

Insulin Biosimilars – Ensuring Access for America's Diabetes Patients May 2019



**Biosimilars
Council**
A Division of AAM

Insulin Biosimilars Whitepaper

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Introduction

Insulin has been available to America's diabetes patients for decades, and millions of patients rely on this medicine every day to control their diseases and maintain their health and quality of life. Yet even as the number of Americans suffering from Type I and Type II diabetes continues to rise, patients are facing increasing difficulties in paying for this life-saving medicine. FDA-approved biosimilar medicines have the potential to make insulin more affordable and accessible to patients. However, realizing the promise of biosimilar insulins requires addressing a series of challenges that threaten their future.

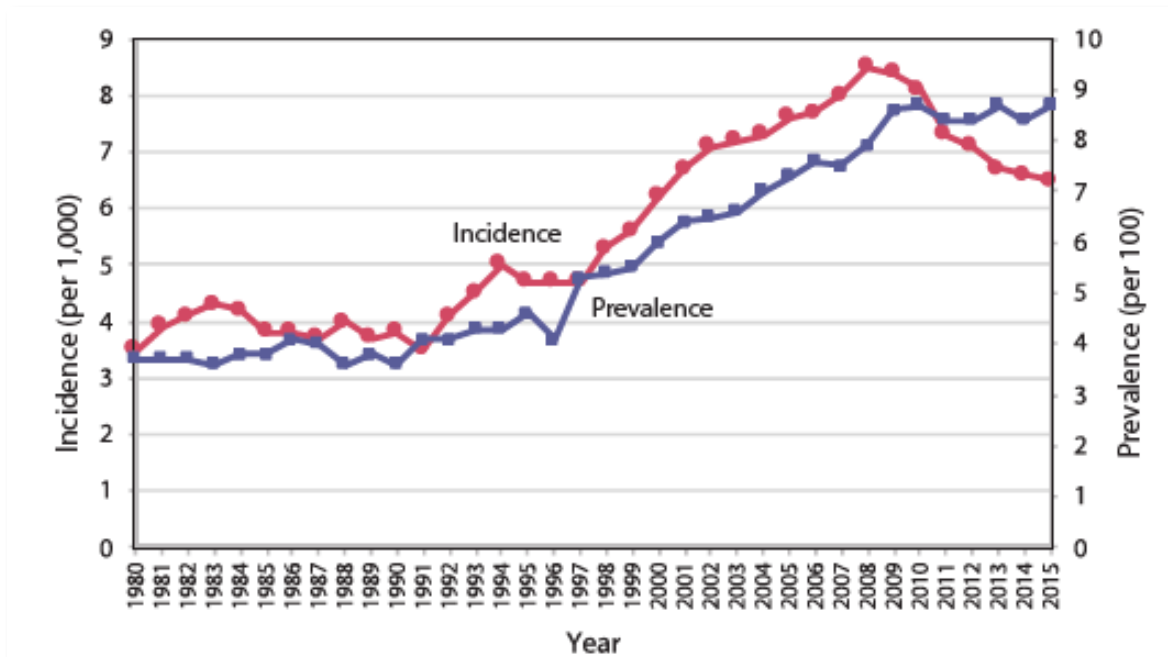
This paper outlines those challenges and recommends actions for policymakers to foster the development of biosimilar insulins for America's patients.

Background

According to the Centers for Disease Control and Prevention (CDC), more than 30 million people in the U.S. have diabetes (more than 9 percent of the U.S. population). An additional 84 million adults have prediabetes. From 1996 to 2015, the prevalence of diabetes has more than doubled.¹ And, as the prevalence has increased, so has its costs. In 2012, the total direct and indirect estimated cost of diagnosed diabetes in the U.S. was \$245 billion.²

¹ Centers for Disease Control and Prevention. "2017 Diabetes Report Card." Available: <https://bit.ly/2GvhC0S>.

² Ibid.



Discovered 100 years ago,³ insulin is a key therapy for more than 7.5 million Americans each day.⁴ Despite its age, there has never been a generic insulin – due in large part to regulatory challenges in navigating the FDA generic drug approval pathway. In fact, former FDA Commissioner Scott Gottlieb noted, “it was hard to bring a substitutable generic insulin to the market under the conventional drug pathway.”⁵

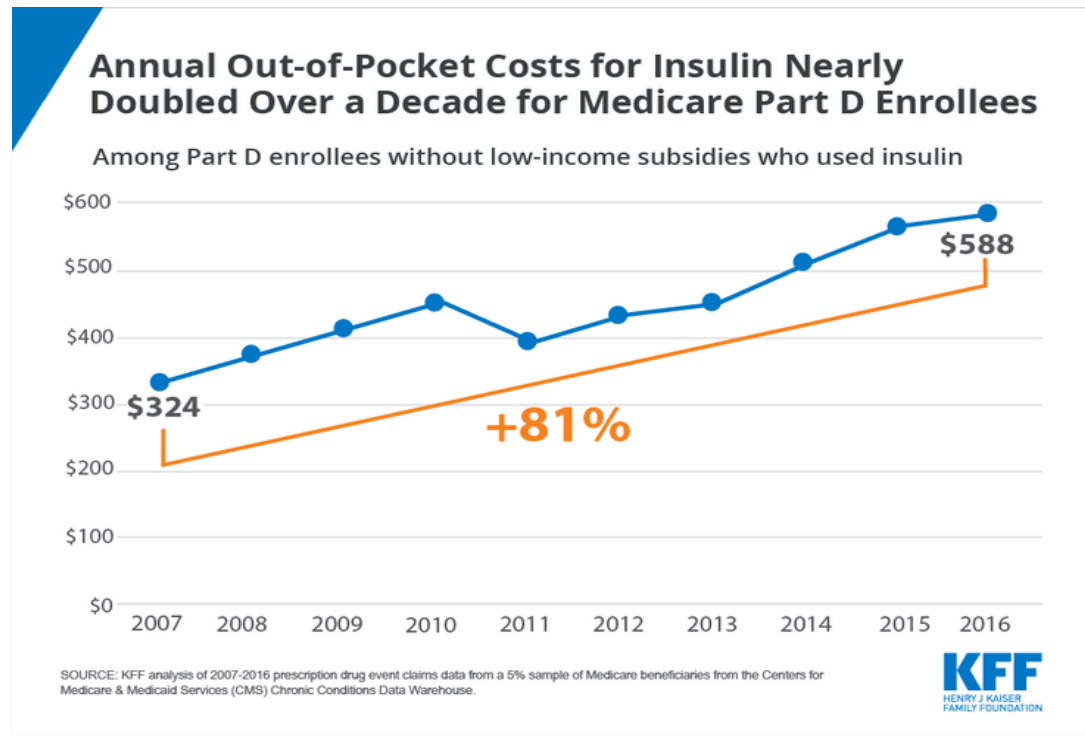
As a result, the insulin market is now dominated by only three manufacturers. This has contributed to a recent increase in the cost of insulin. These rising out-of-pocket costs have highlighted a significant challenge for patients unable to afford their insulin.⁶

³ Congressional Diabetes Caucus Report. “Insulin: A lifesaving drug too often out of reach.” Available: <https://bit.ly/2QcViOu>.

⁴ *Ibid.*

⁵ FDA Press Release. “Statement from FDA Commissioner Scott Gottlieb, M.D., on new actions advancing the agency’s biosimilars policy framework.” Available: <https://bit.ly/2Ggr38N>.

⁶ Congressional Letter to the FDA. “Durbin, Cramer, Cassidy, Smith To FDA: Price Of Insulin Is Unacceptable”. Available: <https://bit.ly/2C8sKR7>.



The Food and Drug Administration (FDA) announced steps to encourage biosimilars, more-affordable versions of brand insulin beginning in March 2020.⁷ Former FDA Commissioner Gottlieb called the Agency's efforts "a watershed moment for insulin products."⁸ However, realizing the promise of biosimilar insulins means addressing barriers that threaten patient access to affordable treatment.

Promise of Biosimilar Savings

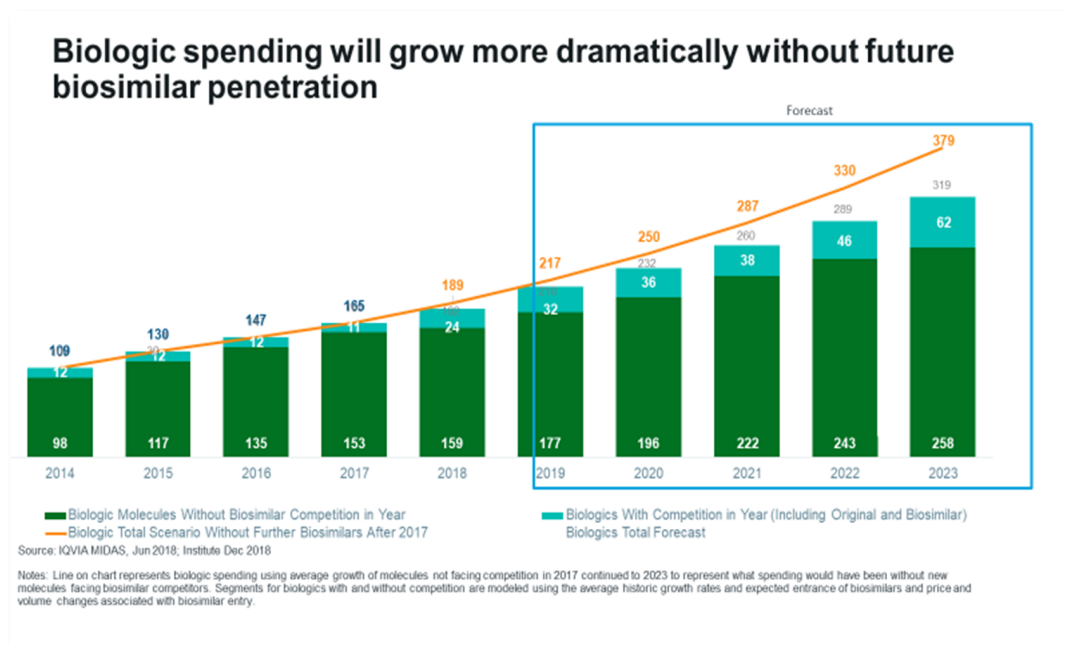
Estimates from recent economic studies put the projected savings from biosimilars utilization at \$44 billion to as high as \$250 billion over 10 years, and \$378 billion over 20 years.⁹ In the near-term, IQVIA expects biosimilars to lower overall spending on biologic medicines by \$153 billion from 2019 to 2023 as a result of competition. Experts agree on the transformative

⁷ FDA Press Release. "Statement from FDA Commissioner Scott Gottlieb, M.D., on new actions advancing the agency's biosimilars policy framework." Available: <https://bit.ly/2Ggr38N>.

⁸ *Ibid.*

⁹ RAND Corp. "Biosimilar Cost Savings in the United States" <https://www.rand.org/pubs/perspectives/PE264.html>; The \$250 Billion Potential of Biosimilars, Express Scripts International (April 23, 2013). Available at: <http://bit.ly/2qYlu4Z>;

potential and significant savings from biosimilars. A study done by Avalere Health found that the availability of biosimilars could increase overall access to biologic medicines by an additional 1.2 million patients.¹⁰



Early signs confirm the potential for robust price competition among biosimilar medicines. Currently marketed biosimilars average a 47 percent list price discount and nearly 20 percent net price discount.¹¹ These competitively priced options fulfill their promise to patients and the U.S. health care system.

Several major payors and pharmacy benefit managers have preferred biosimilars over their brand counterpart. In fact, a recent study from Magellan found that preferring just one biosimilar over the brand product saved its health plan members 34 percent on prescription drug costs for that category.¹²

¹⁰ Avalere Health and The Biosimilars Council, Biosimilars in the United States: Providing More Patients Greater Access to Lifesaving Medicines. (2017) Available at <https://bit.ly/2fAWtXB>.

¹¹ AAM Analysis of IQVIA WAC Data April 2019; CMS ASP Pricing Files April 2019.

¹²The Center for Biosimilars. "PBM Says Its Biosimilars Strategy Led to 86% Use of Biosimilar Infliximab." Available: <http://bit.ly/2VVP9Mu>.

Current Challenges to Biosimilars Competition

Rebates and Pricing

Nonetheless, biosimilars – including potential biosimilar insulins – face challenges to success. In many ways, insulin is a poster child for pricing practices that have generated negative policymaker attention.¹³ One of brand insulin manufacturers' major competitive tools is to offer significant rebates to pharmacy benefit managers (PBM) and payors in exchange for favorable formulary placement. This has contributed to significant increases to the list price of insulin over the past decade.

In fact, six of the most highly-utilized brand-name insulins increased in list price by more than 500 percent from 2006 to 2015.¹⁴ Because patient cost-sharing is often based on the product's list price, before rebates or discounts, increases in list price directly impact a patient's ability to afford their medicines and can cause increased patient abandonment and lower adherence.¹⁵

However, the perverse incentives of brand drug rebates can cause a PBM to disadvantage even a generic or biosimilar with a lower list and net price.¹⁶ This prevents a generic or biosimilar from market penetration and, combined with the difficulty of development and obtaining automatic substitution, as Dr. Gottlieb has noted, can further discourage generic or biosimilar manufacturers from developing a lower-cost product.

Policymakers can address this by ensuring that Medicare Part D plans cover and prioritize use of biosimilars when the list price of a biosimilar drug is less than its reference product. Where applicable, CMS or Congress can require the establishment of a Part D specialty tier with lower-cost sharing for biosimilars that exceed the specialty cost threshold. The ability for plans to impose a lower coinsurance rate on biosimilar products through the establishment of a generic specialty tier, as well lower cost-sharing for those biosimilars that do not meet the specialty threshold on lower cost-sharing generic tiers, would help to mitigate high costs for patients and drive utilization toward lower-cost alternatives.

¹³ Inspector General Office Health and Human Services Department (HHSIG), Fraud and Abuse Removal of Safe Harbor Protection for Rebates Involving Prescription Pharmaceuticals. Available: <https://bit.ly/2Y7vabV>; Congressional Diabetes Caucus Report. "Insulin: A lifesaving drug too often out of reach." Available: <https://bit.ly/2QcViOu>.

¹⁴ STAT News. "'Everyone is at fault': With insulin prices skyrocketing, there's plenty of blame to go around." February 19, 2019. Available: <https://bit.ly/2VG92ne>.

¹⁵ Forbes. "Rebates And Drug Costs: What The New Proposal Would Mean." February 28, 2019. Available: <https://bit.ly/2Tv4pyW>.

¹⁶ Drug Channels. "Payer Power: Why Eli Lilly, Janssen, and Merck Deeply Discount Their Drug Prices." <http://bit.ly/2JCIEYF>.

As manufacturers invest in bringing biosimilar competition to high-priced biologics facing patent and exclusivity expiration it is essential that policymakers act immediately to create a market that encourages investments in developing biosimilar alternatives to high priced brand biologics. This will be critical to ensuring a sustainable market and increased patient access to new biosimilars and interchangeable biologics.

Patent Abuse

While the 1990s and early 2000s witnessed significant innovation in new forms of insulin (i.e. analog insulin), recent years have seen only incremental changes (i.e. multiple variations of a pen delivery system) that effectively “evergreen” the same medicine and delay competition by patenting these tweaks without developing new therapies.¹⁷

This prevents generic manufacturers from pursuing the development of follow-on alternatives of older insulin formulations under the conventional drug pathway. Merck’s decision to halt commercialization of their “follow-on” insulin to Lantus highlights this challenge, despite tentative FDA-approval, as they were in a protracted patent litigation battle.¹⁸ Merck also cited manufacturing cost and pricing as factors in their decision.¹⁹

Policymakers can support future biosimilars by addressing patent abuse – including by safeguarding the *inter partes* review (IPR) process, an important tool for biosimilar developers to challenge non-innovative patents, increasing transparency in the FDA’s Purple Book,²⁰ and “moving up” the patent dance as outlined in the Biologics Price Competition and Innovation Act (BPCIA) to allow biosimilar manufacturers greater flexibility when addressing brand manufacturer patent fortresses.

Regulatory Barriers

Congress sought to encourage biosimilar insulins through the BPCIA, including by transitioning certain protein products, including insulin, to be regulated as biologics after March 23, 2020. However, because of delays in FDA’s final guidance and its plan to require new user fees for applications not approved before the transition date, generic and biosimilar developers have generally delayed their development programs until after March 2020 to submit applications under the biosimilar pathway. Policymakers can support development of biosimilar insulins by changing FDA’s “non-approval” policy regarding pending applications

¹⁷ STAT News. “Patent abuse is driving up drug prices. Just look at Lantus.” December 7, 2018. Available: <https://bit.ly/2Ek5oe8>.

¹⁸ The Pharma Letter. “Merck decides not to enter insulin market after all.” Available: <https://bit.ly/2HiKkoS>.

¹⁹ *Ibid*.

²⁰ Regulatory Focus. “House Unanimously Passes Bills Updating FDA’s Orange and Purple Books.” Available: <http://bit.ly/2LzqcCl>.

which creates a regulatory “dead zone” and by providing for FDA to “carry-over” applications for products “transitioned” from the previous pathway in March 2020.

Moreover, FDA guidance related to the naming of biosimilar and interchangeable biologics will have a particularly burdensome effect on the post-March 2020 biosimilar insulin market.

Naming of Biosimilar and Interchangeable Biologics

FDA policy requires four letter random suffixes be added to the biosimilars international non-proprietary name (INN). FDA contends that suffixes support pharmacovigilance, despite a global consensus that a suffix only leads to patient and prescriber confusion.²¹

FDA recently announced²² that it will abandon its prior commitment to add suffixes to previously approved originator biologics, which includes insulin products. Different requirements for originator biologics and biosimilar competitors will create provider and patient confusion, compounding reference biologic manufacturer-sponsored misinformation campaigns.²³

This will be particularly challenging for insulins approved as interchangeable biologics. It would differentiate automatically substitutable interchangeable biologics from their reference products, undermining interchangeability. The policy further erodes patient and provider confidence in biosimilars and result in billions in lost savings if interchangeable biologics are not automatically substituted for their reference products. In fact, depending on state pharmacy substitution laws, which vary state to state, a pharmacist may not automatically substitute an

interchangeable biosimilar for its reference product because it would not have the same INN. Additionally, even if state law allowed the practice, studies show pharmacists are less likely to substitute products with different INNs.²⁴

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Policymakers can support a robust and competitive market for biosimilar insulin by urging FDA to reverse its policy to add random suffixes to biosimilars and interchangeable biologics.

²¹ International Generic and Biosimilar medicines Association (IGBA). Press Release: “IGBA Congratulates Health Canada For Decision on Biologics Naming That Supports Growing Global Consensus.” February 17, 2019. Available: <https://bit.ly/2ueftlz>.

²² FDA. “Nonproprietary Naming of Biological Products: Update; Draft Guidance for Industry.” Available: <https://bit.ly/2ue9woQ>.

²³ Comments from The Association for Accessible Medicines (AAM) and the Biosimilars Council regarding Docket # FDA-2018-P-3281. Available at: <https://bit.ly/2Cu4toj>.

²⁴ Journal of Managed Care and Specialty Pharmacy. “Biosimilar Naming Conventions: Pharmacist Perceptions and Impact on Confidence in Dispensing Biologics.” Available: <https://bit.ly/2UDhvHz>.

Recommendations

While there remain significant challenges to successful development of a robust biosimilars market in the United States, the good news is that most of these can be surmounted by thoughtful policymaking by FDA, CMS and Congress. Opportunities to foster patient access to biosimilars include addressing brand company spread of misinformation on biosimilar safety and efficacy, aligning payer and provider incentives to encourage early adoption of biosimilars, and ending brand patent-gamesmanship. In particular, policymakers must:

- Ensure that rebates and formulary gamesmanship does not prevent patient access to biosimilars that are priced lower than their brand counterparts;
- Address over-patenting by brand manufacturers to block biosimilar competition, including by strengthening IPR, increasing patent transparency in the Purple Book, and speeding up the patent dance to help biosimilars get to market; and
- Remove regulatory barriers to competition such as the naming of biosimilar products.

The confluence of market-based factors, including rebates and pricing, over-patenting by brand manufacturers, and regulatory mis-steps have created an insulin market which suffers from high prices and a lack of competition. Biosimilar competition offers the promise of significant savings and increased patient access. Policymakers can and should take immediate steps to ensure patient access to lower cost biosimilar insulins.



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