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August 20, 2024

The Honorable Robert Califf
Administrator
Food and Drug Administration
Department of Health and Human Services

Submitted electronically via regulations.gov

RE: Considerations in Demonstrating Interchangeability With a Reference Product: Update

Dear Administrator Califf:

On behalf of the 9,600 American College of Rheumatology (ACR) members, I write to provide comments in response to the Food and Drug Administration's (FDA) proposal to no longer require switching studies for interchangeable products. As you know, rheumatologists and rheumatology healthcare professionals provide primarily non-procedure-based care to patients with severe conditions that can be difficult to diagnose and treat, including rheumatoid arthritis, and other forms of inflammatory arthritis, vasculitis, systemic lupus erythematosus, and multiple other debilitating diseases that require complex diagnosis and treatments. The ACR supports the use of biosimilars to treat many of these diseases, and to reduce costs and increase patients' access to biologics. As such, we commend the FDA's continued thoughtful review of the processes required to approve biosimilars. Our comments on the proposal and the FDA's evolution on "interchangeability" status follow.

Interchangeable biosimilars differ from standard biosimilars as they may be substituted for the reference product without the intervention of a prescribing practitioner. The requirement for switching studies for designation as an interchangeable biosimilar was intended to assure that such switches can be done safely by examining any immunogenicity risks. As the FDA notes, switching between biosimilars has been found to generally be safe and effective, with no differences in efficacy, safety, or immunogenicity. Requiring switching studies for biosimilar approval thus appears superfluous and may represent a barrier to patient access.

The FDA, in abrogating the requirement for switching studies, has removed the only significant barrier to interchangeability. Rather than conducting studies, applicants can use modeling to support interchangeability, drastically decreasing the investment necessary to obtain approval of a biosimilar as interchangeable. While we emphasize the need for continued scientific rigor to protect patient safety, the ACR supports the FDA's lowering of this standard because it would increase access to interchangeable drug products.

However, the ACR cautions the FDA to maintain strict guardrails that uphold patient safety when a biosimilar is granted "interchangeable" status. Per the Guidance:

> *If the FDA makes such a determination and approves the interchangeable biosimilar, the statute* (Biologic Price Competition and Innovation Act) *provides that the interchangeable biosimilar may be substituted for the reference product without the intervention of the healthcare provider who prescribed the reference product. Therefore, the switching standard is intended to provide added assurances regarding safety and efficacy in cases where the decision to switch a patient's treatment from the reference product to the interchangeable biosimilar is not made by the prescribing healthcare provider.*

A recent report has shown that the proliferation of "interchangeable" status among biosimilars leads to more pharmacy-level substitutions, often occurring without timely notification of the prescribing provider and the patient.[1] Additionally, these switches are frequently the result of mandates from insurers or pharmacy benefit managers. They are often implemented for cost-related reasons with minimal regard for the patient's well-being. They also create a significantly high degree of administrative burden for the prescribing provider and logistical challenges for the patient, who may be required to procure a new co-pay card if the biosimilar manufacturer did not develop the reference product.

The ACR strongly encourages the FDA not to overlook these potential downstream effects. We are very concerned about, and opposed to, mandates from health insurers and pharmacy benefit managers to switch from originator products to biosimilars. As such, all pharmacy-level switching must be fully transparent. The prescribing provider and the patient should be informed in a timely manner when a switch at the pharmacy counter occurs. FDA labels (package inserts) should clearly indicate whether a biosimilar is interchangeable with the reference (originator) biologic. FDA labels should also clearly delineate all indications for which a biosimilar is approved and specify whether the supporting clinical data for the indication are derived from studies of the biosimilar or the reference biopharmaceutical.

Conclusion

The ACR is dedicated to working with the FDA to ensure that unnecessary barriers are removed from rheumatic patients having access to biosimilars and that the process for switching a patient to a biosimilar is comprehensive and fully transparent to both the prescribing provider and the patient. We look forward to serving as a resource to you and working with the agency and other policy makers to explore changes and improvements needed to ensure patients with rheumatic diseases have better access to high quality medications. Please contact Colby Tiner, MA, Manager of Regulatory Affairs, at ctiner@rheumatology.org if you have any questions.

Sincerely,

Deborah Dyett Desir, MD
President, American College of Rheumatology

[1] https://gpa.informz.net/gpa/data/images/22354-Focus-on-Interchangeable-Biosimilars.pdf