



## Drug Policy 101: Biosimilars

Biologics – drugs derived from living organisms that are used to treat conditions such as rheumatoid arthritis, multiple sclerosis, and some cancers – are the fastest growing component of prescription drug spending.

While some of these drugs have fostered significant advancements in medicine, some biologics cost hundreds of thousands of dollars per year, imposing crippling costs on patients, the health care system, and the government.

Furthermore, generic competition with brand-name biologics is severely lacking in the United States, despite the existence of an abbreviated pathway for follow-on drugs, known as biosimilars.

This paper:

- Provides background on biologic drugs
- Explains how biosimilar products could bend the cost-curve
- Discusses the barriers to achieving cost reductions
- Highlights key trends to watch

As biologic drugs gain further momentum, a variety of flaws in the market – such as a significant lack in competition among drug makers – must be addressed.

### Specialty drugs and biologics

Specialty drugs are often used to treat complex, chronic, and rare diseases. They often require a prescription by a specialist, special handling, intravenous administration, and a high degree of patient management to ensure compliance and safety.

In recent years, the specialty drug sector has experienced monumental – and disproportionate – growth in utilization and spending.<sup>1</sup> While spending on other medications has been in decline, spending on specialty drugs reached \$318 billion in 2018 – up from \$172 billion in 2013 – which represents 41 percent of overall pharmaceutical spending in developed markets. Spending on specialty drugs is projected to reach 48 percent of total spending in these markets by 2022.<sup>2</sup>

Biologics are a subset of specialty drugs. Unlike traditional “small molecule” medications made from chemical compounds, biologics are large, complex protein molecules that provide groundbreaking therapies for conditions such

as anemia, diabetes, multiple sclerosis, hepatitis, and cancer. Annual treatment prices for some of these products can reach hundreds of thousands of dollars, and for some patients the costs can be crippling.<sup>3</sup>

### Biosimilars

The rapid uptake of high-priced biologics generated support for developing an accelerated approval process for follow-on products that, much like generic drugs in the traditional pharmaceutical market, could spur competition and provide lower-priced options. These treatments are known as biosimilars.

Generic versions of traditional small-molecule drugs approved under the Food, Drug, and Cosmetic Act can go through an expedited review pathway by filing what is called an Abbreviated New Drug Application. Created under the Hatch Waxman Act of 1984, this pathway establishes whether the generic drug is “bioequivalent” – or essentially identical – to the brand-name drug, also referred to as the original product.<sup>4</sup>

For follow-on versions of branded biologics, the law provides a different approval pathway created under the Biologics Price Competition and Innovation Act. Known as biosimilars, these follow-on products are highly similar variants of already approved biologic drugs that show no meaningful clinical difference in terms of safety, purity and potency.<sup>5</sup> The Food and Drug Administration requires biosimilars to meet higher evidentiary thresholds to establish “biosimilarity” or “interchangeability” to the original product than small-molecule generic drugs.

The law allows manufacturers to pursue the heightened standard of interchangeability if the following criteria are met:

- 1) The biosimilar and original products produce the same clinical result, and
- 2) Switching between the different products results in no additional risks in terms of safety or efficacy<sup>6</sup>

Products deemed interchangeable may be substituted by a pharmacist without intervention of the prescriber, similar to how generics are treated.<sup>7</sup>

Biosimilar products have significant potential to expand treatment options and reduce costs through increasing competition and expanding patient choice in the biologic

space.<sup>1</sup> In fact, biosimilars are projected to cost 10 to 30 percent less than original biologics and estimates suggest that they may save as much as \$44 billion in U.S. health care costs over the next 10 years.<sup>8</sup>

However, despite a process in place for approving biosimilar products, FDA has licensed 12 biosimilars, only four of which are available to patients.<sup>9</sup> The primary cause of delays are patent disputes. To date, FDA has not designated any biosimilar products as interchangeable. By comparison, as of March 2018, the European Commission has approved more than 40 biosimilar products across 15 different biologic classes.<sup>10</sup>

The evidentiary standard to which biosimilar products are held – though essential – is rigorous, and requires extensive analytical testing plus supportive clinical studies, more so than generic small-molecule drugs. Biosimilars are expensive to produce, the cost of research, development, and manufacturing is high relative to generics, and their market share and revenue potential is uncertain. These and other issues create barriers to market entry for biosimilar manufacturers.

## Moving forward: What to watch

Several distinct areas of policy in the biosimilars space are worth tracking.

**Patents and exclusivity:** A patent, which is typically granted for 20 years, gives the drug manufacturer sole rights to produce a drug. Exclusivity, however, is granted by the FDA after a drug is approved and gives the manufacturer sole marketing rights to a biologic for 12 years.<sup>11</sup>

Recently, more payers and policy experts have supported changing the 12-year period of exclusivity to seven years, thereby allowing lower-priced alternatives, such as biosimilars, to enter the market.

Length of exclusivity has also been widely discussed in trade negotiations, including the Trans Pacific Partnership and United States-Mexico-Canada Agreement.<sup>12</sup> According to proponents, lowering the exclusivity period to seven years would provide an opportunity for lower-priced biosimilars to enter the marketplace and foster competition, providing an estimated savings to taxpayers of nearly \$7 billion over the next 10 years.<sup>13</sup>

**Interchangeability:** To be an interchangeable biosimilar, the product must not only meet biosimilarity standards, but also must produce the same clinical result as the original product in any given patient.<sup>14</sup>

Additionally, for patients needing continuous treatment, switching between the original and interchangeable products must result in no additional risk in terms of safety or efficacy.

Currently, pharmacists may generally substitute brand-name drugs for cheaper generic versions without consulting a patient's prescribing provider. This is not always the case for a biosimilar product. State laws often create barriers to substituting biosimilars for original biologics, hampering competition and intensifying the market dysfunction that drives drug prices upward.

In places where a biosimilar is deemed interchangeable, pharmacists may substitute the biosimilar for the original biologic without physician approval.<sup>15</sup> But because the FDA has not yet finalized guidance on how to determine interchangeability, no approved interchangeable products exist in the United States.

**Naming conventions:** Brand-name chemical drugs and their identical generic counterparts share a common nonproprietary name based on the drug's core substance, such as ibuprofen or acetaminophen. The drug goes by its proprietary brand name when sold by the company that owns the brand. For example, Pfizer sells ibuprofen under the brand name Advil.

Biologics and biosimilars, however, must abide by different nonproprietary naming guidelines. In January 2017, FDA issued guidance stating that the original product and the follow-on product share a core drug substance name but that each be distinguished by a unique, randomly assigned four-letter suffix.

By FDA's definition, the suffix is "devoid of any meaning" on its own.<sup>16</sup> Take the brand name biologic "Remicade," for example. Under the FDA's guidance, Remicade's nonproprietary name is "infliximab-hjmt," infliximab being the core substance in the drug, and hjmt being the random four-digit suffix. Its biosimilar, "Inflectra," has the nonproprietary name infliximab-dyyb.

FDA says its proposal prevents practitioners' inadvertent substitution of products not determined interchangeable and mix-ups over drug names during market research.<sup>17</sup> Experts in some pharmaceutical industry sectors agree that a unique suffix is necessary to avoid such confusion.

Others, however, argue that such suffixes interferes with the emerging biosimilar market because the naming conventions are not intuitive and could increase confusion.

Another concern is that some patients might think unique suffixes – something most drug names do not have – indicate that the products are significantly different from and possibly inferior to the related brand-name drugs.

## Conclusion

One of the biggest threats to the sustainability of the American health care system and affordability for consumers and payers is the high price of prescription drugs.

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Today, prescription drug expenditures are the fastest growing component of the health care market, making up nearly 20 percent of all health care costs.<sup>18</sup> In an otherwise heavily regulated health care industry, the high price of many biologics is another example of how drug makers have an unfair advantage when it comes to pricing their products.

As the development and use of biologic drugs gain further momentum, a variety of flaws in the market – such as a

significant lack in competition among drug makers – must be addressed. Competition from biosimilar drugs is a promising step in the right direction. But many barriers that limit their market entry remain.

While there is no one-size-fits-all solution to the significant financial impact of drugs such as biologics on the health care system, opportunities for reform exist, and we must explore a variety of strategies.

## References

1. Anthony A. Barraeta, Letter to U.S. Senate Finance Committee re: “The Price of Sovaldi and Its Impact on the U.S. Health Care System,” Kaiser Permanente, March 4, 2016.
2. “2018 and Beyond: Outlook and Turning Points,” IQVIA Institute, March 13, 2018, [iqvia.com/institute/reports/2018-and-beyond-outlook-and-turning-points](http://iqvia.com/institute/reports/2018-and-beyond-outlook-and-turning-points)
3. Francis Megerlin, et al., “Biosimilars and the European Experience: Implications for the United States.” Health Affairs, Vol. 32, No. 10, October 2015, doi.org/10.1377/hlthaff.2009.0196
4. “Abbreviated New Drug Application (ANDA): Generics,” U.S. Food and Drug Administration, November 2016 <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/>
5. See note 3.
6. Benjamin P. Falit, Surya C. Singh, and Troyen A. Brennan, “Biosimilar Competition in The United States: Statutory Incentives, Payers, and Pharmacy Benefit Managers,” Health Affairs. Vol. 34, No. 2. February 2015 [doi.org/10.1377/hlthaff.2014.0482](http://doi.org/10.1377/hlthaff.2014.0482)
7. See note 3.
8. Ed Silverman, “Unintended twist in Obamacare may cost some Medicare patients more for biosimilars,” Stat, April 18, 2016 [statnews.com/pharmalot/2016/04/18/medicare-drug-prices-biologics/](http://statnews.com/pharmalot/2016/04/18/medicare-drug-prices-biologics/)
9. Biosimilar Product Information, U.S. Food and Drug Administration <https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm580432.htm>
10. Hamzah Aideed, “The European Biosimilars Landscape: What to Expect in The Year Ahead,” Biosimilar Development, April 10, 2018 [biosimilardevelopment.com/doc/the-european-biosimilars-landscape-what-to-expect-in-the-year-ahead-0001](http://biosimilardevelopment.com/doc/the-european-biosimilars-landscape-what-to-expect-in-the-year-ahead-0001)
11. “Frequently Asked Questions on Patents and Exclusivity.” U.S. Food and Drug Administration. 18 July 2014. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079031.htm>
12. Vicki Needham, “Five groups urge President Obama to forego longer protections for biologics in the TPP,” The Hill, October 26, 2016 [thehill.com/policy/finance/303010-five-groups-urge-president-obama-to-forego-longer-protections-for-biologics-in](http://thehill.com/policy/finance/303010-five-groups-urge-president-obama-to-forego-longer-protections-for-biologics-in)
13. See note 6.
14. “Information for Consumers (Biosimilars),” U.S. Food and Drug Administration. Drugs, August 27, 2015 <https://wayback.archive-it.org/7993/20170111062916/http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/default.htm>
15. See note 3.
16. Jennifer C. Day and Douglas Monroe, “The Biosimilars Compass: Where Are We Going.” Power Point Presentation
17. “Nonproprietary Naming of Biological Products,” U.S. Food and Drug Administration, Guidance for Industry, August 2015 <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm459987.pdf>
18. “Riddle Me This...When is 10% not 10%? How PhRMA Confuses the Numbers Around Drug Spending,” Campaign for Sustainable Rx Pricing, 2015 [csrxp.org/wp-content/uploads/2015/12/PhRMA-10-percent.pdf](http://csrxp.org/wp-content/uploads/2015/12/PhRMA-10-percent.pdf)