Twenty Years Not Too Late: FDA Issues Guidance to Help PhRMA Talk Health Care Economic Information with Payers

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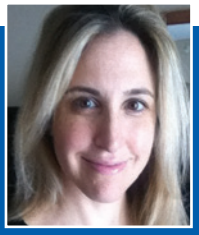

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KEY POINTS . . .

The FDA draft guidance on health care economic information (HCEI) communications between pharmaceutical manufacturers is in line with passages of the 21st Century Cures Act on the same topic.

Updated guidance expanded the audience to whom manufacturers can communication HCEI information, HCEI safe harbor, and the definition of HCEI, which recognizes clinical data.

Under the expanded HCEI safe harbor, manufacturers can now provide HCEI to payers if it is "related" to an approved indication.

Almost 20 years have passed since the Food and Drug Administration Modernization Act (FDAMA) introduced Section 114, amending the Food, Drug and Cosmetic Act. FDAMA114 allowed manufacturers the ability to communicate truthful and non-misleading health care economic information (HCEI) based on competent and reliable scientific evidence to formulary committees or similar entities, provided the HCEI was related directly to the product's approved indication. During these 20 or so years, the pharmaceutical industry had waited patiently for the Food and Drug Administration (FDA) to issue guidance on FDAMA114. While waiting, tools such as the Academy of Managed Care Pharmacy (AMCP) Format for Formulary Submissions provided a vehicle for health plans to get needed HCEI (including HCEI related to uses under investigation) from drug manufacturers [1]. In this way, manufacturers could submit necessary dossiers to managed care entities that included off-label information in response to an unsolicited request for information.

With lots of chatter around manufacturer First Amendment rights, PhRMA's issuance of *Principles on Responsible Sharing of Truthful and Non-Misleading Information About Medicines with Health Care Professionals and Payers (the Principles)* [2], along came passage of the 21st Century Cures Act (the Act), which was signed into law on December 13, 2016. For those who waited 2 decades for FDA guidance on FDAMA114, the newly signed law was reinvigorating as Section 3037 specifically addressed the topic of HCEI [3]. Then, in a little over a month from the Act being signed into law, the FDA dispelled its silence and issued draft procedural guidance entitled *Drug and Device Manufacturer Communications With Payers, Formulary Committees, and Similar Entities – Questions and Answers* to help manufacturers better understand how they can communicate HCEI with payers and similar entities [4]. A summary of this draft guidance in context of the new law is provided below.

The Draft Guidance

Since FDA guidance documents describe the FDA's current thinking on a topic, it is not surprising that the FDA's thinking is in line with Section 3037 of the newly enacted law. The draft guidance considers the expanded HCEI safe harbor and HCEI loosened restrictions as promulgated in the Act. In particular, the draft guidance reiterates the following key elements of the Act:

- Expanded audience to whom manufacturers can communicate HCEI information;
- Expanded HCEI safe harbor; and
- Expanded definition of HCEI which recognizes clinical data.

Through a question-and-answer format, the FDA helps manufacturers better understand best practices they can follow for truthful and non-misleading HCEI communications with payers.

Expanded Audience

In addition to formulary committees, under the Act, the audience to whom manufacturers can communicate HCEI information now expressly includes:

- Payers;
- Other similar entities with knowledge and expertise in the area of health care economic analysis; or
- Those persons responsible for selecting drugs for coverage or reimbursement.

Under the draft guidance, pharmacy and therapeutics committees, pharmacy benefit managers, drug information centers, and technology assessment panels are listed as examples of groups falling into this payer category. Furthermore, the draft guidance is expressly clear that this audience does not include consumers or health care providers who make individual patient prescribing decisions.

Expanded HCEI Safe Harbor

Rather than HCEI that "directly relates" to an approved indication, under the amended law, manufacturers can now provide HCEI to payers if it "relates" to an approved indication. While this is a seemingly small change, it is less restrictive than original FDAMA114 language. The draft guidance gives some clarification as to the types of analyses that it considers to "relate" to a product's approved indication. In a list that is not intended to be comprehensive or >

restrictive, the FDA provides examples of the types of HCEI analyses that it would consider to be related to the product's approved indication. The majority of examples hinge on analyses based on the use of the drug for its approved indication. While variations are present for dosing, practice setting, and duration of treatment, among other things, in general, the examples of HCEI analyses that relate to the approved indication suggest that the FDA prioritizes consistency with the product-approved indication. However, one of the examples cites analyses derived from clinical data particularly as it relates to the use of surrogate endpoints, which warrants discussion on the next element: the expanded definition of HCEI.

> "The 21st Century Cures Act was likely the impetus that the FDA truly needed to issue guidance for manufacturer HCEI communications to payers."

Expanded HCEI Definition

Perhaps most important, the draft guidance takes advantage of the Act's modified definition of HCEI, which now encompasses "analysis (including clinical data, inputs, clinical or other assumptions, methods, or results, and other components underlying or comprising the analysis) that identifies, measures, or describes economic consequences. These may be based on the separate or aggregated clinical consequences of the represented health outcomes, of the use of a drug." [4] This revised definition recognizes that economic endpoints cannot be separated completely from clinical endpoints. Since real-world uses of products are largely based on clinical usages that may be beyond the product's intended use, this modification allows manufacturers to communicate HCEI analyses concerning off-label indications if such communications relate to at least one on-label indication. However, the Act expressly states that HCEI "does not include any analysis that relates only to an indication that is not approved for the drug." [4]

With the Act now in effect and guidance issued, how does the FDA recommend a manufacturer disseminate HCEI that relates to an approved indication and is based on the lesser evidentiary standard of competent and reliable scientific evidence? Similar to PhRMA's Principles, manufacturers must clearly and prominently include the needed background and context to allow the payer audience to fully understand the HCEI. Contextual information should include:

- Study design and methodology – this includes biases and/or confounders, type of analysis, modeling, patient populations, assumptions, and study perspectives, among other things (To support study credibility, manufacturers should ensure all HCEI studies are conducted in accordance with good practice guidelines that consider the specific analyses being performed. The International Society for Pharmacoeconomics and Outcomes Research [ISPOR] outlines recommendations for generating evidence, synthesizing evidence [research methods good practices] and using evidence [decision-making best practices]. Specifically, when designing HCEI studies, manufacturers should consider ISPOR's Economic Evaluation Methods and other good practice recommendations).
- Study generalizability – applicability of HCEI obtained in one setting or population to another
- Limitations (e.g., design, data sources, exclusions)
- Sensitivity analysis and sufficient disclosure of its rationale
- Material information for balanced and complete presentation (e.g., material differences from the label, risk information, FDA-approved indication/label, financial affiliations, disclosure of omitted studies or data sources)

As required under the Act, material differences between HCEI and the approved drug label must be identified by a conspicuous and prominent statement.

The FDA draft guidance also brings some clarity to scientific exchange, a topic it has wrestled with since 1987, as it relates to manufacturer communications about investigational products to payers. Through this draft guidance, the FDA suggests manufacturers can conduct proactive scientific discussions with payers. Previously, manufacturers could only provide formulary committees with information related to investigational products in response to the health plan's request for this information. However, through the draft guidance, the FDA recognizes the need for manufacturers to be able to provide this information to payers without the payer having made the request.

Provided these communications are unbiased, factual, accurate, and non-misleading, are presented with a clear statement noting the product is under investigation and has not yet been proven to be safe and effective, and include product development stage information, the FDA will not object to manufacturers proactively providing payers with information about investigational products. This type of information could include:

- Product information (e.g., drug class)
- Information about the sought indication (e.g., clinical study protocol endpoints, patient population under investigation)
- Results from clinical or preclinical studies (no characterizations or conclusions of safety or efficacy)
- Proposed FDA approval timeline
- Product pricing information
- Marketing strategies
- Product-related programs or services

If manufacturers communicate this information and then at some point, this information becomes outdated as a result of significant changes or new information regarding the product, the FDA recommends that manufacturers provide follow-up information to payers.

While the FDA should not object to manufacturer proactive communications regarding investigational products to payers, provided they adhere to the recommendations noted above, manufacturers should note communications of HCEI regarding unapproved uses of approved drugs should conform to the FDA's 3 previously issued draft guidance documents. These provide recommendations for manufacturers responding to unsolicited requests for off-label information [5] and distribution of scientific and medical publications discussing unapproved uses of approved drugs [6,7].

Original FDAMA114 definitions were not well articulated, leaving quite a bit of room for interpretation. After 20 years, at last, some clarification came. The 21st Century Cures Act was likely the

impetus that the FDA truly needed to issue guidance for manufacturer HCEI communications to payers. As a result, manufacturers were perhaps apprehensive about leveraging FDAMA114. While professional organizations, like the AMCP, presented manufacturers with the option to provide real-world clinical data through an unsolicited request using its Format for Formulary Submissions, and PhRMA, which represents industry, had issued sensible guidelines to assist manufacturers in responsibly sharing truthful and non-misleading information to payers, the Act and draft guidance have put manufacturers on a more level playing field and perhaps a bit more at ease. While previously used tools and guidelines will remain useful and are needed, the expansion afforded under the Act and draft guidance help manufacturers better understand how they can communicate HCEI with payers, formulary committees, other similar entities with knowledge and expertise in the area of health care economic analysis, or those persons responsible for selecting drugs for coverage or reimbursement. The comment period for this draft guidance closed on April 19, 2017.

References

[1] AMCP Format for Formulary Submissions, Version 4.0. A Format for Submission of Clinical and Economic Evidence in Support of Formulary Consideration April 2016. Available at: http://www.amcp.org/FormatV4/. [Accessed, February 12, 2017]. [2] PhRMA Principles on Responsible Sharing of Truthful and Non-Misleading Information about Medicines with Health Care Professionals and Payers. Available at: https://www.bio.org/sites/default/files/PrinciplesReport_FINAL.pdf. [Accessed February 12, 2017]. [3] H.R.34 - 21st Century Cures Act. 114th Congress (2015-2016). Available at: https://www.congress.gov/bill/114th-congress/house-bill/34/text#toc-H3D7C9B659A254C679E8E7BD5F77A7603. [Accessed February 12, 2017]. [4] Drug and Device Manufacturer Communications with Payers, Formulary Committees, and Similar Entities—Questions and Answers; Draft Guidance for Industry and Review Staff. Availability, Federal Register 2017;82(12). [5] FDA's draft guidance Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices. Available at: http://www.fda.gov/downloads/drugs/guidances/ucm285145.pdf. [Accessed February 12, 2017]. [6] FDA's guidance 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 (January 2009). Available at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm. [Accessed February 12, 2017]. [7] FDA's revised draft guidance Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices (February 2014). Available at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm387652.pdf. [Accessed February 12, 2017]. ■

Additional information:

To read more about ISPOR's Economic Evaluation Methods, read the Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force at www.ispor.org/Health-Economic-Evaluation-Publication-CHEERS-Guidelines.asp.

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