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SAFER HARBOR

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FDA guidance released on June 12 clears up regulatory ambiguities that have restricted drug and device company communications with payers, physicians and patients. A primary goal is to make it easier to base payments on outcomes not mentioned on product labels, but there could be broader effects in the loosened restrictions on communications between medical product developers and payers.

If sponsors exercise the ability to discuss healthcare economic data before drugs are approved, that could prevent payers from being surprised by high demand, as they were for the HCV drug Sovaldi sofosbuvir from Gilead Sciences Inc.

The guidance also should support use of and encourage studies to develop non-clinical data, such as quality-adjusted life years (QALYs) and reduction in hospital admissions or stays.

And if the Department of Health and Human Services (HHS) takes steps to remove regulatory impediments outside FDA's jurisdiction, the guidance will enable payers and medical product manufacturers to experiment more broadly with alternative reimbursement arrangements, including outcomes- and indication-based payments.

The final guidance broadens a safe harbor that allows medical product manufacturers to communicate with payers, PBMs, formulary committees and similar entities. The safe harbor was created by draft guidance on communications about investigational drugs in January 2017. It is now extended to medical device manufacturers, and to some unapproved uses of approved products.

The guidance defines healthcare economic information as communications related to the economic consequences of treating, preventing or diagnosing a disease. Economic consequences include but are not limited to monetary costs or resource utilization.

FDA believes payers should be permitted to receive this information because, according to the guidance, they are a "sophisticated audience" that is capable of assessing data and motivated to "closely scrutinize information about medical products as part of their decision-making process, including an evaluation of the limitations and reliability of that information."

"It really does address some of the key fears that pharmaceutical executives have about outcomes-based contracting."

Roger Longman, Real Endpoints

Drug companies have been reluctant to stray from the label, or to discuss unapproved products with payers, because they feared that doing so would expose them to liability for illegal off-label promotion.

The guidance specifically allows sponsors to communicate with payers about clinical outcome assessments, such as patient-reported outcomes, and about health outcomes measures such as QALYs. It also gives the green light to providing payers with analyses "derived from studies comparing the safety or effectiveness of a drug for its approved indication to another drug or intervention or to no treatment."

There are limits to the healthcare economic information manufacturers may provide.

The information must be consistent with a product's label. FDA provides several examples, including data on a duration of treatment that is longer than studies described on the label of a drug for long-term use, and analyses derived from data on the burden of disease, such as the economic consequences of treatment.

FDA also provides examples of prohibited communications.

These include information based on "studies limited to patient populations that are not within the indicated patient population," and data on uses that are unrelated to the approved indications. For example, if a drug or device is approved to treat the symptoms of a disease, communication of economic analyses about its ability to

change the course of the disease would not be permissible.

To be both truthful and non-misleading, the communication must be based on "competent and reliable scientific evidence," and companies must provide a complete, scientifically accurate depiction of data. For example, this could include information about "study design and methodology, generalizability, limitations, sensitivity analyses, and information relevant to providing a balanced and complete presentation."

In evaluating whether data meet this threshold, FDA will use standards from "authoritative bodies" such as International Society for Pharmacoeconomics and Outcomes Research (ISPOR), International Society for Pharmacoepidemiology (ISPE), Patient-Centered Outcomes Research Institute (PCORI), and Agency for Healthcare Research and Quality (AHRQ).

AIMED AT VALUE-BASED CONTRACTS

The guidance fits into HHS' effort to support and encourage a shift toward paying for medical products based on value, FDA Commissioner Scott Gottlieb said in a statement.

He said the guidance will "inform market participants developing contracts that include value-based arrangements how to communicate information about how a drug might impact outcomes that are important to purchasers like a health plan or hospital, but is not an endpoint that is expressly described in the drug's approved labeling."

Manufacturers have told FDA that without clear guidance, they were "inhibited" from sharing economic information and even from generating additional data that could be used as the basis for value-based contracts, Gottlieb said.

Roger Longman, CEO of reimbursement consultancy Real Endpoints LLC, provided a current example. "We are working on a value-based contract right now where this has been an issue," he told BioCentury.

"There isn't a long history of companies getting into trouble for what they say to payers."

Daniel Kracov, Arnold & Porter Kaye Scholer

His client has been cautious about negotiating a contract based on endpoints that are not on the product label because of concerns that it would contravene FDA's prohibition of off-label promotion.

The new guidance will give the company confidence to proceed, Longman said. "It really does address some of the key fears that pharmaceutical executives have about outcomes-based contracting."

Daniel Kracov, a partner at Arnold & Porter Kaye Scholer LLP, told BioCentury the guidance provides meaningful assurances to manufacturers.

"There isn't a long history of companies getting into trouble for what they say to payers, but in an environment where companies have compliance programs and review processes, it is not easy to say 'technically it could be a violation of the law, let's do it anyway.' That's not the way responsible companies behave," he said.

Kracov added that the guidance could protect companies against allegations that their communications with payers constituted illegal off-label communication.

Longman thinks the guidance could lead to gathering new evidence, for instance in unlabeled subpopulations.

"Companies are afraid to write a contract where a drug is used in an unlabeled subpopulation," he said. The guidance could persuade a payer to enter into a contract to reimburse a drug for "patients in the subpopulation for whom it works, and simultaneously agree with a third party to gather the evidence to independently confirm its value."

According to Longman, "real-world evidence gathered in this way would be less expensive than a randomly controlled trial, yet quite credible."

Kracov also believes that the guidance creates new opportunities for contracts tied to data collection. "What could have been perceived as a seeding study in the past is now a legitimate way to gather data and measure value," he said. Seeding studies are clinical trials that are primarily intended to promote the use of a drug rather than to answer legitimate research questions.

FDA's decision to include certain unapproved uses of approved drugs -- a change from the draft guidance that PhRMA and drug companies had requested -- will facilitate outcomes-based contracts for new indications.

"The types of things payers are interested in don't always align with the label," Michelle Drozd, deputy VP, policy & research at PhRMA, told BioCentury. "I've heard payers express interest in performance-based contracts for unapproved uses [and the final guidance] gives manufactures potentially more comfort in that type of arrangement."

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Some drug companies and payers have found ways to navigate past these barriers. According to PhRMA, at least 39 value-based contracts were negotiated in 2016.

Goldberg said these were the exceptions.

"We need to broaden the path through the woods. Only certain carefully constructed contracts could make it through the regulatory forest," she said. "I can imagine that more kinds of contracts can make it through now, but there are still challenges."

TWO MORE HURDLES

The Medicaid best price rule and the anti-kickback law are two such challenges, and are not addressed by the guidance.

Drug companies are legally required to give Medicaid plans the lowest price that they provide any other payer except the Department of Veterans Affairs and some public hospitals.

Best price can stymie outcomes-based contracts because if a contract specifies that an 80% or even a 100% discount will be provided if a drug doesn't help a specific patient, best price could be interpreted to mean that the company must provide the drug at an 80% discount or free to all state Medicaid programs.

The second obstacle is the Anti-Kickback Statute, which is intended to prevent medical product manufacturers from paying providers to prescribe their products or services.

Because they include discounts or other provisions that reduce a payer's costs if they cover a drug, outcomes-based contracts could be interpreted as illegal inducements under the law.

The HHS Office of Inspector General (OIG) could state that it will not interpret the law to include value-based contracts, including those based on outcomes.

As part of the Trump administration's blueprint for lower drug prices, HHS expressed strong support for value-based contracts, and asked for public comment on steps the administration can take to facilitate them.

PhRMA is confident that HHS could act administratively to modify the way Medicaid best price and anti-kickback are implemented so they do not stand in the way of value-based contracting, Goldberg told BioCentury.

COMPANIES AND INSTITUTIONS MENTIONED

Agency for Healthcare Research and Quality (AHRQ), Rockville, Md.
Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
International Society for Pharmacoeconomic and Outcomes Research (ISPOR), Lawrenceville, N.J.
International Society for Pharmacoepidemiology (ISPE), Bethesda, Md.
Patient-Centered Outcomes Research Institute (PCORI), Washington, D.C.
Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.
U.S. Department of Health and Human Services (HHS), Washington, D.C.
U.S. Department of Veterans Affairs, Washington, D.C.
U.S. Food and Drug Administration (FDA), Silver Spring, Md.

REFERENCES

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