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BIOSIMILARS: LOWER COST VERSIONS OF BIOLOGIC DRUGS

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Most of us are familiar with the concept of generic drugs. Lower cost generic versions of drugs become available when the patent of the brand name product expires. The introduction of multiple generic products for a brand name drug, especially a blockbuster brand name drug, typically signals the beginning of significant cost savings for patients and payers.

Many of the newer blockbuster drugs that are driving today's drug trend don't have generic versions – and never will. That's because many of the remaining brand name blockbuster drugs are actually biologic products for which the generic drug approval pathway does not apply.

What is a biologic?

According to the FDA, biologics are medicines that generally come from living organisms, which can include humans, animals, and microorganisms, such as yeast and bacteria. Insulin was the first biopharmaceutical product approved for therapeutic use, made using recombinant DNA technology in 1982. Since then, biologics have grown in both approval and acceptance and are now believed to account for 20% of the worldwide pharmaceutical market.

Traditional non-biologic products (also known as small molecule drugs) have a relatively simple chemical structure that can be easily replicated in a laboratory environment using standard organic chemistry reactions. In contrast, biologic products must be derived or produced from living material, and there is a degree of natural variability in all biologic products – it is simply not possible to generate an exact copy of a product that comes from living cells.

Approval pathway for generic drugs

Before a manufacturer can market a generic version of a small molecule product, the manufacturer must submit an Abbreviated New Drug Application, or ANDA to the FDA. In the application, the manufacturer must demonstrate that the generic is bioequivalent – meaning that the same amount of active ingredient will be available to the patient who takes the medication – to a previously approved product. When a manufacturer submits an ANDA, clinical trials demonstrating safety and efficacy are not required. Without a

need for costly clinical trials, the barriers to entry for generic manufacturers are low which leads to additional competition and ultimately lower prices for consumers and payers.

Biosimilars

Prior to 2010, an abbreviated pathway did not exist to allow other manufacturers to produce versions of already-licensed biological products. While other manufacturers could market biologic products after the initial patent expired, those additional manufacturers would need to submit the complete biologic approval application, including safety and efficacy data, for approval as entirely new biologics.

The marketplace for biologic drugs changed when the 2010 Affordable Care Act created a pathway for biosimilar approval. Under the new process, the manufacturer must provide evidence that the biosimilar version is highly similar to the reference product with no clinically meaningful differences. While the biosimilar approval process is more streamlined than the initial approval process for a new biologic, it requires significantly more data and analysis than does the ANDA required for generic drugs.

Most states do not allow pharmacists to substitute biosimilar drugs for the brand product without approval from the prescriber. While the ACA created a pathway for some biosimilar drugs to be deemed interchangeable to the original products following additional evaluation and testing, no biosimilars to date have been approved as interchangeable biologics.

Currently available biosimilars

The first biosimilar product in the US, Zarxio®, biosimilar for Neupogen®, entered the market in September 2015. Since then, several other biosimilars have been introduced, including three which compete against the blockbluster Remicade® – Inflectra®, Renflexis™ and Ixifi™. Patent disputes and litigation have delayed the launch of biosimilars for the inflammatory drugs Enbrel® and Humira®.

Biosimilar naming conventions

Each new biosimilar is assigned a trade name as well as a generic name. The generic name is hyphenated with an additional 4-letter suffix to differentiate it from the generic name of the original branded biologic or any other biosimilars. For example, the generic name for Remicade® is infliximab, while the generic name for Inflectra® is infliximab-dyyb and the generic name for Renflexis™ is infliximab-abda.

Anticipated effects on pricing

While biosimilars are expected to create cost savings for payers and patients, the savings are not anticipated to be as significant as seen with traditional generic drugs. This disparity is due both to the more rigorous FDA approval process as well as the additional capital investment required for a **biologic production facility.** Early data has shown that biosimilars can reduce prices by as much as 35% once two biosimilars are available for the same biologic. In contrast, traditional generic drugs can be sold at discounts of 75% or more once multiple products are available in the market. Nonetheless organizations such as RAND estimate that biosimilars will reduce US spending on biologic drugs by over $50 billion dollars over the next 10 years.