American College of Rheumatology Oral Presentation to the Food and Drug Administration on Facilitating Competition and Innovation in the Biological Products Marketplace

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My name is Dr. Angus Worthing. I am grateful to speak on behalf of the American College of Rheumatology (ACR) which represents over 9,500 rheumatologists and rheumatology professionals who see the benefits of biologics in our patients every day, and who eagerly anticipate increased access to treatments with more affordable biosimilars.

The ACR strongly believes that safe and effective treatments should be available to patients at the lowest possible cost. In the absence of other large-scale levers to control U.S. biologic drug prices, FDA approvals of biosimilars may be one of the only tools to keep costs within reason.

The safe adoption of biosimilars into the U.S. marketplace remains a top priority for the ACR. Biologics are a lifeline for patients living with rheumatic disease, helping many to avoid pain, long-term disability, and life-threatening complications. Unfortunately, many of our patients struggle to afford these complex therapies due to high costs and coverage restrictions like step therapy, cost sharing, and tiering that result from biologics’ high prices.

ACR supports:

1. **Prescribing safe, effective biosimilars for the purpose of lowering costs and increasing patient access to treatment**

   The ACR welcomes the introduction of biosimilars to the U.S. healthcare system and is hopeful that the decrease in cost resulting from the availability of safe and effective biosimilars in the U.S. will increase our patients’ access to life-changing therapies and improve their overall health. Extrapolation of indications is crucial for the biosimilar pathway to reduce drug prices. The ACR does not support automatic extrapolation, but does support extrapolation after carefully identifying a minimum slate of diseases and outcomes to be studied, depending on factors including mechanism of action and predicted immunogenicity.

   a. The demonstration of safety of a biologic in one population of patients does not guarantee the safety of that biologic in another population of patients. Furthermore, efficacy of one biologic for a particular indication does not suggest that a related biologic will be efficacious for the same disease state. Nevertheless, the FDA has indicated that clinical data could be extrapolated in select cases and approval for a biosimilar could be granted, without specific testing in relevant patients, to additional indications already approved for the reference biologic.

   b. Because some populations of patients with rheumatic diseases may be more susceptible to adverse drug reactions, and because disease states in some organ systems respond differently to one biologic compared to another, extrapolation...
should be pursued with caution and only when deemed by the prescribing provider to be appropriate and in the best interests of the patient. Extrapolation should not be allowed in response to policies conceived by payers to substitute a biosimilar for a reference drug in a stable patient for the sole purpose of cost savings. Finally, if extrapolation is allowed by the FDA, then regulatory agencies and manufacturers should identify a minimum slate of disease states in which biosimilars should be tested before extrapolation to additional indications is granted.

2. Finalizing the approval pathway for interchangeability in all due haste, to include 3-switch studies as drafted

We strongly support the FDA’s proposal to require manufacturers to use robust switching studies to determine whether alternating between a biosimilar and its reference product impacts the safety or efficacy of the drug. Exposing patients in the experimental arm to each drug twice (A, B, A, B), a protocol that requires three switches, is a reasonable attempt to simulate what our patients are likely to experience with changing formularies in a multi-payer, multi-state, and ever-changing market. The requirement for multiple-switch studies to demonstrate the safety of interchangeability is particularly vital in light of the fact that providers will often not know their patient’s medication has been switched.

The ACR was pleased to see the FDA issue draft guidance on biosimilar interchangeability. This guidance brings us one step closer to the shared goal of lowering prices in the biologics marketplace. We believe the draft guidance strikes a good balance between ensuring safety and efficacy while also getting biosimilar products to market as efficiently as possible, while also providing prescribers with confidence about robust data from 3-switch studies, and we therefore encourage the FDA to finalize the guidance will all due haste.

3. Inclusion of a statement of whether or not a drug is biosimilar, and also whether or not a drug is interchangeable, in the PI

FDA labels (package inserts) should clearly indicate whether or not a compound is biosimilar and whether or not it is interchangeable with the reference 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. This will ensure that FDA labels remain a trusted source of information for US prescribers. This will also advance access to biosimilars by increasing transparency of biosimilar data, and improving prescriber understanding and confidence regarding biopharmaceuticals.

4. Robust pharmacovigilance programs to maximize patient safety and prescriber confidence

Post-marketing surveillance studies are needed in children as well as adults, as toxicities and long-term sequelae may be different in these disparate populations. The Best Pharmaceuticals for Children Act (BPCA), which reauthorizes the pediatric studies provision of FDA
Modernization and Accountability Act to improve safety and efficacy of pharmaceuticals for children, should apply to biosimilars.

The ACR strongly supports clinical trial development to focus on markers of immunogenicity, such as trough drug levels, induction of antidrug antibodies and loss of clinical efficacy, as well as adverse effects due to switching between drugs. These data should be made available in the interchangeable drug’s label via text or hyperlink. Data collection should continue through robust post-marketing surveillance. The ACR suggests that FDA allow ready access to pharmacovigilance data for investigators to analyze, and that the FDA promote and disseminate information about the program and the available data. The FDA should also consider requiring manufacturers to submit updated and standardized pharmacovigilance data as a prerequisite to certain post-market labeling changes.

5. **Transparency of transactions between manufacturers and pharmacy benefits managers (e.g., rebates) which can reduce incentives for biosimilars to be covered on payer formularies**

Rheumatologists are discouraged that our prescriptions for the only biosimilar available to our patients have been denied coverage in many cases – including for one of my patients – in favor of the costlier bio-originator. Transparency should be encouraged in the interactions between pharmaceutical manufacturers, pharmacy benefit managers and health insurance companies that determine prescription drug prices and availability.

6. **Non-Medical Switching**

We are further concerned about non-medical switching, also known as forced switching, whereby payers force patients from one biopharmaceutical to another using formulary changes. This already occurs in the absence of interchangeable status and will no doubt accelerate with the availability of biosimilars. Individual treatment decisions should be made by physicians and patients who are informed about an individual patient’s unique condition, comorbidities and circumstances. Such decisions should be made in the best interests of the patient and should not be determined solely by population-based cost considerations. We encourage the FDA to consider the issue of non-medical switching as future guidance is developed.

The ACR shares the FDA’s goal of ensuring that more affordable treatments reach patients as quickly as possible. We applaud the FDA’s measured and thoughtful approach to addressing provider confidence concerns while also prioritizing the safety of our patients. We look forward to being a resource for you and working with you to address these and other matters.