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PARTITIONING HCV

BY ERIN MCCALLISTER, SENIOR EDITOR

Gilead Sciences Inc. and AbbVie Inc. continue to vie for preferred coverage of their HCV drugs in the U.S. private payer market, and Gilead is out to an early lead when it comes to total lives covered. But much of the population is still up for grabs, and the real victor in share of lives could be determined by how the U.S. Department of Veterans Affairs and Medicaid plans respond.

Since FDA approved AbbVie's Viekira Pak paritaprevir/ritonavir/ombitasvir/dasabuvir regimen to treat HCV genotype 1, the pharma and Gilead have been competing for exclusive formulary status by trading rebates for access. Gilead markets Harvoni ledipasvir/sofosbuvir and Sovaldi sofosbuvir.

The contest in genotype 1 has been decided by at least seven payers in the commercial private coverage market. AbbVie immediately won exclusive status for Viekira with the largest pharmacy benefits manager in the U.S., Express Scripts Holding Co., and secured an agreement that will see the PBM drop all restrictions on utilization.

Gilead then scored exclusive deals for genotype 1 with three private payers, and for genotypes 1-4 with CVS Health Corp. and with Aetna Inc.

The PBM Prime Therapeutics LLC gave Viekira and Harvoni co-preferred status.

A back-of-the-envelope comparison suggests that in any realistic rebate scenario, a drug company's potential revenue pool increases significantly when access is granted to all eligible HCV patients — which is why some payers and PBMs are refusing to loosen restrictions even though it shrinks their discounts.

AbbVie obviously won't get all of Express Scripts' patients immediately, and perhaps not even during the undisclosed term of the deal. But what's noteworthy is the size of the pie is so much bigger with a discount and the potential for all-comer access than it was at list price with strict utilization restrictions.

For example, with access to all of Express Scripts' patients, a 30% rebate would translate to more than double the market opportunity for AbbVie, more than off-setting a knock-on effect of best pricing rules in Medicaid, even assuming the state programs continue to restrict access to patients with severe fibrosis.

However, if the rebate gets bigger than 41%, the increased market potential AbbVie gets from the Express Scripts deal is not enough to offset the reduction in Medicaid revenues, assuming Medicaid remains restrictive (see "Coming Out Ahead, Maybe" page 4).

All in, the announced deals tie up about 83% of all the genotype 1 patients in the private commercial market, but only 23% of all U.S. genotype 1 patients (see "HCV Landgrab," page 3).

One other PBM has told BioCentury it expects to announce a deal soon, but the deciding factor will be how Medicaid and the VA react. Medicaid accounts for 31% of the U.S. HCV genotype 1 market, and the VA accounts for 15%.

The biggest losers could be other HCV companies that are on or close to market. Achillion Pharmaceuticals Inc., Merck & Co. Inc. and Bristol-Myers Squibb Co. each have HCV regimens — in Phase II, Phase III and registration, respectively.

Olysio simeprevir from Johnson & Johnson has been on the market for 13 months, but needs to be combined with Sovaldi to be competitive in terms of efficacy in genotype 1, meaning the total cost of treatment is very high.

Depending on the length and terms of the AbbVie and Gilead deals, the other competitors could be shut out of the market and would have to match or offer higher rebates if they hope to make it onto formulary.

DRAWING BATTLE LINES

Payers and PBMs began laying the groundwork for an HCV price war shortly after Gilead launched Sovaldi to treat HCV genotypes 1-4.

Sovaldi was launched in December 2013 with a WAC of $84,000 for a 12-week course. Patients who cannot tolerate interferon must take it for twice as long, at twice the cost.

Because the drug's unparalleled efficacy and tolerability were likely to drive extremely high rates of utilization compared with the similarly priced previous standard of care, most public and private payers limited access to Sovaldi to only the sickest patients whose Metavir scores — a measure of liver fibrosis — were F3 or F4.

Last April, Express Scripts cautioned that as new HCV therapies came to the market it might be appropriate to "exclude unreasonably priced medications from our formulary if more affordable options deliver the same or better results."

ROOM FOR APPEAL?

All the exclusive formulary deals for HCV drugs allow patients to access excluded products if the preferred drug is contraindicated. Physicians who spoke to BioCentury had different opinions about how many patients might be in that boat with respect to Viekira Pak from AbbVie Inc., which lists 12 contraindications on its label compared to none for Harvoni from Gilead Sciences Inc.

Rena Fox, a physician at the University of California, San Francisco, said "only a small fraction of patients will be unable to take Viekira Pak," while Sammy Saab, a digestive disease physician at the Pfleger Liver Institute at the University of California, Los Angeles, said 15-20% of patients may be unable to take the AbbVie regimen due to contraindications.

Express Scripts Holding Co. CMO Steven Miller told BioCentury the PBM will "strictly enforce" requirements for evidence that a patient cannot tolerate Viekira Pak before the PBM would allow the patient to have Harvoni.

Prior to cutting deals with the HCV companies, both public and private U.S. payers had been covering the drugs only for patients with severe disease, and the process for demonstrating a patient qualified for access has been described as onerous.

"Anecdotally, we've heard from some doctors who say that they don't even prescribe a drug unless the patient is dying because the hurdles to jump through were so onerous and time-consuming," said Emalie Huriaux, director of state and federal affairs at Project Inform. While severity is demonstrated by a standard test to measure liver fibrosis scores, Huriaux said it often took multiple steps of paperwork and submissions to verify whether the prescribed drug would be reimbursed.

Gilead President and COO John Milligan told investors at last week's JPMorgan conference that in many cases it had been taking about 45 days from when the drugs were prescribed until the patient received the prescription.

Patient groups like Project Inform will be watching to make sure payers make good on their promise to allow access in cases where the preferred drug isn't appropriate.

"If it's a meaningful exception that patients do in fact really have access if they can't take the preferred drug, then that's great," said Huriaux. "But if it's not meaningful, it won't be good for those patients who can't tolerate the preferred drug."

Ryan Clary, executive director of the National Viral Hepatitis Roundtable, agreed. "That is where advocates will need to engage and be looking very closely. We'll want to make sure that patients aren't falling through the cracks."

— ERIN MCCALLISTER

At the same time, Express Scripts threatened a boycott, asking plan sponsors to "stand side-by-side" with the PBM to pressure Gilead to provide Sovaldi at a "more reasonable price."

The next HCV drug launched was Gilead's Harvoni, a fixed-dose combination of Sovaldi and ledipasvir, approved in October to treat genotype 1. The drug is a single-pill once-daily regimen recommended as a 12-week course for most patients and as an 8-week course for some non-cirrhotic treatment-naïve patients. Gilead has estimated that up to 45% of genotype 1 patients could be eligible for the shorter treatment course.

Harvoni was launched at a WAC of $94,500 for a 12-week course and $63,000 for an 8-week course.

In clinical trials, AbbVie's Viekira had SVR 12 rates as high as 99%, similar to Harvoni. The WAC is $83,319 for a 12-week course.

Viekira consists of four pills: two containing a fixed-dose combination of paritaprevir, ritonavir and ombitasvir that are taken together in the morning, plus two dasabuvir tablets taken separately — one in the morning and one in the evening.

Viekira also must be taken with ribavirin except in non-cirrhotic genotype 1b individuals, or about 25% of patients. A 24-week course is recommended in cirrhotic genotype 1a patients, while a 12-week course is recommended for all other genotype 1 patients.

SHOTS FIRED

Viekira was approved on a Friday. By Monday, Express Scripts announced the decision to exclude the other drugs from its National Preferred Formulary.

In return for an undisclosed rebate, the PBM agreed to make Viekira available to all genotype 1 patients regardless of fibrosis score or any other measure of disease severity. The National Preferred Formulary covers 25 million lives and accounts for about 25% of Express Scripts' commercial business. BioCentury estimates the PBM would have about 112,500 patients with genotype 1 based on its share of the commercial market.

CMO Steven Miller said the remaining 75% of Express Scripts' clients have the option to adopt the National Preferred Formulary. He did not specify if these were the PBM's commercial or non-commercial clients, but spokesperson David Whitrap told BioCentury "the vast majority" of the PBM's commercial employer sponsored plans typically have adopted the National Preferred Formulary.

Miller told BioCentury Express Scripts and AbbVie had been in discussions prior to Viekira's approval, but had not settled on anything, including the relevant patient populations, until the drug was approved.

"There were details that we couldn't work out until the drug was approved, and up to this point we had only been able to treat the most advanced patients, those with fibrosis scores of F3 or F4, and we'd like to treat everyone," he said. "AbbVie was also very interested in getting everyone treated and willing to work with us to do that."

Express Scripts said the rebate for Viekira would narrow the price gap between what the U.S. and European countries were paying for Sovaldi; however, the PBM didn't say by how much. In Europe, the price of Sovaldi ranges from $51,373 in France to $66,000 in Germany — 21-39% lower than Viekira's list price.

HCV LANDGRAB

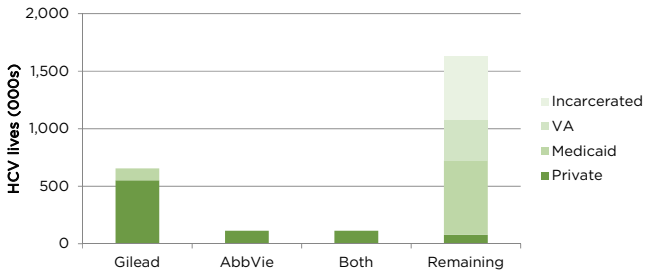
The battle between **Gilead Sciences Inc.** (NASDAQ:GILD) and **AbbVie Inc.** (NASDAQ:ABBV) to secure HCV lives for their new drugs has been mostly focused on patients with genotype 1 infection who are covered under private commercial plans.

Gilead is out to an early lead. Among the 2.4 million genotype 1 patients in the U.S., BioCentury estimates Gilead has gained about 655,000 lives (27%), including about 99,750 Medicaid lives that will be covered under an exclusive deal with **CVS Health Corp.** (NYSE:CVS) for Sovaldi sofosbuvir and/or Harvoni ledipasvir/sofosbuvir. AbbVie has gained about 112,500 lives (5%) for its Viekira Pak paritaprevir/ritonavir/ombitasvir/dasabuvir via its exclusive deal with **Express Scripts Holding Co. Inc.** (NASDAQ:ESRX). That deal still could be expanded into Medicaid.

The companies will share access to about 112,500 lives via co-preferred deals with **Prime Therapeutics LLC**.

About 68% of the genotype 1 population is still up for grabs, including lives covered by private plans that haven't announced a preferred drug, Medicaid plans not included in the deals announced so far, and the **Veterans Health Administration** as well as incarcerated patients. Data on the 800,000 patients with genotypes 2-4 are not included below, although Gilead's deals with CVS and **Aetna Inc.** (NYSE:AET) also include those populations.

The CVS private estimate is based on 57.4 million lives, including the 10.8 million it has from Aetna plans. CVS is Aetna's PBM, and both selected Gilead's HCV drugs. *Source: BioCentury analysis based on data from CDC, Kaiser Family Foundation, VA, Anthem, CVS/Caremark, Express Scripts, Harvard Pilgrim, Humana and Prime Therapeutics*



Although the duration of the deal isn't disclosed, Miller said "the deal will afford AbbVie enough time for financial gain."

COUNTER ATTACK

Gilead's response was swift, suggesting the company also was in discussions with payers and PBMs prior to Viekira's approval.

On Jan. 5, CVS said it would grant Sovaldi and Harvoni exclusive status across a broad range of formularies, including its CVS/Caremark Standard Commercial formulary and its state marketplace exchange, Medicare Part D and Medicaid formularies.

By choosing Gilead, CVS was able to secure a single supplier to provide HCV drugs across all of its affected members regardless of genotype.

"Our goal was to create the lowest net-cost solution for the entire population of patients with all genotypes of hepatitis C," CVS spokesperson Christine Cramer said. "When making this decision, we evaluated a wide variety of factors, including the duration of therapy, relative distribution of genotype and cost of the individual agents in the

category, as well as the results of a comprehensive clinical review of the different hepatitis C regimens."

She added: "This strategy meets patients' needs while delivering excellent value and clinical options to both clients and plan members."

However, CVS didn't completely open the floodgates. At the JP Morgan Healthcare Conference in San Francisco last week, Gilead President and COO John Milligan told investors, "The CVS deal is not as broad as the AbbVie deal with Express Scripts" when it comes to restrictions on disease severity.

The prior authorization and utilization management details aren't disclosed.

Just two days after the CVS announcement, Anthem Inc. said it also chose Harvoni as its preferred HCV regimen for the payer's employer-sponsored plans. The size of those plans isn't disclosed. However, Anthem

COMING OUT AHEAD, MAYBE

A back-of-the-envelope analysis of plausible rebate scenarios under the exclusive HCV deal between **AbbVie Inc.** (NASDAQ:ABBV) and **Express Scripts Holding Co.** (NASDAQ:ESRX) suggests the pharma could come out ahead in total market opportunity, even after accounting for knock-on effects of best pricing rules in Medicaid plans — so long as the rebate wasn't more than 41%.

The PBM agreed to allow all its HCV genotype 1 patients unrestricted access to AbbVie's Viekira Pak paritaprevir/ritonavir/ombitasvir/dasabuvir combination in return for an undisclosed rebate. By eliminating restrictions that had previously limited access to new HCV drugs to patients with liver fibrosis scores of F3-F4, Express Scripts has increased the treatable patient pool available to AbbVie from 32,600 to 112,500 lives.

Comments from Express Scripts that benchmarked the rebate against the difference in U.S. and EU pricing for a competing drug from **Gilead Sciences Inc.** (NASDAQ:GILD) set the boundaries of the rebate between about 20% and 40%.

The light green bars on the left show that even at a discount much higher than what AbbVie likely gave, the increase in treatable patients covered by Express Scripts results in a larger market opportunity. As an example, if AbbVie provided a 30% discount to Express Scripts, which is possible, the market opportunity at the PBM would increase to $6.6 billion from $2.7 billion in a base case scenario that includes no discounts and continued restricted access.

That gain would more than offset the decline in revenue potential in Medicaid that could result if the state plans do not loosen their restrictions on utilization. By law, Medicaid gets a discount that is the greater of either 23% off list price or the best price given to any commercial payer, inclusive of rebates.

The dark green bars on the right show the total market opportunity in Medicaid plans if those plans continue to restrict access to HCV patients with fibrosis scores of F3-F4. At a 30% discount, the pharma's Medicaid market opportunity shrinks from $12 billion to $10.9 billion. Combined with the increase in market potential within Express Scripts, AbbVie comes out $2.8 billion ahead. The break-even point for AbbVie is about a 41% rebate, which is likely higher than what it actually gave.

Calculations are based on a WAC of $83,319 for a 12-week course of Viekira Pak and take into consideration Gilead's deal with **CVS Health Corp.** (NYSE:CVS) and **Humana Inc.** (NYSE:HUM), which included the PBM's Medicaid plans. *Sources: BioCentury reporting; company documents; A. C. Moorman, et al., "Mortality and progression to decompensated cirrhosis in chronic hepatitis C patients with liver biopsy confirmed fibrosis in the Chronic Hepatitis Cohort Study," American Association for the Study of Liver Diseases (AASLD) abstract, 2014*

is one of the largest payers, with 37 million total members and 28% of the commercially insured market.

In a statement to BioCentury, Anthem said it chose Harvoni over Viekira because the latter requires ribavirin, which has "significant side effects," including anemia.

The payer added: "Viekira also requires more pills and a more complex dosing regimen. There are more drug interactions with Viekira as compared to Harvoni and length of therapy can also be shorter with Harvoni."

The label for Viekira lists 12 different drug classes as contraindications. There are none for Harvoni.

Anthem will list Harvoni as a Tier 3 or Tier 4 drug, which typically require co-insurance. The payer did not disclose the level of cost-sharing that would be required, but did say access would be restricted based on disease severity. It couldn't confirm whether this means only F3 and F4 patients.

Anthem also said it will seek to list Harvoni as a preferred drug on its Medicare Part D plans. This move first needs to be cleared by CMS, as payers are required to cover at least two drugs in a therapeutic class. Anthem has 1.5 million Medicare members.

Express Scripts is the PBM for Anthem. However, the payer works with its own P&T committee to select its own formulary, which Express Scripts then administers.

Regional payer Harvard Pilgrim was able to secure a lower price for Harvoni while maintaining its restrictions on the drug.

According to CMO Michael Sherman, the Massachusetts payer will continue to restrict access to F2-F4 patients. According to a study by the Centers for Disease Control and Prevention (CDC), about 58% of HCV patients fall into this category.

Sherman said the payer approached both companies, and AbbVie was willing to give larger rebates if the payer allowed all patients access to Viekira.

"It's great that we'd be getting a discount, but if utilization doubles, total expenses would go up," he told BioCentury.

Additionally, the deal with Gilead is only for one year.

"We heard from both companies that a longer deal would get us a better rebate. But with other new drugs on the horizon, we're not going to get locked in for that long," Sherman said.

Harvard Pilgrim covers about 1.2 million lives.

Humana Inc. and Aetna also selected Gilead's drugs. Humana selected Harvoni as its exclusive treatment for HCV genotype 1 on its formularies for commercial, Medicare and Medicaid plans, which account for over 10 million lives. No details were disclosed.

Aetna selected Harvoni and Sovaldi for all HCV patients, including Sovaldi for genotypes 2, 3 and 4. The payer said its current clinical restrictions related to disease severity would remain in place. It also will cover Viekira for patients who first fail treatment with the Gilead drugs.

A DRAW

Prime was able to secure lower prices while offering both companies a spot on its formulary, a trend Gilead and AbbVie think will continue.

David Lassen, chief clinical officer, told BioCentury that Prime evaluated "the effectiveness of managing these drugs from a Metavir score relative to loosening that for prior authorization, and what the net best course of action will be financially."

The PBM also took into consideration the different durations of therapy. "We made assumptions around what we believe in terms of percent of use in each duration, and then looking at the overall best pricing that we can achieve based on that," Lassen said.

"The co-preferred position has the best advantages in both cost and access for our clients and members. It also became very clear that neither Gilead nor AbbVie wanted to be left off formulary. We secured market-leading rates from both companies on both sets of products, providing significantly better value than exclusive deals," said Peter Wickersham, SVP of integrated care and specialty.

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>
> MICHAEL SHERMAN, HARVARD PILGRIM

Prime is owned by 13 Blue Cross and Blue Shield Association plans and manages benefits for more than 25 million lives across 23 Blue Cross plans. Prime said the plans will make decisions about tier placement and utilization management.

Gilead and AbbVie have suggested that they expect more private payers to select the co-preferred option, and that the deals will include rebates based on the size of the population treated and whether the payer is willing to loosen its restrictions.

"We are very pleased with the prices we've been able to secure, and we are pleased with the access we've been able to get," Milligan said at JP Morgan. However, he noted there are still "dozens" of contracts to negotiate and added: "I think that we are going to see more parity deals."

AbbVie CFO William Chase voiced a similar perspective at JPMorgan. "We are not all the way through the game yet, but we feel confident that whether from a parity perspective or exclusivity option that we can compete," he said.

"There is a lot at play and some have made public announcements and some have not," Chase added.

Catamaran Corp. spokesperson Lauren Denz told BioCentury the PBM plans to announce a coverage decision for the HCV drugs "soon." It serves over 25 million members.

THE PUBLIC FRONT

While these commercial deals in many cases increase access, it's unknown how they will affect the large swath of patients on Medicaid, which to this point has been more restrictive than commercial plans.

For example, in California and Illinois, patients must undergo screening for illegal drug and alcohol use prior to and during treatment. Moreover, in California, only hepatologists are allowed to prescribe the drugs. These requirements are on top of limiting access to patients with fibrosis scores of F3 or F4.

The first determinant of whether Medicaid will loosen its restrictions will be the size of the rebates commercial plans are getting.

By law, Medicaid gets at least a 23% discount off a drug's list price. However, if the best price offered to a commercial payer is less than the average manufacturing price (AMP) minus a 23% discount, the difference between the reimbursed price and the best price must be rebated to state agencies on a quarterly basis.

The public payer impact of the private payer deals won't be known immediately, as the calculation lags actual sales and rebates by six months. Thus, any rebates offered in 1Q15 won't be evident to state Medicaid groups until 3Q15 at the earliest.

"Costs could come down, but by how much, nobody really knows," said Matt Salo, executive director of the National Association of Medicaid Directors.

Jeff Myers, president of Medicaid Health Plans of America, said states could get an early idea of the rebate for commercial plans based on the quarterly sales and prescription data reported for the drugs.

He is skeptical the rebates will be large enough.

"The challenge with HCV pricing has been that so many people, theoretically, could derive benefit from the drug," he said. "Even at a 50% discount, that is still a substantial cost. If you are dropping restrictions because you are getting a lower cost, more people will be covered and the states have to look carefully at how many people are now going to go through the gate."

Incarcerated patients are another wild card.

While the 550,000 incarcerated HCV patients aren't entitled to Medicaid benefits, Salo said states are trying to figure out how to "Medicaid-ize" these individuals. For example, the prison could discharge the inmate to a half-way house or work-release program for eight or 12 weeks, depending on the necessary duration of treatment. The prisoner could then receive HCV treatment as a Medicaid beneficiary.

The VA also accounts for a large chunk of the market but did not respond to BioCentury's request for information on its coverage plans for the new HCV drugs.

The VA's formulary currently lists Harvoni and Sovaldi.

LOCK OUT

While Harvard Pilgrim's deal is only for one year, the time frame for the remaining deals is undisclosed. Thus it is unknown how long at least two new drug candidates, along with Olysio, will be locked out of the genotype 1 market.

This half, Merck plans to submit regulatory applications for its all-oral regimen of grazoprevir (MK-5172) and elbasvir (MK-8742).

Bristol-Myers has submitted an NDA to FDA for daclatasvir for genotype 1b. In December, FDA issued a complete response letter in which the agency requested additional safety and efficacy data. The pharma did not provide a timeline for submitting a response.

BMS also plans to submit an NDA this quarter for its fixed-dose oral combination of asunaprevir, daclatasvir and BMS-791325 to treat genotype 1. The combination has breakthrough therapy designation in the U.S. for HCV.

Achillion plans to start a Phase IIa trial of its ACH-3102 plus ACH-3422 this half.

J&J did not share its reimbursement plans, but told BioCentury it continues to work with payers to secure access.

While Express Scripts has said its deal with AbbVie is "multi-year," Miller said the PBM will continue to evaluate the clinical implications of any newly approved HCV medications before it decides whether to keep them off the formulary in favor of AbbVie's regimen.

However, AbbVie's Chase told investors last week "there are built in protections that those [deals] are sustainable short of something revolutionary coming to the market."bc

COMPANIES AND INSTITUTIONS MENTIONED

AbbVie Inc. (NYSE:ABBV), Chicago, Ill.
Achillion Pharmaceuticals Inc. (NASDAQ:ACHN), New Haven, Conn.
Aetna Inc. (NYSE:AET), Hartford, Conn.
Anthem Inc. (NYSE:ANTM), Indianapolis, Ind.
Blue Cross Blue Shield Association, Chicago, Ill.
Bristol-Myers Squibb Co. (NYSE:BMY), New York, N.Y.
Catamaran Corp. (NASDAQ:CTRX), Schaumberg, Ill.
CVS Health Corp. (NYSE:CVS), Woonsocket, R.I.
Express Scripts Holding Co. (NASDAQ:ESRX), St. Louis, Mo.
Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Harvard Pilgrim Health Care Inc., Boston, Mass.
Humana Inc. (NYSE:HUM), Louisville, Ky.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Medicaid Health Plans of America, Washington, D.C.
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
National Association of Medicaid Directors, Washington, D.C.
National Viral Hepatitis Roundtable, San Francisco, Calif.
Prime Therapeutics LLC, Eagan, Minn.
Project Inform, San Francisco, Calif.
University of California, Los Angeles (UCLA), Los Angeles, Calif.
University of California, San Francisco (UCSF), San Francisco, Calif.
U.S. Centers for Disease Control and Prevention (CDC), Atlanta, Ga.
U.S. Centers for Medicare & Medicaid Services (CMS), Baltimore, Md.
U.S. Department of Veterans Affairs (VA), Washington, D.C.
U.S. Food and Drug Administration (FDA), Silver Spring, Md.

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McCallister E. "The price of success." *BioCentury* 1-7 (March 24, 2014)