RADAR on Specialty Pharmacy
Strategies and Analysis for Managing High-Cost Specialty Products

September 2018
VOLUME 15 | NUMBER 09

NHIA, Others Call for Changes to Proposed Home Infusion Rule

Although legislation signed earlier this year established a transitional payment to plug a reimbursement gap for home infusion therapy, a proposed rule is threatening both the temporary and permanent reimbursement for this service. The National Home Infusion Association (NHIA) and other stakeholders are calling for the administration to modify the final rule in order for it to align with the legislation.

Specifically, NHIA is calling for the removal of language requiring the physical presence of a nurse when a drug is administered to a patient and for there to be a specific definition of the professional services that are associated with home infusion.

Traditionally Medicare reimbursed for home infusion drugs but not the professional services associated with the infusions themselves. This changed in December 2016 with the signing of the 21st Century Cures Act, which established a reimbursement structure for the professional services that are provided with home infusion therapies *(RSP 2/18, p. 1)*. However, this does not take effect until Jan. 1, 2021.

The act also changed the reimbursement methodology for Part B infusible drugs furnished through durable medical equipment (DME). The Medicare Modernization Act established an average sales price (ASP)-based methodology for most Part B drugs. However, it excluded Part B infusible drugs furnished through DME — such as chemotherapy administered with an infusion pump — from shifting to ASP, instead basing these therapies' reimbursement on October 2003 average wholesale prices (AWPs). The law went into effect Jan. 1, 2005 *(RSP 10/04, p. 7)*, and reimbursement for these therapies continued to be based on those same AWPs.

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Indication-Based Formularies in Part D Offer Benefits and Risks

The administration continues to take steps that it hopes will bring down drug prices. In the latest move, CMS Administrator Seema Verma said in an Aug. 29 memo to Medicare Part D plan sponsors that they can begin using indication-based formularies in contract year 2020. Industry experts tell AIS Health that the decision definitely has benefits, including giving plans the ability to negotiate higher discounts and providing biosimilars an advantage. On the flip side, potential risks are inherent in the approach, including challenges with operationalizing the policy and the evidence needed to prefer one product over another.

Currently, plan sponsors can use prior authorization (PA) to apply varying approval criteria — a certain diagnosis or result of a diagnostic test, for example — for specific indications. In addition, plans must cover any drug on a formulary for all the indications for which it has FDA approval except for those drugs excluded from Part D based on statutory and regulatory requirements. But starting in 2020, "Part D sponsors may utilize step therapy-like requirements within their PA to promote cost-effective drug therapy by requiring the use of one formulary drug for a certain

Published by AIS Health, Washington, DC. An independent publication not affiliated with insurers, vendors, manufacturers or associations.

indication prior to authorizing coverage of a second drug for that indication," explains the memo, which notes that some commercial health plans already use this approach.

The memo makes clear that a plan taking an indication-based approach "must ensure that there is another therapeutically similar drug on formulary for the non-formulary indication," or CMS may decide that it is not adhering to the anti-discrimination requirements outlined in the Social Security Act. All other Medicare formulary requirements apply, including coverage of drugs within protected classes.

"If a Part D sponsor excludes specific indications for a Part D drug from its formulary, requests for coverage for those excluded indications should be treated as an exception request for an off-formulary drug," says the memo. Plans that take this approach must update their beneficiary materials for 2020 to make sure prospective enrollees are aware of the policy. Plans also must submit the indication information to CMS's Health Plan Management System.

Multiple benefits to using indication-based formularies exist. Plan sponsors will have the "ability to negotiate steeper discounts in the specialty space — not tied into a single rate for utilization of a product across multiple indications," says Andrew Cournoyer, R.Ph., vice president, director – payer access solutions at Precision for Value. "For example, a drug may have strong utilization in one indication, driving meaningful rebate revenue, but weaker utilization in another indication. Payers won't be handcuffed based upon performance in a single indication and can maximize rebate potential across multiple indications."

Plans will be able "to assign a combination of higher payment and/or lower cost share for a treatment used for a particular indication, where evidence shows that this treatment for that indication is likely to yield a better outcome compared to alternative treatments," says Elan Rubinstein, Pharm.D., principal at EB Rubinstein Associates. In addition, for uses of a drug in which evidence offers worse outcomes compared with alternatives, plans can "assign a lower payment and/or a higher cost share."

Firms Need New Contracting Strategies

"Drug manufacturers will need to alter their contracting strategies to match their competition in various segments," says Cournoyer, as "preferred access across the board will be harder to achieve, and, as a result, discounts may increase."

In addition, he tells AIS Health, "Manufacturers of biosimilars may also gain advantage. Aggressive WAC [i.e., wholesale acquisition cost] pricing coupled with a contracting approach may provide net cost benefits to the payer across a number of indications, or a biosimilar could be more aggressive in one indication over another to gain initial market entry. Either scenario could result in favorable access for a biosimilar entrant."

While the Medicaid best price rule may be an impediment to value-based pricing in commercial markets, prices for drugs covered by Part D don't trigger that rule, points out Rubinstein, so discounts for these products don't impact Medicaid pricing.

The policy, however, has multiple potential downsides and risks. Cournoyer points out that it won't impact the broader population: "The benefit enhancement is simply a catch-up play for the Medicare population, which represents only about 15% of the population. Moreover, its impact is most likely targeted at specialty drugs, which are utilized by approximately

Radar on Specialty Pharmacy (ISSN: 2576-4438) is published 12 times a year by AIS Health, 2101 L Street, NW, Suite 400, Washington, D.C. 20037, 800-521-4323, www.AISHealth.com.

2% to 3% of the population. So, when combining these numbers, the overall impact to the insured population is quite low."

Beneficiaries, he says, "will likely not 'feel' the impact from an affordability perspective. The goal of the initiative is to enhance the negotiating leverage of payers, which in turn should increase the rebate stream. Without any pass-through of rebates to the member" — which a handful of payers have said they will begin applying at the point of sale *(RSP 6/18, p. 1)* — "the benefit to the member is really only felt in premium expenditures, which are relatively flat year over year."

What Is Sufficient Evidence to Prefer?

Rubinstein questions "what constitutes sufficient evidence to support preference for one product over another as a matter of policy and benefit design, if there are patient-specific variables such as severity, age, mobility, comorbidities or other matters that should be taken into consideration?" For this reason, he wonders what the role of real-world data will be in this decision making. "Aside from clinical benefit for a particular indication, how will differences in adverse event frequency and severity reflect in the plan's preference decision, particularly if adverse event importance varies with patient-specific factors such as age, comorbidity and condition?"

"If Part D plans evaluate the same evidence and come to a different conclusion, will that decision process be transparent and defensible to prescribers who may treat patients from different Part D plans and who might not agree with one or the other of the Part D plan interpretations of the evidence?" asks Rubinstein. He tells AIS Health that "it's easier to defend step-therapy preference of therapeutically similar products A vs. B in a drug formulary due to a favorable contract with a manufacturer, but a more difficult challenge to defend diametrically opposed interpretations of published evidence with respect to products A vs B. So will indication-based formulary decisions only apply where the evidence is strong, reflect the evidence in a defensible and transparent manner, and always yield the same preference?"

With prescriptions not needing to show an indication for a drug and systems for PBMs and specialty, community and mail-order pharmacies not recording the indication "if [it's] not part of a prior-authorization protocol that specifically requires it," Rubinstein questions how this policy will be operationalized.

Will It Affect Pharmacies' Gross Margins?

"If the indication for which a prescription is dispensed is reflected in reimbursement to the pharmacy, and given that the pharmacy purchased the inventory at a particular price from the wholesaler, will dispensing a drug for a non-preferred indication impact the dispensing pharmacy gross margin — and if yes, how does pharmacy financial risk reflect its ability to influence the indication for which the drug is prescribed?" asks Rubinstein. "That is, might the dispensing pharmacy be penalized for something that is confusing (e.g., on the basis of the same evidence, plan A prefers product #1, while plan B prefers product #2 for a given indication), does not have sufficient transparency to explain to the patient, sufficient clinical or patient-specific condition information to judge if/whether to try to influence the prescriber's decision vs. call the plan to seek an exception, nor sufficient information to audit that it was paid appropriately by the PBM?"

Another challenge will be how payers can "verify the correctness of a drug written for a preferred indication," Rubinstein says. "Can indication-based pricing be gamed?"

In addition, he says, if manufacturers vary purchase prices and discounts for products based on their formulary position, "how will that be implemented, and what's to stop purchasing for preferred indication A, but administering/dispensing for non-preferred indication B?"

Policy Could Encourage Rebate 'Games'

According to an Aug. 29 research note from Evercore ISI analysts Ross Muken and Michael Newshel, indication-based formularies "make sense and should give PBMs some incremental negotiating leverage by multiplying their options for building formularies. But at the same time this could encourage more of the rebate 'games' described by HHS where manufacturers raise list price and rebate dollars to get onto formularies, highlighting the tension between the administration's consideration of restricting rebates and its desire to broaden the negotiating leverage of PBMs," including the new policy change allowing Medicare Advantage plans to apply step therapy to Part B drugs *(RSP 8/18, p. 4)*.

As far as drug classes likely to be affected by the policy, specialty drugs "are the most likely targets on the basis of high cost per prescription, high year-over-year trend of specialty relative to non-specialty pharmaceuticals…and the prediction that specialty will soon comprise half of drug benefit spend," says Rubinstein. Cournoyer agrees that these drugs are likely targets due to their high prices and "multiple indications with varied competition in each indication."

Within the specialty medications, the anti-inflammatory products used in conditions such as rheumatoid arthritis, psoriasis and Crohn's are likely, with Verma even mentioning the tumor necrosis factor (TNF) inhibitors in her memo. This is a class with numerous high-cost therapies, and some payers, including CVS Health, have launched indication-based formularies for it. Hepatitis C drugs, expensive therapies that are approved for different genomes of the virus, also could be contenders.

Grandfathering Is Likely for Most Plans

Both Cournoyer and Rubinstein believe that plans will grandfather in those beneficiaries who are on a drug for an indication that's not on formulary. "I envision that most plans will grandfather patients," says Cournoyer. "Disrupting existing care, especially treatment that has been effective, is generally frowned upon by CMS. Furthermore, patient disruption on this front could result in Medicare complaints, which can adversely affect star ratings. Transition policies will also continue to take effect, and plans will need to provide ample notice to beneficiaries if they opt not to grandfather patients (which opens the door for CMS auditing opportunities)."

Patients who already are on a drug for an indication in which it is preferred "will also enjoy the lower cost-share (relative to what they were paying out of pocket before the change) or whatever other benefits are bestowed for use of a preferred product for a preferred indication," points out Rubinstein.

So what should drug manufacturers do to make sure their drugs receive favorable formulary positions? For one, Rubinstein tells AIS Health, they will need to "ramp up demonstration of efficacy and value via real world data/'big data' analysis."

"Payers will be in a position to redefine market baskets," says Cournoyer. "No longer will TNF inhibitors be a market basket across an indication set but rather a market basket within an indication subset. As a result, manufacturers will need to look at their value propositions (clinical and financial) within an indication and across indications. Bid proposals will need to look at total value and have the added flexibility of varying contracting rates across different indications (as opposed to one flat rate). There is also an opportunity to expand value or outcomes-based contract opportunities to look at holistic drug performance across all utilizing populations. For example, will a manufacturer hedge its drug's performance across an indication-agnostic measure such as adherence or persistence, and does this arrangement give a competitive edge?"

View the CMS memo at https://tinyurl.com/y86fbpuc. Contact Cournoyer through Tess Rollano at trollano@coynepr.com and Rubinstein at elan.b.rubinstein@gmail.com. ✧

CVS Will Exclude Certain Drugs Based on ICER Analyses of QALY

At the time of year when PBMs are rolling out their 2019 strategies, CVS Health has unveiled a bold new approach to managing certain specialty drugs based on data from the Institute for Clinical and Economic Review (ICER). However, industry experts are divided on how much of an impact it truly will have on drug prices.

In a white paper out last month, titled *Current and New Approaches to Making Drugs More Affordable*, CVS revealed that it's starting a program focused on bringing down launch prices of pricey me-too drugs. The approach allows clients to exclude those medications that come onto the market with a price more than $100,000 per quality-adjusted life year (QALY) as determined by publicly available ICER analyses. Drugs to which the FDA has given breakthrough therapy status will not be eligible for exclusion.

Program Focuses on Costly Me-Too Drugs

By focusing on "expensive, 'me-too' medications that are not cost effective," the approach, contends the white paper, will help "put pressure on manufacturers to reduce launch prices to a reasonable level." Noting that drugmakers are the only stakeholder with the ability to control launch prices, the PBM maintains that "this new approach, harnessing the power of the market, could change manufacturer behavior. CVS Caremark continues to use other PBM techniques to help lower costs for payors and their members, but lower launch prices could help bring about real deflation in drug prices."

CVS spokesperson Christine Cramer confirms that the company is beginning to roll out the program now, which is "focused on new drugs entering the market moving forward." She notes that the PBM has not announced which drugs would be excluded under the program.

The white paper includes a chart that shows high launch prices for certain drugs starting in 1997 with Teva Neuroscience, Inc.'s Copaxone (glatiramer acetate). Interestingly, of the seven drugs included in the graphic that were first approved starting in 2013 — the breakthrough therapy designation, which was created as part of the Food and Drug Administration Safety and Innovation Act, was unveiled July 9,

2012, when FDASIA was signed into law — six had breakthrough therapy designation, so they would have been ineligible for the CVS program.

CVS's approach is "another example of how payers and PBMs are looking at opportunities to manage drug costs by tying access to competitive cost-effectiveness," according to Ami Gopalan, Pharm.D., vice president, director, payer access solutions at Precision for Value. "As therapeutic classes become more competitive, encompassing multiple products with similar efficacy and safety, programs like the one promoted by CVS provide another option for formulary management."

The program is "a credible approach to better managing drug spend for its clients," maintains Elan Rubinstein, Pharm.D., principal at EB

Drug Prices Increases Are Expected to Slow, but Specialty Prices Continue to Dominate Spending

Pharmaceuticals are expected to undergo a 4.92% price increase from 2018 to 2019, according to the recently released July-August 2018 *Drug Price Forecast* from Vizient. That's actually a slowing from the 7.61% increase for 2018. The company conducted its analysis using price and volume data from hospital and non-acute facilities participating in its Vizient Pharmacy Program. Among Vizient members, therapeutic classes with the highest spend include many with specialty drugs (see table below).

Disease-modifying antirheumatic agents lead the way with an estimated 8.57% increase, followed by the immunomodulatory agents for multiple sclerosis, at 7.33%. According to the report, "Based on the total amount of spend across care environments, the types of molecular entities approved by the FDA, and the investigational products in the development pipeline, it is certain that specialty pharmaceuticals will continue to play an increasingly important role in pharmacy budgeting." However, a handful of events have occurred that are helping slow drug price increases, including CMS giving biosimilars a unique reimbursement code and pass-through status, as well as the administration's initiative to bring down drug prices.

Challenges within the system include the fragility of the pharmaceutical supply chain, which is leading to multiple drug shortages, and novel new medications that launch at very high prices.

Download the report at https://tinyurl.com/ycbfcjmg.

Summary of Highest-Spend Therapeutic Classes Among Vizient Members

Therapeutic category	Key products in class	Class-estimated price change (%)
Antineoplastic agents	Rituxan, Keytruda, Avastin	4.32
Disease-modifying antirheumatic agents	Remicade, Humira, Enbrel	8.57
Immunomodulatory agents	Tysabri, Copaxone, Ocrevus	7.33
Anti-infectives		1.24
Hepatitis C	Harvoni, Epclusa, Zepatier	0.00
Antibacterials/antifungals (systemic)	Daptomycin, Invanz, AmBisome	1.45
Plasma critical care		3.10
Immune globulin, intravenous (IgIV)	Gamunex, Privigen, Gammaguard	3.78
Albumin	AlbuRx, Albutein, Flexbumin	0.00
Hematopoietic agents	Neulasta, Aranesp, Procrit	2.03
Vaccines	Prevnar, Gardasil, Pneumovax	5.76

Vizient data, April 2017-March 2018.
SOURCE: Vizient Inc., *Drug Price Forecast*, July-August 2018, released August 2018. Download the report at https://tinyurl.com/ycbfcjmg.

Rubinstein Associates. "This approach strengthens PBMs' business case for how PBMs add value, which has come under increasing fire from all sides and which may be under even more pressure if the safe harbor which protects manufacturer class of trade discounts and rebates is eliminated" *(RSP 6/18, p. 1)*.

Approach Needs Careful Evaluation

Other reactions were more skeptical. "Already 'me-too' drugs are subject to negotiation such that they can be excluded from formularies — I'm not sure if this is going to have such a material effect on them," says Lisa Kennedy, Ph.D., chief economist at Epiphany, a company that performs health economics, reimbursement and market access studies. "The question is how this will affect innovative drugs where there are fewer alternatives for patients. Any decision to use this approach needs to also be carefully evaluated in the context of how it could help or harm patients, which I'm sure CVS will do.…I can't see a lot of benefits to this approach."

In response to the program, "manufacturers may increase the weight of value criteria to assess candidate viability and inform pipeline culling considerations during the R&D process," Rubinstein tells AIS Health. "Self-insured employers may face pushback from employees and dependents who are denied access to me-too products excluded from coverage on the basis of value below threshold. HR departments will need to find ways to communicate about rationale and justification for this."

According to Gopalan, "One point to keep in mind is there can be different interpretations of what is considered a me-too medication. In addition, a QALY pricing threshold of $100,000 may not be appropriate for all scenarios."

Cramer did not respond to a question about why CVS chose drugs exceeding $100,000 per QALY as opposed to another amount, such as $50,000 or $150,000 per QALY.

According to Kennedy, QALYs are "as complicated as the concept sounds. The purpose of using the QALY is to be able to compare all innovations with a common unit of benefit. The problem is that QALYs are hard to understand and exhibit extraordinary methodological and practical problems: They aren't reliable across the same patients over time, across different patients and, additionally, fall down when required to measure more difficult things such as QALYs in the elderly or the very young. QALYs are often mapped from quality-of-life measures collected in a trial. What can happen is that the quality-of-life instruments used are not sensitive enough to capture meaningful change for the patient."

Move Is Step in Right Direction for U.S.

Yet although "one might argue with the methodology" used to assess value, Rubinstein tells AIS Health, "the fact of the matter is that this is a step in the right direction for the United States, where pursuing value is something of a new thing that has had difficulty getting established — and in light of a health care cost trend which regularly exceeds CPI-U [i.e., Consumer Price Index for All Urban Consumers], and which likely holds down wage increases since employers look at the whole 'package' of employee costs. When other package costs rise faster, then wages have less room to rise."

"I'm not sure how this will affect products at launch, but it could function to put pressure on manufacturers not to raise their prices over time — this combined with competitive pressure," Kennedy tells AIS Health.

Lower Net Prices May Be Outcome

"While it may not hold down list prices of me-too products, CVS's move may result in lower net prices for PBMs and insurers that go this route, as manufacturers negotiate to avoid flat-out exclusion from a drug formulary," Rubinstein states. "Me-too products with similar efficacy and safety as ones already on the market will face a higher bar to launch than they have in the past, if PBMs and insurers follow CVS's lead in using a QALY threshold for product formulary listing vs exclusion. That will mean deeper price concessions but not necessarily commensurately lower launch prices."

"Manufacturers will need to evaluate their launch pricing scenarios closely to understand the potential impact of a program offering like CVS's," Gopalan says. "For manufacturers entering highly competitive categories, alternative pricing strategies will need to be considered."

In order for drugmakers to successfully launch their products, "beyond safety and efficacy, manufacturers need to plan to demonstrate the clinical and economic value their product brings to the marketplace," she maintains.

"Generating evidence that supports the value of their product will be important to be successful."

View the CVS white paper at https://tinyurl.com/ybgm4n8n. Contact Cramer at Christine.Cramer@CVSHealth.com, Gopalan through Tess Rollano at trollano@coynepr.com, Kennedy at lisa.kennedy@epiphanomics.co and Rubinstein at elan.b.rubinstein@gmail.com. ✧

Express Scripts Will Exclude Some HAE, HIV, Factor Products

With 48 new exclusions on its 2019 National Preferred Formulary (NPF), Express Scripts Holding Co. is getting more aggressive in its attempt to broaden access to pharmaceuticals and bring value to its clients. But some industry stakeholders are questioning its strategy of excluding more specialty drugs, including some for rare conditions, as well as a low-cost pangenomic hepatitis C medication.

The new exclusions are on top of the 196 drugs Express Scripts already is excluding in 2018. In 2019, the NPF will cover more than 25 million lives and will include 3,886 medications. The PBM estimates that it will save $3.2 billion. Those plans that have continuously used the NPF since Express Scripts introduced it in 2014 will save $10.6 billion total through next year, projects the company.

Among the new exclusions are the following:

✦ ***Novartis Pharmaceuticals Corp.'s multiple sclerosis drug Extavia*** (interferon beta-1b);

✦ ***Four factor VIII recombinant products for hemophilia:*** Eloctate from Bioverativ, a Sanofi company; Shire US Inc.'s Recombinate; and Pfizer Inc.'s Xyntha and Xyntha Solofuse;

✦ ***AbbVie Inc.'s hepatitis C medication Mavyret*** (glecaprevir/pibrentasvir);

✦ ***CSL Behring LLC's Berinert*** (C1 esterase inhibitor, human), indicated for the treatment of acute abdominal, facial or laryngeal hereditary angioedema (HAE) attacks in adult and pediatric patients; and

✦ ***Gilead Sciences, Inc.'s HIV drug Atripla*** (efavirenz/emtricitabine/tenofovir disoproxil fumarate).

Express Scripts has a formulary exception process by which patients who cannot use a preferred therapy can seek an exception.

Jennifer Luddy, a spokesperson for Express Scripts, tells AIS Health that "no formulary decision is based strictly on price. First, our independent P&T [i.e., pharmacy & therapeutics] committee reviews medications and makes recommendations based on clinical evidence. Medications they deem 'mandatory include' are included. Medications which are a 'may add' have therapeutic alternatives available, and then we can make a decision based on price."

"After clinical considerations, formulary preference is given to high-value therapies with the lowest net cost, achieved through low list price, rebate, or both," says Express Scripts.

Some Exclusions Were Surprising

According to Jeremy Schafer, senior vice president at Precision for Value, "The inclusion of categories like HIV, hereditary angioedema and hemophilia was certainly a surprise. Rare disease categories such as these were commonly seen as too sensitive and individualized to be managed by something as blunt as an exclusion. Even though Express Scripts is grandfathering current users, this move represents an aggressive step in the management of rare disease drugs."

But with multiple therapies in hemophilia, HIV and HAE, why shouldn't PBMs exclude some of them?

Schafer tells AIS Health that "a primary reason may be that patient care in these diseases is so individualized. The diseases included here are very nuanced, and patient presentation is highly variable. For categories like HAE and hemophilia, product supply, site of care and variances in dose play additional roles. As a result, different drugs often have carved out niches in unique subpopulations. An exclusion doesn't take into account these nuances and instead blocks out affected products. Although appeals for coverage may be made, it is a blunt instrument in drug management."

Within the HAE space, says Luddy, "we leveraged increased competition in that class to maintain access to a variety of therapies (there are eight preferred alternatives in that class) at a lower cost."

However, "some patients respond better to certain products, so physicians might experiment with one or more products to see which ones are most effective in managing the disease and symptoms," Elizabeth Duruz, R.Ph., director of clinical program services at Diplomat Specialty Infusion Group, a brand of Diplomat Pharmacy Inc., tells AIS Health *(RSP 3/18, p. 1)*. For example, some patients may think that one HAE product works really well for facial attacks, but another works better for abdominal attacks.

PBM Will Exclude Four Hepatitis C Drugs

Within the hepatitis C class, in addition to Mavyret, the PBM also will continue to exclude Bristol-Myers Squibb Co.'s Daklinza (daclatasvir), Janssen Therapeutics' Olysio (simeprevir) — which Janssen discontinued earlier this year — and Gilead's Sovaldi (sofosbuvir). On the 2019 NPF are Gilead's Epclusa (sofosbuvir/velpatasvir), Harvoni (ledipasvir/sofosbuvir) and Vosevi (sofosbuvir/velpatasvir/voxilaprevir) and Merck & Co., Inc.'s Zepatier (elbasvir/grazoprevir), which currently is excluded.

"We have successfully driven down the cost to cure hepatitis C over the last four years, and once again we're taking action to further lower client costs," says Luddy. "In July 2018, Mer-

ck announced a 60% price reduction for Zepatier that will take place in the fourth quarter of 2018. That will make Zepatier the lowest-cost agent for a 12-week course of therapy. Because of this market dynamic shift, Zepatier will be added to formulary effective Jan. 1, 2019. At the same time, Mavyret will be excluded on the NPF. All current utilizers of Mavyret will be grandfathered to allow completion of their treatment course. For 2019, the Express Scripts NPF will have a combination of the market leading products (Harvoni and Epclusa) and the low-cost leader (Zepatier) on the formulary, as well as Vosevi."

Adam Fein, Ph.D., author of the Drug Channels blog and CEO of Drug Channels Institute, noted in an Aug. 16 blog that excluding Mavyret is a "patient unfriendly change to the hepatitis C category." That's because while that therapy is indicated for genotypes 1 through 6 — as is Epclusa — Zepatier is indicated for only genotypes 1 and 4. Harvoni is indicated for genotypes 1, 4, 5 and 6.

As he wrote in his blog, "Until recently, Mavyret had the lowest list price. AbbVie launched Mavyret in

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New FDA Specialty Approvals

✦ ***Aug. 15: The FDA expanded the approval for Kalydeco*** (ivacaftor) to include the treatment of children with cystic fibrosis at least 12 months old who have at least one mutation in their cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to Kalydeco based on clinical and/or in vitro assay data. The agency first approved the Vertex Pharmaceuticals Inc. drug in January 2012 *(RSP 2/12, p. 8)*. Dosing is age- and weight-based. The product is available as a 150 mg tablet and oral granules. Website GoodRx lists the price of one carton containing 56 150 mg tablets as more than $23,700. Visit www.kalydeco.com.

✦ ***Aug. 16: The FDA granted an additional approval to Lenvima*** (lenvatinib) for the first-line treatment of people with unresectable hepatocellular carcinoma (HCC). The agency initially approved the capsule from Eisai Inc. and Merck & Co., Inc. for the treatment of differentiated thyroid cancer in 2015 *(RSP 3/15, p. 11)*; it's also approved for renal cell carcinoma *(RSP 6/16, p. 6)*. Dosing for the newest indication is 12 mg once daily for people weighing at least 60 kg and 8 mg once daily for people less than 60 kg. According to Reuters, Eisai will price the recommended starting dose for HCC at $15,970 for a 30-day supply. Visit www.lenvima.com.

✦ ***Aug. 17: The FDA gave accelerated approval to Opdivo*** (nivolumab) for the treatment of people with metastatic small cell lung cancer whose cancer has progressed after platinum-based chemotherapy and at least one other line of therapy. The FDA first approved the Bristol-Myers Squibb Co. programmed death receptor-1 (PD-1) inhibitor in December 2014 for the treatment of unresectable or metastatic melanoma *(RSP 1/15, p. 6)*. Dosing for the newest indication is 240 mg as a 30-minute intravenous infusion every two weeks. GoodRx lists the price of one 100 mg/10 mL vial as more than $2,600. Visit www.opdivo.com.

✦ ***Aug. 17: The FDA gave an additional indication to Eylea*** (aflibercept) for the treatment of wet age-related macular degeneration on a 12-week dosing schedule. The Regeneron Pharmaceuticals, Inc. intravitreal injection already was approved for use every four weeks and every eight weeks after three initial monthly doses. The FDA initially approved the drug in November 2011 *(RSP 12/11, p. 8)*. Website Drugs.com lists Eylea's price as more than $1,900. Visit www.eylea.com.

✦ ***Aug. 20: The FDA expanded the label of Keytruda*** (pembrolizumab) to include its use in combination with Alimta (pemetrexed) and platinum chemotherapy for the first-line treatment of people with metastatic nonsquamous non-small cell lung cancer (NSCLC) with no epidermal growth factor receptor (EGFR) or ALK genomic tumor aberrations. The agency initially gave the Merck PD-1 inhibitor in combination with Alimta and carboplatin accelerated approval in 2017 *(RSP 6/17, p. 6)*. Dosing is 200 mg of the intravenous infusion every three weeks. GoodRx lists the price of three 50 mg vials as more than $6,700. Visit www.keytruda.com.

✦ ***Aug. 21: The FDA expanded the use of the Dako PD-L1 IHC 22C3 pharmDx assay*** to identify people with urothelial carcinoma who may benefit from Keytruda. The agency

New FDA Specialty Approvals *(continued)*

has approved the Agilent Technologies Inc. companion diagnostic for use in multiple other cancers. Visit https://tinyurl.com/ybmruoyo.

✦ ***Aug. 22: The FDA approved Dompé farmaceutici S.p.A.'s Oxervate*** (cenegermin-bkbj) for the treatment of neurotrophic keratitis in people at least two years old. The agency gave the recombinant human nerve growth factor priority review and fast track status, as well as breakthrough therapy and orphan drug designations. The company says it will launch the ophthalmic solution in the U.S. by early 2019. Dosing is six times per day for eight weeks. Visit https://tinyurl.com/ya86gayo.

✦ ***Aug. 23: The FDA approved Biocodex SAS's Diacomit*** (stiripentol) for the treatment of seizures associated with Dravet syndrome in people at least two years old who are taking clobazam. The agency gave the product orphan drug designation. It is available in two formulations: capsules and powder for oral suspension. The company says it expects the drug to be available in early January 2019. Visit www.biocodex.com/en.

✦ ***Aug. 23: The FDA gave another indication to the cobas EGFR Mutation Test v2*** as a companion diagnostic for AstraZeneca's Iressa (gefitinib) in people with NSCLC. The FDA has approved the Roche Diagnostics test as a companion diagnostic for other drugs to determine NSCLC EGFR mutation status. Visit www.cobasegfrtest.com.

✦ ***Aug. 23: The FDA approved Shire plc's Takhzyro*** (lanadelumab-flyo) for prophylaxis to prevent hereditary angioedema attacks in people at least 12 years old. The plasma kallikrein inhibitor is the first monoclonal antibody the agency has approved for this indication. The drug, which can be self-administered, had breakthrough therapy and orphan drug designations, as well as priority review. The recommended starting dose for the subcutaneous injection is 300 mg every two weeks, which may shift to every four weeks if the patient is well controlled for more than six months. Visit www.takhzyro.com.

✦ ***Aug. 27: The FDA expanded the indication for Imbruvica*** (ibrutinib) in combination with Rituxan (rituximab) to treat adults with Waldenström's macroglobulinemia (WM). This approval makes the drug, which is jointly developed and commercialized by Pharmacyclics LLC, an AbbVie Inc. company, and Janssen Biotech, Inc., the first and only chemotherapy-free combination treatment for the disease. The Bruton's tyrosine kinase inhibitor came onto the U.S. market after the agency gave it accelerated approval in 2013 for the treatment of mantle cell lymphoma *(RSP 12/13, p. 7)*; it now has approval for multiple indications. It is available in capsule and tablet formulations. Dosing for WM is 420 mg once daily. GoodRx lists the price of 90 140 mg capsules as more than $12,100. Visit www.imbruvica.com.

✦ ***Aug. 30: The FDA approved Bayer Corp.'s Jivi*** (antihemophilic factor [recombinant] PEGylated-aucl) for the prophylactic treatment of hemophilia A, as well as on-demand treatment and perioperative management, in previously treated people at least 12 years old. The initial recommended dosing regimen for prophylaxis is 30-40 IU/kg twice weekly with the ability to dose 45-60 IU/kg every five days and then individually adjust to less or more frequent dosing based on bleeding episodes. Dosing of the intravenous infusible for on-demand treatment is based on the degree of bleeding, and dosing for perioperative management is based on the type of surgery. Visit www.jivi.com.

✦ ***Aug. 31: The FDA approved Merck's Delstrigo*** (doravirine/lamivudine/tenofovir disoproxil fumarate) for the treatment of HIV-1 infection in adults with no prior antiretroviral treatment. It is a once-daily, fixed-dose combination tablet, and it's priced at $70 per day, or $25,550 per year. The company says it expects the drug to be available within one month. Visit www.delstrigo.com.

✦ ***Aug. 31: The FDA approved Merck's Pifeltro*** (doravirine) in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults with no prior antiretroviral treatment. The recommended dose of the non-nucleoside reverse transcriptase inhibitor is one 100 mg tablet daily. Its price is $46 per day, or $16,790 per year. The company says it expects the drug to be available within one month. Visit www.pifeltro.com.

NPF Excludes Rare Disease Drugs

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2017 with a wholesale acquisition cost (WAC) list price for a one-month supply that was more than 50% lower than the list price of other therapies." Citing *Pharmaceutical Technology*, Fein said that the list price for an eight-week course of Mavyret is $26,400, and a 12-week course is $39,600. That's compared with the 12-week Harvoni list price of $94,500 and Epclusa's $74,760. "Rebates can be substantial, so the list prices do not meaningfully reflect the net cost to a payer," he noted.

"Express Scripts has excluded Mavyret, the lowest list price product that can treat the one in four patients who has HCV [i.e., hepatitis C virus] genotype 2 and 3," he said. "These patients can't take Zepatier, which treats only genotypes 1 and 4. They will therefore most likely be treated with Harvoni, a product with a higher list price and presumably high rebates."

With discounts reflected in average sales price, this "translates into savings for a payer compared with paying from WAC," notes Schafer.

Fein also pointed out that "patients with commercial insurance often have prescription drug deductibles and coinsurance, so their out-of-pocket costs are linked to undiscounted, pre-rebate list prices. Patients with HCV genotypes 2, 3, 5, and 6 will face higher costs due to these formulary exclusions. They won't benefit from a low net price. If physicians end up prescribing Harvoni or Epclusa over Zepatier, then patients with genotypes 1 and 4 will also get stuck with higher out-of-pocket costs tied to the higher list prices."

When Fein queried Express Scripts about patients' higher out-of-pocket costs due to Mavyret's exclusion, he said a spokesperson told him that "the copay card would be an option."

Luddy tells AIS Health that those members on the excluded factor VIII, HIV and hepatitis C excluded drugs "will be grandfathered per guidance from our internal clinical team and our independent pharmacy & therapeutics committee." However, this doesn't apply to all the excluded drugs but rather only "for those where it is clinically necessary." The PBM also will grandfather "a few others" outside these three therapeutic classes.

View the exclusions at https://tinyurl.com/y78jy5kf. View Fein's blog at https://tinyurl.com/y89wr82l. Contact Schafer through Tess Rollano at trollano@coynepr.com. ✧

Groups Call for Language Changes

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The Cures Act, however, changed the reimbursement methodology for these drugs to ASP as of Jan. 1, 2017. So rather than being reimbursed at AWP -5%, these drugs are now paid at the ASP +6% rate used for most Part B drugs. About 30 drugs have been affected by the shift to ASP, and while the impact hasn't been negative for all of those therapies, two drugs in particular are taking the biggest hits. Reimbursement for inotropic agent milrinone dropped about 92%, and subcutaneous immune globulin (IG) Hizentra dropped about 31%. Other subcutaneous IG products such as Gamunex and Gammagard have suffered hits between 21% and 31%.

In 2017, members of Congress introduced legislation to plug the gap between the ASP reimbursement change that went into effect Jan. 1, 2017, and the professional services reimbursement that goes into effect Jan. 1, 2021. The House passed it July 25, 2017, and the Senate introduced a similar bill shortly thereafter. The Medicare Home Infusion Therapy Access Act of 2017 finally was enacted earlier this year when President Trump signed the Bipartisan Budget Act of 2018 on Feb. 9. The act establishes a transitional payment that kicks in Jan. 1, 2019.

However, a proposed rule issued this summer, titled *Medicare and Medicaid Programs; CY 2019 Home Health Prospective Payment System Rate Update and CY 2020 Case-Mix Adjustment Methodology Refinements; Home Health Value-Based Purchasing Model; Home Health Quality Reporting Requirements; Home Infusion Therapy Requirements; and Training Requirements for Surveyors of National Accrediting Organizations* (83 Fed. Reg. 32340, July 12, 2018) is threatening to undo much of what that other legislation established.

Comment Period Ended Recently

The comment period on that proposed rule ended Aug. 31. NHIA spokesperson Marilyn Tretler notes that CMS typically will finalize rules 60 days after the comment period closes, so by that approach, CMS will issue the final rule on or around Nov. 1. That said, "It's a bit of a moving target. They can choose to move forward with one part and not the other." But it needs to be implemented by Jan. 1 for the transitional payments to kick in.

NHIA shared its comment letter with AIS Health in response to questions about the proposal and potential ramifications were it to be implemented as is. The association, as well as some members of Congress, takes issue with two provisions of the proposed rule: the physical presence requirement and the definition of professional services required for home infusion.

In describing the "infusion drug administration calendar day," the pro-

posed regulation explains that it understands the act to mean that "payment is only for the day on which the nurse is in the patient's home when an infusion drug is being administered.…Payment is made only for the day on which the administration of the infusion drug occurs even if professional services were furnished on a different day. Therefore, we propose to define in regulation that payment for an infusion drug administration calendar day is for the day on which home infusion therapy services are furnished by skilled professional(s) in the individual's home on the day of infusion drug administration. The skilled services provided on such day must be so inherently complex that they can only be safely and effectively performed by, or under the supervision of, professional or technical personnel."

Physical Presence Contradicts Intent

In a letter commenting on the proposed rule, Sens. Johnny Isakson (R-Ga.) and Mark Warner (D-Va.) — authors of the Medicare Home Infusion Therapy Access Act of 2017 — state that in their legislation, the benefit was intended to cover "professional services, including nursing services." But the physical presence required in the proposed rule "contradicts our intent in drafting and enacting this legislation and makes the reimbursement required by the bill inadequate."

According to Isakson and Warner, "In preparing this legislation, we worked to mirror this benefit as closely as possible to private sector and other governmental home infusion programs. No other payers for home infusion (commercial plans, Medicare Advantage Plans, the Veterans Administration, or others) have such a requirement for a professional to be physically present in order to reimburse for the beneficiary's home infusion. To remain true to both the legislation and our intent, CMS should withdraw the requirement that a nurse or other professional be physically present 'in the home' for reimbursement to occur, and instead to recognize that reimbursement be made for each day that a home infusion drug is infused."

Goal of Bill Was Patient Freedom

The goal of the bill, they say, "was to give patients freedom to receive these infusions in the comfort of their own home, without having to make the sometimes onerous journey to a healthcare facility to receive an infusion. Congress intended to give freedom to the patients in this legislation, allowing them to administer their own infusions at home without a healthcare worker."

Another benefit to patients — many of whom have compromised immune systems — of receiving infusions in their home is this location is safer health-wise in that they aren't at risk of getting a health care-associated infection from a site of care such as a hospital outpatient department.

In addition, Isakson and Warner note that their "intent was that home infusion providers' professional services, such a drug preparation, clinical care planning, care coordination, nursing and other associated professional work should be a component of the home infusion benefit.…The legislation is clear that the 'nursing services' are a subset of 'professional services,' and we made reference to nursing services to clarify that they were not to be separately billable from the other professional services." The senators urge CMS to come up with "a definition of professional services that is unique to home infusion." They also clarify that the services are not covered under the DME benefit.

Through the proposed rule, says Rep. Earl "Buddy" Carter (R-Ga.) — who is the lone pharmacist in Congress — "CMS has virtually eliminated any reference to pharmacy services as professional services for reimbursement. It is vital that professional services include drug preparation and dispensing. The drugs that home infusion suppliers provide to patients require extensive pharmacy services, including the compounding of the drugs. By ignoring pharmacy services as a professional service CMS has created a home infusion benefit that incorrectly focuses solely on nursing services," he says in a letter commenting on the proposed rule.

Rule Impacts Permanent Payment Also

According to NHIA, "For the permanent payment, the proposed rule would adopt the same definition to limit the payment in the same way. By tying this definition to face-to-face nursing services, this definition would exclude coverage and reimbursement for the myriad of other professional services needed for safe and effective delivery of home infusion therapy, including sterile compounding, clinical care planning, care coordination, nursing and other associated professional services." This means that through the proposed rule, both temporary and permanent reimbursement would be limited "to only a small subset of the many professional services furnished in connection with home infusion therapy."

NHIA maintains that the limitation of reimbursement is "inappropriate for two reasons. First, this limitation is contrary to the text and structure of the statutes directing CMS to reimburse home infusion therapy services. Second, providing for pay-

ment only on a day on which nursing services are furnished fails to take into account the many professional services that are necessary to deliver home infusion therapy to the patient, and would therefore make it impractical for home infusion therapy suppliers to continue to provide these services."

NHIA explains that home infusion pharmacists prepare and compound drugs, assess the possibility of medication interactions and coordinate with care teams, as opposed to nursing services, which almost always are face-to-face encounters with patients. With the proposed rule specifically referencing a face-to-face interaction, this "would treat the home infusion therapy pharmacy components of professional services reimbursement as a nursing benefit and would assume away the crucial additional professional services necessary to deliver home infusion therapy." This, says the association, "would fail to implement Congress's instruction."

NHIA also points out that the proposed rule equates "a day the drug is administered" with its proposed definition of infusion drug administration calendar day, a day when a nurse is in the home of the patient. This is problematic because a nurse is not present for every infusion of a drug. "Depending on the specific circumstances, a patient may only need a single visit per week in connection with drugs that can be self-infused or infused by the patient's caregiver on each of the remaining six days," says NHIA. "In failing to take such an arrangement into account, in effect, the proposed rule would demand that a supplier accept one day of payment for one week of professional services."

In a letter responding to the proposed rule, Rep. Pete Sessions (R-Texas) notes another problem. The Congressional Budget Office estimated that the home infusion benefit as part of the budget act would cut down on federal costs and boost the number of home infusion days to 25 million infusions for each of the two transitional years. "This estimate is in direct conflict with the CMS projections of payment once a week or once a month resulting in 305,000 total visits of care" in 2019, as indicated in the proposed rule.

The upshot?

"The proposed rule, ironically, would cost the Medicare program significantly more money by shifting Medicare beneficiaries unable to access infusion in the home into far costlier inpatient settings and skilled nursing facilities."

View NHIA's resources page for the transitional reimbursement law, which includes links to the congressional letters, at https://tinyurl.com/y6v9g4w9. Contact Tretler at marilyn.tretler@nhia.org. ✧

News Briefs

✦ ***A group of industry stakeholders, including insurers, hospitals, pharmacists, CVS Health and Prime Therapeutics LLC, recently sent a letter to FDA Commissioner Scott Gottlieb, M.D., calling for the FDA to finalize the draft interchangeable biosimilars guidance*** — which it issued in January 2017 *(RSP 2/17, p. 4)* — in order to increase competition within the pharmaceutical marketplace. Interchangeable designation would allow pharmacists in states that allow therapeutic substitution to automatically substitute an interchangeable biosimilar for its reference product without intervention from the health care provider who prescribed the reference product. While the FDA has approved 12 biosimilars, it has not granted interchangeable status to any of them. View the letter at https://tinyurl.com/y85qebqh.

✦ ***Pfizer Inc. filed a citizen petition last month asking the FDA's Gottlieb to "issue guidance clarifying appropriate sponsor communications about the nature and properties of biosimilar products."*** It cites specific companies and their communications that it says are false and misleading. The company maintains that part of the reason behind the slow uptake of biosimilars is "a lack of market confidence in biosimilars resulting from the efforts of certain reference product sponsors to disseminate false and misleading information that casts doubt about the safety and efficacy of biosimilars in the minds of patients and prescribers." View the petition at https://tinyurl.com/ybtcy8lp.

✦ ***PEOPLE ON THE MOVE:*** Village Fertility Pharmacy named ***Richard J. Burkett*** CEO. He previously was U.S. head of sales, marketing, and strategic partnerships within EMD Serono Inc.'s U.S. fertility business. Village also named ***Michael Abramo*** chief financial officer. He was the chief administrator of the Massachusetts Bay Transportation Authority most recently.