

# **Arthritis Foundation Position Statement: Access, Notification Substitution, Labeling and Approval of Biosimilars Entering the US Pharmaceutical Market**

## **Background**

On March 30, 2010, President Obama signed into law a reconciliation bill that finalizes Congress's health care reform legislation, the Patient Protection and Affordable Care Act. The Affordable Care Act creates a regulatory pathway for the approval of follow-on biologics, often called biosimilars. The relevant statutory text is subtitled "Biologics Price Competition and Innovation Act."<sup>1</sup>

## **The PPACA currently recognizes three types of biologic products:**

1. Reference/innovator/pioneer biologic: Unlike chemically synthesized drugs, biologic products are produced from genetically engineered animal and human proteins. Today there are several different biologic products used to treat patients with arthritis. These original, reference biologic products have met all required FDA standards for safety, efficacy and potency.
2. Biosimilar: This is a biological product that is biologically similar to the reference biologic. A biosimilar product will include genetically engineered protein substances that are "similar" to a reference or innovator biologic. There must be no "clinically meaningful differences between the biosimilar product and the reference biologic in terms of safety, purity, and potency."<sup>2</sup> Through additional testing, some biosimilars may be determined to be interchangeable with a reference biologic product.
3. Interchangeable biosimilar: This is a biosimilar product that has met additional FDA review requirements and has been determined to be interchangeable with a reference or innovator biologic. Interchangeability has yet to be defined by the FDA in terms of a defined pathway and research protocols.<sup>3</sup> A biosimilar product which meets additional "interchangeability" standards can be substituted for the reference biologic product. Thus, an interchangeable biosimilar product may be substituted for the reference biologic without the intervention of the health care provider who prescribed the reference biologic. In order to meet the interchangeability standard, the product must be:
  - Biosimilar to the reference product and expected to produce the same clinical result as the reference product in any given patient; and
  - For a biological product that will be administered to a patient more than once, the risk in terms of "safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation."<sup>4</sup>

## **Why are biosimilars such an important issue?**

- For many people with arthritis, as well as for those with various other types of chronic diseases, access to biologic therapies is limited or non-existent due to the extremely high cost or limited availability of treatments.<sup>5</sup> The average cost for a biologic treatment is \$16,000 per year, though some treatments can be as much as \$10,000 per month.<sup>6</sup>
- Biologic sales are increasing at a much faster rate than for non-protein-based drugs, and by 2015, eight of the 10 top-selling medications are expected to be biologics.<sup>7</sup>
- For patients who need biologic therapies to control their disease, its symptoms and pain, but who struggle to afford these therapies, biosimilars may hold the key to improving access to safe, effective, and less expensive treatments. The Congressional Budget Office expects biosimilars to save approximately \$13 billion over the next ten years and cost between 60 and 80% (a 20 to 40% cost reduction) of the reference biologic drug upon market entry.<sup>8</sup> Other studies indicate the cost of biosimilars might be closer to 80 to 90% of the reference biologic.<sup>9</sup>
- By 2020, biosimilars are expected to account for up to 50% of the off-patent biological drug market, assuming there is a price discount of at least 20-30%.<sup>10</sup>

## **What problems are related to the introduction of biosimilar drugs?**

- Biologic products are complex medicines manufactured from living organisms. Minor changes in the manufacturing process can cause variations in the final product that could dramatically change the way a patient responds to the medication.
- The FDA has not yet set explicit standards for approval of biosimilars or interchangeable biologic products. The FDA may request different information when approving applications for biosimilar drugs compared to reference biologics. For example, some phases of clinical testing required for a reference biologic may not be required for a biosimilar (this falls under FDA's discretion).
- Biosimilar drugs, such as those to be possibly used in the treatment of RA and certain types of cancer, will likely enter the US market in 2014 or later, having undergone the same premarket approval system as their reference biologics, and the long-term side effects are not yet known.
- Biologic medications often work differently for different people, making it difficult for physicians to ascertain whether the biosimilar will work as well for them; even a medicine that has a good track record in the population at large may not have as positive an effect on a particular patient. Predicting the response of a particular patient receiving treatment with a biosimilar or interchangeable biologic may prove difficult.

### **Some states are taking action to ensure patient protection.**

A growing number of states are proposing legislation regulating biosimilars and their potential substitutions for biologics. The structure of these bills varies, and several do not include both of the following points:

- to notify both the patient and their prescribing physician any time a biosimilar medication is substituted for a biologic medication; and
- to require that the pharmacist and/or prescriber retain records of patients who receive biosimilars for a set period of time.

### **Recommendations for Action**

**The Arthritis Foundation believes the provider-patient relationship should be the key place where decisions about drug and biologic therapies should be decided and recommends the following:**

- Access to safe therapeutics:
  - Patient safety must remain the number one priority in any discussion of the introduction of biosimilars to the market; even if a drug is less expensive and more accessible than a brand name alternative, these advantages mean nothing if the drug does not successfully treat the patient – or worse, harms the patient. Physicians and patients should have access to both interchangeable biosimilars and non-interchangeable biosimilars that have obtained FDA approval. Patients should have access to all FDA-approved products in a class.
- Notification and substitution:
  - There must be a clear substitution process where physicians have the right to declare whether substitutions are prohibited.
  - The patient and prescribing physician should be notified within 24 hours by the pharmacist when a substitution has taken place. Since biosimilars are not exact replicas of biologics, the labeling of the biosimilar should be as clear as possible so that pharmacist, patient, and physician know exactly which product the patient is receiving.
  - Substitution of a biosimilar product should only occur when the product has been determined by FDA to be interchangeable with the prescribed product for the specified indicated use.

- Patients who are stable on a reference biologic should not be required to switch to a biosimilar product.
  - New patients may be started on an interchangeable biosimilar product with approval of patient and physician.
  - The pharmacist and the prescribing physician should keep records of any substitutions made for a minimum of 5 years, as this will provide records that document how and when a patient was treated. Such records may be invaluable in case the patients' condition changes over time, or an adverse reaction or disease evolution occurs.
- Labeling and Approval:
    - Biosimilars should have distinct names allowing them to be easily distinguished from their reference products so that the pharmacist, patient and physician know which product the patient is receiving.
    - Long-term, post marketing, registry-based data collection is necessary to monitor for less common – but nonetheless important- adverse events.
    - Post-marketing surveillance studies are needed in children as well as adults because toxicities and long-term sequelae may be different. 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.

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<sup>1</sup>Fish News: Biosimilars Legislation Update, Fish & Richardson, Spring 2010, found at <http://www.fr.com/Biosimilars-Legislation-04-08-2010/>, citing Patient Protection and Affordable Care Act (“PPACA”), Pub. L. No. 111-148, §2702, 124 Stat. 119, 318-319 (2010). (Title VII, Subtitle A, § 7002, titled “Approval Pathway for Biosimilar Biological Products,” explains this pathway. The link to the federal legislation can be found at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/ucm216146.pdf>). § 7002 explains the requirements for submitting an application for a biosimilar or interchangeable biologic product.

<sup>2</sup>PPACA, Title VII, Subtitle A, § 7002, definitions section (this section amends Section 351(i) of the Public Health Service Act (42 U.S.C. 262(i))).

<sup>3</sup>Shea, Timothy J. “The New Biosimilars Act: Overview of the Legislation and IP Implications,” GEN Theater, BIO International Conference, Chicago, IL, May 5, 2010. (This presentation provides a good overview of the biosimilars act and what each definition means within the PPACA. It can be found at <http://www.skgf.com/media/pnc/9/media.1299.pdf>).

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<sup>5</sup>New York State Assembly Member Micah Z. Kellner, Address to New York State Assembly: Prohibiting Specialty Tiers in Prescription Drug Formularies (2010), found at <http://www.micahkellner.net/pubs/Specialty%20Tiering%20Report.pdf>. (This report lists the cost of Humira in 2009 as being \$1,500 per month, or \$495 with a 33% coinsurance).

<sup>6</sup>Maiese, Brett A., Lee, Edward H. Toscani, Michael. “Follow-on Biologics & Biosimilars Literature Review: the Current Landscape and Implications of Recent Healthcare Legislation for the U.S. Market.” Specialty Pharma Journal, last updated 2012, citing Shapiro R, Singh K, & Mukim M. “The potential American market for generic biological treatments and the associated cost savings.” February, 2008.

<sup>7</sup>Maiese, Brett A., Lee, Edward H. Toscani, Michael. “Follow-on Biologics & Biosimilars Literature Review: the Current Landscape and Implications of Recent Healthcare Legislation for the U.S. Market.” Specialty Pharma Journal, last updated 2012.

<sup>8</sup> Maiese, Brett A., Lee, Edward H. Toscani, Michael. “Follow-on Biologics & Biosimilars Literature Review: the Current Landscape and Implications of Recent Healthcare Legislation for the U.S. Market.” Specialty Pharma Journal, last updated 2012.

<sup>9</sup>Howell, Peyton. “How much cheaper will biosimilars be?” FiercePharma, March 2, 2012, found at <http://www.fiercepharma.com/story/how-much-cheaper-will-biosimilars-be/2012-03-02>

<sup>10</sup>“Shaping the biosimilars opportunity: A global perspective on the evolving biosimilars landscape.” IMS Health, December 2011, page 6, found at [http://www.imshealth.com/ims/Global/Content/Home%20Page%20Content/IMS%20News/Biosimilars\\_Whitepaper.pdf](http://www.imshealth.com/ims/Global/Content/Home%20Page%20Content/IMS%20News/Biosimilars_Whitepaper.pdf)

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