While the rest of the healthcare system is paying for value, payments for drugs largely continue to be stuck in a 20th century construct that focuses on price, regardless of the health outcomes of each patient. Anthem and Eli Lilly and Company are collaborating to help accelerate the transition towards a value-based system with policy proposals that will help drive payment innovation. Read more at ThinkAnthem and LillyPad.

Facilitating Open Communication About Emerging Therapies

Eli Lilly and Company and Anthem | January 29, 2016

The following memorandum outlines Eli Lilly and Company and Anthem's joint perspective on creating a legislative or regulatory exemption that would allow manufacturers and health plans to communicate about emerging products prior to U.S. Food & Drug Administration (FDA) approval.

POLICY GOAL: Clarify federal law to confirm that manufacturers may speak openly with health plans about drugs going through the FDA approval process, particularly with regard to product efficacy, safety, and pharmacoeconomic information.

Background and Context

Aligning drug coverage decisions with rate development and budgeting timelines – that is, making a new drug available within an insurance premium that reflects expected spending on that drug, among many other factors – requires thoughtful synchronization over a several-month period. Two recent developments have created an environment where this alignment is difficult for health plans[1], state and federal governments, and manufacturers to achieve, ultimately creating downstream consequences for consumers.

First, with changes to commercial insurance processes included in the Affordable Care Act, insurance rates in most lines of business (including the individual market, employer market, Medicaid, and Medicare) are set – and unchangeable – well before the coverage year begins (see Appendix A). Accurate rate development relies on detailed assumptions about the use of healthcare services, including prescription drugs. Manufacturers are the best source of reliable and accurate clinical and pharmacoeconomic information about emerging therapies, but face significant restrictions on communicating to plans information about not-yet-approved products. When plans cannot accurately account for a drug when setting rates, they may overestimate the drug's cost, setting premiums higher than is ultimately needed to cover the costs of the drug, and perhaps discouraging some consumers from purchasing coverage. Alternatively, plans might underestimate the cost of the drug, thus setting premiums that do not cover costs. As a result, plans may need to consider mid-year solutions to control budgets like more stringent utilization management criteria.

At the same time, the new U.S. Food & Drug Administration (FDA) "breakthrough" therapy designation process means that blockbuster drugs will likely be moving more efficiently through the development, review, and approval processes. While more rapid approval of breakthrough medicines means that these products are available to consumers sooner, health plans, employers, and state and federal governments have less time to plan for their utilization. "Breakthrough" drugs by definition offer significant benefits for consumers – the designation is granted when preliminary clinical evidence shows they may represent substantial improvement over available therapies for treatment of a serious condition – but can have significant budget impacts on health plans, employers, and state and federal governments. Given current health plan rate development and budgeting requirements, some of the most promising new medicines are most vulnerable to timing challenges and their potential implications for patient access.

Clarifying that manufacturers and health plans may discuss critical scientific evidence and other drug features (e.g., dosage, pharmacoeconomic information, and clinical indications) for products under FDA review would encourage these discussions, allowing health plans to better anticipate effects on the target patient population and consider available pharmacoeconomic and efficacy data. Stakeholders could design the clarification to preserve FDA's interests, as discussed below.

[1]While this document references health plans throughout, the policy solution would also aid other stakeholders including pharmacy benefit managers and certain providers who purchase drugs.

Existing law and regulations are intended to achieve a very specific and important goal: preventing the marketing of a drug before FDA determines that it is safe and effective for its intended use. However, the FDA regulations on this subject, namely 21 C.F.R. § 312.7, are broadly written and could be interpreted to sweep in beneficial and otherwise non-harmful communications. Health plans have long used sophisticated methods for assessing the evidence base and patient access considerations for new medicines, and are well positioned to assess manufacturer-generated evidence and consider any existing limitations in evidence available prior to FDA approval. However, given the lack of clarity on the boundaries of permissible, pre-approval scientific exchange, manufacturers are hesitant to discuss clinical data or pharmacoeconomic information until FDA approves a product.

While pre-approval communication between manufacturers and health plans should explicitly be lawful and permissible, policy safeguards could prevent the distribution of pre-approval information to other audiences, such as patients, who may not be equipped to interpret it. For example, manufacturers and health plans could enter into appropriate non-disclosure agreements. As is the case today, a therapy would not be used prior to FDA approval under the proposed solution, and health plans would still have ample opportunity to review the label post-approval. In addition, manufacturers might commit to follow up with health plans when necessary to correct any assumptions made in pre-approval discussions that materially differ from the final product labeling agreed with FDA.

Facilitating Open Communication

Removing the existing uncertainty about as to when and how manufacturers and health plans can communicate about certain critical clinical and safety aspects of a drug's attributes before FDA approval could benefit patients, health plans, state and federal governments, employers, and manufacturers. Patients could directly benefit in the form of less restricted access to new medicines and more predictable trends in insurance rates from year to year. Health plans would have additional, directly relevant information when establishing rates and benefits for the upcoming year. Manufacturers would have the opportunity to engage in more timely conversations with health plans, providing targeted and well-timed information that may be helpful when price negotiations occur.

The Unfortunate Lack of Communication: A Case Study

The Case

- Health Plan X is developing its rate for the upcoming year. Final rates are due in April.
- Health Plan X knows that breakthrough Drug Y is undergoing FDA review. Drug Y is expected to significantly improve outcomes and experience for patients with a certain type of cancer. However, Health Plan X does not know which patients will be eligible to take Drug Y. The manufacturer of Drug Y is unable to discuss Drug Y's target patient population or potential price with Health Plan X.

Options for Health Plan X	OPTION ONE: Health Plan X Overestimates Utilization of Drug Y	OPTION TWO: Health Plan X Underestimates Utilization of Drug Y
Health Plan X Pre-Approval Assumption	Health Plan X assumes that 3 percent of its members will take Drug Y during the year. Health Plan X also estimates price and factors these assumptions into rates and thus into the budgets of health plans, employers, state and federal governments.	Health Plan X assumes that 1 percent of its members will take Drug Y during the year. Health Plan X also estimates price and factors these assumptions into rates and thus into the budgets of health plans, employers, state and federal governments.
Drug Y is Approved	Drug Y is approved by the FDA in September. Based on the FDA-approved label, only 1 percent of Health Plan X's members are candidates for Drug Y.	Drug Y is approved by the FDA in September. Based on the FDA-approved label, 3 percent of Health Plan X's members are candidates for Drug Y.
End Result	Health Plan X overestimates the aggregate costs associated with Drug Y and develops rates that are higher than they would have been, had Health Plan X had access to more complete information. Fewer consumers purchase coverage because rates are higher than they should have been, and other areas of employer, state and federal budgets are potentially unnecessarily cut.	Health Plan X underestimates the aggregate costs associated with Drug Y and develops rates that do not adequately reflect actual costs. Health plan X and its customers (employers, state and federal governments) more seriously consider aggressive utilization management criteria and stakeholders scramble for mid-year solutions.

FDA's interests would be protected as well. Manufacturers would continue to have the same strong incentives to seek FDA approval, as commercialization would continue to be dependent on it. Further, new guidance could contain explicit safeguards to protect patient safety and to ensure that communications are truthful and non-misleading, and do not compromise FDA's interest in ensuring the safety and effectiveness of new medicines. For example, manufacturers could include prominent disclaimers on data shared with health plans, making it clear that the data are not FDA-approved. A more detailed analysis of potential stakeholder impacts is included in Appendix B.

Therefore, policymakers and regulators should clearly acknowledge through clarification of federal law and regulations that manufacturers may communicate with health plans about drugs undergoing FDA review, including potential indications, clinical performance and pharmacoeconomic information.

Existing Legislative and Operational Barriers

Current rules prohibit manufacturers from communicating promotional claims of a drug's safety or efficacy for an investigational use, and manufacturers must avoid commercialization of the drug before it is approved for commercial distribution.[2] FDA's chief concern is that such communication may undermine the approval process, as products' safety and efficacy are not considered to be established until FDA grants marketing authorization. Further, FDA is concerned that pre-approval communication could create confusion if stakeholders share safety and efficacy information that is not ultimately included in the FDA-approved label. Currently, an existing regulation provides that:

> *A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.*[3]

However, targeted pre-approval conversations between manufacturers and health plans are not inherently promotional, and in the absence of definitive negotiations or a signed agreement, such conversations would also not amount to commercialization. In any event, use of a medical product would not be allowed prior to FDA approval. While such conversations are not clearly covered or prohibited by existing legislation or regulations, ongoing concerns about FDA's interpretation have a chilling effect on industry and create a compelling need for clarification.

Key Considerations for Implementation

Clarifying manufacturers' right and ability to communicate with health plans about certain pre-approval, product-specific information raises several practical considerations. First, key stakeholders (i.e., FDA, manufacturers, health plans) would need to define the specific types of information that are critical to inform desired discussions. We expect this information would include data from pivotal Phase III clinical trials (supported by substantial evidence) or pharmacoeconomic data (supported by competent and reliable evidence). Additionally, stakeholders should consider what limitations and parameters must guide these discussions (e.g., the discussions should be limited to indications undergoing FDA review, should be within a certain time period of the expected PDUFA date, should be subject to confidentiality restrictions, and should contain appropriate disclaimers). Manufacturers and health plans would need clear guidance from FDA on these topics, as well as compliance and oversight expectations.

FDA's existing regulatory framework for post-approval communications – that they be truthful and non-misleading – offers one potential path forward for setting expectations and guardrails for pre-approval discussions.[4] Applying a standard to pre-approval communications that is similar to the truthful and non-misleading standard applied to post-approval communications has several important benefits. Notably, this would ensure consistency over time (pre- and post-approval). Key stakeholders are already familiar with the standard, which would facilitate implementation of such an approach for pre-approval discussions. By applying a familiar but rigorous standard to pre-approval communications, while clarifying the parameters of these discussions, FDA can inject greater consistency into its regulatory framework and encourage richer discussions among stakeholders, ultimately benefitting patients and other stakeholders.

[2] 21 C.F.R. § 312.7
[3] 21 C.F.R. § 312.7
[4] See 21 U.S.C §§ 352(a), 321(n); 21 C.F.R. § 202.1(e)(3)(i).

Appendix. Health Insurance Rating Filing and Approval Process