $1.16 billion for its first year and Opdivo from BMS is 16th with $0.87 billion.

Lesson #3 – Success Can Be Fleeting

A big first year of sales doesn't always portend a robust future. Three of the top ten drugs on Urquhart's list are no longer on the market. Two are hepatitis C drugs. In 2011, Vertex launched Incivek which registered $1.72 billion in its first year. Two years later, J&J brought out Olysio which exceeded $2.0 billion. Unfortunately, these drugs proved inferior to the next generation hepatitis C drugs from Gilead and AbbVie (e.g., Mavyret). As a result, Vertex and J&J discontinued the sales of their drugs in 2014 and 2018, respectively.

The tenth ranked drug on this list is Vioxx, the osteoarthritis drug that was pulled from the market due to concerns about adverse cardiovascular effects. Ironically, because they acted by the same mechanism (inhibition of the COX-2 enzyme), Vioxx's problems impacted the prescribing patterns for Celebrex. As a result, sales of Celebrex never exceeded those seen in its first 12 months on the market.

Lesson #4 – Impact on R&D Investments

The billion dollar launches of drugs that can command high prices and which are used for modest or small patient populations have greatly influenced the direction of R&D investments for biopharma companies for a variety of reasons. First, clinical trials for rare disease drugs or for targeted cancer therapies are much smaller than the mammoth trials needed to get drugs approved for diabetes, heart disease, etc. Second, large sales forces are not needed to detail such niche drugs as there are far fewer physicians who prescribe such drugs. Finally, pricing is attractive.

One can simply examine the research priorities of companies to see what has happened. Take Pfizer, a company with roots in antibiotics, cardiovascular diseases, and neurosciences. Its research pipeline is now focused on oncology, immunology, liver disease, rare diseases and

vaccines – all areas of major medical need, and also areas where an effective drug can command high pricing.

It is hard to envision a drug will someday replace Harvoni at the top of the list of biggest drug launches. But given the medical breakthroughs being made, it is likely that in the coming years there will be new entries in this list – and high priced ones at that.

John LaMattina
I was the president of Pfizer Global Research and Development in 2007 where I managed more than 13,000 scientists and professionals in the United States, Europe, and Asia. I've received numerous awards including an Honorary Doctor of Science degree from the University of New Hampshire. I am also the author of "Drug Truths: Dispelling The Myths Of R&D" and the recently published Devalued And Distrusted: Can The Pharmaceutical Industry Restore Its Broken Image?" I am also a senior partner at PureTech Health.

N. NHS England plans to eliminate Hep C by 2025 – with the help of pharma price cuts

Richard Staines

January 31, 2018

Source:

https://pharmaphorum.com/news/englands-nhs-plans-eliminate-hep-c-2025/

NHS chiefs in England have announced an ambitious plan to make it the first country in the world to eliminate hepatitis C – and hopes to make it possible by further squeezing drug prices.

Gilead's Sovaldi kicked off a revolution in 2014 by becoming the first drug to offer a cure to most patients with hepatitis C, but also sparked fears of huge cost to healthcare systems globally, including Europe.

However, the arrival of rival products from Abbvie, Janssen and MSD, combined with heavy discounts has helped drive down the cost of using the drugs.

NHS England in particular has been using a contract tendering process, and pharmaphorum understands this means it is paying around £10,000 for a course of treatment for a single patient, rather than the list price of around £35,000.

Now NHS England have called on the pharma industry to provide "best value for money" treatments so that the health service can step up its use of the drugs so that it can eliminate the disease by 2025 – five years ahead of a global target set by the World Health Organization.

Next month NHS England will launch the single largest medicines procurement it has ever undertaken, in order to drive down the cost of the drugs further.

Peter Huskinson, National Commercial Director, NHS England, said: "The NHS has made major headway in the last three years in the treatment of Hepatitis C, which has enabled a once in a generation opportunity to eliminate a major disease.

"With the right response from pharma companies in the coming months, we can strike the most competitive deal possible – improving the future for patients with Hep C alongside securing the best value for money for taxpayers."

NHS England says it aims to treat a further 5,000 patients by October on top of the 25,000 already treated, **prioritising the sickest patients first**.

Significantly, it has also unveiled plans to work more closely with drug companies to identify people living with Hepatitis C who need to be treated.

This approach, combined with sustained levels of investment from the NHS could lead to hepatitis C being eradicated in the near future.

They have also been launching pan-genotypic treatments, including Gilead's Epclusa and AbbVie's Maviret, the latter offering an eight week course in some patients.

While Gilead and its rivals still make good profits on the drugs, global revenues have flattened out, as health systems around the world face the same struggle to identify and treat the many thousands of Hep C patients in each country who remain undiagnosed and untreated.

Hepatitis C campaigners and pharma companies have until now been loudly protesting that NHS England's restrictive use of the drugs has meant that eradication of the disease would take decades.

The new measures, including greater collaboration on finding more undiagnosed patients have been welcomed by all sides – but pharma will have to drop their prices further to be part of the programme.

Further progress in hepatitis C has included creation of 22 'operational delivery networks' in each area of England.

The NHS has also established a national hepatitis C registry to record and monitor uptake, outcomes and diagnosis rates in real time.

Stelios Karagiannoglou, general manager, Gilead Sciences UK & Ireland, said:

"Gilead welcomes the announcement from NHS England about its commitment to make England one of the first countries to eliminate hepatitis C. This is an ambition that we share, and we are committed to working collaboratively with all stakeholders and NHS England to bring new hope to all patients living with hepatitis C."

One of the problems facing greater hep C diagnosis and treatment is that many people with the disease are marginalised and stigmatised in society, often suffering from deprivation, drug and alcohol problems.

This makes them hard to reach, so Gilead and other companies in the field have set up outreach programmes to test and treat these individuals.

Karagiannoglou added: "Since 2016, Gilead has invested in a team dedicated to working in partnerships with prisons, drug and alcohol addiction teams and other key stakeholders to help find and link patients with hepatitis C into care – through awareness campaigns, training and pathway support, patient management software, and awards through the Gilead Fellowship programme."

Great to have a target for elimination but devil in the detail – what is pharma's role to 'identify more people living with hep c'? what about harm reduction and when and how will resources reach community services? Who decides?

Read our response to the @NHSEngland announcement on #hepatitisC

"We welcome this plan to make England the first country in the world to eliminate Hepatitis C by 2025, but there is a long way to go and this deal still needs to be completed"

— HepatitisCCoalition (@HCVCoalition) January 30, 2018

Until now, NHS England's tendering system has meant that there has been clear winners and losers on the pharma side, with one company winning all the business for a period, with all firms invited to tender again once this period elapses.

Whether or not this system will remain in place is not yet clear, but pharma companies will be hoping the new expansion of treatment will be a win for them as well as patients.

O. Wall Street Wants the Best Patents, Not the Best Drugs

Curing diseases like Hepatitis C just doesn't pay.

By Joe Nocera
November 27, 2018, 8:00 AM EST

Executives are likely to take a lesson from the Humira monopoly: a drug to take for life, not just for months.
Photographer: JB Reed/Bloomberg
Joe Nocera is a Bloomberg Opinion columnist covering business.

It's probably unfair to start a column about the new drugs that are curing Hepatitis C by referencing Jonas Salk and the discovery of the polio vaccine, but I'm going to do it anyway. It's worth remembering what the world used to look like as we contemplate what it looks like now.

In the late 1940s and early 1950s, there was nothing that scared American parents more than polio, a disease that (a) caused partial paralysis, (b) was easily transmitted, and (c) primarily affected children. Salk, who had worked on flu vaccines during World War II, joined the University of Pittsburgh in 1947 and soon began working on a possible polio vaccine. In 1953, he announced — on a national radio broadcast, no less — that he had developed a vaccine that prevented the disease; two years later, once its efficacy had been proved, the country undertook a national inoculation program, paid for by the federal government.

Did his discovery of the polio vaccine make Salk rich? It did not. When the CBS journalist Edward R. Murrow had Salk on his interview show, "See It Now," he asked the scientist, "Who owns the patent on this vaccine?"

"The people, I would say," Salk replied, after a moment's hesitation. "There is no patent. Could you patent the sun?"

In 2014, Gilead Sciences Inc. introduced Sovaldi, the first drug that cured Hepatitis C, a liver disease that may affect as many as 150 million people worldwide, and that can be life-threatening if untreated. As is always the case in the modern age, Sovaldi was surrounded by a thicket of patents, some of which wouldn't expire until 2034.

The company knew, however, that AbbVie Inc. was less than a year away from coming out with its own Hep C drug, and thus its monopoly was likely to be short-lived. Under pressure to capitalize on its invention during a short window, the company priced Sovaldi at $84,000 for a 90-day course of treatment. Less than a year later, the Food and Drug Administration approved a

second Gilead drug, Harvoni, which in some cases could cure Hep C patients in 60 days instead of 90. Harvoni cost $94,000.

The reaction was predictable. Hep C sufferers expressed outrage at the price. Insurers — including Medicare — balked at paying so high a price; even after rebates the price was still over $50,000. Some of them limited the drug to only to the sickest patients.

The Senate Finance Committee conducted an investigation and concluded that Gilead's pricing strategy was "a calculated scheme" aimed at "maximizing revenue." Gilead, the committee wrote, "knew these prices would put treatment out of reach of millions and cause extraordinary problems for Medicare and Medicaid, but the company still went ahead."

But because the drugs worked so well, most insurers swallowed hard and paid for them. Even after AbbVie came out with its first Hep C drug, the Gilead drugs remained dominant, largely because the AbbVie products didn't work as well. Between 2014 and 2017, Gilead's generated $50 billion from its Hep C "franchise," curing hundreds of thousands of patients while leaving rivals in the dust.

I first starting paying attention to Gilead's Hep C drugs in the spring of 2016, when I noticed that its stock had begun to drop precipitously. I couldn't understand why Wall Street was down on a company with a near-monopoly on a drug that actually cured a disease rather than simply treated symptoms, as most drugs do. Isn't a cure the holy grail of drug discovery?

Success in the Lab, Stumble in the Markets

GILD stock price chart – See separate document posted for this – end of document.

For patients and doctors, it certainly is. But it turns out that Wall Street much prefers a drug like AbbVie's Humira, which treats — but doesn't cure — rheumatoid arthritis, Crohn's disease and a variety of other illnesses. Patients who need it use it forever. With an estimated $38,000-a-year price tag (after rebates), and patents that won't expire for years, it is the biggest selling drug in the world.

Gilead, meanwhile, began to see its patient population dwindle as its Hep C drugs worked their magic. There are only 3.5 million chronic Hep C sufferers in the U.S., but many of them are in prison or on Medicare or Medicaid, which had rules that made using the drug difficult. By some estimates, as many as 85 percent of the people with chronic Hep C lacked access to treatment. In addition, while Gilead allowed generic manufacturers to make Hep C competitors in many poorer countries, it declined to do so in such countries as Argentina, Brazil, China and most of Western Europe.

Enter a group called the Initiative for Medicines, Access and Knowledge, or I-MAK for short. I-MAK is funded in part by John Arnold, a billionaire energy trader who once worked at Enron. Its mission is to challenge key pharma patents in an effort to enable generic competition and bring down the price of important, life-saving drugs. Tahir Amin, one of I-MAK's co-founders, told me that his group had had its eye on Sovaldi as long ago as 2012, even before the drug received approval by the Food and Drug Administration. I-MAK's position is that the basic compound at

the heart of Gilead's drugs, sofosbuvir, is simply not novel enough to merit 20 years patent protection.

In the U.S. that argument hasn't gotten very far; despite numerous challenges, Gilead's patents have been sustained by the U.S. patent office. But elsewhere I-MAK had considerable success.

In 2015, in the face of an I-MAK patent challenge in India, Gilead decided to allow generics to copy its Hep C drugs. Ukraine rejected a key Gilead patent. Argentina turned thumbs down on Gilead's patents. In May, a court in Brazil rejected an important Gilead patent. And most recently, in August, I-MAK's challenge succeeded in getting Gilead to withdraw key patent claims to sofosbuvir in China, where 8.9 million people have chronic Hep C. All of these victories have increased the likelihood that low-priced generics will replace Gilead's Hep C drugs in those nations.

I told Amin that it struck me as a little unfair that a company that actually cured a disease was getting hammered like this while AbbVie's gaming of the patent system to maintain its Humira monopoly has gone largely unchallenged. At the very least, I had a hard time seeing why any pharma company would want to work to find cures. All the incentives seemed to skew in the direction of drugs that treated symptoms – and would have to be used for years.

"This is certainly a question we've thought about," Amin responded. "But drugs aren't annuities. The problem is that the patent system has allowed companies to keep extracting payments where they either don't deserve a patent or where they are over patenting well beyond the intended 20-year term." He added: "When you have a drug with a list price of $84,000, you can't just stand back and let people die because they can't afford it."

Amin told me that the real problem is that the incentive structure is all wrong under the current patent system: There needs to be a way to give drug companies an incentive to invest in potential cures and get a return that doesn't depend on a 20-year patent." The Gilead Hep C story is certainly a case in point, from the outrageous early prices, to the Senate investigation, to Wall Street's disapproval, to the strenuous effort to remove the patent protection abroad.

The truth is, though, as pharmaceutical development has become ever more oriented to Wall Street, protection from generics is the only bankable asset.

Could you patent the sun? No need. The universe of Big Pharma now orbits around patents themselves.

1. It is hard to know how many people have Hepatitis C because many of those infected don't know it. It can be years, and even decades, before the liver damage Hep C causes becomes apparent.
2. I should note that I-MAK did a comprehensive study of Humira's manipulation of the patent system. You can read it here.

P. How an $84,000 drug got its price: 'Let's hold our position ... whatever the headlines'

Source: https://www.chicagotribune.com/business/ct-gilead-sciences-hepatitis-c-sovaldi-drug-20151201-story.html

Sovaldi, a new pill for hepatitis C, cures the liver-wasting disease in 9 of 10 patients, but treatment can cost more than $90,000.

Gilead Sciences executives were acutely aware in 2013 that their plan to charge an exorbitantly high price for a powerful new hepatitis C drug would spark public outrage, but they pursued the profit-driven strategy anyway, according to a Senate Finance Committee investigation report released Tuesday.

"Let's not fold to advocacy pressure in 2014," Kevin Young, Gilead's executive vice president for commercial operations, wrote in an internal email. "Let's hold our position whatever competitors do or whatever the headlines."

Gilead gained federal approval for its drug Sovaldi in late 2013 and ultimately settled on the price of $84,000 for a 12-week course of treatment. To the company, that price seemed to deliver the right balance: value to shareholders while also not so high that insurers would "hinder patient access to uncomfortable levels," according to internal documents. But they also got more than they bargained for: an outpouring of outrage from the public, a backlash from government and private payers, and political scrutiny.

The 18-month Senate committee investigation reviewed more than 20,000 pages of company documents.

"The documents show it was always Gilead's plan to max out revenue, and that accessibility and affordability were pretty much an afterthought," said Sen. Ron Wyden, D-Ore., who co-led the investigation with Sen. Charles Grassley, R-Iowa, in a press conference.

In a statement released Tuesday, Gilead disagreed with the conclusions of the report, saying that the price was "in line with previous standards of care." The company noted that it has programs in place to help uninsured patients and those who need financial assistance access the treatments. More than 600,000 patients around the world had been treated with Gilead's hepatitis C drugs since 2013, according to the company.

Here are four key takeaways from the investigation:

1) It could have been priced at $115,000 for a course of treatment.

Gilead considered a range of prices for Sovaldi and weighed the value to its shareholders against the "reputational risks," meaning the potential outrage from patients, physicians and payers. The potential prices ranged from $50,000 to $115,000.

Executives believed a $50,000 price would build good will and ensure easy access to the drug because it would be covered by most plans. But it would cause "significant foregone revenue," and activists would still critique the price, even at this relatively low level.

At $115,000, executives were concerned about "external considerations" and predicted: "High levels of advocacy group criticism and negative PR/competitive messaging could be expected at $115K and it would be increasingly difficult to manage at these levels."

2) Gilead priced Sovaldi partly based on the expectation it would set a benchmark for the next drugs in the pipeline.

A company presentation noted that Gilead has "considerable pricing potential" for Sovaldi, but that future pricing for next-generation drug launches would be limited by competition -- what it referred to as a second wave of treatments.

"Wave 1 will set a price benchmark against which Wave 2 will ultimately be evaluated," the presentation stated.

"By elevating the price for the new standard of care set by Sovaldi, Gilead intended to raise the price floor for all future hepatitis C treatments, including its follow-on drugs and those of its competitors," the report states.

Its next hepatitis C drug, Harvoni, was priced at $94,500.

3) Patients were warehoused to limit access to Sovaldi.

Facing pent-up demand for a hepatitis C treatment, insurers quickly began to implement restrictions -- essentially, warehousing patients by putting sick people aside until they were even more sick. Medicaid programs in 27 states limited which patients could get access to Sovaldi. Private insurers did, too.

In a letter, the Oregon Health Authority reported that while more than 10,000 Medicare patients were deemed good candidates for Sovaldi and its competitors in fall of 2014, the estimated cost of treating half of them would more than double the entire $600 million spent on all drugs in the previous year. Instead, because treating more advanced patients would be more cost effective, the state implemented a plan to treat at the rate of 500 patients a year for the first six years.

Kentucky's Medicaid program noted that the state's heroin epidemic exacerbated its hepatitis C problem -- people who had injected drugs were being tested for the disease, raising the tricky question of when to start treatment.

"Given the current cost of the newer treatment options and to remain fiscally responsible we will be forced to make difficult decisions regarding who does and does not get access to treatment medications upon diagnosis," Samantha McKinley, pharmacy director of the Kentucky Department for Medicaid Services, wrote in a letter to Grassley and Wyden.

4) Cost-per-cure, not cost of development.

The report suggests that the factors Gilead used to set its price were not based on the research and development needed to bring the drug to market, or on the $11.2 billion it paid for Pharmasset, the company that developed Sovaldi. Instead, Gilead executives looked at what previous treatments had cost and the effect of future waves of competition on the revenue it could bring in.

"Company officials surmised that its drug had a 'value premium' because of increased efficacy and tolerability, shorter treatment duration, and its potential to ultimately be part of an all-oral regimen," the report states.

In its statement Tuesday the company said, "We stand behind the pricing of our therapies because of the benefit they bring to patients and the significant value they represent to payers, providers, and our entire healthcare system by reducing the long-term costs associated with managing chronic [hepatitis C virus]."

With another Senate committee now probing price increases at four other pharmaceutical companies, the final conclusion of the report may be one we see repeated.

"This might be an example that received the most attention in some time, but it won't be the last," Grassley said in a statement.

Q. Gilead Stock Price (Ticker: GILD)

Source: https://www.nasdaq.com/market-activity/stocks/gild/advanced-charting

Gilead: Sovaldi and Harvoni

You can also see: https://finance.yahoo.com/quote/GILD?p=GILD&.tsrc=fin-srch
for more details