AMERICAN COLLEGE OF RHEUMATOLOGY
POSITION STATEMENT

SUBJECT: Biosimilars

PRESENTED BY: Committee on Rheumatologic Care

FOR DISTRIBUTION TO: Members of the American College of Rheumatology
Medical Societies
Members of Congress
Health Care Organizations/Third Party Carriers
Managed Care Entities

POSITIONS:

1. The ACR supports the use of biosimilars to reduce costs and increase patients' access to biologics.

2. The ACR opposes insurer-mandated switching to biosimilars and is concerned over frequent non-medical switching with biosimilars.

3. The ACR supports the omission of manufacturer rebates to payers in the calculation of the average sales price (ASP) of biosimilars to discourage unfair misrepresentation of market drug costs.

4. The Best Pharmaceuticals for Children Act (BPCA) should apply to biosimilars.

5. 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.

Background:

Biologic medications are complex molecules produced by living cells using recombinant DNA technology. Biologics became widely used in the late 1990s and since then have revolutionized the approach to treatment in many rheumatologic diseases with dramatically improved outcomes (1). Compared to conventional medications, where chemical compounds can be mass-produced at a lower cost, biologics are more costly to produce due to the nature of their complexity. These high costs strain the financial sustainability of both the healthcare system and the patients who rely on biologic therapies.

Biosimilars are biologic medications highly similar to the reference biologic product, also known as the originator. A product can be considered biosimilar to a reference product if, based on data derived from analytical studies, animal studies, and a clinical study or studies, the product is shown to be "highly similar" to the reference product, notwithstanding minor differences in clinically inactive components, and if there are no clinically meaningful differences in terms of safety, purity, and potency (2). Biosimilars and bio-originators have the same treatment risks and benefits, the same strength and dosage, and are made with the same organic source. Biosimilars offer a market-based solution to help with the affordability of specialty drugs by promoting a sustainable, robust, marketplace that encourages competition and cost savings.

Biologics are created by incorporating DNA sequences into living cells and utilizing the genetic transcription, protein translation, and processing machinery of the specific cell line to produce an engineered protein product. Once the biologic protein is produced in the living cell, an extensive purification process is required to isolate the desired protein. Biologics used in rheumatic diseases are typically large (1000-fold larger than aspirin) monoclonal antibodies (a type of protein) with complex three-dimensional structures. This structure determines their function but also gives rise to the risk of adverse events that they may cause. The structure is determined not only by the original DNA sequence but also by multiple post-translational modifications which can vary significantly based on the details of the manufacturing process (3). Companies that produce biosimilars use the reference biologic to reverse engineer the biosimilar product and do not have access to proprietary manufacturing procedures of the original biologic (4). Therefore, the biosimilar is not expected to be identical to the reference product.

The ACR commends the Food and Drug Administration (FDA) in its commitment to stringent regulation of processes required to approve biosimilars. To gain FDA approval, a biosimilar must provide comprehensive evidence through detailed chemical testing, purity testing, and clinical trials involving diverse patient populations with different diseases. The results of this testing must match up to the original biologic medication. Clinical trials ensure that biosimilars are safe and effective, with no clinically meaningful differences to the reference product. In December of 2017, the FDA approved the use of 7 biosimilar medications. There are 50 different FDA-approved biosimilars available to date. Not all biologics have biosimilar alternatives, and the availability of biosimilars varies by the specific medication and region.

Biosimilar Interchangeability:

A biosimilar product may be deemed interchangeable if it meets certain standards. According to the FDA, an interchangeable biological product is biosimilar to the reference product and can be expected to produce the same clinical result as the reference product in any given patient. If administered more than once to an individual (as many biological products are), the risk in terms of safety or diminished efficacy of alternating or switching between the biologic product and the reference product will not be greater than the risk of using the reference product without such alternation or switch (5).

Once determined interchangeable two biological products may be substituted for each other (i.e., interchanged) by a pharmacist as specified by state statutes without intervention from the prescriber. Pharmacists will be responsible for knowing which biological products are interchangeable and which will require a new prescription from the prescribing clinician before

dispensing. A pharmacist who exchanges a reference biologic prescription for an interchangeable biologic must immediately notify the prescriber and patient of such a change.

Biosimilars in Pediatric Rheumatology:

The efficacy and safety of therapeutics in adults does not guarantee safety and efficacy in children. For this reason, the Best Pharmaceuticals for Children Act (BPCA), which reauthorizes the pediatric studies provision of the FDA Modernization and Accountability Act to improve the safety and efficacy of pharmaceuticals for children, should apply to biosimilars. Understanding the unique considerations of pediatric patients, care must be taken to ensure that children are on an appropriate treatment path. The ACR also supports continued comparative effectiveness research efforts to better define the role of biologics and biosimilars in the treatment of diverse populations of adult and pediatric patients (6).

Increasing Patient Access, An Unmet Goal:

The ACR recognizes the importance of safe and cost-effective biological therapies. It had been hoped that free market price competition between biologic manufacturers and a gradual increase in prescribing biosimilars would lower prices and increase patient access (7). Unfortunately, despite best efforts, this goal has only been marginally realized to date.

Despite increasing attention to the impacts of pharmacy benefit managers (PBMs) on drug costs, agreements negotiated between PBMs and pharmaceutical manufacturers still form the basis of drug placement on a payers' formulary. Under these agreements, PBMs receive a rebate from drug manufacturers in exchange for the PBM's favorable placement of a pharmaceutical on a payer's preferred formulary tier. The PBM's disproportionate sway on the formulary has pressured manufacturers to offer significant rebates to get their biosimilar versions on payers' formularies.

Manufacturers that agree to high rebate demands report these rebates to the Center for Medicare and Medicaid Services (CMS) as part of their quarterly average sales price (ASP) reporting. The manufacturer experiences a subsequent reduction in ASP as a result. The ASP serves as the basis for CMS, and private payer, reimbursement of physician-administered pharmaceuticals using the ASP+6 equation. The rebates paid by manufacturers may reduce the ASP to a level at or below the acquisition cost of the medication. Additionally, the rebates paid by manufacturers to payers and PBMs are not passed along to the medical providers who purchased the product. The rebate value artificially reduces the ASP to a value that does not accurately reflect the true cost for rheumatologists and rheumatology professionals to acquire biosimilars.

Unfortunately, the drop in ASP has not been matched by a similar decrease in acquisition cost for certain biosimilars, leaving physicians who buy and bill biosimilars at a loss when infusing them. This problem occurs across multiple suppliers, indicating an industry-wide phenomenon. In many regions of the country, biosimilars are no longer accessible to patients for this reason. In a national survey of rheumatologists, 97% have reported that their practice has been affected by reimbursement rates which are lower than acquisition costs. Of these responses, 91% reported a discrepancy in reimbursement vs acquisition rates as more pronounced for certain biosimilars than others (8). Ironically, the lowest-cost medication, the biosimilar, cannot be administered due to economically unviable reimbursement. These circumstances force practitioners to make the

difficult financial decision to either take a financial loss to administer needed therapy or to send patients away to hospital infusion centers, where the cost to the health system can increase significantly (9).

Financial solvency in rheumatology practices is critical for patient access to high-quality rheumatology care in their communities. To mitigate the growing disparity between the cost to administer a biosimilar and its reimbursement, commercial payers should eliminate biosimilar version mandates for physician-administered drugs, or at a minimum limit them to more expensive hospital infusion sites, not independent clinics. CMS and commercial payers must also adjust the ASP formula and/or the add-on calculation. This adjustment could include an 8% add-on to the actual acquisition cost and/or the removal of manufacturer rebates to PBMs from the ASP equation. The ACR calls upon federal and state regulators to continue increasing scrutiny and oversight of PBM practices, which can serve to increase transparency in the rebate process and mitigate the perverse incentives affecting drug pricing and formulary placement.

The ACR recognizes that increasing cost pressures and formulary placement may cause payers to push patients toward biosimilars. The decision to choose one treatment option over another requires careful clinical evaluation and consideration by the physician or rheumatology professional, and the patient. Should the appropriate medication chosen have a biosimilar option, the ACR supports initial biosimilar use. However, if the most appropriate biologic does not have a biosimilar option, it should be approved by the patient's insurer, and not be switched to a different biologic class or to the biosimilar of another agent in the same class.

The ACR opposes step edits, fail-first policies, tiering, forced switching, or excessive out-of-pocket costs for all biologics and biosimilar counterparts (10). Due to the large molecular size of biosimilars, some patients may develop drug-specific antibodies that influence the efficacy of subsequent treatments. Additional variables, including anti-drug antibodies and immunogenicity, influence the choice of biologic treatment. Non-medical switching in biologic and biosimilar therapy may harm patients and lead to disease relapse. Payers should provide transparent guardrails around any form of non-medical switching. Payers should not determine the treatment of the patient, nor should the use of one therapy over another be mandated based on cost alone.

Conclusion:

Biosimilars are safe and clinically effective rheumatic disease treatments that offer a market-based solution to increase patient access to affordable specialty drugs at a lower cost. The ACR is concerned about the role of payers and PBMs in dictating the choice of therapy, especially if cost savings are prioritized over the appropriateness of a particular therapeutic agent. Insurers should not mandate switching to a different biosimilar medication for patients on established biologic therapy. If the appropriate medication does not have a biosimilar option, it should be approved by the patient's insurer and not switched to a different biologic class.

PBMs are adversely affecting the physician-administered biosimilar market in ways that harm providers, hinder patient access, and stymie uptake of biosimilar use. Increasing transparency regarding rebates paid from manufacturers to PBM's, as well as patient-centered guardrails regarding forced switching to and between biosimilar versions, will foster a healthier biosimilar

marketplace and promote increasing use of biosimilars and subsequent cost savings to patients and the healthcare system and increased patient access to effective therapies.

Approved by ACR Board of Directors: 11/2022, 8/2024

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