August 28, 2020

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"); Establishment of a Public Docket; Request for Comments

Dear Dockets Management Staff:

Thank you for the opportunity to comment on Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the "Orange Book." The National Health Law Program (NHeLP), founded in 1969, protects and advances health rights of low-income and underserved individuals and families by advocating, educating, and litigating at the federal and state levels.

The Orange Book is an important and informative resource for a range of stakeholders, including consumers, health care professionals, and drug developers. In this comment we offer a number of suggestions that would make the Orange Book more widely and readily accessible to the communities actually using the medications.[1]

I. Types of People or Entities Using the Orange Book

The Orange Book preface recognizes that the document is traditionally used by pharmacists and prescribers for education and advice on drug product selection.[2] State health agencies also use it for cost containment of health care costs.[3] Unmentioned, however, is the Orange Book's critical function for advocates working on the state and federal level to advance health care access.

NHeLP relied on the Orange Book to develop California's Contraceptive Coverage Equity Act in 2014. The Act requires that health plans cover all formulations of FDA-approved contraceptives with no cost-sharing, unless there is a therapeutic equivalent (TE) of the contraceptive; in that case, only one of the TE formulations must be covered with no cost-sharing.[4] Since then, versions of this legislation have been introduced in 40 jurisdictions and enacted in 14 states and Washington, D.C.[5] After enactment, NHeLP provides technical assistance to advocates, regulators, and policymakers on what these laws mean in practice for state prescription drug coverage. The Orange Book has been a key document in formulating our analysis, primarily the Prescription Drug Product List section found in the Orange Book Annual Edition.[6]

In partnership with a pharmacist, NHeLP reviewed all contraceptives in the 2018 Orange Book. We used the information gathered in our review to publish a model formulary tool.[7] The tool describes each unique Food and Drug Administration (FDA)-approved contraceptive and any associated TE generics.[8] Under Contraceptive Equity laws that require coverage of all FDA-approved products, at least one product from each line on the tool should be covered without cost-sharing.[9] To create this tool, we utilized Orange Book information on active ingredient, trade name, route of administration, strength, TE code, and applicant. We used both the web-based and PDF versions available on the FDA website.

The Orange Book is also vital for implementing state laws that allow for, or even mandate, generic substitution of brand-name drugs with a less-costly TE.[10] It is important for the Orange Book to be accessible and user-friendly, not only for pharmacists and practitioners, but also for patients, advocates, and policymakers.

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[1] 85 Fed. Reg. 33165 (June 1, 2020), https://www.federalregister.gov/documents/2020/06/01/2020-11683/approved-drug-products-with-therapeutic-equivalence-evaluations-the-orange-book-establishment-of-a.
[2] FDA, *Approved Drug Products with Therapeutic Equivalence Evaluations* iv (2020) [hereinafter Orange Book], https://www.fda.gov/media/71474/download.
[3] *Id.*
[4] CAL. HEALTH & SAFETY CODE § 1367.25.
[5] Nat'l Health Law Prog., Contraceptive Equity, https://healthlaw.org/contraceptive-equity/ (last visited Aug. 13, 2020).
[6] Orange Book, *supra* note 2, at 3-1.
[7] Liz McCaman, Nat'l Health Law Prog., *Contraceptive Equity in Action: A Toolkit for State Implementation* 57 (2019), https://healthlaw.org/wp-content/uploads/2019/07/NHeLP-ContraceptiveEquityInAction-Toolkit2-July-2019.pdf.
[8] *Id*.
[9] *Id*.
[10] William H. Shrank et al., *State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid*, 29 HEALTH AFF. 7 (2010), https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2009.0424.

II. Additional Information and Features To Incorporate into the Orange Book

A. Sorting and Organization

Currently the Prescription Drug Product List is organized alphabetically over approximately 1,500 pages. This makes searching for a class of drug products, such as all preventatives or opioids, extremely difficult. Additional organizational schema, such as the ability to sort drugs by medical indication or United States Pharmacopeia class, would be useful. This would be especially helpful for people with or interested in a particular condition to understand what the prescription drug options are to treat that condition.

RECOMMENDATION: FDA should modify the online version of the Orange Book to support additional organizational schema, such as the ability to sort drugs by medical indication or United States Pharmacopeia class.

B. Integrated Updates

FDA publishes periodic supplements to the Orange Book in addition to the full annual version. These supplements account for changes such as new drugs coming to market, or alternatively discontinued drugs that are no longer in use. Unfortunately, the PDF supplements are very difficult to use. For drug products like contraception, where there are so many formulations, searching for an update is time consuming and requires coming prepared with information about hormonal ingredients.

The web-based version of the Orange Book is more user-friendly and reliable for updates, especially since they are added monthly. However, with this version users are unable to view TE codes for discontinued products. There is also no clear indication of an original source product; even if that product is no longer available, the information is valuable for understanding historical context.

RECOMMENDATION: FDA should make changes to the online and PDF versions of the Orange Book, including supplements, to clearly indicate source product and TE code no matter current market availability.

C. Language Access and Accessibility

The Orange Book is a helpful tool for consumers who rely on prescription medication, because it allows them to explore alternative dosage forms, potentially cheaper generics, and new drugs with the same approved use. Unfortunately, language access and accessibility is a current barrier to consumer use. In 2018, the American Community Survey estimated that over

25 million people were limited English proficient (LEP).[11] Additionally, the Centers for Disease Control and Prevention reported that in 2015 a total of 1.02 million people were blind, and approximately 3.22 million had visual impairments.[12] As a result, millions of consumers cannot easily use a cumbersome document like the Orange Book.

To ensure that patients are empowered and informed during their medication process, we suggest development of a consumer-friendly guide that would explain the Orange Book's purpose and how to use it. While we recognize that full translation of the entire Orange Book may not be feasible, a short guide should still be available in English (including large print and Braille) and at least 15 non-English languages, and posted on the same webpage as the Orange Book. The Orange Book guide should also be created and distributed in a way that is compatible with technology assisted reading devices to allow for visually impaired people to have access to this crucial information.

RECOMMENDATIONS: FDA should develop a short, consumer-friendly guide explaining the Orange Book's purpose and how to use it, available in English (including large print and Braille) and at least 15 non-English languages, and posted on the same webpage as the Orange Book. FDA should also ensure that the guide is compatible with technology assisted reading devices.

III. Therapeutic Equivalence Information

The information in the Orange Book regarding therapeutic equivalence is generally useful, but not always sufficient to distinguish medications. Pharmacists and advocates alike often struggle to determine whether a formulation is the same, especially when considering characteristics like release time.

The coding system for therapeutic equivalents (TEs) is intended to allow users to determine quickly whether FDA has evaluated a particular approved product as therapeutically equivalent to other products.[13] The letter codes do this easily; "A" codes indicate drug products that FDA considers to be TEs to other pharmaceutically equivalent products, while "B" codes mean a drug has no TEs.[14]

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[11] U.S. Census Bureau, ACS 5-Year Estimates, Custom Table (2018), https://data.census.gov/mdat/#/search?ds=ACSPUMS5Y2018&cv=ENG&wt=PWGTP.
[12] CDC, The Burden of Vision Loss, https://www.cdc.gov/visionhealth/risk/burden.htm (last visited Aug. 13, 2020).
[13] Orange Book, *supra* note 2, at xii.
[14] *Id. at xiii.*

In certain instances, numbers are supposed to be added to an "A" code when more than one reference listed drug of the same strength has been designated under the same heading.[15] Still, there are many instances in the Orange Book when lack of number codes causes great confusion. For example, under Desogestrel and Ethinyl Estradiol there are 12 brand name drugs as well as 9 generic drugs listed, and all list the code "AB."[16] There is no numerical information on which of these Desogestrel and Ethinyl Estradiol products are TEs of one another. It is clear from the strength information that not all of these products are interchangeable, but some are; nonetheless, there is no such clarification in the listed TE code.

FDA could provide additional clarity by revising its numerical coding to clearly demonstrate exactly which formulations are interchangeable for every listed product. It would also be useful, especially in the web-based version of the Orange Book, to be able to easily pull up all TEs for a specific drug. NHeLP could use this information to better advocate for comprehensive prescription drug formularies, in accordance with state and federal law.

RECOMMENDATIONS: FDA should revise TE codes to ensure clear demonstration of exactly which formulations listed under a given heading are interchangeable. FDA should modify the web-based version of the Orange Book to facilitate easy viewing of all TEs for a specific drug.

IV. Conclusion

We strongly recommend FDA consider our suggested recommendations for the Orange Book. If you have further questions, please feel free to contact me at mccaman@healthlaw.org.

Thank you,

Liz McCaman
Staff Attorney

[15] *Id. at xv.*
[16] *Id. at 3-122.*