



## Research Report

### » Ten-Year Potential Savings from Biosimilars in California

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<b>Table of Contents</b>	
<b>Executive Summary</b> .....	<b>3</b>
<b>Background</b> .....	<b>3</b>
<b>Methodology</b> .....	<b>4</b>
<b>Results</b> .....	<b>6</b>
<b>Conclusions</b> .....	<b>7</b>

## Executive Summary

This study calculated the potential 10-year saving to patients and payers in California should an improved biosimilars pathway be developed by the Food and Drug Administration (FDA) for evaluation and approval of generic biologic medications (biosimilars).

Using data from the Express Scripts Drug Trend Report and IMS, Express Scripts modeled the saving opportunities for 11 widely used biologic medications. Total estimated saving over a 10-year period was approximately \$27.6 billion. The projected unrealized saving is significant. It warrants regulatory and legislative consideration at both federal and state levels to improve the pathway for biosimilar evaluation and reject industry requests to enact legislative barriers to interchangeable biosimilar substitution.

## Background

For the 12 months ending November 2012, total U.S. sales of biologic drugs were estimated at \$55 billion.<sup>1</sup> As patents for many biologic drugs expire over the next 10 years, opportunities for billions of dollars in saving are possible if biosimilars – highly comparable generic-like alternatives to original (reference) biologic medications – are made available to the market. However, considerable roadblocks currently make the path to biosimilars highly uncertain.

Roadblocks arise from both the nature of biologic drugs and the recent FDA regulatory pathway established for the approval of biosimilars. Biologic drugs are very large, complex proteins. Due to natural variability in living cells, uncontrollable small differences are inevitable in both the biological manufacturing processes and the resulting molecules. Intra-lot variability occurs even within brand biologics medications.<sup>2</sup> Traditional drugs are chemically synthesized, they are much smaller molecules, and they can be manufactured with far less variability.

The Hatch-Waxman Act of 1984 provided a regulatory pathway for the approval of generics for traditional chemically synthesized drugs. In brief, it allowed competition to drugs with expired patents, but did not require generic manufacturers to repeat the entire original approval process (mainly bypassing clinical trials). At that time, however, few biologic drugs were on the market. The nature of biologics requires a unique biosimilar approval pathway, separate from the pathway for traditional generic drugs. To address the issue, the Biologics Price Competition and Innovation Act (BPCIA), originally proposed in 2007, was passed as part of the Patient Protection and Affordable Care Act of 2010.<sup>3</sup> The BPCIA created a parallel abbreviated pathway for the manufacture biosimilars for reference biologics. However, the burden of demonstrating that a biosimilar is therapeutically equivalent to and interchangeable with the reference drug is much more onerous, time-consuming and expensive than for a chemically derived small molecule. In addition, BPCIA stipulated that a sponsor of a biosimilar drug may have to share proprietary details of its manufacturing process with

the reference drug's manufacturer. Under those terms, the biosimilar sponsor has no protection for its intellectual property.

Presently, no biosimilars have been approved under the BPCIA pathway. Given the retroactive 12-year exclusivity guaranteed to biologics by the BCPIA and the current expired patent status of many biologic drugs, we believe that 11 current brand biologic drugs are good candidates for the introduction of biosimilars over the next 10 years.

The European Union (EU) is ahead of the United States, having already developed both a legal pathway and an abbreviated approval process for biosimilars. The EU has one drug regulatory body, the European Medicines Agency (EMA), which is the counterpart to the U.S. FDA. Although the EMA has approved 14 biosimilar products since 2006, only three unique biosimilars presently are on the EU market: filgrastim (for white blood cell deficiency), epoetin alfa (red blood cell deficiency), and somatropin (human growth hormone deficiency). Long-term saving estimates (through 2020) for existing biosimilars and those projected to be introduced in the EU range from €11.8 billion to €33.4 billion<sup>4</sup> (currently about \$15.4 billion to \$43.7 billion), under the assumption that biosimilar monoclonal antibodies (mainly used to treat autoimmune diseases and cancer) will be approved during the next seven years. In addition, biosimilars have been launched in India and other parts of Asia. One example is Cipla, which recently launched Etacept, a biosimilar for Enbrel® (etanercept) in India at a 30% discount from the reference product.<sup>5</sup>

## Methodology

We developed the biosimilar saving model based on 11 biologic drugs that currently are available in the United States. They are commonly used biologic medications with U.S. patents that have expired or will expire in the near future unless new patents are granted. The medications included are used to treat a number of conditions including anemia, blood deficiencies, cancer, rheumatoid arthritis and other inflammatory conditions, such as Crohn's disease. They all have a high potential for biosimilar development if a better pathway to biosimilars is established.

The brand drugs included in the model, their generic names, manufacturers, approval dates, patent expiration dates and U.S. sales for 2012, and estimated California sales for 2012 are shown in Table 1. Several drugs previously predicted to have expiration dates prior to 2024 were not included, because brand drug makers continue to develop new dosage forms, seek new indications and apply for additional patents years after the original products are approved and launched. Such is the case with three interferons — Avonex® (interferon beta-1a), Betaseron® (interferon beta-1b), and Rebif® (interferon beta-1a), which are used to treat multiple sclerosis. Estimates of California sales were based on the 11% percent of national total healthcare spend that is represented for the state of California.

Biologic drugs still in the development pipeline were not considered in our model. Biosimilar versions for reference biologic drugs were assumed to be introduced one year after patent expiration or end of exclusivity, whichever is later. Additionally, the model assumed that corresponding biosimilars for all 11 biologic drugs will be marketed.

Under patent protection, annual cost increases due to brand inflation are much higher than typical consumer price inflation. However, as the number of biosimilars increases over time, brand inflation is likely to decline as brand manufacturers attempt to keep pricing for original biologic products competitive. If regulatory hurdles or technical difficulties keep biosimilars from being introduced in the U.S., brand inflation also will decrease, due to increasing availability of alternate therapies (which now include oral medications) and more aggressive contracting from consolidations of payers. In the model, we estimated a gradual decrease in brand inflation to 10% without biosimilars and to 8% with biosimilars because the competition generated by biosimilars is likely to drive down brand inflation more than in the scenario with no biosimilars.

In addition, consumer price inflation was factored in for the model with biosimilars at 2.5% starting in the year following introduction of the biosimilar. This assumption may not align with actual future inflation but we considered it to be a reasonable estimate and the inclusion created a more conservative estimate of biosimilar savings<sup>6</sup> while recognizing biosimilar manufacturers will be affected by normal increases in energy and labor costs.

Among other parameters we included are biosimilar price discount and utilization changes. As new biologics are introduced, the average discount included in the model for all available biosimilar drugs was 30% which was selected as it is consistent the highest discount seen in other studies<sup>7</sup> and is on the lower end of the 30-50% discounts seen in Europe.<sup>8</sup> Utilization increases were set to a relatively flat 0.1% annually, which allows for expected growth in utilization but at a very conservative rate given the factors that may increase or decrease utilization.

Another major controversy in the introduction of biosimilars is substitutability or interchangeability. Questions proposed in legislation under consideration in several states, including California, include whether pharmacists will be required to notify physicians of biosimilar substitutions, what information needs to be shared with patients and how much administrative recordkeeping will be necessary from pharmacies and physician's offices.<sup>9</sup> Patients who are treatment-naïve may be more likely to be initiated on an available biosimilar, but physicians of patients currently on a brand biological might be more cautious about the interchangeability of biosimilars and chose to continue prescribing the brands. Since substitution and therapeutic interchange rates for biosimilars are likely to increase over time as prescribers and patients gain experience with their use, the model increases substitution and interchangeability rates slightly to reflect growing confidence in biosimilars.

» Table 1 | Biologics Included in Express Scripts' 10-Year Savings Model

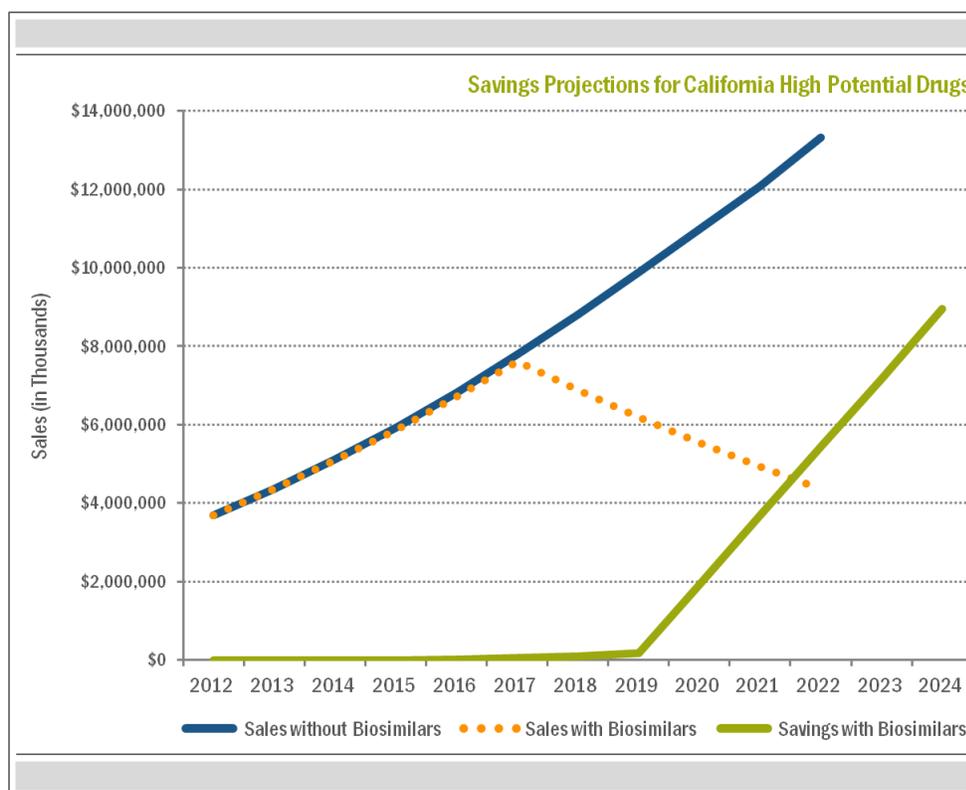
Brand	Generic	Manufacturer	Approval	Patent Exp	US 2012 Sales (in thousands)	CA 2012 Estimated Sales (in thousands)
Avastin	bevacizumab	Genentech	02/06/2004	06/18/2019	\$2,662,842	\$ 292,912.62
Epogen	eopetin alfa	Amgen	06/01/1989	05/26/2015	\$2,254,245	\$ 247,966.95
Herceptin	trastuzumab	Genentech	09/25/1998	08/27/2019	\$ 1,837,693	\$ 202,146.23
Humira	adalimumab	AbbVie	12/31/2002	12/31/2016	\$4,505,380	\$ 495,591.80
IntronA	Interferon alfa-2a	Merck	06/04/1986	08/26/2020	\$ 94,009	\$ 10,340.99
Neulasta	pegfilgrastim	Amgen	01/31/2002	10/20/2015	\$3,472,988	\$ 382,028.68
Neupogen	filgrastim	Amgen	02/20/1991	11/10/2013	\$ 1,007,172	\$ 110,788.92
PEG-Intron	Peginterferon alfa-2b	Merck	01/19/2001	08/26/2020	\$ 121,828	\$ 13,401.08
Procrit	eopetin alfa	Janssen Products	06/01/1989	05/26/2015	\$ 1,127,024	\$ 123,972.64
Remicade	infliximab	Janssen Biotech	08/24/1998	09/04/2018	\$3,796,422	\$ 417,606.42
Rituxan	rituximab	Genentech	11/26/1997	07/05/2015	\$3,183,625	\$ 350,198.75

## Results

Based on our initial assumptions, in the all-brand scenario, estimated sales of the 11 included biologic drugs in California were \$3.7 billion in 2014 increasing to \$13.3 billion in 2024.

Assuming that each potential biosimilar becomes available one year after the reference biologic drug's patent expires, the estimated total combined 2024 sales of biologics and biosimilars was reduced to \$4.4 billion; a saving of about \$8.9 billion in 2024 and a 10-year saving of \$27.6 billion for the period 2014 through 2024. Figure 1 illustrates the saving over time. Interestingly, as more biosimilars are marketed, the dollar amount of total sales in the "with biosimilars" scenario starts to bend downward due to competition and growing biosimilar utilization.

» Figure 1 | Biologic Sales and Biosimilars Savings Opportunities



## Conclusions

Costs for prescription drugs are more than twice as high in the United States than in any other country.<sup>10</sup> Biologics are the most costly medications available, ranging in price from \$1,000 to more than \$50,000 per treatment. In some cases, treating only one patient costs hundreds of thousands of dollars per year. And these drugs are not experimental; they are approved medications widely used to treat chronic conditions that touch all of us — cancer, rheumatoid arthritis, multiple sclerosis and others.

This model focused on a relatively small number of biologics, for which patents are expiring in the next decade. Sales of each are large enough to warrant investment by biosimilar manufacturers, but only if the regulatory pathway is conducive for the manufacturer to develop and seek approval for biosimilars while maintaining profitable business operations.

The saving we predict reflects both California sales of biologic drugs and the impact of an improved biosimilar pathway on these sales. The assumptions, which were based on conservative estimates of utilization, cost and consumer inflation used the most generous anticipated early discounts from biosimilars. In addition, new drugs, drug recalls and other influences on biosimilar cost and utilization were not considered in this model. Based on the current biologic pipeline, we fully anticipate that new

biologics will become available during the next decade. Furthermore, the U.S. market also is likely to see expanded indications for some existing biologic drugs. This model considers only a limited number of reference biologic drugs. However, the importance of a biologic pathway on saving is likely to grow quickly as U.S. patents on drugs such as Avonex<sup>®</sup>, Betaseron<sup>®</sup>, Rebif<sup>®</sup> and Enbrel<sup>®</sup> expire in the coming years.

A pathway enabling approval of biosimilars will spur market competition and reduce prices not only for the patients who depend on these medications, but also for payors, including private employers, insurance companies and government organizations. State legislation that frustrates pharmacist and prescriber efforts to use biosimilars will undoubtedly jeopardize these savings.

<sup>1</sup> IMS Health. National Prescription Audit<sup>®</sup>, 2012.

<sup>2</sup> Zelenetz AD, Ahmed I, Braud EL, et al. NCCN Biosimilars white paper: regulatory, scientific, and patient safety perspectives. JNCCN. 2011;9(Suppl 4):S1-S22.

<sup>3</sup> Grabowski H, Long G, Mortimer R. Implementation of the Biosimilar Pathway: Economic and Policy Issues. *Seton Hall Law Review*. 2011;41(2):512- 557. Available at: <http://erepository.law.shu.edu/shlr/vol41/iss2/2> . Accessed Apr 14, 2013.

<sup>4</sup> Rice M. Europe could save billions. *Generics Bulletin*. May 4, 2012. Available at: <http://www.generics-bulletin.com/media/15194/genbiosimart.pdf>. Accessed Apr 9, 2013.

<sup>5</sup> Grogan K. Cipla launches Enbrel biosimilar in India. PharmTimes. April 17, 2013. Available at: [http://www.pharmatimes.com/Article/13-04-17/Cipla\\_launches\\_Enbrel\\_biosimilar\\_in\\_India.aspx](http://www.pharmatimes.com/Article/13-04-17/Cipla_launches_Enbrel_biosimilar_in_India.aspx). Accessed April 17, 2013.

<sup>6</sup> Savings are \$7.7 billion higher if the factor for consumer inflation is removed (\$257.7 billion)

<sup>7</sup> Grabowski H, Long G, Mortimer R. Implementation of the Biosimilar Pathway: Economic and Policy Issues, *Seton Hall Law Review*. 2011;41(2):512- 557. Available at: <http://erepository.law.shu.edu/shlr/vol41/iss2/2> . Accessed Apr 14, 2013.

<sup>8</sup> Apro M, Cornes P, Sun D, Abraham I. Comparative cost efficiency across the European G5 countries of originators and a biosimilar erythropoiesis-stimulating agent to manage chemotherapy-induced anemia in patients with cancer. *Ther Adv Med Oncol*. 2012;4(3):95-105.

<sup>9</sup> Dunkelberger L. Bill sets high standards for 'biosimilar' drugs. *Sarasota Herald-Tribune*. Feb. 19, 2013. Available at: <http://politics.heraldtribune.com/2013/02/19/bill-sets-high-standard-for-biosimilar-drugs/>. Accessed Apr 9, 2013.

<sup>10</sup> Organization for Economic Co-operation and Development. Why is health spending in the United States so high? November 2011. Available at: <http://www.oecd.org/health/health-systems/healthatagance2011.htm>. Accessed May 6, 2013.