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Submitted via the Federal eRulemaking Portal: http://www.regulations.gov

Stephen M. Hahn, M.D.
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Approved Drug Products With Therapeutic Equivalence Evaluations (the "Orange Book"); Establishment of a Public Docket; Request for Comments (Docket No. FDA-2020-N-1069)

Dear Commissioner Hahn:

Vizient, Inc. appreciates the opportunity to comment on the Food and Drug Administration's (FDA) recently published draft guidance for industry, "Approved Drug Products With Therapeutic Equivalence Evaluations (the "Orange Book"); Establishment of a Public Docket; Request for Comments". Vizient also appreciates FDA's ongoing efforts to support pharmaceutical competition and work to gain insights from stakeholders related to Orange Book use.

Background

Vizient, Inc. provides solutions and services that improve the delivery of high-value care by aligning cost, quality and market performance for more than 50% of the nation's acute care providers, which includes 95% of the nation's academic medical centers, and more than 20% of ambulatory providers. Vizient provides expertise, analytics, and advisory services, as well as a contract portfolio that represents more than $100 billion in annual group purchasing volume, to improve patient outcomes and lower costs. Headquartered in Irving, Texas, Vizient has offices throughout the United States.

Recommendations

Vizient has supported the introduction and adoption of generic drugs as safe and effective alternatives to branded products. As described in Vizient's recent report, "Drug Price Forecast 2020", generic competition and biosimilars have curbed the impact of routine price increases for frequently used medications. As part of FDA's Drug Competition Action Plan and the agency's continued effort to improve transparency and provide useful information to regulated industry and the public, the agency is seeking comments on how stakeholders and the public use the Orange Book and whether it can be improved. Vizient is pleased to respond to the various questions FDA poses regarding the Orange Book.

What types of people or entities use the Orange Book?
One role that Vizient plays for our members is as a group purchasing organization (GPO), where we leverage the collective purchasing power of our members to negotiate lower prices for goods and services, including pharmaceuticals. As the sourcing partner for our members, Vizient utilizes the Orange Book as it is a trusted source of information regarding generic drugs. We are also aware that our member hospitals use the Orange Book.

For what reasons do these people or entities use the Orange Book? What additional information or features (*e.g.,* additional search functions) could be incorporated into the Orange Book to make it more useful?
Vizient uses information from the Orange Book primarily to determine the relationship between brand and generic drugs, including to help inform substitution-related decisions. In addition, Vizient has used the Orange Book to make inferences that certain products (e.g., unapproved drug initiative products) are not approved if they do not appear in the Orange Book or other FDA data sources (e.g., Drugs@FDA).

Regarding features, Vizient appreciates the functionality of the Orange Book as a searchable database. As FDA considers enhancements to the Orange Book, FDA should ensure the content of the Orange Book remains easily searchable.

Other information that should also be included in the Orange Book (as well as the Purple Book) and easily accessible to clinicians are the extent of indication coverage as compared to the brand/originator product and the impact of orphan drug exclusivity on that labeling. When searching for a generic drug or biosimilar, users should quickly be able to see the similarities and differences between a generic drug and its originator reference product, including which differences are the result of orphan drug exclusivity.

In addition, the health care community needs information on the origination point of active pharmaceutical ingredients (API) and other critical components of medications. We request that FDA include additional information about the location where all components of pharmaceuticals (e.g. API, excipients, etc.) are made as well as the quality of manufacturing at those sites. The Orange Book would be a useful location for users to access this information given the familiarity of this resource.

Is the information in the Orange Book regarding therapeutic equivalence generally useful?
In general, the information regarding therapeutic equivalence is very useful for pharmacists who substitute medications when dispensing in a retail setting and for those in a hospital environment making purchasing decisions. However, during the last twenty years, the health care community has been extremely challenged by drug shortages, particularly as a result of manufacturing issues. The COVID-19 outbreak has further worsened the concern about drug shortages, manufacturing quality of pharmaceuticals, and the origination point for API and other critical components of medications licensed for use in the U.S. Therefore, there is an opportunity to better inform the healthcare community not only about the molecular and pharmaceutical comparability of related products, but also the extent to which those medications meet similar standards of quality. Therapeutic equivalency ratings should not be a characterization from a single point in time that remains static but should reflect the continued vigilance of good manufacturing adherence and resiliency.

How useful is the second letter of a therapeutic equivalence evaluation code?
For the majority of use cases of which Vizient is aware, the second letter in the therapeutic equivalence code is not used to an extensive degree. Most users, including our member organizations, are concerned with whether a drug is "A" or "B" rated.

How could the therapeutic equivalence information be made more user-friendly or otherwise be tailored to meet the needs of people or entities that use the Orange Book (*e.g.,* the therapeutic equivalence evaluation code)?
As stated above, the most helpful addition to the characterization of medications listed in the Orange Book, beyond their therapeutic equivalency, is an indication of their manufacturing quality. Prescribers and providers increasingly demand additional assurance of the quality of the products they purchase or prescribe as well as their pedigree. Beyond the extent to which a generic is molecularly comparable to a reference product, end users want more information about ongoing product quality. Therefore, Vizient recommends FDA include a designation reflecting the results of the most recent quality inspection of a medication.

If you use the information regarding therapeutic equivalence, how do you use it? Does the information regarding therapeutic equivalence promote drug competition? And if so, how?
Products that are "A" rated are preferable to "B" rated drugs as they can be substituted for the originator product without prescriber intervention. Therefore, any product that has an "A" rating will be more competitive due to ease of use. Furthermore, beyond simply the characterization of the therapeutic equivalency of a pharmaceutical, increased disclosure of information related to product quality could make such medications even more desirable and competitive. As a result, we continue to advocate for greater transparency of product quality attributes.

Is there any other information regarding the Orange Book that would be useful for FDA to consider?
As stated previously, Vizient uses tools such as the Orange Book to identify by exclusion those medications that remain "unapproved". The transition of medications from an unapproved to an approved status has presented many challenges for health care organizations. The lack of a definitive list of unapproved drugs has made it difficult to anticipate which medications might make this transition and suddenly be marketed at much higher prices. Once FDA grants an approval and then requires the removal of remaining "unapproved" competitors, the manufacturer of the newly approved entity leverages market exclusivity and patent protection to prevent additional competition. As a result, a previously inexpensive medication can become extremely costly.

An analysis[1] conducted by Vizient in February 2020 estimates that the approval of four previously unapproved medications (vasopressin, neostigmine, selenious acid, and dehydrated alcohol) has already cost the U.S. health system an additional $2.6 billion in spending and could contribute an additional $17.59 billion if ongoing patent challenges are unsuccessful. If hospitals and health systems are to contend with this degree of financial risk, they must have greater pre-emptive notice of the medications for which similar increases could occur. Based upon Vizient's

[1] Vizient (February 2020). Financial Consequences of Good Intentions: The unanticipated costs of the Unapproved Drugs Initiative (UDI), available at: https://newsroom.vizientinc.com/sites/vha.newshq.businesswire.com/files/doc_library/file/UDI_Analysis_US_Market_Spend_FINAL_022420.pdf, last accessed August 20, 2020.

estimates, there are another 19 drugs commonly used in the U.S. health system that could pursue a similar path to the four examples cited above and could add another $8.75 billion in expenses.

Conclusion

In closing, on behalf of Vizient, I would like to thank the FDA for providing us this opportunity to comment on the Orange Book. Vizient looks forward to continuing to work with the FDA to support strategies that increase generic drug utilization, minimize health care costs and mitigate increasing drug expenditures to preserve access to care. Please feel free to contact me or Jenna Stern at (202) 354-2673 or jenna.stern@vizientinc.com if you have any questions or if Vizient can provide any assistance as you consider these issues.

Respectfully submitted,

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