The Value of Pre–FDA Approval Healthcare Economic Information Exchange Between Payers and Drug Manufacturers

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In October 2014, ledipasvir plus sofosbuvir (Harvoni) became available in the United States, providing renewed hope for patients with certain chronic hepatitis C virus (HCV) genotypes. At the same time, payers were suddenly trying to factor the $92,000 cost of therapy with this medication into budgets created before its approval by the US Food and Drug Administration (FDA).1 An example for this dilemma was presented by Qualchoice Health Plan Services (QHPS) at a hearing held by the US House Energy and Commerce Committee’s Subcommittee on Health in July 2017.2

QHPS, a health plan organization with 22,500 members, set its 2015 premium rates by June 2014. To set its premiums, QHPS utilized the most recent full year of data it had available (ie, from 2013). In 2015, after the FDA approval of Harvoni, QHPS had 101 claims for the drug for 32 patients. This amounted to 0.14% of QHPS’s patient population, accounting for almost 10% of its total spending in 2015. As a payer, QHPS was unable to adequately forecast the impact that Harvoni would have on its drug spending, because of the lack of preapproval communication between the company and the manufacturer of Harvoni (Gilead).

Similar scenarios have been replayed many times in the past decade, with new pharmaceuticals bringing new hope to patients and new challenges to private and public payers in seeking to forecast the economic impact of the new medications. In this case, the manufacturer admitted that it could have handled the situation about Harvoni, as well as the earlier, single-agent anti-HCV drug sofosbuvir (Sovaldi) better, by having more detailed conversations with third-party payers before the FDA approval of these drugs.3 Increasingly, this situation highlights an underlying deficiency in communication between plan sponsors (or payers) and drug manufacturers about healthcare economic information (HCEI) throughout a drug’s development and approval processes (Figure).4

Overall, a 20-year-old part of legislation, Section 114 of the Food and Drug Administration Modernization Act of 1997 (FDAMA),5 represents the primary regulatory structure for how drug manufacturers can distribute and use pharmacoeconomic information in the promotion of their drugs. However, in the absence of subsequent FDA guidance, uncertainty has prevailed regarding some key features of FDAMA Section 114, including the interpretation of who can be included in the target audience, the definition of “competent and reliable scientific evidence,” and the focus on shared information having to be related to FDA-approved indications for the medications.5,6 In addition, the sharing of general economic information, such as proposed pricing, is not clearly addressed in this legislation.5

Recent Drug-Related Regulatory Updates

The current regulatory and legislative climates recognize the need to address the shortcomings of FDAMA Section 114. The passage, on December 13, 2016, of the 21st Century Cures Act, updates the language of FDAMA Section 114.7 Section 3037 of the Cures Act takes a step forward to clarify the vague wording and definitions of HCEI and the audience for which HCEI is intended.7 The new law solidifies that “clinical data, inputs, clinical or other assumptions, methods, results, and other components underlying or comprising the analysis” are considered HCEI, and that such information “may be comparative to the use of another drug, to another health care intervention, or to no intervention.”7 Section 3037 of the Cures Act also broadens the reach of HCEI to include information that relates to an FDA-approved indication and updates the HCEI audience to include “a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement.”7

The FDA builds on Section 3037 of the Cures Act in a recent draft guidance.8 This guidance provides examples of HCEI that do and do not relate to an FDA-approved indication, and of information that should be
disclosed to the audiences receiving the HCEI, and discusses the communication of information on investigational drugs. A separate FDA guidance further clarifies the communication of material that is not explicitly included in an FDA-required drug label but that “may be consistent” with the FDA-required drug label.

Drug manufacturers have generally been supportive of these regulatory updates, but many submitted comments highlighting their concerns and requests for further clarification from the FDA. For example, Eli Lilly worked with the health insurer Anthem to submit joint commentary on the importance of increased communication between drug manufacturers and payers to “mitigate the challenges associated with the limited information that currently exists during insurer rate development and stakeholder budgeting timelines.” They also highlighted the desire for the FDA guidance to be extended beyond new molecular entities to include new indications and treatment line extensions, especially in light of the trend toward indication-based pricing for certain drugs.

Other pharmaceutical companies have also started to test their approaches to the dissemination of HCEI and seem ready to move forward, despite some lingering questions left unanswered by the recent guidances. For example, in response to these recent guidance drafts, Genentech established 5 pilot programs that are testing different approaches to communicating HCEI to payers. These efforts are intended to inform the development of effective internal procedures to support increased engagement between Genentech and all stakeholders in the future. The development of such procedures is important for enhancing communication pre- and post-FDA approval based on the FDA’s recent draft guidance.

**Need for Communication Pre–FDA Approval**

The clarification of ambiguous language is only part of the need for HCEI communication. The need for adequate exchange of HCEI is readily apparent in the pre- and post–FDA approval phases of a drug’s life cycle. Traditional randomized clinical trials establish a drug’s efficacy and safety profiles, but evidence of the drug’s effectiveness or its full safety profile in the real world requires additional monitoring and analysis. The use of real-world data to assess a drug’s effectiveness has recently gained the attention of the US healthcare system. Discussions held in 2016 at an Academy of Managed Care Pharmacy (AMCP) Partnership Forum between various stakeholders emphasized that a significant part of the difficulties in forecasting the financial impact of future drug approvals come from the absence of HCEI exchange about a drug’s assets preapproval. Primarily, such discussions reflected the difficulty of formulary planning and budgeting 12 to 18 months in advance without any economic data for drugs entering the market after a health plan submission of its insurance premiums. Such difficulties have been more recently exacerbated as a result of the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA).

The 2012 FDASIA created the Breakthrough Therapy designation, which provides an accelerated approval path for medications that “treat a serious or life-threatening disease or condition” for which “preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies.” Breakthrough therapies provide new treatment options for patients, but they make it difficult for payers to predict the impact of such therapies when the FDA accelerated approval precedes the publication of clinical data and comes with little information regarding the drug’s price.

At the 2016 AMCP Partnership Forum, key stakeholders—including managed care organizations, pharmaceutical companies, academia, healthcare professionals, and patients—discussed how they might facilitate communication of HCEI about a drug’s assets before the FDA approval of the drug. Based on their discussions, the AMCP Partnership Forum developed the following recommendations:

- Allowing for proactive and continuous “preapproval information exchange” of clinical and economic information about investigational drugs between manufacturers and decision makers who manage a population’s health at least 12 to 18 months before a drug’s approval
- Part of the shared information should include items such as anticipated indications, place of therapy, routes of administration, distribution channels, and potential budget impact
- A specific format should be developed collaboratively between the manufacturers and population health decision makers exchanging this information
- Preapproval information exchange should not be worked into existing regulations, and the information would need to have its own safe harbor in a manner consistent with existing law.

In January 2017, the FDA issued a draft guidance that includes the agency’s current thoughts on communication of HCEI preapproval. In this document, the FDA...
directly mentions that preapproval communication is permitted, provided the information is “unbiased, factual, accurate, and non-misleading,” and that it is presented with “a clear statement that the product is under investigation and that the safety or effectiveness of the product has not been established.” The FDA also explicitly lists what types of information can be shared, including details about the drug and its clinical and preclinical data, anticipated timeline for approval, pricing information, and marketing strategies. The guidance supports the exchange of healthcare information before a drug’s approval and emphasizes the importance of maintaining the communication channel regarding drugs and devices.

Uncertainty remains regarding some of the specifics of the HCEI related to a specific drug preapproval. For example, although the AMCP’s recommendations specifically highlight the importance of sharing economic information before a drug’s approval, the FDA guidance is vague about this and only directly speaks to sharing drug-pricing information before the FDA approval. In addition, a clarification is needed about where the FDA will draw the line on what constitutes “unbiased” and “non-misleading” information that is shared with payers for investigational drugs. Executives from Genentech and Bristol-Myers Squibb (BMS) have cautioned against waiting too long before acting on these guidance updates. This is especially so because it is unclear how long it may take the FDA to issue further direction on the development and dissemination of HCEI. Lauren Carter, BMS’s Vice President and Head of Strategic Care Marketing, argued that “you’ve got this nexus of a desire in the…payer and provider marketplace as well as legislation and regulation to open the door. So it’s incumbent on us to step through.”

Conclusion

The current US healthcare system falls short in utilizing HCEI to accurately manage spending on prescription drugs, diagnostics, and devices. Recent legislation, regulatory guidance from the FDA, and key stakeholder involvement have improved preapproval and postmarketing HCEI communication between drug manufacturers and payers. These steps have provided a framework for both sides to share information that extends beyond traditional clinical trial data, but the implementation and uptake of HCEI remain to be seen.

The adequate adoption and use of HCEI communication could play a role in improved formulary decision-making and increase the accuracy of budget forecasts and premium rates. In turn, this could translate to more affordable access to drugs for patients. However, in the absence of additional updates to these FDA guidances, it will fall to drug manufacturers and payers to develop internal processes and, through collaborative efforts, support the adoption and use of HCEI. Such efforts could result in market-driven regulatory change at the FDA and other agencies, such as the Department of Labor, the Treasury (ie, the Internal Revenue Service), and the Department of Health & Human Services (ie, the Centers for Medicare & Medicaid Services, Health Resources and Services Administration).

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