Written Statement for the Record

Energy & Commerce Committee, Subcommittee on Health

"Examining Medical Product Manufacturer Communications"

July 12, 2017

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Summary of Statement

Existing laws and regulations hinder the ability of biopharmaceutical manufacturers to share information proactively on emerging therapies with population health decision makers, who have indicated that waiting until FDA approval is often too late for the critical planning, budgeting, and forecasting associated with health benefit design, especially given the recent influx of high-cost medications and focus on value-based payment models, and that they need access to information about emerging therapies at least 12-18 months prior to FDA approval. Therefore, in September 2016, a diverse group of stakeholders came together to develop consensus recommendations on how to enable preapproval communications, while still maintaining appropriate safeguards to prevent this information from reaching unintended entities.

In January 2017, the FDA released a draft guidance document explaining how "FDA does not intend to object" to certain types of information being shared prior to approval. However, the draft guidance remains non-binding and does not provide the level of certainty needed to truly operationalize Pharmaceutical Information Exchange (PIE). Therefore, there is a need for Congress to engage in this topic to create a legislative safe harbor for PIE so that it is clear that the proactive dissemination of certain information does not violate the prohibitions against preapproval promotion and does not run afoul of the labeling, misbranding, and intended use provisions of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. *H.R. 2026 – The Pharmaceutical Information Exchange (PIE) Act of 2017* incorporates the consensus recommendations developed by the multi-stakeholder group, creates a very narrow safe harbor for a very specific purpose, and will improve patient access to emerging medication therapies.

Statement

As the U.S. health care system evolves from a historical payment system based upon quantity and process to a modernized system rewarding quality and improved patient outcomes, the need for timely communication between biopharmaceutical manufacturers and population health decision makers (e.g. payors, provider sponsored health plans, pharmacy benefit managers, accountable care organizations, and integrated delivery networks) about emerging therapies is critical for the successful shift to a value-driven system. The current pipeline of therapies awaiting Food and Drug Administration (FDA) approval offer promising, but often costly, treatments or cures for chronic diseases that previously had few options for long-term management. However, existing laws and regulations hinder the ability of biopharmaceutical manufacturers to share information proactively on emerging therapies with population health decision makers. Allowing for proactive Pharmaceutical Information Exchange (PIE) on these pipeline therapies will help population health decision makers to identify cost offsets for other medical interventions that impact patient costs.

Three Main Imperatives Driving the Need for Communications Prior to FDA Approval

A. **Planning, Budgeting, and Forecasting for Benefit Design -** As a result of federal laws and state mandates, population health decision makers are required to evaluate their plan designs, formularies, and rates 12-18 months in advance to meet submission deadlines 6-9 months before the beginning of the intended plan year. For example, for the 2016 coverage year, population health decision makers analyzed 2014 data to submit their 2016 rates by spring 2015. The budget impact of new therapies that were approved by the FDA after spring 2015 could not be integrated into the 2016 rates.

As detailed in Appendix I, a recent prime example of the need for population health decision makers to account for new medications entering the marketplace was the introduction of novel treatments for hepatitis C infection in 2013. Population health decision makers were not properly prepared for the impact of these new therapies and the inaccuracies in budgeting and forecasting resulted in limited patient access to these medications. Had PIE been available during this timeframe, population health decision makers would have had better knowledge of the impact of the new hepatitis C medications, would have been able to better plan, budget, and forecast, and would have been able to minimize disruptions to patient access to these medications.

Therefore, accurate forecasting and rate setting is critical to ensure patients have continued access to affordable coverage for their health care needs. With rates being filed over a year in advance, proper planning, budgeting, and forecasting are integral for population health decision makers to accurately account for the impact of new therapies that will enter the market.

B. **Value-Based Payment Models -** There is an increased focus on value-based payment models as evidenced by the Medicare Shared Savings Program and a range of initiatives launched and proposed by the Center for Medicare and Medicaid Innovation (CMMI). Successful implementation of value-based payment models requires understanding the overall value of a therapy, including how pharmacy spending can offset medical costs and vice versa. In addition, it requires downstream planning for population health decision makers to change plan design, formularies, and necessary contracts in advance of submitting rates at least a year in advance of the intended coverage year. Therefore, to increase the utilization of value-based payment models, it is important for

biopharmaceutical manufacturers and population health decision makers to be able to share information prior to FDA approval about emerging therapies to provide sufficient time to implement these models in a timely and effective manner upon FDA approval.

C. **Patient Access to Breakthrough Therapies** - *The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)* created an expedited approval pathway allowing the FDA to grant priority review if preliminary clinical trials indicate a therapy may offer substantial treatment advantages over existing options for patients with serious or life-threatening diseases. Under the expedited approval pathway, therapies may be approved by the FDA before clinical trial data is published and made publicly available, thereby making it very difficult for population health decision makers to determine whether a therapy is appropriate for a patient if they receive a coverage request prior to publication of the data. Guidelines and peer-reviewed compendia sources are even further delayed in providing population health decision makers with reputable reference material for making sound clinical judgements when published clinical data is not available.

In 2016, of the 22 new molecular entities approved by the FDA, 32% received breakthrough therapy designation. This percentage is expected to increase in the future as a result of provisions included in the *21st Century Cures Act* to advance medical product innovation and ensure that patients get access to treatments as quickly as possible.

As detailed in Appendix I, I personally experienced a situation where we received a coverage request for pembrolizumab, a medication approved by the FDA under the breakthrough therapy designation to treat head and neck squamous cell carcinoma. The medication was approved by the FDA on August 5, 2016. However, three weeks later when we received our first patient coverage request,

clinical trial data was still not published and not available. We had no information available to us to determine whether the medication was appropriate for our patient and that resulted in an undue delay in her care. Had we been able to communicate with the manufacturer leading up to FDA approval of the medication, we would have had access to the data available at the time of FDA approval and been able to make a coverage decision for our patient, minimizing delays in her care.

In these situations, enabling communications prior to FDA approval is critical to ensuring population health decision makers are aware of the information available to date on emerging therapies granted breakthrough designation by the FDA so they are prepared to make coverage decisions for patients immediately upon FDA approval.

Multi-stakeholder Group Develops Consensus Recommendations for Enabling Communications Prior to FDA Approval

In September 2016, the Academy of Managed Care Pharmacy (AMCP) convened a Partnership Forum with a diverse group of stakeholders representing population health decision makers, biopharmaceutical manufacturers, patient advocacy groups, health care providers, health economists, and others. As a participant in the Partnership Forum, I worked alongside the key professionals and entities affected by the current restrictions on the sharing of preapproval information to develop consensus recommendations on how to improve patient access to emerging medication therapies by clarifying the scope of permitted health care economic and scientific information communications between biopharmaceutical manufacturers and population health decision makers, while still maintaining appropriate safeguards to prevent this information from reaching unintended entities. The full

recommendations from the Partnership Forum were published in the January 2017 issue of the *Journal of Managed Care & Specialty Pharmacy* and are also included as Attachment A.[1] The consensus recommendations from the Partnership Forum included the following provisional recommendations:

- Create a safe harbor to allow biopharmaceutical manufacturers to share truthful and non-misleading clinical and economic information about medications in the pipeline with population health decision makers proactively at least 12-18 months prior to FDA approval during the forecasting and rate setting process.
    - Forum participants agreed that a safe harbor for PIE was necessary to confirm that the proactive dissemination of certain information does not violate the prohibitions against preapproval promotion and does not run afoul of the labeling, misbranding, and intended use provisions of the Federal Food, Drug, and Cosmetic Act and its implementing regulations.
    - Forum participants agreed that information shared under PIE should meet the competent and reliable scientific evidence standard as defined by a prior AMCP Partnership Forum[2] to be "truthful and non-misleading tests, analyses, research, studies, models, or other evidence. Such evidence would be based on the expertise of professionals in the relevant area and be derived using methods that are transparent, disclosed, reproducible, accurate, and valid."
    - Forum participants agreed that the specific format or process for sharing PIE should not be prescribed in legislation but should be developed collaboratively between the

[1] Enabling the Exchange of Clinical and Economic Information Pre-FDA Approval. Journal of Managed Care & Specialty Pharmacy 2017 23:1, 105-112
[2] AMCP Partnership Forum: FDAMA Section 114—Improving the Exchange of Health Care Economic Data. Journal of Managed Care & Specialty Pharmacy 2016 22:7, 826- 831

biopharmaceutical manufacturers and population health decision makers who would be exchanging this information.

- Limit exchange to narrow audience: biopharmaceutical manufacturers and population health decision makers (e.g. payors, provider sponsored health plans, pharmacy benefit managers, ACOs, and IDNs) only.
    - Forum participants debated the scope of preapproval communications and also considered whether providers and patients should be considered within scope. After much debate, forum participants agreed that given that information shared under PIE is prior to a product being deemed safe and effective by the FDA, information should only be shared proactively with those entities that have accountability for forecasting costs to ensure patient access and coverage. In addition, PIE should be limited to a sophisticated audience who has the education, training, and expertise to critically analyze and evaluate health care economic information for credibility. Therefore, PIE should be limited to a narrow audience and should only be permissible for biopharmaceutical manufacturers and population health decision makers.
- Limit exchange to new molecules and expanded indications with an intent to file only.
    - Forum participants debated whether PIE should be limited to new molecular entities only, or should also include expanded indications. During the debate, population health decision makers articulated that expanded indications can have a major impact on budgeting, forecasting, and rate setting if the expanded indication increases the patient population eligible to receive the product significantly. For example, if the indication for PCSK9 inhibitors were expanded to include generalized hypercholesterolemia, it would result in a major increase in the eligible population and corresponding costs associated

with the treatment of hypercholesterolemia. However, population health decision makers also noted that while they want to receive information about expanded indications preapproval, they do not want to receive information about all off-label uses of a product. In addition, they wanted to ensure that incentives were still in place to encourage biopharmaceutical manufacturers to file for an expanded indication as FDA approval remains the gold standard for formulary placement for most classes of medications. Therefore, forum participants recommended that PIE should be applicable to both new molecular entities and expanded indications with an intent to file. An intent to file would be demonstrated by submission of a Supplemental New Drug Application (sNDA) or other similar steps. However, forum participants also noted that in certain situations, especially for rare diseases, a financial incentive to file for an expanded indication may not be viable and therefore an avenue should be available for PIE to be applicable absent a regulatory filing in certain circumstances.

- Allow for bidirectional exchange of information that does not necessarily have to be clinical or scientific evidence.
    - Forum participants agreed that bidirectional exchange of information was a key element of PIE to encourage a continuous and ongoing dialogue between biopharmaceutical manufacturers and population health decision makers throughout a product's preapproval lifecycle. The bidirectional communication would also allow population health decision makers to share with manufacturers what they are looking for in clinical endpoints and level of evidence to make coverage decisions for patients. This notion has become increasingly important recently with the approval of new therapies for Duchenne's Muscular Dystrophy. These products were approved by the FDA as safe and effective,

but population health decision makers are hesitant to cover the products as the level of evidence does not meet their needs to make a coverage decision, resulting in patients being unable to access these products. Had PIE been permissible during the development phase of these products, population health decision makers could have shared their expectations for the level of evidence generated from clinical trials and perhaps avoided the gap in patient access that exists today.

- Forum participants debated whether PIE should be limited to "evidence" or "information." After much debate, it was agreed that "information" was the more appropriate term as some elements shared under PIE would always amount to information and not evidence, such as anticipated indications, place in therapy, routes of administration, and budget impact. It was also discussed that economic models cannot be considered evidence and limiting the standards to "evidence" may cause legal concern and be interpreted as requiring a level of research or replicability for all information disclosed, which might be unattainable at certain stages of the product's development.
- Forum participants discussed the need to establish a minimum set of standards that information shared under PIE should meet, including the need for a dynamic standard that would support the evolution of information to evidence as a biopharmaceutical product approaches FDA approval. Forum participants suggested that an independent objective entity comprised of a multi-stakeholder collaborative of representatives from various organizations could be responsible for developing consensus recommendations regarding good research practices for information shared under PIE. The independent objective body would also be responsible for continually updating the established good

research practices to reflect updates in scientific rigor and other advances in evidentiary standards.

- Forum participants also emphasized that because the information about a product could change and augment over time, information shared under PIE should include appropriate disclosures including transparency regarding the methods and results with appropriate disclosures of uncertainty and limitations inherent in such information.

FDA Releases Draft Guidance and Shares Its Current Thinking on Preapproval Communications

In January 2017, the FDA released a draft guidance document[3] outlining its current thinking on manufacturer and payor communications. The draft guidance took a helpful first step in creating a safe harbor for manufacturer communications to payors regarding investigational products, but did not include expanded indications. While population health decision makers were pleased to see that the FDA draft guidance allows the proactive communication of certain information by biopharmaceutical manufacturers to payors prior to FDA approval, the draft guidance remains non-binding and these provisions must be codified by law. Therefore, there is a need for Congress to engage in this topic to create a legislative safe harbor for PIE so that it is clear that the proactive dissemination of certain information does not violate the prohibitions against preapproval promotion and does not run afoul of the labeling, misbranding, and intended use provisions of the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

[3] FDA Draft Guidance - Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities—Questions and Answers [FDA-2016-D-1307]" as published in the Federal Register on January 19, 2017. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf. Accessed July 10, 2017.

H.R. 2026 – The Pharmaceutical Information Exchange (PIE) Act of 2017 is Introduced

In April 2017, Representative Brett Guthrie (R-KY) championed this issue by introducing *H.R. 2026 – The Pharmaceutical Information Exchange (PIE) Act of 2017* to improve patient access to emerging medication therapies by clarifying the scope of permitted health care economic and scientific information communications between biopharmaceutical manufacturers and population health decision makers. The bill, as amended, incorporates the consensus recommendations developed by the multi-stakeholder group and creates a very narrow safe harbor to allow for biopharmaceutical manufacturers to share proactively health care economic or scientific information with population health decision makers. The bill also solidifies the current thinking of the FDA and includes expanded indications, an area that the FDA did not include in their draft guidance, but an area that the multi-stakeholder group felt was integral to improving the ability of population health decision makers to properly plan, budget, and forecast for the impact of an expanded indication. The bill also requires that information provided under PIE must include a conspicuous and prominent statement describing any material differences between the information provided and the FDA-approved product labeling.

There is a Need for Congress to Engage in This Topic

PIE is an acute issue that a broad group of stakeholders came together and agreed needs clarification. While the FDA draft guidance took a helpful first step in creating a safe harbor for manufacturer communications to population health decision makers regarding investigational products, the draft guidance remains non-binding and does not provide the level of certainty needed to truly operationalize PIE. Absent a legislative safe harbor, PIE will likely not be utilized to its full potential by

biopharmaceutical manufacturers and population health decision makers for fear of enforcement, and unfortunately patients will not realize the benefits of PIE.

Therefore, there is a need for Congress to engage in this topic to create a legislative safe harbor for PIE so that it is clear that the proactive dissemination of certain information does not violate the prohibitions against preapproval promotion and does not run afoul of the labeling, misbranding, and intended use provisions of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Congressional action is needed to create a safe harbor for PIE to improve patient access to emerging medication therapies.

Appendix I

In practice, the importance of the need for PIE and where access to PIE would have improved patient access to care is demonstrated in the following scenarios. The answer to improving access here is having necessary information 12-18 months ahead of FDA approval, and having legislative support that not only grants access, but provides the necessary framework and safe harbor enabling a sophisticated audience the ability to have a bidirectional dialogue concerning this information.

(1) Scenario Ia – Hepatitis-C: All Medicare bids for 2014 benefit offerings use the 2012 experience to structure benefits offered to patients ('members'); all clinical, actuarial and cost analyses due to submit to CMS for approval 5/31/2013, including our formulary covering at least 2 drugs in every therapeutic category

- Sovaldi: groundbreaking treatment for Hepatitis C, approved by FDA 12/6/2013 with novel mechanism; changing the landscape for an estimated 3.2 million people known to the CDC as diagnosed with Hepatitis-C (note, 7 months after we've already analyzed our costs and planned our 2014 benefits)
- 1/1/14-12/31/14: Drugs to treat Hepatitis C accounted for $500k (1/2 million dollars) for 4 patients in our plan. Two additional patients opted not to pick-up their medications, which would have accounted for another $160k in spend. For that time-period, we had another 16,000 people to take care of, and cancer was the only category with higher spend.

(2) Scenario Ib. Hepatitis-C 2014: bids for 2015 benefits due 6/2/2014 based on base period of 2013 drug use trends, Harvoni approved 10/10/2014; 2015 benefit year saw 101 claims for 32 of our

22,500 patients accounted for 10% of our spend, while only caring for 0.14% of our member patients.

In the first two scenarios, had we been able to discuss proactively with Gilead their emerging evidence, treatment options, and had a better grasp on understanding their pricing strategy for a 'cure', the restrictive coverage criteria and multiple iterations of coverage criteria revisions might not have occurred over the ensuing years.

(3) Scenario II – Oncology:

- Key timeline: follow the timeline presented previously - bids for 2016 were submitted 6/2015 & bids for 2017 submitted 6/2016 – we are always playing a game of catchup for planning and communication of benefits to our members
- Let me introduce you to a patient, one of our enrolled members – a 67 year old diagnosed with inoperable lip cancer which has spread to tongue, clinically called 'squamous cell carcinoma':
- Patient is eligible for a low-income subsidy based on annual income (annual single income ≤135% FPL ($16,278)
- Provider tells patient about a new treatment the FDA granted **accelerated** approval 8/5/2016 for pembrolizumab (Keytruda) to treat head and neck squamous cell carcinoma due to overall risk reduction of 16% seen in clinical trials;
- 200mg/dose every 3 weeks = plan pay $7,178 (pt pay $1,830)/dose x 8 visits = $57,424 (pt pay $14,640)/treatment course until $6,500 Maximum-Out-of-Pocket (MOOP) Limit
- Out of pocket limits update annually, so potential for full patient liability since treatment crosses 2016-2017.

- Without being a head and neck cancer specialist, how can I have an informed discussion with my provider regarding the level of evidence showing 16% overall response rate when clinical trial evidence is not yet publicly available without a specific data request to the manufacturer?
- In this scenario if we were able to talk with the manufacturer, in this case Merck, about their pipeline and treatments ahead of time, or better yet have a portal for secure login and review the information available, thus understand their value statement and clinical data; I could better plan for this treatment and have an open dialogue with my provider once the product is approved, rather than scrambling to review the evidence and appropriateness of care on 9/1/16 when I received the request for coverage of the product and the patient already scheduled to receive treatment on 9/2/16.

Reflecting on historical 'what if' scenarios can only be made more impactful if we look at what is ahead:

(4) Scenario III – Future State: In the next 12-18 months there are approximately 60 new products that have filed for, or are anticipated to file for, approval within categories including diabetes, anti-infective agents, dermatologic, inflammatory conditions, multiple sclerosis, cancer, and others.

- As a reminder, we submitted our 2018 Medicare bids for formulary and coverage criteria on June 5, 2017, and will submit our 2019 benefits and formularies the first week of June, 2018; thus each of these potential new treatments represent coverage uncertainty for payors, providers, and ultimately a patient who is at the receiving end of coverage decisions.
- Because we can only estimate when therapies will be approved, if we receive a coverage request shortly after FDA approval, the landscape still remains one of chaos and requires special requests

to biopharmaceutical companies to access the data until the data is published, compendia and treatment guidelines are updated, and coverage criteria reflect new and novel treatments.

- These new drug application estimates do not include expanded label indications – which adds additional importance for continued communication as the label of products evolve over time as new indications are studied.

As demonstrated in my previous scenarios, each of these breakthrough therapies represent innovation and the potential to change a patient's life IF they can gain access to therapy. The barrier to access to novel therapies is a population health decision maker's ability to have sufficient data and sophisticated discussions with those most informed about the utility of the products in a timely enough fashion to plan, budget, and forecast for the therapies coming to market. Payors represent an extremely sophisticated audience who has the education, training, and expertise to critically analyze and evaluate health care economic information for credibility. These individuals are trained to review evidence and understand clinical endpoints resulting in better information applied to patient access

Attachments

Attachment A: Enabling the Exchange of Clinical and Economic Information Pre-FDA Approval. Journal of Managed Care & Specialty Pharmacy 2017 23:1, 105-112

AMCP Partnership Forum: Enabling the Exchange of Clinical and Economic Information Pre-FDA Approval

SUMMARY

Current federal laws and FDA regulations have significantly restricted the sharing of clinical and health economic information on biopharmaceuticals that have yet to receive FDA approval. Over the past several years, organizations that make health care coverage decisions, including those that set copayments, premiums, and formulary placement, have expressed a need for receiving this information before approval, as long as appropriate safeguards exist to prevent this information from reaching unintended entities. Population health decision makers have indicated that waiting until FDA approval is often too late for the critical planning, budgeting, and forecasting associated with health benefit design, especially given the recent influx of high-cost medications and scrutiny for better evaluation and preparation. Recognizing that securities laws restrict the disclosure of nonpublic information and may need to be amended, permissible early dissemination would allow population health decision makers to incorporate clinical and economic information for pipeline drugs or expanded indications into financial forecasting for the following year's plan. Access to this information is needed 12-18 months before FDA approval when organizations are deciding on terms of coverage and budgetary assumptions for state health insurance rate filings, Medicare and Medicaid bids, contracts with health care purchasers, and other financial arrangements.

The need for exchange of clinical economic information before FDA approval was first introduced at a previous Academy of Managed Care (AMCP) forum in March 2016, which addressed section 114 of the Food and Drug Administration Modernization Act and the communication of such information after FDA approval. To address preapproval information specifically, AMCP convened a Partnership Forum on September 13-14, 2016. This forum included a diverse group of stakeholders representing managed care, the biopharmaceutical industry, providers, patients, health economists, academia, and others. The multistakeholder group represented the key professionals and entities affected by the federal laws and FDA regulations that restrict the sharing of preapproval information and the collective credibility necessary for proposing this new communication process.

Forum participants primarily focused on 6 items of discussion: (1) creating and defining new terms for how biopharmaceutical manufacturers may provide clinical and economic information 12-18 months before FDA approval; (2) defining the clinical and scientific standards that this information should meet; (3) determining which entities should have access to this information and the value to each; (4) the format and process by which this information should be disseminated; (5) developing definitions for existing terms referenced in current laws, regulations, or guidance documents that would need to be modernized to align with the identified new term; and (6) providing safeguards to prevent this information from reaching unintended entities.

Forum participants selected "preapproval information exchange" (PIE) as the correct term to describe this proposed new communication process and to be inclusive of data from pivotal phase III clinical trials, pharmacoeconomic data, and patient-reported outcomes, as well as other relevant items, including anticipated indications, place in therapy, and routes of administration. Stakeholders agreed that PIE should be truthful, nonmisleading, and include a broad range of information to meet the needs of population health decision makers and health care technology evolution. Recipients of PIE would be limited to population health decision makers who need this information for coverage decisions. The format and process for PIE disseminated should allow for a bidirectional exchange between manufacturers and population health decision makers but should not be proscribed in legislation. Furthermore, new legislative language may be beneficial, since PIE is a novel category of information. New legislation could provide a safe harbor and clarity that PIE does not violate preapproval promotion and the Federal Food, Drug, and Cosmetic Act and its regulations.

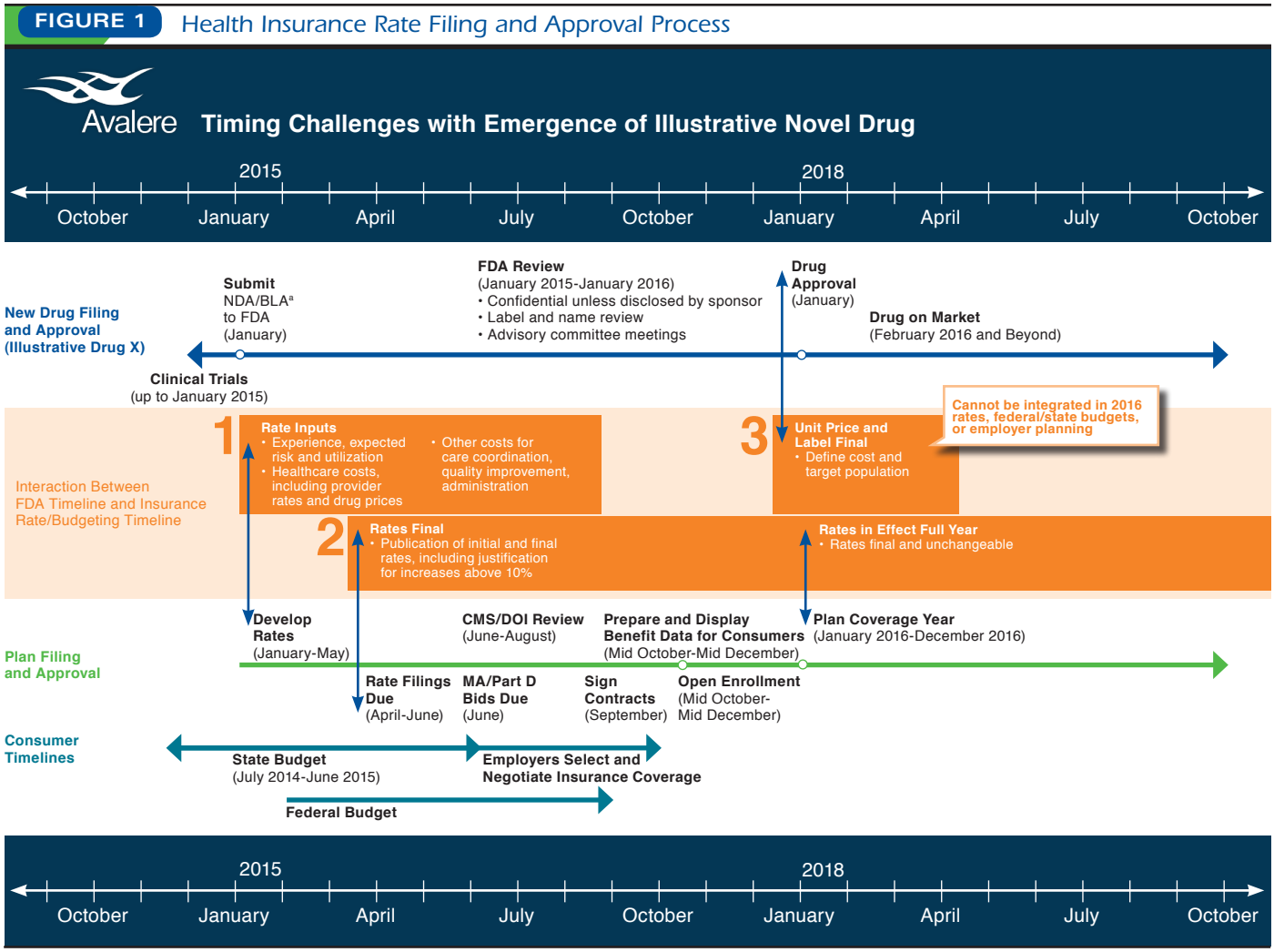
J Manag Care Spec Pharm. 2017;23(1):105-12

As the U.S. health care system evolves from a historical payment system based on quantity and process to a modernized system rewarding quality and improved patient outcomes, the need for timely communication between biopharmaceutical manufacturers and population health decision makers about emerging therapies is critical for the successful shift to a value-driven system. There are 3 main imperatives driving the need for communications before approval by the U.S. Food and Drug Administration (FDA).[1,2]

First, as a result of new laws such as the Affordable Care Act and state mandates, population health decision makers are required to evaluate their plan designs, formularies, and rates 12-18 months in advance to meet submission deadlines 6-9 months before the beginning of the intended plan year. With rates being filed over a year in advance, proper planning, budgeting, and forecasting are integral for population health decision makers to accurately account for the effect of new therapies that will enter the market. For example, for the 2016 coverage year, population health decision makers analyzed 2014 data in order to submit their 2016 rates by spring 2015 (Figure 1). The budget impact of new therapies that were approved by the FDA after spring 2015 could not be integrated into the 2016 rates. Accurate forecasting and rate setting is critical to ensure that patients have continued access to affordable coverage for their health care needs. Changes are necessary to FDA regulations to expressly permit biopharmaceutical manufacturers to proactively communicate with population health decision makers about emerging therapies before FDA approval so that more accurate forecasting and rate setting are supported, enabling affordable access for all patients to new therapies upon FDA approval.

Second, there is an increased focus on value-based payment models as evidenced by the Medicare Shared Savings Program and a range of initiatives launched and proposed by the Center for Medicare & Medicaid Innovation. Successful implementation of value-based payment models requires understanding the overall value of a therapy, including how pharmacy spending can offset medical costs and vice versa. In addition,

FIGURE 1 Health Insurance Rate Filing and Approval Process



From Eli Lilly and Company and Anthem. Facilitating open communication about emerging therapies. January 29, 2016. Appendix.[2] Reproduced with permission from Eli Lilly and Company.

[a]Median review time 1-2 years.

BLA = Biologic License Application; CMS = Centers for Medicare & Medicaid Services; DOI = Department of Insurance; FDA = U.S. Food and Drug Administration; MA = Medicare Advantage; NDA = New Drug Application.

it requires downstream planning for population health decision makers to change plan design, formularies, and necessary contracts in advance of submitting rates at least a year in advance of the intended coverage year as previously outlined. Therefore, to increase the use of value-based payment models, it is important for biopharmaceutical manufacturers and population health decision makers to be able to share information about emerging therapies before FDA approval in order to provide sufficient time to implement these models in a timely and effective manner upon FDA approval.

Finally, the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) created an expedited approval pathway allowing the FDA to grant priority review if preliminary clinical trials indicate that a therapy may offer substantial treatment advantages over existing options for patients with serious or life-threatening diseases.[3] Under the expedited approval pathway, therapies may be approved by the FDA before clinical trial data are published and made publicly available, thereby making it very difficult for population health decision makers to determine whether a therapy is appropriate for a patient if they receive a coverage request before publication of the data. Guidelines and peer-reviewed compendia sources are even further delayed in providing population health decision makers with reputable reference material for making sound clinical judgements when published clinical data are not available. In these situations, enabling preapproval information

TABLE 1 FDA Guidance and Other Initiatives Regarding Clarification of the Dissemination of Off-Label Drug Information

Year	Topic	Title (if applicable)
1997	Guidance on the scientific exchange of original trial results and off-label information	Industry-Supported Scientific and Educational Activities[4]
2009	Guidance on the distribution of peer-reviewed scientific and medical publications regarding unapproved new uses of approved drugs and approved/cleared medical devices	Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices[5]
2011	Guidance reflecting responses to unsolicited requests	Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices[6]
2011	MIWG petition regarding clarification on off-label communication	Citizen Petition, FDA-2011-P-5012[9]
2013	MIWG petition requesting a constitutional response to 2011 petition (above)	Citizen Petition, FDA-2013-P-1079[10]
2014	Update to 2009 guidance	Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices[7]
2015	Declaration that detailed the FDA's initiatives to accommodate policies to foster stakeholder interests in off-label communication	Declaration by Janet Woodcock[11]

FDA = U.S. Food and Drug Administration; MIWG= Medical Information Working Group.

exchange (PIE) is critical to ensuring that population health decision makers are aware of the information available to date on emerging therapies granted breakthrough designation by the FDA so that they are prepared to make coverage decisions for patients immediately upon FDA approval.

Restricting Information Dissemination

Current federal laws and FDA regulations have significantly restricted communications between biopharmaceutical manufacturers and population health decision makers for emerging therapies before FDA approval, despite clear recognition that budgeting and forecasting by payers is critical to ensure that patients have access to new treatments as soon as possible following market approval. Over the past 3-4 decades, the FDA has disseminated various policy documents addressing this issue.[4-7] While safe harbors for off-label communication already exist, the interpretation is unclear, and enforcement involves various entities with differing approaches (i.e., Health and Human Services Office of the Inspector General, Federal Trade Commission, Department of Justice, and state governments).[8] FDA regulations ensure access to safe and effective medications, while other agencies must ensure prevention of fraud, waste, and abuse, and marketplace competition. Uncertainty regarding safe harbors and the fear of enforcement has limited the dissemination of preapproval information by manufacturers, despite population health decision makers and others expressing a strong need for this information much earlier in the drug development process. There is a definitive need to refine and clarify laws governing activities under the purview of the FDA to help diminish concerns about the possibility of legal action by other agencies. More recently, the FDA has drafted guidance to take steps to support solutions to distinct, yet related, communication challenges; granted petitions to elucidate on this topic; and announced a public hearing to review policies and clarify standards for off-label communication.[4-11] This topic has also been heavily discussed outside of the FDA, including at AMCP's FDAMA Section 114 forum, 21st Century Cures proposals for reform of Section 114, Biotechnology Innovation Organization and Pharmaceutical Research and Manufacturers of America's principles on responsible sharing for truthful and non-misleading information, among others (Table 1).[12-14]

Given these circumstances and others discussed in the following proceedings, further recommendations, guidance, and legislation are needed to provide clarity on the dissemination of information before FDA approval.

Forum Purpose and Discussion Points

To address the long-debated issue of proactive dissemination of clinical and health economic information on products before FDA approval, the Academy of Managed Care Pharmacy (AMCP) held a Partnership Forum on September 13-14, 2016, in Tysons Corner, Virginia, with a diverse group of health care stakeholders to provide recommendations for Congress and the FDA. The purpose of this forum was to discuss the following 6 items:

1. The term that would be used to describe the ability of biopharmaceutical manufacturers to proactively share clinical and economic information about medications in the pipeline with payers and other entities before FDA approval.
2. The standards that clinical and economic information should meet before FDA approval.
3. Stakeholders who should have access to clinical and economic information before FDA approval and the value of this information to each of these entities or individuals.
4. The preferred format and process by which eligible entities would like to receive clinical and economic information from biopharmaceutical manufacturers before FDA approval.
5. The definitions for existing terms referenced in current laws, regulations, or guidance documents (i.e., labeling, misbranded, or intended use) that would need to be modernized to align with the identified new term for the exchange of clinical and economic information before FDA approval.

TABLE 2 Summary of the AMCP FDAMA 114 Partnership Forum[12]

Objective	AMCP convened a Partnership Forum for stakeholders to discuss clarification and possible expansion of FDAMA Section 114 to obtain consensus recommendations on how information related to this statute should be disseminated.
Key stakeholders	Pharmaceutical industry, managed care industry, health care providers, pharmacoeconomic experts, health policy experts, and patient advocates

Recommendations: Terms, Definitions, and Key Points

Term	Definition	Key Points
Competent and reliable scientific evidence	"Truthful and non-misleading tests, analyses, research, studies, models, or other evidence. Such evidence would be based on the expertise of professionals in the relevant area and be derived using methods that are transparent, disclosed, reproducible, accurate, and valid."	Models would be left behind with reproducible methods.
Formulary or other similar entity	"Health care decision makers beyond health plan formulary committees, including organizations, or individuals in their role in an organization, who make health care decisions for patient populations and organizations that evaluate HCEI or develop value frameworks and compendia, including individuals in such organizations."	• "Other entity" needs to be flexible as the health care industry evolves over time. • The role of the individual needs to be a key consideration. • Inclusion of patient advisory groups was debated, since some of these groups are sophisticated and have the ability to interpret this information, but not all do, so proper protections need to be considered.
Health care economic information	"Any analysis that identifies, measures, or compares the economic, clinical, or quality of life consequences for any treatment. This includes the costs and resource utilization of a drug or health technology relative to another drug, health technology, or no intervention."	Includes noneconomic information as well, since clinical and quality life endpoints are a part of economic evaluation.

AMCP=Academy of Managed Care Pharmacy; FDAMA=Food and Drug Administration Modernization Act; HCEI=health care and economic information.

6. The public health protections that should be considered to prevent the dissemination of clinical and economic information to unintended entities before FDA approval.

AMCP previously held a Partnership Forum in March 2016 to address communications of health care economic information (HCEI) after FDA approval. More specifically, the March forum discussed the clarification and possible expansion of Section 114 of the Food and Drug Administration Modernization Act (FDAMA) to obtain consensus recommendations on how information related to this statute should be disseminated.[12] While the recommendations from the March forum (Table 2) were focused on HCEI dissemination after FDA approval, a key recommendation was that further discussion was warranted to create recommendations for information exchange before FDA approval.

Stakeholders participating in the September Partnership Forum on preapproval communications were separated into 3 groups. Throughout the forum, each group, which was composed of representatives from the biopharmaceutical industry, payers, provider organizations, academia, health economists, and patient advocacy groups, among others, began its discussion with the question of whether the recommendations from the March forum on post-FDA approval communications were applicable to pre-FDA approval communications or whether the latter required adjustments given the differences in purpose and use before versus after FDA approval. The following recommendations and discussion points are reported to reflect where there was agreement, and where further discussion is warranted.

Terminology to Describe the Sharing of Preapproval Clinical and Economic Information

When considering the terminology that should be used to describe the ability of biopharmaceutical manufacturers to proactively share clinical and economic information about medications in the pipeline with payers and other entities before FDA approval, debate among the 3 groups focused on 3 areas: (1) the term "preapproval," (2) whether the information to be communicated should be information or evidence, and (3) whether the method of conversation should be deemed an exchange or information sharing.

Preapproval

The groups discussed the need for a term that is narrow enough to be included in legislation or adopted in guidance. Whether to include "preapproval" in this term was debated. Stakeholders reached consensus that the final recommended term should differentiate what type of information is to be shared. Including the word "preapproval" in any such term would highlight that the term refers to information disclosed for forecasting, planning, and budgeting before FDA approval. A key point of discussion was when pricing information would be available for medicines initially entering the market. Some stakeholders noted that pricing may only be known shortly, if not immediately, before product launch, while other stakeholders expressed an interest in receiving pricing information, or at least a range of possible prices, as early as possible. Stakeholders recognized, however, that manufacturers must

comply with securities and trade secrets laws that restrict the dissemination of material nonpublic information, which could include pricing, as well as certain clinical trial data.

Information Versus Evidence

The terms "information" and "evidence" were used to describe the clinical and economic data to be communicated. Although the term "scientific information" was proposed, stakeholders agreed that this term may be misinterpreted as being limited to research studies subject to scientific rigor, when instead, the proposed term should be inclusive of additional purposes (e.g., identifying potential patient-populations, distribution requirements, and budgeting). Some stakeholders indicated that as biopharmaceuticals move through the early phases of development, information builds over time and eventually leads to a body of evidence in the later phases of development and throughout the product life cycle. Furthermore, the term "information" was deemed appropriate by some because "evidence" may be viewed as only the types of data that involve a statistical comparison and may limit the use of models and valuable cost analyses. Stakeholders expressed that models cannot be classified as evidence, since they are simply tools to develop estimations, and there was a strong concern among many stakeholders that deeming a model as evidence would lead to misinterpretation as to what such models can and cannot demonstrate and depict from a level of certainty. Those who supported use of the term "evidence" stated that "information" is a broader and more encompassing term that may not have as much weight in the scientific community. The concept of information versus evidence is discussed in more detail throughout this proceedings document.

Exchange Versus Information Sharing

The third area of discussion focused on the terms "exchange" versus "information sharing." Supporters of the term "exchange" felt that the use of this term would signify bidirectional conversations between decision makers and manufacturers and reinforce an ongoing dialogue between the 2 parties. Proponents of the term "information sharing" thought that the term "exchange" would be confused with scientific exchange, which has traditionally been interpreted to be applicable to investigational new drugs under 21 CFR 312.7(a) and therefore expressed hesitance in using this term.

After thorough discussion, stakeholders agreed on the term "preapproval information exchange" (PIE), which referred to the proactive sharing of clinical and economic information by manufacturers to decision makers (entities are discussed later in the proceedings) at least 12-18 months before FDA approval and the ongoing discussions between the 2 sharing entities as information evolves into evidence throughout drug development. Furthermore, stakeholders agreed that this preapproval communication only applies to those biopharmaceutical manufacturers who intend to file for a new indication (new molecules and new indications), thereby limiting the risk for off-label promotion. Stakeholders agreed that the intent of a biopharmaceutical manufacturer to file would need to be justified by submission of an Investigational New Drug (IND) application, New Drug Application (NDA), Supplemental New Drug Application (sNDA), or other similar steps.

Standards for Preapproval Information

Discussion on the question "What standards should clinical and economic information shared prior to FDA approval meet?" began with the definition of "competent and reliable scientific evidence" as developed in the FDAMA 114 forum (Table 2) and how to differentiate the preapproval setting from the postapproval setting. Overall, stakeholders agreed that the standards for this information should be based on the FDAMA 114 forum definition, with a few proposed exceptions:

- "Information" should be either added to the definition or should replace "evidence."
- A minimum set of standards should be set for this information, but as a biopharmaceutical product approaches approval, the information would become stronger and evolve into evidence.
- It was emphasized that because the information about a product could change and augment over time, any disclosure of information for PIE purposes needed to include transparency regarding the methods and results (all of which would need to be done in a truthful and non-misleading manner) with appropriate disclosures of uncertainty and limitations inherent in such information, and methods would need to be reproducible—not the results).

Some stakeholders expressed that all-inclusive information sharing, with ultimately no restrictions, may allow too much lenience, while being too specific may inhibit manufacturers from sharing important information with population health decision makers that would be of value to their decisions and ultimately be important for planning and forecasting purposes. As mentioned in the previous section, limiting the standards to "evidence" may cause legal concern and be interpreted as requiring a level of research or replicability for all information disclosed, which might be unattainable at certain stages of the product's development, whereas the intent is to be able to include additional items such as anticipated indications, place in therapy, routes of administration, distribution channels, and potential budget impact.

Entities and Individuals Who Should Receive Preapproval Information

During the FDAMA 114 forum, it was decided that entities who should receive HCEI after FDA approval would be "health care decision makers beyond health plan formulary

committees, including organizations, or individuals in their role in an organization, who make health care decisions for patient populations and organizations that evaluate HCEI or develop value frameworks and compendia, including individuals in such organizations" (Table 2). Stakeholders were asked to consider these same entities for preapproval purposes, in addition to pharmacy and therapeutic committees, managed care pharmacy, health care providers, accountable care organizations (ACOs), integrated delivery networks, patient advocacy groups (PAG), organizations that develop value frameworks (e.g., American Society of Clinical Oncology and National Comprehensive Cancer Network), organizations that develop clinical practice guidelines (e.g., American College of Cardiology and American Diabetes Association), research societies (e.g., International Society for Pharmacoeconomics and Outcomes Research), actuaries, contract specialists, and others.

All stakeholders agreed that population health decision makers such as managed care organizations and pharmacy benefit managers would be eligible to receive preapproval information. In addition, certain integrated delivery networks (IDNs) and ACOs that bear financial risk for biopharmaceuticals would also be eligible to receive preapproval information. These population health decision makers were included because entities and individuals within these organizations need to receive this information in advance of FDA approval for budgeting, forecasting, and coverage decision purposes.

Forum stakeholders also considered whether other entities that are "influencers," such as groups that develop value frameworks and clinical practice guidelines should be included in PIE. Some stakeholders thought that clinical practice guidelines developers would need to know this information, since the evolution of guidelines is a lengthy process, and it would be beneficial to know this information for the next guideline update. A limited number of stakeholders thought that some benefit exists in expanding this information sharing to PAGs, since the FDA is moving toward more patient-focused drug development. However, the majority of stakeholders strongly argued that the need for HCEI is for entities that have accountability for forecasting costs to ensure patient access and coverage, which is not the case for influencers or PAGs. While preapproval information sharing with influencers and PAGs was considered, there was consensus that the pre-FDA approval information most valuable to influencers and PAGs was clinical in nature, not preliminary economic or financial data. Furthermore, entities such as influencers or PAGs could receive this information through the usual channel of unsolicited requests. Therefore, the majority of stakeholders agreed that only entities who manage a population's health should receive preapproval information.

Preferred Format and Process for Receiving Preapproval Information

After reviewing the recommendations set forth at the FDAMA 114 forum, stakeholders were asked the question "What is the preferred format and process by which eligible entities would like to receive clinical and economic information prior to FDA approval from biopharmaceutical manufacturers?". Overall, stakeholder consensus supported the creation of a flexible means of providing this information that allows for a bidirectional exchange between manufacturers and population health decision makers and that a specific format or process should not be prescribed in legislation. Furthermore, AMCP was identified as a potential driver and leader in this space, given that AMCP has an established process for communication of information about biopharmaceutical products to inform decisions made by formulary committees. This process is currently restricted to unsolicited requests but could be adapted for PIE. Conversely, a few key points were debated:

1. *Central repository versus repositories for each manufacturer.* Some stakeholders thought that having multiple repositories (each for a different biopharmaceutical manufacturer) would simplify the risk of unintended users gaining access to preapproval information. Others stated that having the ability to compare medications and technologies in a central repository during a single log-in would allow for a more simplified, effective process. The central repository would allow for alerts once information is updated—decision makers could choose to opt-in and the frequency of the alerts they would like to receive (e.g., once a month or once a week). Later in the discussion, stakeholders noted that AMCP already has a central repository system in place for dossier submissions and viewing; therefore, this same system could be adapted as an option for communicating information in the preapproval setting.
2. *Standardized format versus flexible format.* An AMCP dossier-light format was initially suggested by many stakeholders, while others were concerned that not all end users, such as IDNs and ACOs, would be as familiar with this format; therefore, the format would need to be adaptable and flexible to suit the needs of organizations or entities. Furthermore, technology is rapidly evolving and developing, so a format developed today may not be useful tomorrow. Others disagreed, stating that a standardized format with the ability to locate the same information in the same location between 2 products would allow for a more simplified, consistent process.
3. *Communication and notification.* Communications via a repository would include notifications to decision makers once information was updated, options for manufacturers to share models and slide-decks, and one-on-one conversations between manufacturers and decision makers. More importantly, manufacturers and decision makers would have the option to choose the type and frequency of

engagement, depending on their individual needs, and whether to use a central repository or another process for exchanging this information.

Stakeholders ultimately agreed that the forum discussion is a starting point for the consideration of format options and that a specific format or process should *not* be prescribed in legislation but should be developed collaboratively between the manufacturers and population health decision makers who would be exchanging this information. The group agreed that given AMCP's history of providing this type of information, it is in a good position to serve as a leader and developer for providing information under PIE.

Definitions for Existing Terms in Current Laws, Regulations, or Guidance Documents

Given the existing terms included in current laws, regulations, and guidance documents, stakeholders were asked the question "How should the definitions for existent terms, referenced in current laws, regulations, or guidance documents (such as labeling, misbranded, or intended use) be modernized to align with the identified new term for the exchange of clinical and economic information before FDA approval?". Stakeholders quickly reached a consensus that PIE would need to have its own safe harbor, in a manner consistent with existing law.

Public Health Protections to Prevent the Dissemination of Preapproval Information

Stakeholders considered the public health protections required to prevent the dissemination of preapproval information and agreed that it should function similarly to the system in place for HCEI under FDAMA Section 114. The stakeholders agreed that certain public health protections are already in place through other legislation, so there may not be a need to create further protections beyond those already enacted.

Conclusions

Currently, the sharing of clinical and health care economic information on new products and indications before FDA approval is significantly restricted by federal laws and FDA regulations regarding product promotion. Population health decision makers have expressed a need for receiving this information at least 12-18 months before FDA approval to properly plan, budget, forecast, and care for the populations they serve, as long as safeguards are in place to prevent preapproval information from reaching unintended entities. The recommendation from this Partnership Forum is for Congress to establish a safe harbor for preapproval information exchange between biopharmaceutical manufactures and population health decision makers to encourage better decision making, without interfering with innovation in the biopharmaceutical and health technology industry.

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DISCLOSURES

The AMCP Partnership Forum on Enabling the Exchange of Clinical and Economic Data Pre-FDA Approval and the development of this proceedings document were supported by AbbVie, Boehringer Ingelheim Pharmaceuticals, Bristol-Myers Squibb, Celgene, Intarcia Therapeutics, Eli Lilly and Company, GlaxoSmithKline, Merck, National Pharmaceutical Council, Novo Nordisk, Pfizer, Pharmaceutical Research and Manufacturers of America, Precision for Value, Sanofi, Takeda Pharmaceuticals, U.S.A., and Xcenda. All sponsors participated in the forum and in revising and approving the manuscript.

ACKNOWLEDGMENTS

The AMCP Partnership Forum on Enabling the Exchange of Clinical and Economic Data Pre-FDA Approval was moderated by Susan Denzter, President and CEO, The Network for Excellence in Health Innovation (NEHI). The proceedings document was written by Emily Zacherle, MS, Evidence Strategy, Generation and Communication, Precision Health Economics.

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