Biosimilars in the United States:

Providing More Patients Greater Access to Lifesaving Medicines

The Biosimilars Council

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Biologics are innovative treatment options for patients affected by debilitating and life-threatening diseases. However, they are often associated with high costs and limited patient access. Biosimilar medicines are a solution that provide greater access to these advanced therapies for patients. As biosimilars become more widely available in the United States, they expand therapeutic options, enhancing the likelihood that patients will be able to begin treatment with biologic medicines. An analysis by Avalere Health for the Biosimilars Council shows that **1.2 million U.S. patients could gain access to biologics by 2025 as the result of biosimilar availability.[i] This data also suggests that women, lower income, and elderly individuals would disproportionately benefit from access to biosimilar medicines.**

Introduction

Biologics are medicines extracted from a variety of natural sources—human, animal or microorganism—and include a wide range of products such as vaccines, blood components, gene therapy, tissues, and recombinant therapeutic proteins.[ii] In contrast to traditional small molecule prescription drugs that are chemically synthesized, biologics are large molecule products that involve complex research, development and manufacturing processes. Biologics represent the cutting-edge of biomedical research and often offer the most effective treatment for such serious and life-threatening conditions as cancer, HIV/AIDS, rheumatoid arthritis and heart disease. However, biologic medicines can cost thousands of dollars per treatment keeping them out of reach for many patients.

Biosimilars are biologic medicines that are approved for use based on data showing they are highly similar to an existing brand name biologic, known as the reference product. Biosimilar manufacturers must prove that their biosimilar product has no meaningful clinical differences in terms of safety and effectiveness from the reference

product.[iii] Some biosimilars can be designated as "interchangeable" with the reference product, meaning they can be substituted for the brand name biologic by a pharmacist without the intervention of the prescribing health care provider. Biosimilars typically can be approved and licensed for use after expiration of the exclusivity period granted to the brand name product. Because biosimilar approvals can rely, in part, on information attained from the original reference product, thereby diminishing the need for repeating extensive new drug clinical trials, they are less costly than the brand biologic. Consequently, biosimilars offer safe, effective, and more accessible treatment alternatives for patients needing biological therapy.

In an environment where health decisions increasingly are made based on value and cost, biosimilars will play a vital role in improving patient access to needed medicine. The launch of new biosimilars over the next decade will expand treatment options for chronically ill patients and allow greater use of biologic medicines overall by providing more affordable access to individuals who in the past have either forgone treatment or settled for less effective medicine.

Key Findings

1. Biologic Medicine Use Will Grow Significantly over the Next Decade

More than 200 biologic products are now approved for use in the United States.[iv] Sales of these biologics have increased 65 percent since 2011, reaching more than $105 billion in 2016, as a variety of new biologic treatments for autoimmune disorders, immunology and cancer have come to market.[v] As of 2013, there were over 900 biologics targeting over 100 diseases under development in the United States. With patents due to expire for several of the approved brand biologics that are currently on the market, biosimilar development is booming. The FDA reported that as of April 2017, there were 66 biosimilar product development programs underway.[vi] The Agency noted further that it has received requests from biosimilar companies for pre-development meetings involving 23 different reference products.[vii] All of this adds up to robust pipelines both for new brand-name biologics and for prospective biosimilars. Based on these data, market analysts forecast that annual sales of biological medicine in the U.S. will reach between $250 billion and $275 billion annually by 2025[viii].

2. Access to Biosimilars Will Drive Further Growth in Biologic Use

The benefits of biosimilars in terms of cost savings and patient access to needed medicine are just beginning to be realized in the United States. In Europe, however, where biosimilars have been available since 2007, market data show that biosimilars lead to increased overall use of biologic medicine. A June 2016 report by IMS Health, "The Impact of Biosimilar Competition," describes the effects on total biologic utilization following the arrival and presence of biosimilar competition in the European Union.[ix] Specifically, introduction of biosimilars led to an average increase in utilization, compared to the year prior to the biosimilar entrance, of 32 percent[x]. The two primary reasons for this growth are: (1) the availability of lower-cost medicine, which opens up access for more patients to previously cost-prohibitive treatment; and (2) market competition, which provides choices in medicine and tends to moderate price increases that typically occur in a monopoly market. In other words, by expanding therapeutic options, biosimilars enhance the likelihood that patients will be able to begin treatment with biologic medicine.

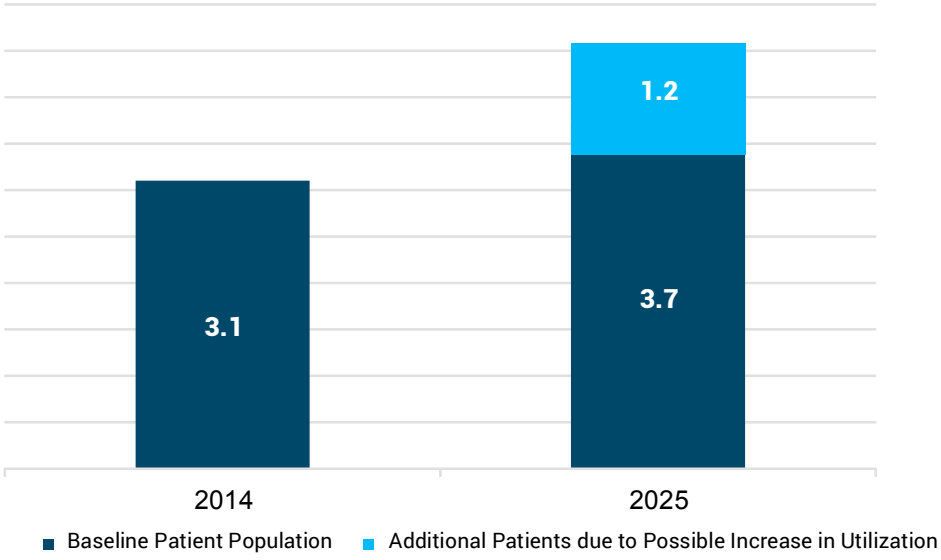
3. Biosimilars Will Advance Biologic Treatment Use in the U.S.

The availability of biosimilars could also make life-saving biologic medicines available to patients in the United States, according to the Avalere analysis. In order to estimate the impact, the analysis looked at seven leading biologics currently on the market whose exclusivity period either has ended or will expire prior to 2025 opening the door for biosimilar approval: Humira® (adalimumab), Remicade® (infliximab), Neulasta® (pegfilgrastim), Enbrel® (etanercept), Avastin® (bevacizumab), Lucentis® (ranibizumab) and Rituxan® (rituximab). Five of these seven products are among the top-10 biggest selling brand biologics in the U.S., accounting for more than 30 percent of total U.S. biologic sales.[xi] (The analysis does not account for any delays in biosimilar launches due to patent issues.)

In 2014, there were 3.1 million patients in the U.S. being treated with one of these seven biologics. Based on the general population growth rate estimates[xii] and the growth rate specific to the Medicare population[xiii], this number is projected to grow to 3.7 million patients by 2025. This represents *all* patients who will be treated with one of the seven medicines, whether it be the reference brand or a biosimilar for the reference brand. Applying assumptions based on IMS Institute for Healthcare Informatics

European findings with respect to the potential increased utilization of biologics due to the introduction of biosimilars[xiv] shows that an additional 1.2 million patients could begin therapy for one of these products as a result of a biosimilar version being available for the reference brand. Accordingly, the potential patient population for these seven therapies will grow to 4.9 million by 2025, an increase of 55 percent over an 11-year period. This number does not account for increased patient access due to improved coverage and formulary tier placement as more biosimilars become available (see Fig. 1).

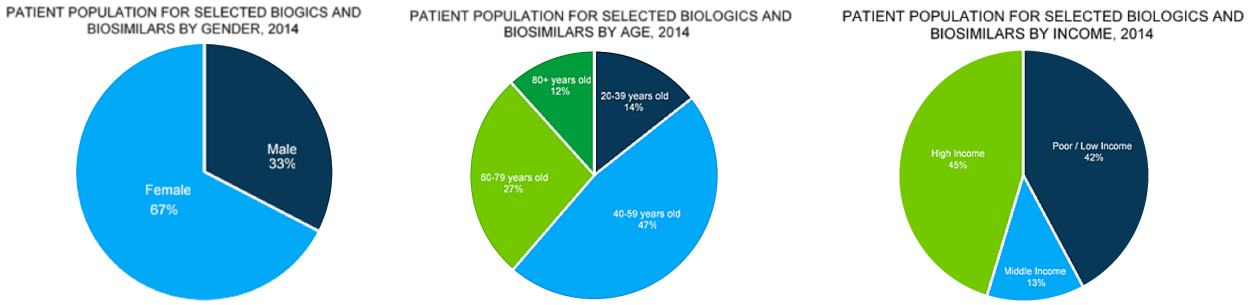
Fig. 1 Additional U.S. Patients with Biologic Access by 2025



4. Biosimilar Access will Benefit Women, Seniors and Low-Income Patients

As an increasing number of biosimilars enters the U.S. market, patients currently treated with biologic medications will have access to a broader set of treatment options at lower prices than now available. The Avalere analysis found that this benefit could be significantly applicable to women, older adults, and low-income individuals. While the seven drugs included in this study represent only about one-third of all U.S. biologic sales, utilization demographics show that two out of three patients being treated with these products are women; 86 percent of the total patients are above the age of 40; and 42 percent are either poor or low-income patients[xv] (see Fig. 2).

Fig. 2 Utilization Demographics for Select Biologics



Conclusion

The addition of biosimilars into the U.S. market is expected to increase patient access to biologic medicines across the board. Specifically, based on market data from seven leading biologics included in this study, the introduction of affordable biosimilars over the next 10 years could boost access to biologic treatments for an additional 1.2 million patients in 2025. Women, the elderly and lower income individuals are likely to be most impacted by enhanced biosimilar competition. Lower income individuals have been linked in the past to higher incidence of disease and worse disease progression, and they are often associated with overall worse health outcomes in comparison to the rest of the population. As such, this segment of the patient population may disproportionately benefit from biosimilars, and also could benefit from increased access to new and innovative therapies.

While these populations may realize improvements in access more noticeably than others, most individuals with health insurance regardless of their demographic will benefit from having greater options for biologic therapy, including originator, biosimilar and interchangeable biologics.

Methodology for Cited Avalere Analysis

In order to select the seven originator biologics included in this analysis, Avalere used the Centers for Medicare & Medicaid Services (CMS) 2014 Medicare Drug Spending Dashboard[xvi] that includes information for high spending Medicare Part D and Part B drugs and the 2014 Medical Expenditure Panel Survey (MEPS)[xvii] that is the most complete source of data on the cost and use of health care and health insurance coverage of US population. The seven reference products were selected based on three criteria: total Medicare program spending on the product, loss of exclusivity within the next ten years, and total volume of patients.

Avalere then extrapolated the Medicare data to estimate the total population size of current product use. Specifically using the CMS' Dashboard data to obtain the count of Medicare beneficiaries, both fee-for-service (FFS) and Medicare Advantage (MA), who were prescribed each of the seven selected medications. The analysis then applied a Medicare share of the payer mix associated with each drug to estimate total patient population taking a medication. To arrive at the payer mixes, Avalere queried the MEPS data using ICD-9-CM diagnosis group[xviii] for top clinical indications associated with the selected medications and determined the insurance coverage for patients with those indications. The exception was Humira and Enbrel, which were able to be identified in MEPS and capture insurance coverage for the patients utilizing those drugs.[xix]

Neulasta: 288.xx (diseases of white blood cells)
Lucentis: 362.xx (retinal disorders)
Avastin: 362.xx (retinal disorders [off-label use])
Rituxan: 202.xx (other malignant neoplasm of lymphoid and histiocytic tissue) and 204.xx (lymphoid leukemia)
Remicade: 714.xx (rheumatoid arthritis and other inflammatory polyarthropathies)
Humira: 714.xx (rheumatoid arthritis and other inflammatory polyarthropathies)
Enbrel: 714.xx (rheumatoid arthritis and other inflammatory polyarthropathies)

Avalere also used MEPS data for those top indications to describe patient demographics for each drug. It's important to note that the top indication for each drug does not account for the whole patient population utilizing the medication.

To approximate the number of patients that could have access to biosimilars over the next 10 years, the model grew medication user estimates using an average growth rate of 2.8% for

Medicare patients between 2015-2025[xx] and 0.8% projected general US population growth for non-Medicare patients[xxi].

Finally, to arrive at the final numbers of people who may have access to biosimilars, Avalere created an assumption of increased utilization after the introduction of a biosimilar based on the experience in Europe. Using the June 2016 IMS Health report on "The Impact of Biosimilar Competition," Avalere averaged the increased utilization for the product, compared to the last year prior to the introduction of the biosimilar, across the six products in the paper. The model used used the European Union average of 30%, rather than any of the individual countries. That 30% average increased utilization was then applied to the products in this analysis to determine the "increased utilization due to biosimilars introduction" component of the paper.

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[i] Avalere modeling of expected growth of top seven originator biologics volumes through 2025. The modeled
[ii] U.S. Food and Drug Administration. "What Is a Biological Product?" Access August 10, 2017, from www.fda.gov/aboutfda/transparency/basics/ucm194516.htm
[iii] U.S. Food and Drug Administration. "Information on Biosimilars." Access August 10, 2017, from www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/default.htm
[iv] U.S. Food and Drug Administration. "Biological Approvals by Year." Accessed August 12, 2017, from www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/
[v] QuintilesIMS. April 2017. "Medicines Use and Spending in the U.S. A Review of 2016 and Outlook to 2021."
[vi] U.S. Food and Drug Administration. "Cumulative Number of Biosimilar Development Programs." Accessed August 10, 2017, from www.accessdata.fda.gov/scripts/fdatrack/view/track.cfm? program=cder&id=CDER-RRDS-Number-of-biosimilar-dev-programs-in-BPD-Program
[vii] Janet Woodcock, Director, FDA Center for Drug Evaluation and Research. March 2, 2017. Testimony before the House Energy and Commerce Committee.
[viii] Transparency Market Research. Global Biologics Market Forecast. October 6, 2016.
[ix] IMS Health. The Impact of Biosimilar Competition. June 2016.
[x] ibid.
[xi] IMS presentation to the Association for Accessible Medicines Annual Meeting, February 2017.
[xii] U.S. Census Bureau. 2014 National Population Projections. Accessed August 11, 2017m from www,census.gov/population/projections/data/national/2014.html
[xiii] Centers for Medicare and Medicaid Services. Accessed August 13, 2017, from www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/
[xiv] IMS Health: Delivering on the Potential of Biosimilar Medicines: The Role of Functioning Competitive Markets Report, March 2016.
[xv] Analysis of the 2014 Medical Expenditure Panel Survey for the selected conditions.
[xvi] Centers for Medicare and Medicaid Services.
[xvii] Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey.
[xviii] MEPS captures ICD-9-CM diagnosis codes only at the 3rd digit level.
[xix] MEPS allows researchers to identify prescription drugs covered under Medicare Part D; biologics covered under Medicare Part B cannot be identified.
[xx] U.S. Food and Drug Administration.
[xxi] US Census Bureau 2014 National Population Projections.

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