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FDA Biosimilar Approval Foreshadows IP Litigation Issues

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In July 2021, the U.S. Food and Drug Administration granted a determination of interchangeability to a biosimilar drug for the first time.[1]

This approval has raised expectations for the potential of biosimilars to lower the costs of biologic drugs as it is expected to be permitted to be substituted for the reference product at the pharmacy.[2]

Collectively, sales of biologics, including biosimilars, have grown substantially in the past several years.

As of 2018, biologics accounted for 36% of all prescription drug spending in the U.S.[3] As the U.S. biologics marketplace continues to evolve, it will be important for both branded biologic manufacturers and biosimilar manufacturers to understand the changing dynamics of the market and how those dynamics may impact biosimilar litigation.

One critical consideration is the possibility that originator biologics may experience price erosion due to biosimilar entry as this can have a significant impact on issues such as launch-at-risk decisions, potential damages, settlement evaluation and the assessment of irreparable harm.

Below we discuss key features of the biologics marketplace and explain how these economic issues impact biosimilar IP litigation.

Biosimilar and Generic Competition

Biologics are large-molecule drugs derived from living organisms and are often used to treat chronic, complex and rare diseases. Whereas most small-molecule drugs are chemically synthesized, biologic drugs are more complex and therefore require a more complex, and costly, manufacturing process.[4]

In 2019 there were only 400 FDA-licensed biologic products out of the 20,000 prescription drug products approved for marketing in the U.S.[5] Although biologics account for only about 2% of all prescriptions, many of the best-selling drugs are biologics.[6] Notably, half of the 10 best-selling drugs in 2020 were biologics.[7]

The biologics marketplace can be segmented into originator biologic products and biosimilar products. A biosimilar is a highly similar version of an already approved reference biologic product and has no clinically meaningful differences in safety, purity and potency with the reference product.[8]

Biosimilars have captured 20% of volume in the portion of the biologics marketplace that faces biosimilar competition.[9] By contrast, among small-molecule drugs, generics have captured 97% of volume in market segments that face generic competition.[10]

In addition to obtaining a much smaller share of the marketplace, biosimilars capture share more slowly.[11]

The more rapid uptake of generics may be explained by factors such as tiered formularies with lower patient copayments for generics than for branded drugs, health plan restrictions limiting formulary coverage to generics in certain categories, and, perhaps most importantly, state laws allowing pharmacists to automatically substitute generics for brand-name drugs prescribed by physicians.

In addition to uptake, biosimilars and generic drugs differ in the price competition they offer. Although the vast majority of small-molecule prescriptions are filled with generic products, generics account for only 22% of net spending.[12] This is due to the fact that generics are priced at a significant discount to branded products.

A recent study by the FDA demonstrated that a greater number of generic manufacturers selling a given drug is associated with lower generic prices.[13] For example, when there are six or more generic competitors, prices fall to less than 10% of the original branded drug.[14]

Price erosion for biosimilars is more muted. A recent study that analyzed the net pricing of seven biologics facing biosimilar competition found that each additional biosimilar entrant resulted in a 5.4%-7% reduction of the weighted average price for the product line, where the product line is defined as the branded biologic and all biosimilar versions.[15]

Branded small-molecule drugs dispensed at pharmacies do not typically try to compete with generics based on price and, in some cases, branded small-molecule drugs may even increase list price after generic entry.

In contrast, two recent studies that looked at the list and net price of branded biologics in the U.S. following the launch of biosimilars found that net prices of the reference products decreased following the launch of biosimilars, although list prices remained flat.[16]

Implications for Biosimilar IP Litigation

Price erosion of the reference product appears more likely to occur with biologics than with small-molecule drugs, according to the recent literature noted above.

Additionally, when price erosion does occur, the resulting profit loss is likely to be more significant for biologic reference products than for small-molecule reference products.

When marginal costs are very low for the originator, as is typically the case in the context of small-molecule drugs, then a given percentage reduction in the originator's price has approximately the same effect on its profits as the same percentage reduction in its unit sales.

However, as marginal cost is greater and the per-unit profit margin narrows, this is no longer the case: A percentage reduction in price when marginal cost is high has a greater effect on profits than the same percentage reduction in unit sales. Since biologics tend to be associated with higher marginal costs, lost profits arising from price erosion are more likely to be a concern in the context of a biosimilar launch than a generic launch.

The competitive dynamics of biosimilars create three important considerations for patent infringement litigation.

First, price erosion may affect biologic innovators more than branded small-molecule drugs, so an at-risk launch may have a more significant effect on a biologics innovator.

Second, the likelihood that the originator product suffers price erosion may be a significant factor in the analysis of irreparable harm, which is part of the four-factor test that plaintiffs generally must satisfy when seeking a preliminary injunction.[17]

Third, while the launch of a potentially infringing biosimilar is unlikely to lead to as rapid a decline in the reference product's share as would be expected with a generic drug example, if even a small decline in the price of a reference product can be attributed to the biosimilar, the potential damages exposure could be quite substantial.

This potential exposure should be considered in any damages or settlement analyses performed by either party involved in the litigation.

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[1] FDA, "FDA Approves First Interchangeable Biosimilar Insulin Product for Treatment of Diabetes" at https://content.govdelivery.com/accounts/USFDA/bulletins/2ea6ffc; "Letter from FDA to Mylan Pharmaceuticals, Inc. re BLA 761201, July 28, 2021, https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/761201Orig1s000ltr.pdf, p. 2.

[2] Joshua Cohen, "Approval of First Interchangeable Biosimilar, Semglee, is Sign of an Improving U.S. Biosimilars Market, Despite Challenges," Forbes, August 1, 2021 at https://www.forbes.com/sites/joshuacohen/2021/08/01/approval-of-first-interchangeable-biosimilar-semglee-is-sign-of-an-improving-us-biosimilars-market-despite-challenges.

[3] Total net spending on prescription drugs in 2018 was $344 billion with biologics accounting for $125.5 billion or 36 percent of the total. Medicine Use and Spending in the U.S.: A Review of 2018 and Outlook to 2023, IQVIA Institute, May 9, 2019, p. 2 and 26.

[4] R. Otto, A. Santagostino, and U. Schrader, "Rapid growth in biopharma: Challenges and opportunities," McKinsey & Company, December 1, 2014 at https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/rapid-

growth-in-biopharma#.

[5] US Food and Drug Administration, Fact Sheet: FDA at a Glance, October 2019, https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance.

[6] Medicine Use and Spending in the U.S.: A Review of 2018 and Outlook to 2023, IQVIA Institute, May 9, 2019, Introduction and p. 10, https://www.iqvia.com/insights/the-iqvia-institute/reports/medicine-use-and-spending-in-the-us-a-review-of-2018-and-outlook-to-2023.

[7] Urquhart L., "Top companies and drugs by sales in 2020," Nature Reviews Drug Discovery, 2021 March; 20: 253.

[8] FDA, "Biosimilar Product Regulatory Review and Approval," https://www.fda.gov/files/drugs/published/Biosimilar-Product-Regulatory-Review-and-Approval.pdf.

[9] Medicine Use and Spending in the U.S.: A Review of 2018 and Outlook to 2023, IQVIA Institute, May 9, 2019, Introduction and p. 10, https://www.iqvia.com/insights/the-iqvia-institute/reports/medicine-use-and-spending-in-the-us-a-review-of-2018-and-outlook-to-2023.

[10] M. Aitken, "Biologics Market Dynamics: Setting the Stage for Biosimilars," IQVIA, March 9, 2020, p. 7.

[11] M. Aitken, M. Kleinrock, and E. Muñoz, "Biosimilars in the United States 2020-2024: competition, savings, and sustainability," IQVIA, September 29, 2020, p. 2, https://www.iqvia.com/insights/the-iqvia-institute/reports/biosimilars-in-the-united-states-2020-2024; Grabowski, Henry et al., "Updated trends in US brand-name and generic drug competition," Journal of Medical Economics, 2016, p. 8.

[12] Association for Accessible Medicines, "The case for competition. 2019 Generic Drug & Biosimilars Access & Savings in the U.S. Report," 2019, https://accessiblemeds.org/sites/default/files/2019-09/AAM-2019-Generic-Biosimilars-Access-and-Savings-US-Report-WEB.pdf.

[13] Ryan Conrad and Randall Lutter, "Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices," FDA, Center for Drug Evaluation and Research, December 2019, at https://www.fda.gov/media/133509/download.

[14] Ibid, p. 2.

[15] Richard G. Frank, Mahnum Shahzad, William Feldman and Aaron Kesselheim, "Biosimilar Competition: Early Learning (March 2021)," NBER Working Paper No. w28460, https://ssrn.com/abstract=3799809. The maximum number of biosimilar entrants observed in the reported data is three entrants and the time period studied varied by product given the different market entry dates for each biosimilar.

[16] AlvaroSan-Juan-Rodriguez, Walid F.Gellad, and Chester B.Good, et al., "Trends in List Prices, Net Prices, and Discounts for Originator Biologics Facing Biosimilar Competition," JAMA Network Open, 2019 Dec 2;2(12):e1917379, https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2757480; Alex Brill and Benedic Ippolito, "Biologics are not natural monopolies," Health Affairs Blog, July 2, 2019, https://www.healthaffairs.org/do/10.1377/hblog20190701.349559/full/.

[17] Anna Majestro, "Preparing for and Obtaining Preliminary Injunctive Relief," ABA Section of Litigation, The Women Advocate, Practice Points, June 4, 2018, at https://www.americanbar.org/groups/litigation/committees/woman-advocate/practice/2018/preliminary-injuction-relief/. In the context of non-interchangeable biosimilars, lost share to the originator biologic may also be an important consideration when analyzing irreparable harm to the extent that patients receiving a biosimilar cannot automatically be switched back to the reference product.