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Phone: +1 646 783 7100 | Fax: +1 646 783 7161 | customerservice@law360.com

Purple Is The New Orange: A New Book On Biosimilars

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Christopher J. Betti

On Sept. 9, 2014, the U.S. Food and Drug Administration published the first edition of the Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations. The Purple Book is the biological equivalent of the pharmaceutical Orange Book and seeks to aid regulatory agents, generic manufacturers and physicians by arming them with information related to biological products, such as biosimilars including, for example, providing information regarding the interchangeability of products.

The publication of the Purple Book comes several years after the enactment of the Biologics Price Competition and Innovation Act in 2010, which established an expedited pathway for FDA approval of biosimilars. Since the enactment of the BPCIA, many organizations have supported the creation of an Orange Book equivalent for biological products.

The Purple Book takes a significant step toward this goal, and will list those biological products that have been "licensed" or approved by FDA under Section 351(k) of the Public Health Service Act. Notably, the FDA's release of the Purple Book comes a little over a month after the filing of the first biosimilar application under Section 351(k) and points to the FDA providing further clarity regarding biosimilars in the coming months.

Purple Book Contents

While the Purple Book has been colloquially referred to as an "Orange Book equivalent," the two contain distinct types of information; most notably, the Orange Book includes a listing of the patents purported to cover the reference drug, while the Purple Book does not include patent information. The differences in the two books reflect the unique nature of biologics and the 351(k) approval process.

The Purple Book is split into two parts: (1) products approved by the Center for Drug Evaluation and Research and (2) products approved by the Center for Biologics Evaluation and Research. The Purple Book's lists include the following information: the date a biological product was licensed under Section 351(a) of the PHSA; whether the FDA evaluated the biological product for reference product exclusivity under Section 351(k)(7) of the PHSA; whether a biological product licensed under Section 351(k) of the PHSA has been determined by the FDA to be a biosimilar or interchangeable with a reference biological product; and biosimilarity or interchangeability evaluations. Notably, the Purple Book will organize biosimilars licensed under Section 351(k) deemed to be biosimilar or interchangeable under the

reference product to which biosimilarity or interchangeability was demonstrated.

As the approval process under Section 351(k) is still in its infancy, the lists in the Purple Book are incomplete and will require updating as biological products are licensed under 351(k). For example, currently, the CBER list does not include reference product exclusivity information or expiry date of first licensure information. The FDA has addressed this missing information in the Purple Book background by stating that, although the FDA has not determined the date of first licensure for all Section 351(a) biological products included in the Purple Book lists, it does not mean that those biological products on the list are not eligible for exclusivity.

The FDA further stated that determinations of date of first licensure and when any remaining reference product exclusivity will expire for biological products submitted under Section 351(a) will generally be made for regulatory necessity and/or at the request of the Section 351(a) license holder. Therefore, it is likely that as the field of biosimilars grows and exclusivity is granted, the Purple Book will be updated over time to accommodate these changes.

Remaining Issues

The publication of the Purple Book is a significant step toward clarifying how certain information pertaining to biosimilars will be made publicly available. However, there are numerous issues related to biosimilars that remain unresolved and that will have an impact on the information loaded into the Purple Book.

For instance, it is currently unknown what naming convention will be used to list the biosimilars in the Purple Book. Of particular concern is whether biosimilars will have the same International Nonproprietary Name as the branded biologic. An INN is a globally recognized generic name for biological, pharmaceutical and other similar products, such as the name filgrastim for the branded biologic product Neupogen. This hotly contested issue remains unresolved.

Generic companies have taken the position that all biologics should have the same INN, regardless of how they came to market. See Sept. 17, 2013, Generic Pharmaceutical Association Citizen's Petition to the FDA. On the other hand, brand companies have taken the opposite position, arguing that distinct INNs should be required in order to avoid ambiguity that would encourage treatment of all biosimilars as biogeneric equivalents, particularly in pharmaceutical references. See Citizen's Petition filed by the Biotechnology Information Institute at 15-17.

Although it is uncertain how the FDA will choose to regulate the naming of biosimilars, it is critical that the naming convention be finalized well before the approval of any biosimilar under Section 351(k). Once that information is known, the Purple Book will be able to be updated to include names of biosimilars as they are approved.

Additionally, as the FDA has yet to approve any biosimilar under Section 351(k), it is unclear how stringent it will be in identifying certain biological products as being interchangeable under Section 351(k)(6) of the PHSA. The Purple Book will list whether a biological product licensed under Section 351(k) of the PHSA has been determined by the FDA to be biosimilar or interchangeable with a reference biological product by designating it as a "B" for biosimilar or as an "I" for interchangeable. However, currently neither the CDER nor the CBER lists have designated any biological products as either a "B" or an "I," and that column in the Purple Book lists remains blank.

The onus on a biosimilar applicant to establish a biological product as being interchangeable with a reference product has yet to be resolved. As the field of biological products continues to grow, states have enacted or are contemplating enacting statutes to regulate the use of biosimilars including those determined to be interchangeable with the reference product. Some states have enacted statutes requiring a biological product to be interchangeable in order for it to be prescribed in place of the reference product. However, there is debate as to whether these statutes are too restrictive and unnecessarily limit patient access to products the FDA recognizes as not clinically different.

The presence of the Purple Book lists should provide a useful tool to both physicians and the general public to see the status of a biological product as 351(k) applications are filed and approved and as designations regarding interchangeability and biosimilarity are made.

—By Christopher J. Betti, Jennifer M. Dienes, Maria E. Doukas and Margaux L. Nair, K&L Gates LLP

Christopher Betti is a partner and Jennifer Dienes, Maria Doukas and Margaux Nair are associates in K&L Gates' Chicago office.