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

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Administration Unveils Blueprint Aimed at High Drug Prices

After more than a year of promising action to counter the high costs of prescription drugs, the Trump administration on May 11 unveiled its *American Patients First* blueprint aimed at lowering medication prices and reducing costs for consumers. It remains to be seen how effective — or even how implementable — the various strategies are, which focus on four areas: better competition, tougher negotiation, incentives for lower list prices and decreased out-of-pocket costs. During a press conference unveiling the blueprint, President Trump called out various stakeholders within the pharmaceutical channel, but it's unclear at this point how concerned they should be.

According to Trump, these strategies will "start to take effect very soon."

The blueprint, says Steve Wojcik, vice president, public policy, National Business Group on Health, "generally followed what was in the Administration's proposed budget, by and large."

Evercore ISI analysts Ross Muken and Michael Newshel agree: "The specific 'immediate actions' included in the blueprint are largely a rehash of prior proposals from February's White House budget that are relatively benign for the industry and not majorly disruptive, driving some relief in the stocks today," they wrote in a May 11 research note.

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Deemed Guidance 2020 Deadline Has Impact Beyond Pharma

When the Biologics Price Competition and Innovation Act of 2009 (BPCIA) was enacted as part of the Affordable Care Act, Congress left much of the details up to the FDA to determine. In addition to creating the 351(k) biosimilar approval pathway, Congress via the BPCIA wanted to bring all biologics together under the same law, which it planned to do through the "deemed to be a license" provision. The FDA issued draft guidance in 2016 on how it interprets that section of the law, which is slated to take effect in less than two years. However, as the countdown continues, many questions remain on how the agency will implement this guidance. Manufacturers should be keeping payers abreast of the status of any impacted drugs, as they could affect the way those drugs are managed, among other things.

While most biologics are licensed under the Public Health Service (PHS) Act and approved through a biologics license application (BLA), some protein products have gained FDA approval under the Federal Food, Drug, and Cosmetic (FD&C) Act through a new drug application (NDA). The BPCIA did two things to impact this: First, it modified the definition of a "biological product" to include a "protein (except any chemically synthesized polypeptide)." Second, it said that biologics approved under the FD&C Act on or before March 23, 2020 — 10 years after the BPCIA was enacted — would transition over to the PHS Act. Thus, an approved

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marketing application for one of these drugs under section 505 of the FD&C Act would be deemed to be a license for the product under section 351 of the PHS Act.

On March 11, 2016, the FDA released draft guidance on this provision of the BPCIA (81 Fed. Reg. 13373, March 14, 2016). Titled *Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009,* the guidance describes how the FDA interprets the BPCIA provision *(RSP 4/16, p. 4)*. The agency accepted comments for 60 days; 13 comments currently are posted online.

The agency has yet to issue final guidance. However, included in the FDA's Center for Drug Evaluation and Research's guidance agenda for calendar year 2018, released Jan. 19, is *Implementation of the "Deemed to be a License" Provision of the BPCI Act: Questions and Answers.*

An FDA spokesperson tells AIS Health that the agency "is carefully considering the comments received on the draft guidance, as the Agency considers next steps regarding implementation of the 'deemed to be a license' provision of the BPCI Act. While FDA cannot provide a specific timeline for the release of any guidance, we are working very hard to finalize the guidance related to statutory transition of certain biological products."

The spokesperson clarifies that that Q&A draft guidance "is not intended to take the place of a final guidance. Instead, the 'Q&A' draft guidance is intended to facilitate planning for the March 23, 2020, transition date."

One aspect — among many — of the FDA's proposed guidance that has come under fire is its stance that an application under the FD&C Act that is pending or has tentative approval as of March 23, 2020, will need to be withdrawn and resubmitted as an application under the PHS Act. As more than one commenter contended, this seems to be directly at odds with the BPCIA, which said companies could submit applications until that date.

In the draft guidance, the FDA acknowledges that its interpretation "could have a significant impact on development programs for any proposed protein products intended for submission under section 505 of the FD&C Act that are not able to receive final approval by March 23, 2020." To address this, the agency recommends manufacturers planning submissions of NDAs or abbreviated NDAs (ANDAs) for protein products consider instead submitting a BLA under section 351(a) of the PHS Act or an abbreviated BLA (ABLA) under section 351(k), respectively.

505(b)(2) Products Pose 'Conundrum'

For companies that are considering submitting 505(b)(2) applications, a kind of hybrid approval that has some aspects of an NDA and some of generic ANDAs, the guidance notes that "Congress did not provide an approval pathway under the PHS Act that precisely corresponds to section 505(b)(2) of the FD&C Act." Such manufacturers should consider modifying their development programs in order to file for approval through either the 351(a) or 351(k) pathway, says the FDA. Drugs that would meet the requirements of a 351(k) biosimilar could apply for approval through that pathway "after the NDA for the listed drug is deemed to be a BLA (or after another product that could be a reference product for the proposed product is licensed under section 351(a) of the PHS Act)."

Without an equivalent pathway in the PHS Act, 505(b)(2) products represent a "conundrum," contends

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an industry expert who declines to be identified. "I think some will be biosimilars (Omnitrope, Basaglar), but the hyaluronidases are not remotely highly similar (different amino acid sequences), and their reference product (Wydase) is not available for them to even try to do clinical studies."

In its comments on the draft guidance, Mylan Inc. maintains that the FDA's interpretation "creates a regulatory 'dead zone'" that "will be highly disruptive" on development programs, "delaying the development and approval of competing transitional biological products for several years in at least two ways." Companies will stop submitting ANDAs "at some point well before March 23, 2020 because of the meaningful risk that such applications will not be approved before that date." In addition, manufacturers won't be able to submit 351(k) applications for a drug already approved under the FD&C Act until after that reference drug transitions over to the PHS Act.

Questions Exist on Interchangeable Status

Questions still remain on the issue of interchangeable biosimilars and how this label applies to drugs transitioning over from the FD&C Act. The FDA has approved 10 biosimilars as of *RSP* press time, but none of them has an interchangeable designation. "If you roll over products" such as all the somatropin growth hormones, "would they be considered interchangeable?" asks the unidentified source. According to Lynn Nishida, area vice president of pharmacy at Solid Benefit Guidance, and Helen Sherman, R.Ph., Pharm.D., senior vice president and chief pharmacy officer at SBG, for products transitioning from the FD&C Act to the PHS Act, "it is unclear as to whether these products will be transitioned to a stand-alone 351(a) BLA product, or (in the case of a product with an ANDA), to an 'interchangeable' biosimilar. Right now the approval pathways under the FD&C do not fully translate to that of the PHS Act, making this unclear regarding how the FDA determines this."

Exactly What Drugs Will Move Is Unclear

Also unclear is exactly what products will transition over to the PHS Act. In the draft guidance, the FDA included some examples of biologics approved under the FD&C Act, but it does not say that this is a comprehensive list of products that will be transitioned over.

For example, would Lovenox (enoxaparin) roll over? It's a product approved under the FD&C Act that is a "complex sugar mixture" but is "scientifically a biologic," according to the unnamed source *(RSP 1/12, p. 1)*. When asked shortly after the draft guidance was issued whether this drug would roll over, an FDA spokesperson told AIS Health it will not. "Enoxaparin products that have been approved under the FD&C Act do not meet the definition of 'biological product,' in the Public Health Service Act and therefore will not be affected by the transition provision," he said.

Andrew Cournoyer, R.Ph., vice president, director, payer access solutions at Precision for Value, maintains that it's important for drugmakers to keep payers apprised of "timelines and expectations.…Payers are continually watching the pipeline and factoring 'generic' or 'biosimilar' drug launches into their spend and bid projections. Uncertainty will impact predictability and diminishes a payer's ability to accurately set premiums or Medicare bids. The more transparent a manufacturer can be, the better for payer predictability."

For those drugs rolled over, "a number of outcomes could occur," Cournoyer tells AIS Health. "If it is a first entrant, the innovator product maintains prolonged time to maintain market share and deploy loss-of-exclusivity strategies to minimize biosimilar uptake upon launch. If not an innovator, other biosimilars will have advantages with building market share and gaining formulary access … or cementing themselves as 'house' biosimilars for retail, mail, LTC [i.e., long-term care] and institutional dispensing channels."

FD&C Act drugs that roll over to the PHS Act will need to be relabeled, point out Nishida and Sherman. Specifically, they tell AIS Health, "Drug chemical names, in the case where a product could roll over as biosimilar, may require a name change (e.g., addition of a suffix). Downstream claims adjudication will need to be addressed by payers." In addition, "Different regulations and labeling requirements apply to drugs approved under an NDA/ANDA vs." those approved as a BLA or ABLA.

'Entire Supply Chain' Is Likely Impacted

The transition "likely impacts the entire supply chain on that date — e.g., presumably an 'old' product labeled as a drug has to get thrown out," the unidentified expert tells AIS Health. Companies "will need to advise their downstream users as to what is happening, especially if all the nonproprietary names get suffixes and so look like they have different APIs [i.e., active pharmaceutical ingredients]."

Keeping payers abreast of the situation is important as these stakeholders "need to be aware of any specific contract language that defines how these products are handled and/or reimbursed," assert Nishida and Sherman.

"For example, payers may have unique contract definitions that define drugs approved under an NDA or ANDA vs. those that are approved via a BLA or considered as a biosimilar adjudicate a certain way (e.g., brand vs. generic status); as a result, this may have potential financial implications for payers."

"Moving to a 351 approval from a 505 pathway may impact coding of drugs from a drug databank perspective (e.g., Medi-Span)," elaborates Cournoyer. "Drugs that were considered 'brands" under 505 pathways may now be considered generics under 351. The resulting designation of 'brand' or 'generic' within the drug databank could impact default coding and ultimately tiering (e.g., 351 generics default to generic tier). The short of it is, the impact to claims systems will have to be analyzed, and new custom functionality may be needed."

View the deemed draft guidance at http://tinyurl.com/j2nd965 and view the comments on the guidance at https://tinyurl.com/y9ed255j.

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Studies Examine Adherence, Cost From Use of Certain Drugs

In some disease states treated with specialty drugs such as hemophilia and hereditary angioedema (HAE), management tactics can help ensure appropriate use of life-saving therapies. But in a condition such as multiple sclerosis (MS), in which neurologic damage accumulates over many decades, more long-term research is needed to truly understand the impact of disease-modifying drugs (DMDs), according to studies recently released by Prime Therapeutics LLC.

The first two studies focused on DMD use among members with relapsing remitting MS. The first study analyzed MS prevalence, DMD use and total pharmacy and medical claims expense, while the second study examined members' DMD adherence, relapses and the association between the two.

FDA Has Approved Multiple DMDs for MS

The FDA has approved more than a dozen DMDs to treat relapsing remitting MS. Primary outcomes in clinical trials of these therapies have focused on measures of clinical relapses.

The first study looked at 15 million commercially insured members who were continuously eligible from October 2013 through September 2017, who were younger than 65 years old as of Sept. 30, 2017, and who had at least two inpatient or at least three outpatient claims with an MS diagnosis code or who had a claim for an MS DMD other than Tysabri (natalizumab), which also is used to treat Crohn's disease.

Researchers examined the number of days covered by a DMD between October 2016 and September 2017 to determine MS prevalence, DMD adherence and annual total pharmacy and medical claims for members with MS. Out of 4.04 million continuously enrolled members, researchers found 8,356 with an MS diagnosis. Of those members, 5,514 had a DMD claim within the most recent 12 months, while another 819 had a DMD claim in the preceding three years.

The study found MS members with a DMD claim between October 2016 and September 2017 had $84,712 in per-patient per-year (PPPY) total claims costs, with DMDs accounting for more than 80% of that total. For all MS members, total claims costs were $63,175 PPPY, with 71.6% of the total attributable to DMDs. Matched members without MS had a total PPPY claims cost of $7,642.

Among the 5,514 with a DMD claim over the most recent 12 months, 37.2% were nonadherent (defined as a proportion of days covered for a DMD less than 80%). If those nonadherent members became adherent, they would add $7,948 PPPY in incremental DMD cost. And if the 819 who had had a DMD claim in the preceding three years became adherent to therapy, they would add $6,710 PPPY.

Better Adherence Would Not Offset Costs

"A clinical program that moves all non-adherent DMD members to adherent and members who had discontinued DMD to a DMD adherent state would add an additional $14,700 PPPY in MS DMD costs to the current $63,200 PPPY total MS health care cost, for a new MS PPPY cost of $77,900," concluded researchers.

"Unfortunately, the $14,700 PPPY in new MS DMD costs is more than could be potentially saved in non-DMD medical care costs, therefore it is not possible to obtain a direct medical cost offset return on investment from improving adherence. The value of treating more MS members with DMDs or improving adherence needs to be assessed from a societal perspective and with a time horizon of many years."

The second study looked at 15 million commercially insured members who were continuously eligible from October 2013 through September 2017, who were younger than 65 years old as of Sept. 30, 2017, and who had at least two inpatient or at least three outpatient claims with an

MS diagnosis code and a pharmacy or medical claim for a DMD between October 2013 and September 2014. Researchers analyzed the proportion of days covered for DMDs to determine whether members were adherent or not — adherent again was considered at least 80% — and claims evidence of a relapse. Based on 4,753 qualifying members, Prime found that 50.2% — 2,859 members — were adherent to DMDs during a three-year follow-up period. Of that group, 18.2% had at least one relapse compared with 24.9% within the nonadherent group.

"If the observed association is causal, this finding implies that, on average, improving adherence to DMD therapy for 15 not adherent MS members for three years would be expected to prevent one member from having a moderate to severe relapse," conclude researchers. "A DMD cost of $3 million to obtain adherence in 15 members would be expected to save $9,000 in direct medical costs from avoidance of moderate to severe relapses for one

Prime Says Managing Soliris Per Its Clinical Trial MG Population Will Help With Appropriate Use

Prime Therapeutics LLC recently released a handful of studies analyzing, among other things, costs for various specialty therapies based on their experience on the U.S. market. But another study examined the potential cost impact of a new indication for which data are not yet available. For this study, researchers based estimates on two already-approved uses of the therapy and underscored the importance of a utilization management program to ensure its appropriate use.

At more than $700,000 for the first year of treatment, Soliris (eculizumab) has the distinction of being one of the costliest specialty drugs available. The FDA initially approved Soliris in 2007 to treat paroxysmal nocturnal hemoglobinuria *(RSP 4/07, p. 4)* and then gave it a second indication for atypical hemolytic uremic syndrome in 2011 *(RSP 11/11, p. 8)*. Most recently, in October 2017, the agency granted it a third indication, for people with myasthenia gravis who are anti-acetylcholine receptor antibody positive (anti-AchR positive), an indication that's approximately 74% to 88% of the MG population *(RSP 11/17, p. 8)*. But, note the researchers, the FDA approved the MG label for a broader population than the drug's phase III REGAIN clinical trial, which looked at people whose MG was refractory, who represent about 10% of the anti-AchR positive MG population.

Prime looked at claims for 15 million commercial insured members in 2016 and found 3,493 members had at least one diagnosis code for MG among five fields within a medical claim. It then narrowed them down to members with a primary field MG code (2,721 members) and then by those members with at least two primary field diagnoses at least 30 days apart who were at least 18 years old (1,574).

Among those, it found 511 members with at least one medical or pharmacy claim for an immunosuppressant drug or immune globulin in 2016. Prime estimated about 51 of these would be eligible for Soliris treatment based on the clinical trial data.

But when Prime evaluated the 1,574 members based on the drug's approved label, it found that 1,165 would be eligible for treatment.

Before the new MG indication, Soliris per-member per-month cost already was increasing: up 51% from first-quarter 2016 ($0.38 PMPM) to third-quarter 2016 ($0.58 PMPM). Prime estimates that if the trend continues, third-quarter 2018 PMPM cost will be $0.74.

If the 51 members based on the clinical trial data were adherent to therapy for one year, the PMPM impact would be $0.20, for a total of $0.94 PMPM in third-quarter 2018. But if 30% uptake by the broader label-based population is assumed, the potential impact is $1.37 PMPM for a total of $2.11 PMPM in third-quarter 2018.

"Without clinical programs in place to manage eculizumab use according to the clinical trial, the PMPM impact could exceed $2.10, more than 2-fold the expected PMPM of $0.94 with active clinical programs," concluded the study's authors. "Clinical programs such as utilization management combined with other strategies to ensure appropriate use and billing should be employed for expensive specialty products, like eculizumab, because there are minimal cost offset opportunities from medical savings."

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MS patient. An investment of $333 to save $1 in direct medical costs." In addition, says the study, DMDs "may delay progression of MS."

Another study examines the use of extended half-life (EHL) recombinant coagulation factor in hemophilia as opposed to conventional standard half-life (SHL) products. The FDA approved the first EHL factor XIII product for people with hemophilia A in June 2014 and the first EHL factor IX product for hemophilia B in April 2014.

Study Analyzed Members Switching to EHL

Prime analyzed pharmacy and medical claims from January 2013 to July 2017 among 15 million members. It identified members who had switched from a SHL product to an EHL one and who had at least 180 days of continuous eligibility before their initial EHL claim and 210 days after it. The company found 34 people with hemophilia A and 20 with hemophilia B who had switched from a SHL factor and remained on an EHL product.

Among those hemophilia A members, the mean six-month SHL cost was $127,168, compared with a post-switch, six-month mean cost for EHL factor of $300,429. Mean SHL units over the same time period were 115,424 compared with 167,282 units of EHL factor.

For people with hemophilia B, the mean six-month SHL cost was $116,909 compared with $230,209 for EHL. The mean SHL units were 104,637 compared with 85,745 for EHL units.

The study also found that while the EHL factor IX products have had more uptake than the EHL factor XIII products, the factor XIII therapies are used by more people because hemophilia A is more common than B.

"In this real-world data analysis using integrated medical and pharmacy claims data, members converting to EHL factor products for both hemophilia A and B were associated with substantially higher costs," conclude the authors. "The clinical value of the doubling in cost will need to be justified." And while there was a decrease in EHL factor units among people with hemophilia B, there was an increase in mean units among people with hemophilia A who switched to an EHL therapy.

According to the study, "Because four in five hemophilia A members still are using a SHL product, there is substantial risk for many more EHL conversions with an anticipated more than doubling in cost, at an additional $300,000 per year cost per EHL treated member. Pharmacy benefit managers and health plans will need to closely assess EHL cost effectiveness."

Most of HAE Care Costs Are for Drugs

In the fourth study, Prime examined the costs of treating someone with HAE. Medications to treat the condition made up more than 97% of the total one-year cost of care.

The FDA has approved HAE medications for prophylactic use to prevent attacks and also for on-demand use during an attack. Treatment guidelines recommend that people with the condition keep both kinds of medications on hand. The drugs may be adjudicated in both the pharmacy and the medical benefit *(RSP 3/18, p. 3)*.

Prime identified 226 members who had at least one pharmacy or medical benefit claim for an HAE drug in the first half of 2016 out of more than 15 million commercially insured members from July 1, 2015, to June 30, 2017. Of those, 111 met continuous enrollment criteria, meaning they were continuously enrolled six months prior to that claim and 12 months following it.

Ten Members' Costs Exceeded $1 Million

Prime analyzed these members for 12 months after their initial claim and found the average one-year total cost of care was $409,925 — of which drug costs represented $395,507 compared with all other medical and pharmacy costs. Of those 111 members, 48 had claims for at least two HAE therapies, and 10 members had drug expenditures totaling more than $1 million. These 10 people represented $13.3 million of the total $43.9 million in overall HAE drug spend in Prime's commercial book of business. Almost one-quarter had HAE drug claims in both the medical and the pharmacy benefits.

Shire's Cinryze (C1 esterase inhibitor [human]) — the first drug the FDA approved to treat HAE, in 2008, for prophylaxis *(RSP 11/08, p. 6)* — had the highest total spend among the drugs studied, at $25.1 million, or 57% of overall HAE drug spend. It was followed by another Shire drug, Firazyr (icatibant injection), indicated for acute attacks, which accounted for $13.2 million, or 30%, of all drug spend.

With the costs of the drugs making up 97% of the total cost of HAE care, "we do not believe medical costs can be lowered through use of HAE drugs," says Catherine Starner, Pharm.D., health outcomes consultant senior principal at Prime. "Rather, diligent pharmacist case management following a patient's first use of HAE drugs must be provided to help ensure appropriate use and realize cost savings

regardless of which benefit (medical or pharmacy) the HAE drug is billed."

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Digest: Plans' Focus Remains on Cancer, Site-of-Care Programs

It should come as no surprise that managing oncology drugs and services remains a challenge for health plans. Respondents to a survey by EMD Serono, Inc. cited it as their top challenge, tied with determining the value of specialty drugs and ensuring clinically appropriate use of specialty therapies, when asked to rank their top five of nine challenges. Those three challenges were also the top ones selected by respondents for the previous edition of the report.

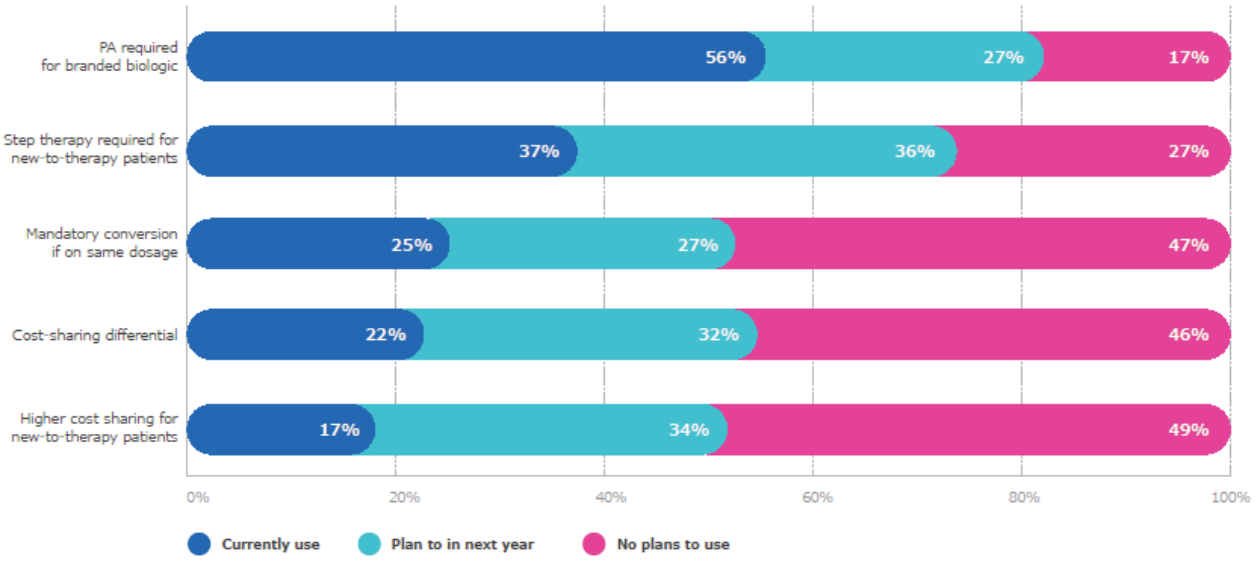
Released at the end of April, the 14th edition of the *EMD Serono Specialty Digest: Managed Care Strategies for Specialty Pharmaceuticals* is based on survey responses from 59 commercial health plans representing more than 76 million covered lives.

Site-of-care programs continue to rise in use, up from 26% of respondents in 2013 to 61% in 2017. That's a 135% increase, points out Robert Truckenmiller, senior vice president, market access and customer solutions, EMD Serono. "And the trend is expected to continue — more than half of those plans without a current site-of-care program said they will implement one in the next 12 months, and 20% of plans said that moving infused drugs to lower-cost sites of care is their highest-priority goal in the next 12 to 24 months. Today, health plans are increasingly turning to site-of-care programs to provide patients with the highest quality experience at the lowest possible cost."

Intravenous immune globulin (89%), rheumatoid arthritis/Crohn's (86%) and multiple sclerosis (MS) (67%) were the top therapeutic categories for site-of-care strategies.

Eighty-four percent of respondents — up from 38% in 2016 — said they collaborate with oncologists to create plan-specific oncology pathways. This, Truckenmiller tells AIS Health, represents "a dramatic shift in how these pathways are created.…Health plans are relying more heavily on oncologist collaboration to develop cancer treatment pathways. In fact, 42% of health plans use at least one clinical pathway in oncology treatment — in line with results seen in the previous edition of the Specialty Digest.…Respondents preferred the collaborative approach over using third-party pathways (28%), creating proprietary pathways internally (24%) or relying on oncologists to develop their own pathways (12%)."

Management Policies in Place or Being Considered for Biosimilars Currently Approved



PA = prior authorization

SOURCE: EMD Serono, Inc., *EMD Serono Specialty Digest: Managed Care Strategies for Specialty Pharmaceuticals,* 14th edition, released April 30. Download a copy of the digest at http://specialtydigest.emdserono.com.

According to Truckenmiller, "These are noteworthy findings as payers are realizing that connecting with the experts directly helps them to better understand how to manage treatment and services as part of their health plans. This more collaborative approach is important, and is also in line with recent recommendations from the American Society of Clinical Oncology (ASCO), which urges all stakeholders to work together to ensure treatment pathways promote high-quality patient care."

As the attention on biosimilars grows, the top management strategy is requiring prior authorization for the branded biologic, cited by 56%

New FDA Specialty Approvals

✦ ***April 17: The FDA approved Rigel Pharmaceuticals, Inc.'s Tavalisse (fostamatinib disodium hexahydrate)*** for the treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to prior therapy. The tablet is the first and only spleen tyrosine kinase inhibitor for adults with chronic ITP. Pricing is not yet available for the drug. Dosing is 100 mg twice daily; it can be increased to 150 mg twice daily after four weeks. Visit http://tavalisse.com.

✦ ***April 17: The FDA approved Ultragenyx Pharmaceutical Inc.'s Crysvita (burosumab-twza)*** to treat people at least one year old with x-linked hypophosphatemia. Crysvita is a fibroblast growth factor 23 blocking antibody, and the agency gave the drug breakthrough therapy and orphan drug designations, as well as a rare pediatric disease priority review voucher. Dosing of the subcutaneous injectable is weight-based. The product will cost about $160,000 annually for children and $200,000 for adults. Visit https://crysvita.com.

✦ ***April 18: The FDA expanded the label of Tagrisso (osimertinib)*** to include the first-line treatment of people with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test (see brief below). The agency initially gave the AstraZeneca tablet accelerated approval in 2015 *(RSP 12/15, p. 8)* and then regular approval in 2017 for another form of NSCLC *(RSP 4/17, p. 8)*. The recommended dose is 80 mg once daily. Website GoodRx lists the price of 30 80 mg tablets as more than $14,500. Visit www.tagrissohcp.com.

✦ ***April 18: The FDA granted another indication to the cobas EGFR mutation test v2*** as a companion diagnostic to Tagrisso for its new use (see brief above). The agency also has approved the Roche Molecular Systems Inc. test for use with Tagrisso's other NSCLC indication, as well as with Tarceva (erlotinib) for NSCLC. Visit https://tinyurl.com/yco88o7g.

✦ ***April 23: The FDA approved Amerigen Pharmaceuticals Ltd. and Dipharma S.A.'s miglustat*** for the treatment of adults with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not an option. It is the first generic of Actelion Pharmaceuticals US, Inc.'s Zavesca. Recommended dosing of the capsule is 100 mg three times daily. GoodRx lists the price of a Zavesca dose pack with 90 100 mg capsules as around $27,000. Visit www.amerigenpharma.com.

✦ ***April 26: The FDA approved Otsuka Pharmaceutical Co., Ltd.'s Jynarque (tolvaptan)*** to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease. The company says the selective vasopressin V2-receptor antagonist is the first approved for this indication. Otsuka says the wholesale acquisition cost of a 28-day pack is $13,041.10. Visit www.jynarque.com.

✦ ***April 30: The FDA approved the combination of Tafinlar (dabrafenib) and Mekinist (trametinib)*** for the adjuvant treatment of people with melanoma with BRAFV600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph nodes following complete resection. The agency first approved the Novartis Pharmaceuticals Corp. drugs in 2013 *(RSP 6/13, p. 8)*, and they have multiple indications. This indication had priority review and breakthrough therapy designation. The recommended dose of BRAF inhibitor Tafinlar is 150 mg twice daily, and for MEK inhibitor Mekinist, it is 2 mg once daily. GoodRx lists the price of 120 Tafinlar 75 mg capsules as more than $9,300 and 30 Mekinist 2 mg tablets as more than $10,200. Visit www.us.tafinlarmekinist.com.

✦ ***May 1: The FDA approved an additional indication for Kymriah***

(see chart, p. 7). That was followed by requiring step therapy for patients new to therapy, with 37% of respondents having this in place; this is the top strategy respondents said they plan to implement in the next year, cited by 36%. Sixty-nine percent said they plan to negotiate rebates on biosimilars.

Among other findings are the following:

✦ ***36% of respondents said new and/or enhanced utilization management and/or prior-authorization programs were the most important initiative*** their company had taken the previous year to manage specialty medications. This was followed by 14% who cited changes to medical and/or pharmacy

New FDA Specialty Approvals *(continued)*

(tisagenlecleucel) for the treatment of adults with relapsed or refractory large B-cell lymphoma after at least two lines of systemic therapy. The agency initially approved the Novartis infusible as the first chimeric antigen receptor T cell (CAR-T) therapy in August *(RSP 9/17, p. 10)*. The price of the one-time treatment for the newest indication is $373,000, the same price as the second CAR-T therapy, Yescarta (axicabtagene ciloleucel) *(RSP 11/17, p. 8)*. Visit www.us.kymriah.com.

✦ ***May 3: The FDA gave accelerated approval to Portola Pharmaceuticals, Inc.'s Andexxa (coagulation factor Xa [recombinant], inactivated-zhzo)*** as an antidote for people treated with factor Xa inhibitors Xarelto (rivaroxaban) and Eliquis (apixaban) when reversal of anticoagulation is necessary due to life-threatening or uncontrolled bleeding. The agency gave the product breakthrough therapy and orphan drug designations. There are two dosing regimens, and the drug's wholesale acquisition cost is $27,500. Visit www.andexxa.com.

✦ ***May 4: The FDA approved the combination of Tafinlar and Mekinist*** for the treatment of anaplastic thyroid cancer that cannot be removed by surgery or is metastatic and is BRAF V600E mutation-positive. This was the second indication granted to the pair of drugs within five days (see brief above). The FDA gave priority review and breakthrough therapy and orphan drug designations for this indication. Visit www.us.tafinlarmekinist.com.

✦ ***May 8: The FDA granted an additional indication to Darzalex (daratumumab)*** in combination with Velcade (bortezomib), melphalan and prednisone for people with newly diagnosed multiple myeloma who are not eligible for an autologous stem cell transplant. The agency first gave the Janssen Biotech, Inc. infusible accelerated approval in 2015 *(RSP 12/15, p. 8)*. Dosing for the CD38-directed antibody is weight-based. Blink Health lists the price of a 20 mg/mL vial as more than $3,200. Visit www.darzalex.com.

✦ ***May 11: The FDA approved another indication for Gilenya (fingolimod)*** for the treatment of relapsing forms of multiple sclerosis in people between 10 and 18 years old. The Novartis capsule is the first disease-modifying therapy to gain FDA approval for use in children and adolescents. The agency gave the drug breakthrough therapy designation and priority review for this use. The FDA initially approved the drug in 2010 for use in adults *(RSP 10/10, p. 1)*. Dosing for people weighing more than 40 kg is 0.5 mg once daily; for people weighing 40 kg or less, dosing is 0.25 mg daily. GoodRx lists the price of one 28-capsule package of 0.5 mg Gilenya as more than $5,400. Visit https://gilenya.com.

✦ ***May 14: The FDA gave another indication to the subcutaneous version of Actemra (tocilizumab)*** to treat active polyarticular juvenile idiopathic arthritis in people at least two years old as a monotherapy or in combination with methotrexate. The agency initially approved the interleukin-6 receptor antagonist from Genentech, Inc., a member of the Roche Group, in 2010 for the treatment of rheumatoid arthritis *(RSP 1/10, p. 6)*. Dosing for the new use is weight-based. GoodRx lists the price of two 162 mg/0.9 mL syringes as more than $2,100. Visit www.actemra.com.

✦ ***May 15: The FDA approved Hospira Inc.'s Retacrit (epoetin alfa-epbx)*** to treat anemia caused by chronic kidney disease, chemotherapy or zidovudine use in people with HIV infection, as well as for use before and after surgery to reduce the need for red blood cell transfusions. The injectable from Pfizer Inc.'s Hospira is the first biosimilar of Epogen/Procrit (epoetin alfa) the FDA has approved. Dosing varies depending on the patient and indication. GoodRx lists the price of four vials of Epogen 10,000 units/mL as more than $660. Visit www.pfizer.com.

benefit coverage or changes to improve parity.

✦ ***High-deductible plans saw a decline in the use of copayments*** (32% to 26%) and coinsurance with a maximum out-of-pocket member share (36% to 30%) in the pharmacy benefit, while coinsurance without a maximum OOP increased (32% to 44%).

✦ ***Standard-deductible plans saw a similar trend within their pharmacy benefit,*** although copays were still the top design, cited by 45%, down from 46%. Coinsurance with a max OOP dropped from 37% to 23%, and coinsurance without a max OOP rose from 18% to 32%.

✦ ***Within the medical benefit, coinsurance remained the top cost-sharing design*** across the physician office, outpatient hospital departments and home infusion sites.

✦ ***The use of partial-fill programs increased to 58% in 2017,*** up from 45% the previous year. While oral oncology remained the top category for these programs, its use declined from 100% in 2016 to 79% in 2017. Fourteen percent of respondents said they plan to implement a partial-fill program within the next year, with oral oncology (88%) and anti-inflammatory biologics for rheumatoid arthritis/Crohn's psoriasis (38%, both oral and subcutaneous/intramuscular) being the most-targeted classes for this tactic.

✦ ***Within the physician office setting,*** 51% of respondents reimburse all physicians at the same rate, an increase from 36% in 2016.

✦ ***Episode-of-care or bundled reimbursement models*** are used on a full-time basis for at least one disease state by only 7% of respondents, with 12% saying they have at least one program in place on a pilot basis, a decline in the trend over the last few years. But 68% of respondents said they have no plans to implement these payments.

✦ ***The use of outcomes-based contracts declined,*** with only 8% of respondents saying they have one in place, down from 16%. Only 19% plan to put one in place over the next year, a drop from 26%. And 73% of respondents said they have no plans to use one, down 59%.

✦ ***Asked what specialty pharmacy services they would rate the highest,*** 53% of respondents said dispensing, followed by 22% citing patient services. Among the lowest-rate services, reporting came in No. 1, cited by 41% of respondents, and then medical management, 19%.

✦ ***78% of respondents said they require mandatory dispensing through specialty pharmacies for certain drugs.*** Injectable MS, inflammatory conditions and hepatitis C drugs were the top classes, all cited by 78% of respondents.

✦ ***20% of respondents reported using MS clinical pathways,*** with 12% planning to implement a program in the next year. Among those with one in place, 63% include infused MS drugs and 58% include oral treatments, and 58% include depression screening and management. Use of the pathways program is mandatory for 42% of respondents.

Download the digest at http://specialtydigest.emdserono.com. ✧

Trump Proposes Rx Pricing Tactics

continued from p. 1

However, they state, the blueprint "does highlight 'further opportunities' that include the potential for more aggressive actions — including 'restricting the use of rebates' by revisiting the Anti-Kickback safe harbor and considering fiduciary status for PBMs."

Trump said that "eliminating the middlemen," which have become "very, very rich," would be among the efforts. "They won't be so rich anymore."

So should PBMs be concerned? "No," maintains Elan Rubinstein, Pharm.D., principal at EB Rubinstein Associates. "Trump does not understand the prescription drug marketplace."

The idea of "considering the fiduciary status for" PBMs is "interesting and is something that some employers have wondered about," Wojcik says. However, points out Rubinstein, "HHS recommends nothing, is looking for suggestions and states that it may implement regulations on this at a later point."

Drug Rebates Are Under Fire

One of the practices within the pharmaceutical system that has received a large amount of attention is rebates. Trump said that the administration will address the ability of "middlemen to pocket rebates." Specifically, the blueprint includes as a "further opportunity" — as opposed to an "immediate action" — "measures to restrict the use of rebates, including revisiting the safe harbor under the Anti-Kickback statute for drug rebates," as well as "additional reforms to the rebating system."

However, Bill Sullivan, principal consultant at Specialty Pharmacy Solutions LLC, questions whether the rebate system is really in jeopardy. For one, he points to legislation defining kickbacks: "The federal Anti-Kickback Statute ('Anti-Kickback Statute') is a criminal statute that prohibits the exchange (or offer to exchange), of anything of value, in an effort to induce (or reward) the referral of federal health care program business. See 42 U.S.C. § 1320a-7b. The Anti-Kick-

back Statute is broadly drafted and establishes penalties for individuals and entities on both sides of the prohibited transaction."

Sullivan points out that "payers and PBMs do not fit the definition of being in a position to 'induce or reward the referral of federal health care program business' since rebates are not paid by manufacturers on federal program transactions."

Anti-Kickback Law Would Need Changes

For drug rebates to be considered kickbacks, he tells AIS Health, "An amendment to the current law would be the first practical step to clarify/define rebates as kickbacks as (I believe) it is not at all clear now. However, since there are no rebates on 'federal' business, it is a moot point. A totally new law prohibiting kickbacks on commercial business would also be required for this campaign to be truly meaningful. Such prohibitions already exist for physicians (e.g., self-referral) but there is no effective 'self-referral' for a payer/PBM."

Asked about the likelihood of drug rebates being considered kickbacks and, thus, illegal, Sullivan replies, "The drug lobby is right up there with the NRA, military manufacturers and insurance companies. Payers (and PBMs) will push back on any legal remedies since their financials would be radically impacted by huge reductions in 'unearned revenue' (= rebates). They would have to put all drugs on a level pricing plane, and that would likely raise costs by eliminating 'preferred' formularies."

The issue of removing the safe harbor for rebates is one that FDA Commissioner Scott Gottlieb, M.D., and HHS Secretary Alex Azar mentioned ahead of Trump's speech. Muken and Newshel point out that Azar criticized PBMs and rebates in a press briefing "and called for 'fundamental structural change.' At this point it's still a threat, and now the question is whether the administration follows through or not on actions that could pose bigger risks to the drug channel. We also await more detail in the rulemaking notice/request for information document from HHS expected to be posted after the close. With that notice kicking off a regulatory process that could still yet result in more disruptive proposals — and in the meantime political rhetoric on drug pricing likely to get louder as the midterm elections approach and Democrats call for even more aggressive actions — we don't think the clouds have cleared yet."

> **"Payers (and PBMs) will push back on any legal remedies since their financials would be radically impacted by huge reductions in 'unearned revenue.'**

Among other targets, Trump also called out pharma, maintaining that the "drug lobby is making a fortune at the expense" of Americans. The reforms, he said, would "derail the gravy train for special interests."

He was slightly more specific in saying that "Medicare Part D plans [will have] new tools to negotiate." In addition, the administration will "ban the pharmacist gag rule" preventing them from telling Part D beneficiaries when paying out of pocket would be cheaper than using their insurance.

The administration "will demand fairness overseas" in drug pricing. "Americans will not be cheated any longer," Trump contended. The blueprint explains that "HHS may support better negotiation by… working in conjunction with the Department of Commerce, the U.S. Trade Representative, and the U.S. Intellectual Property Enforcement Coordinator to develop the knowledge base necessary to address the unfair disparity between the drug prices in America and other developed countries. The Trump Administration is committed to making the appropriate regulatory changes and seeking legislative solutions to put American patients first."

Rubinstein contends that "The most troublesome idea is that HHS suggests leaning on countries that control drug prices to '...address the unfair disparity between the drug prices in America and other developed countries' — as if the market pricing solution in the U.S., if implemented in all industrialized nations, would lead to better control of drug spend internationally."

"They want drug companies to increase their prices in EU and Japan," says consultant Jim Martin, Ph.D. "I like that …. we are going to ask pharma to increase prices overseas so they can lower prices here. Hmm …. We will put tariffs on goods to protect IP [i.e., intellectual property]. It seems like a similar disconnect," he tells AIS Health.

Blueprint Fails to Address 'Key Problem'

On this issue, the blueprint, asserts Rubinstein, "does not address the key problem, which is that net prices for brand name drugs are much higher in the U.S. than in other industrialized nations. The proposed solution does not include using government payer leverage to negotiate better net prices, although Trump's quote on pg. 20 would seem to imply that he supports this: 'We're the largest buyer of drugs in the world, and yet we don't bid properly.'

"But of course, the problem is that the U.S. market isn't a 'we' while most

other industrialized nations have central control of drug price and access — meaning they are a 'we,'" he says.

In a speech following Trump's, Azar mentioned mandating that pharmaceutical ads on TV disclose the drugs' prices. "We're going to look into having the FDA require this," he said.

However, points out Rubinstein, the agency does not have the power to do this. On its website, the FDA spells out exactly what content different types of ads are required to include — based on requirements by Congress that the FDA oversees — and not one of the types says an ad must contain pricing information.

So what actions proposed by the administration would have the most impact on drug prices?

According to Wojcik, "Given the trend and outlook for specialty pharmacy prices and spending, those that would increase biosimilar competition and eliminate Medicare and Medicaid policies that unintentionally drive up prices for specialty pharmacy would have the most impact if implemented."

Some points within Section IV of the blueprint, says Rubinstein, "may help reduce net drug prices — like encouraging value-based prices and site-neutral Medicare payment for drugs. Indication-based pricing is interesting as a way to encourage higher value use of drugs, but it would be difficult and confusing to manage."

That said, Rubinstein maintains that "Several things in this section are potentially problematical — like allowing Part D plans 'flexibility to manage high cost drugs that do not provide Part D plans with rebates or negotiated fixed prices, including in the protected classes,' eliminating the appeals process and restarting the [Medicare Part B] drug competitive acquisition program."

At the close of his speech, Trump contended that "These reforms are just the beginning.…It's going to happen, and it's going to happen quickly.… We're going to see prices go down. It'll be a beautiful thing."

Download the blueprint at https://tinyurl.com/y7wgme35.

Contact Rubinstein at elan.b.rubinstein@gmail.com, Sullivan at wsullivan@specialtyrxsolutions.com and Wojcik through Ed Emerman at eemerman@eaglepr.com. ✧

News Briefs

✦ ***BioScrip, Inc. reported a first-quarter net loss of $13.0 million,*** or 12 cents per share, compared with a net loss of $19.7 million, or 18 cents per share, in the prior-year period. The infusion services provider had revenue of $168.6 million for the most recent quarter, down from $217.8 million in the first quarter of 2017. Visit www.bioscrip.com.

✦ ***Diplomat Pharmacy, Inc. reported a first-quarter 2018 net loss of $0.5 million,*** or 1 cent per share, compared with net income of $4.4 million, or 6 cents per share, for the year-ago period. The specialty pharmacy services provider had revenue of $1.3 billion for the most recent quarter, up from $1.1 billion in the first quarter of 2017. Visit www.diplomat.is.

✦ ***Praluent (alirocumab) will be the exclusive PCSK9 on Express Scripts Holding Co.'s National Preferred Formulary as of July 1.*** The move follows the release of clinical trial data showing the Regeneron Pharmaceuticals, Inc./Sanofi drug "significantly reduced the risk of major adverse cardiovascular events in patients who had suffered a recent acute coronary syndrome event" and was associated with lower risk of death overall *(RSP 3/18, p. 12)*. Those outcomes prompted the companies to lower the high cholesterol therapy's net price "in exchange for straightforward, more affordable patient access" from the PBM. Contact Brian Henry at bhenry@express-scripts.com.

✦ ***PEOPLE ON THE MOVE:*** Diplomat Pharmacy, Inc. named ***Brian Griffin*** CEO and chairman of its board of directors effective June 4. He previously was executive vice president and CEO of IngenioRx, Anthem, Inc.'s PBM. Following former CEO and co-founder ***Phil Hagerman***'s retirement earlier this year *(RSP 1/18, p. 12)*, Diplomat named board member ***Jeff Park*** interim CEO. He resigned that position May 8, and Chief Financial Officer and Treasurer ***Atul Kaythekar*** was named interim CEO on May 11.… Precision for Value named ***Marylou Buyse, M.D.,*** vice president, integrated health solutions; ***Joseph Honcz, R.Ph.,*** vice president, payer access solutions; and ***Elizabeth Oyekan, Pharm.D.,*** senior director for the quality and population health solutions team. Buyse had been a senior medical director at Highmark, Inc., Honcz was an executive director in the network and clinical services division at Aetna Inc., and Oyekan was vice president of operations and quality with Kaiser Permanente.