Your Generics & Biosimilars Industry

January 28, 2020

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Comments from The Association for Accessible Medicines (AAM) and the Biosimilars Council on behalf of our member companies, regarding FDA-2019-D-5255: Draft Guidance: Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products

The Association for Accessible Medicines (AAM) and its Biosimilars Council (Council) appreciate the opportunity to provide input on the draft guidance **Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products** and commend the Agency for addressing this critically important matter.

AAM's Biosimilars Council works to ensure a positive regulatory, reimbursement, political and policy environment for biosimilar products, and educate stakeholders and patients about the safety and effectiveness of biosimilars. Member organizations include companies and stakeholder organizations working to develop biosimilar products with the intent to participate in the U.S. market.

AAM commends the efforts of FDA and the Administration to champion a robust biosimilars market. This is a critical part of efforts to lower drug prices and reduce out of pocket costs for patients. Accordingly, AAM was pleased to take part in FDA's May 2019 Part 15 Hearing on "The Future of Insulin Biosimilars: Increasing Access and Facilitating the Efficient Development of Biosimilar and Interchangeable Insulin Products" and to submit written comments following the hearing.

Background

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) requires that previously approved biological products governed by section 505 of the Federal Food Drug and Cosmetic Act (FD&C) be transitioned to section 351 of the Public Health Service Act (PHSA) on March 23, 2020. FDA has interpreted this transition to include insulin products previously approved through the 505 pathway. In preparation for the transition, and the availability of previously approved 505 products to be reference products under the 351 pathway, this guidance addresses the Agency's interpretation of the statutory immunogenicity assessment requirements outlined in the BPCIA for applicants, pending or future, seeking approval for 351(k) and 351(k)(4) insulin products.

AAM Supports FDA's Current Thinking

AAM fully supports the current thinking of the Agency as outlined in the draft guidance, specifically the Agency's conclusion that, if a comparative analytical assessment demonstrates the proposed insulin product is highly similar to its reference product, "an applicant would not need to conduct a comparative clinical immunogenicity study, e.g., a switching study, to support licensure under section 351(k)(4)". Further, we support the Agency's interpretation of and flexibility in implementing statutory evaluation requirements for biosimilar and interchangeable products. Specifically, the position that an immunogenicity assessment justifying why a comparative clinical study to assess immunogenicity is not necessary to support a demonstration of biosimilarity. This approach will allow for faster and more efficient develop of interchangeable insulin products. Further, it reflects the extensive and broad stakeholder feedback and consensus from the Part 15 hearing related to the lack of clinical relevance of immunogenicity for insulin products.

AAM believes it is important for FDA to ensure that its approach to biosimilar and interchangeable insulin products is consistent with its approach to biosimilars and interchangeable biologic products broadly. Insulins have been commercially available for decades, and we believe these products will provide important experience for FDA to consider and incorporate into its broader regulatory framework for biosimilars and interchangeable biologic products.

Therefore, we urge the Agency to reconsider the position that "well-characterized nature of insulin products ***in comparison to the vast majority of biologics***…generally allows for a comprehensive analytical evaluation. *(emphasis added)*" While insulins may differ in size and weight from monoclonal antibodies (for example), this does not exclude more complex biologics from being "well-characterized." We are concerned this interpretation is indicative of an approach that would necessarily subject well-characterized "more complex" biologics to different approval requirements than "less complex" biologics, seemingly by virtue only of the relative complexity of the molecule instead of the strength of the analytical science to conduct a comprehensive evaluation.

We applaud the Agency on taking this step for well-characterized insulin products and encourage the Agency to build on its experience with insulin, and future approval of 351(k) and 351(k)(4) insulin products, to further streamline regulatory requirements for biosimilar and interchangeable biologics broadly in line with the strong scientific foundation of analytical comparability.

Additional Interchangeability Considerations

AAM believes that the Agency should continue to educate stakeholders that the BPCIA's statutory requirement around interchangeability, along with separate state law requirements, is properly understood as a mechanism for automatic substitution of biosimilars at the retail pharmacy, and that the designation does not confer any additional quality or safety attributes compared to a biosimilar that has not applied for an interchangeability designation.

Availability of biosimilar insulin is likely to increase patient access and savings. As such, FDA's educational efforts should continue to emphasize that a transition from a reference product to a

biosimilar insulin will not result in changes to safety or effectiveness, regardless of whether the biosimilar has applied for an interchangeability designation.

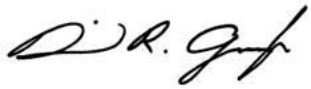
Patients on insulin therapy are deeply involved in their disease management (i.e. blood sugar monitoring and insulin injections multiple time a day). Therefore, they may be receptive to education outreach; however, they also may be vulnerable to misinformation. These patients and their healthcare providers must be made aware that biosimilars provide a therapeutic option without clinical or practical differences in efficacy or safety from the reference product.

Contrary to brand misinformation campaigns around the safety and efficacy of biosimilars, providers do not need to "wait" for interchangeable biologics to use biosimilars with their patients. Significant evidence exists that a physician-led transition from a reference product to a biosimilar medicine does not result in a loss of safety or efficacy.

Conclusion

We applaud the FDA's efforts to ensure insulin biosimilars can efficiently be developed and come to market post-March 2020. We support the Agency's draft guidance and the final guidance on interchangeability, particularly its streamlined data and study design requirements that allow flexibility and the use of global comparator products to support applications.

Sincerely,



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