Has the Food and Drug Administration (FDA) finally ushered in a new era for the U.S. biosimilar marketplace? Many in the industry are hopeful after the Agency approved its first interchangeable biosimilar, Mylan’s Semglee (insulin glargine) on July 28, 2021. Mylan’s Semglee is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. It is both biosimilar to and interchangeable with Lantus (insulin glargine) meaning it can be substituted for Lantus at the pharmacy-level without the need for a prescription from a healthcare professional. This approval is important because it furthers FDA’s commitment to supporting a competitive marketplace for insulin products. The availability of interchangeable biosimilar products can provide more treatment options to patients, lowering the treatment costs and enabling greater access for more patients. One can hope that this approval marks the beginning of a trend in the biosimilar marketplace.

Biosimilars are a subset of biological products, or biologics. Biologics are large complex molecules made from living sources such as bacteria, yeast, and animal cells. Each batch varies slightly due to the composition of living organisms. In addition, they are more complicated to purify, process, and manufacture. Accordingly, a biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product, but it cannot be an identical copy of the reference product. Drugs, on the other hand, are made from chemicals using smaller molecules that are easier to copy. A biosimilar may or may not be interchangeable with its reference product. An interchangeable biosimilar is a biosimilar that meets additional requirements and may be substituted for the reference product at the pharmacy, depending on state laws. In anticipation of the FDA’s approval of interchangeable biosimilars, most, if not all states have enacted laws describing conditions under which pharmacists can substitute these agents. See our prior post summarizing FDA guidance on biosimilar interchangeability.

Biosimilars, including interchangeable biosimilars, are safe and effective biological medications for treating many illnesses, including chronic skin diseases, inflammatory bowel diseases, arthritis, kidney conditions, diabetes, and cancer. Biosimilars and interchangeable biosimilars have the same expected benefits and risks as their reference products, which are existing FDA-approved biologics. In essence, biosimilars and interchangeable biosimilars are analogous to generic drugs in some ways, as both are compared to brand-name drugs and may offer patients more affordable treatment options due to the abbreviated nature of the clinical development program and FDA marketing application.

All FDA-approved biologics, including biosimilars, undergo a rigorous evaluation to ensure safety, efficacy, and quality. For approval, biosimilars and interchangeable biosimilars are approved through an abbreviated pathway that compares to and evaluates the product against a reference product to verify that the biosimilar has no clinically meaningful differences in terms of safety and effectiveness. For approval as an interchangeable biosimilar, manufacturers must provide additional data that reflect how the interchangeable biosimilar may be used in the marketplace with patients. Specifically, a biosimilar can be judged interchangeable with the reference product if the biosimilar manufacturer can show that the biosimilar produces the “same clinical result” as the reference product in “any given patient” and can be switched with the reference product with no additional risks in terms of safety or diminished efficacy. Meeting this higher threshold delays market entry, which explains why the first interchangeable was just approved, over a decade after Congressional enactment of the biosimilar amendments to FDA’s authorizing statute for regulating biologic products. In addition, it is expensive for the biosimilar manufacturer to seek approval as an interchangeable, which may have dissuaded many manufacturers from undertaking such efforts.

This market delay is partly why FDA published its Biosimilars Action Plan (BAP) in July 2018. The BAP acknowledged the lack of competition in the biologics space and recognized the numerous barriers to the development and utilization of biosimilars. Therefore, FDA outlined four key goals to tackle this...
issue including: (1) streamlining the approval process, (2) improving regulatory clarity, (3) increasing educational efforts to improve understanding among stakeholders, and (4) collaborating with the Federal Trade Commission (FTC) to address anticompetitive behaviors. In February 2020, FDA updated the BAP, in coordination with FTC through a joint statement noting several new actions aimed at promoting greater competition in biosimilar markets.

FDA has now approved its first interchangeable biosimilar product and its 30th biosimilar product in the U.S. While it has been improving, the U.S. biosimilar market is still mediocre when compared to Europe. However, insulin may be the next biosimilar target for the U.S. industry. Currently, the insulin market is dominated by a handful of brands and characterized by high prices that have been the subject of various Congressional hearings and reports about high costs. Of the approximately 35 million Americans who have diabetes, about a third require insulin to manage their disease. The out-of-pocket costs for insulin can be a major expense, even with insurance. To date, biosimilars marketed in the U.S. typically have launched with initial list prices 15% to 35% lower than comparative list prices of the reference products. According to Dr. Peter Stein, director of the Office of New Drugs in the FDA’s Center for Drug Evaluation and Research, “Access to affordable insulin is critical and long-acting insulin products, like insulin glargine, play an important role in the treatment of Types 1 and 2 diabetes mellitus, . . . The FDA’s high standards for approval mean health care professionals and patients can be confident in the safety and effectiveness of an interchangeable biosimilar product, just as they would for the reference product.”

Despite barriers to their development and commercialization, biosimilars remain a powerful tool with the potential to lower health care costs and improve patients’ access to valuable therapeutics. This pioneering FDA approval raises the question of whether interchangeable biosimilars could make a bigger dent in the U.S. market for biosimilars including insulin and other products. However, the approval also places more pressure on traditional insulin and other product manufacturers, who have come under heavy criticism for high prices in recent years.

We will be on the lookout for additional movement from FDA and industry regarding interchangeable biosimilars.

Authors

Joanne S. Hawana, Member

Joanne counsels global clients on the regulatory and distribution-related implications when bringing a new FDA-regulated product to market and how to ensure continued compliance after a product is commercialized.

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