Understanding Biosimilars and Projecting the Cost Savings to Employers – Update

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FOREWORD

We have observed from our pharmacy consulting that the prescription drug market continues to undergo dramatic change as most of the blockbuster drug products from the last 15 – 25 years have seen or will see their patents expire and cheaper priced generic products take their place. For most employers, generic drugs represent 85% - 90% of the prescriptions dispensed, but still 50% or more of the total drug dollar expenditures are represented by brand drug products. Brand drug spending is increasingly dominated by specialty drugs because over the past ten years most new drug approvals have been for specialty drugs. Consistent with this trend is the 2014 U.S. (FDA) drug approval list; the FDA approved more new drugs in 2014 than in any of the past eighteen years, and the majority of these were specialty drugs.

A large portion of specialty drugs are biologics and, unlike a generic form of a brand drug, the lower cost alternative is called a "biosimilar." In simplest terms, biologic drugs are those drugs that are grown from biological natural sources rather than chemically processed. Biological sources can be human, animal, protein-based, nucleic acid-based, living cells, tissue, and microorganisms, for example. Many biologic drugs cost greater than $1,000 per prescription or $100 per dose. However, some other biologic drugs, such as insulin analogs and vaccines, are much lower cost, and are not generally categorized by payers as specialty drugs and thus are not included in this employer savings analysis.

Biosimilars are not generic versions, and are therefore approved under the standard of "highly similar," not the bioequivalence or "sameness" standard under the Drug Price Competition and Patent Term Restoration Act. Biosimilars do not meet the definition of sameness, like that of generics, which is why a new regulatory pathway was established. Thus, there is expected to be some variability between a biologic and its biosimilar counterpart, within some tolerance range, for consideration of biosimilarity. This paper addresses the potential savings to employers from the introduction of biosimilars.

One of the highest trending components of healthcare expenditures today is specialty drug products. Depending upon the source (including Milliman's own *Health Cost Guidelines [HCGs]* Research), the average cost per prescription is trending at 8% – 12% and the utilization is trending at 6% – 12%. Whether provided as coverage under the medical benefit or drug benefit, drugs associated with increasingly more common high-cost healthcare conditions, such as Cancer, Hepatitis C, HIV, Rheumatoid Arthritis, Multiple Sclerosis, etc., have become a bigger concern for employers. The recent commercial success of the newer Hepatitis C medications, which have high cure rates and can cost nearly $80,000 (but decreasing) per 12-week treatment, is just one example of how new medicines can impact conditions that were previously undertreated or ineffectively treated and the impact this has of increasing total drug spend.

We performed a cost analysis of the current market for biologic drug products and the future market penetration for biosimilars. Appendix A shows the list of drugs considered to be biologics for this study, which was based on an extensive and subjective review of all specialty type drugs. In total, we included 282 unique drug products and their cost to employers in both a commercially active and retiree setting.

Articles and testimonials on biosimilars generally discuss two important terms, biosimilarity and interchangeability. According to the FDA, the biosimiliarity standard is met if the applicant can prove that the biosimilar is "highly similar" to the reference product notwithstanding minor differences in clinically inactive components and show there are "no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency of the product." In addition to a demonstration of biosimilarity, a product can be deemed "interchangeable" by the FDA. To receive this designation the biosimilar must *also* be proven "to produce the same clinical result as the reference product in any given patient" and "[if] administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the two products is not greater than the use of the reference product without such alteration or switch."[1]

The first approved biosimilar drug in the U.S., Zarxio®, was not deemed interchangeable by the FDA. Zarxio's® manufacturer, Sandoz (a Novartis company), did not seek approval for interchangeability, which would have required more extensive research and documentation to the FDA for approval. From a cost savings and market penetration perspective, interchangeability can be very attractive to payers. For a typical generic drug, a pharmacist has the ability to substitute the generic drug for the brand during dispensing. Depending on state laws, if biosimilars do not have interchangeability, a pharmacist may not have this ability and thus will have less impact on increasing the biosimilars' market penetration.

Biosimilar market penetration will be highly dependent upon the physician, patient, and price, while the Pharmacy Benefit Manager (PBM) and benefit design will also have impact through formulary design and utilization management programs. Interchangeability will be less of a decision driver for new patients who have had no prior history of using either the brand biologic or biosimilar because they may be just starting treatment for a new healthcare condition. For some conditions, such as some cancers, the majority of patients are new to treatment, while other conditions require long-term treatment and have fewer new patients. Interchangeability is an important factor that should be recognized when considering biosimilar market penetration and more importantly patient and physician treatment choice for the condition being managed.

I. INTRODUCTION

The focus of this paper is on the potential for savings to employers in the Commercial and retiree marketplace through the introduction of biosimilar drugs. This paper is an update and expansion of the paper published in 2011, "Understanding Biosimilars and Projecting the Cost Savings to Employers," by Milliman. At that time, Congress, through the Affordable Care Act (ACA), and more specifically the Biologics Price Competition and Innovation Act of 2009 (BPCIA), had determined that patients should have access to lower cost drug alternatives. This legislation brought biologics and biosimilar drugs into the spotlight. Biosimilars, or follow-on biologics as they are often referred to, are approved drugs that attempt to replicate the original biologic manufacturer's drug functionality.

This study covers the time period 2013 – 2019 and is based on Milliman research and cost modeling analysis, using primarily actual employer fully-insured and self-insured 2013 prescription drug experience obtained from the Truven Health MarketScan® database, which contains medical and prescription drug records for millions of commercial and retiree lives. The purpose of this study is to quantify the impact of biosimilar savings to employers and take a close look at the potential drivers of cost savings and their variability.

This study focuses on:

- Identifying biologic drugs and the percentage of overall healthcare costs they represent,
- Consideration for the FDA approval pathway for biosimilar drugs,
- Creating an estimated savings timeline that projects employer savings, and
- Evaluating the importance of physician/patient behavior, market penetration, biosimilar pricing and benefit design for employer savings.

Employers can use this study to help understand the implications of such changes on future healthcare expenditures and to understand the timing of these changes and how benefit design or pharmacy cost management will impact future cost savings.

Since BPCIA was first introduced, the FDA has provided six specific sets of draft guidance from February 2012 through 2014 that provided manufacturers with the agency's view on key topics. An additional draft guidance was published in May 2015. In May 2015, some of the earlier draft guidance was finalized. The FDA considers the various sets of draft guidance to be non-binding but the guidance does address the following biosimilar approval pathway concerns[1]:

1.) Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (Final)

2.) Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product (Final)

3.) Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (Final)

4.) Formal Meetings between the FDA and Biosimilar Biological Product Sponsors or Applicants (DRAFT)

5.) Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product (DRAFT)

6.) Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act (DRAFT)

7.) Additional Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (DRAFT)

The seven specific sets of FDA guidance for biosimilar approval include the following provisions:

- Primary attention to a "stepwise" approach to demonstrating biosimilarity, including extensive analytical comparisons
- The drug approval process will be on a case by case basis that may require varying research and documentation from the biosimilar manufacturer.
- Some degree of pre-clinical and/or clinical trials but not to the same extent as the biologic.
- In some cases separate biosimilarity evidence for each drug indication. (This is not the case for Zarxio®).
- Evidence used in gaining biosimilar approval in Europe through the European Medicines Agency (EMA) will be allowed as evidence for U.S. approval, if scientifically justified.

Expectations around biosimilar emergence and opportunity for employer cost savings as a result of BPCIA legislation six years ago have been dampened due to the FDA delays in biosimilar approval guidance. As a result, the time gap between biosimilar market entry in the U.S. and other countries such as in Europe has widened. In March of 2015, about five years after BPCIA, the first official biosimilar drug in the U.S., Zarxio®, was approved to compete with the biologic Neupogen®. Neupogen® has been on the market for almost twenty-five years and is well beyond any data exclusivity rights. Zarxio® was already approved for use in Europe in 2009 where there are currently nearly 20 biosimilar drugs in use since 2014. Zarxio® is the first U.S. example for makers of biosimilars to follow, compare and learn from. It will also be the first biosimilar product that can be studied to observe market penetration and pricing when compared to its biologic counterpart. One very key point of the FDA guidance so far is that the pathway to approval will vary on a drug by drug basis. Zarxio® has not been brought to market as of May 2015 due to litigation appeals. Consequently the market awaits price and penetration data for the first U.S. biosimilar under the abbreviated FDA approval pathway.

This paper focuses on new information over the past several years about the U.S. market for biosimilars and how the cost savings impact may emerge over the next five years through 2019. In addition to active employees and dependents, the study considers retirees, since employers have been weighing the advantages and disadvantages of providing retiree healthcare coverage in light of changes to employer tax advantages as a result of ACA regulations. Any savings from biosimilars for employers due to an abbreviated biosimilar approval process will begin in the second half of 2015 provided Zarxio® clears litigation and other new biosimilars come to market.

II. PRODUCTS AND UNDERLYING COSTS IN THE COMMERCIAL MARKETPLACE

Less than 1% of employees and their dependents utilize biologic drugs but the average biologic drug cost is roughly 30 – 70 times the average cost of a non-biologic drug, making biologics much more significant for cost than utilization. Biologic drugs represent about 5% – 5.5% of the total healthcare spend (medical plus pharmacy) for a commercial population, so a 30% savings from biosimilar introduction would represent a 1.5% – 1.7% reduction in the employer's cost. However, the 30% savings assumes a 100% substitution rate across all biologics with a price differential of 30% or some combination of factors that achieve this, which might be considered aggressive initially in the U.S. market but less aggressive in the more developed European market. For comparison purposes, a $1.00 increase in the generic drug member copayment translates into about a 1% reduction in the employer cost to provide healthcare benefits.

Table 1 provides a breakdown of 2013 biologic drug cost experience for the nationwide average commercial population based on Milliman research. This data forms the basis for the commercial savings projections provided later in this paper. Note that 16 of the 282 biologic drugs studied comprise 55.8% of the biologic drug cost in 2013 shown in Table1, Neupogen® (Zarxio®) not being one of them.

Table 1
2013 Commercial Population
Biologic Estimated Cost PMPM

Biologic Drug®	Medical Benefit	Pharmacy Benefit	Total
Humira Pen	$0.01	$1.82	$1.83
Remicade	1.51	0.14	1.66
Copaxone	0.01	1.26	1.26
Enbrel Sureclick	0.02	1.22	1.24
Neulasta	0.94	0.09	1.03
Avastin	0.72	0.01	0.73
Herceptin	0.70	0.00	0.71
Rituxan	0.64	0.02	0.66
Enbrel	0.00	0.60	0.60
Rebif	0.00	0.50	0.50
Tysabri	0.42	0.07	0.49
Stelara	0.05	0.41	0.46
Humira	0.00	0.44	0.44
Avonex	0.00	0.43	0.43
Advate	0.24	0.15	0.39
All Other	4.89	4.95	$9.84
Total	**$10.16**	**$12.12**	**$22.28**

Source: Milliman 2013 proprietary data for a large, multi-payer commercial population. See Appendix A for a full list of biologic drugs represented in this study.

The $22.28 per member per month (PMPM) in Table 1 represents the historical 2013 cost of these biologic drugs (see Appendix A) provided in a hospital outpatient setting, physician's office, home health, retail pharmacy, mail pharmacy, or specialty drug pharmacy. The medical PMPM of $10.16 PMPM is likely to be understated to the extent that drugs provided under the medical benefit are improperly coded (proper coding uses Level II HCPCS codes such as J, S, and Q) or are part of a bundled payment. Drugs administered in an inpatient hospital setting, which are typically bundled with other ancillary services, are not included in this analysis. The use of the distinct National Drug Code (NDC) for retail, mail, and specialty pharmacy claims under the drug benefit makes material cost understatement highly unlikely for the $12.12 PMPM pharmacy benefit.

Table 1 provides some evidence for the fact that most drug products, based on dispensing requirements or administrative complexity, are conducive to delivery under either the medical benefit or the prescription drug benefit but not equally across both benefits. An important consideration for employers is where these drugs belong from a benefit design, cost management, and price perspective. Dispensing under the medical benefit is typically per treatment; whereas dispensing under the drug benefit is typically based on a monthly prescription which, for high-cost drugs, creates a significant concern that low medication adherence or unused medication can mean wasted medication. However, there may be more opportunities for clinical pharmacist intervention and, thus, drug management under the drug benefit due to the current retail, mail, special delivery channel management, and point of sale adjudication and drug utilization review edits. Over the past few years, many employers have performed analyses to determine whether it is beneficial to move coverage of certain drugs from the medical to pharmacy benefit.

The BPCIA provided a twelve-year exclusivity period for many new biologic drugs. Given that a large number of new biologics have been approved in recent years or even months, and a large number of biologics remain in the pipeline, it will be at least twelve years for biosimilars to fully penetrate the current biologic market. As such, biosimilar penetration in the market over the next several years will be small. New biologic drugs that entered the market in 2008 and later would not be impacted until 2020 and later, which is outside the study period. New therapies could render older therapies unmarketable, further delaying the impact of biosimilars. Table 2 shows the 2013 biologic cost of $22.28 PMPM incrementally as exclusivity expires over the six projected years in this study. Zarxio® was just approved in March 2015 as the first official biosimilar in the U.S. Products approved prior to this date would have been required to comply with the full FDA drug approval process and clinical trials which we are not measuring.

Table 2
12 Year Exclusivity Expiration for
2013 Historical Biologic Drug Cost of $22.28 PMPM

	Year of Patent Exclusivity Expiration					
	2014 or prior	**2015**	**2016**	**2017**	**2018**	**2019**
2013 PMPM distributed by year drugs 12 year exclusivity expires	$15.71	$1.34	$1.71	$0.80	$0.05	$0.09
2013 % of PMPM distributed by year drugs 12 year exclusivity expires	70.5%	6.0%	7.7%	3.6%	0.2%	0.4%
Cumulative 2013 %	70.5%	76.5%	84.2%	87.8%	88.0%	88.4%

Source: Milliman 2013 proprietary data for a commercial population. See Appendix A for a full list of biologic drugs represented in this study.

Over 70% of the 2013 cost for biologics is represented by drugs whose twelve-year exclusivity has already expired, in some cases several years ago. Thus, the exclusivity time period established by the BPCIA will not be a great barrier to biosimilars. The opportunity is already here for biosimilar manufacturers, but the approval pathway and return on investment are not necessarily appealing for all biologics or specific drug therapy classes.

III. PRODUCTS AND UNDERLYING COSTS IN THE AGES 65 AND OLDER RETIREE MARKETPLACE

Biologic drugs represents about 7% – 7.5% of the total healthcare spend for a retiree population. Less than 1% of retirees utilize biologic drugs. A 30% savings due to biosimilars would represent a 2.1% – 2.3% reduction in the employer cost to provide healthcare benefits to retirees eligible for Medicare benefits. Medicare would be the primary payer of the employer benefits for other than small employers where Medicare is the secondary payer.

Table 3 provides a breakdown of 2013 biologic cost experience for the nationwide average retiree population based on Milliman research. This data forms the basis for the retiree savings projections provided later in this paper.

Table 3
2013 Ages 65 and Older Retiree Population
Biologic Estimated Cost PMPM

Biologic Drug®	Medical Benefit	Drug Benefit	Total
Enbrel Sureclick	$0.00	$1.90	$1.90
Humira Pen	0.00	1.87	1.88
Enbrel	0.00	1.60	1.60
Copaxone	0.00	1.54	1.54
Forteo	0.00	1.00	1.00
Humira	0.00	0.81	0.81
Neulasta	0.54	0.24	0.78
Rituxan	0.67	0.09	0.76
Gammagard Liquid	0.16	0.54	0.70
Avonex	0.00	0.69	0.69
Lucentis	0.54	0.10	0.64
Procrit	0.15	0.46	0.61
Avastin	0.44	0.08	0.52
Gamunex-C	0.12	0.39	0.51
Remicade	0.34	0.11	0.45
All Other	3.88	5.81	9.70
Total	**$6.84**	**$17.24**	**$24.09**

Source: Milliman 2013 proprietary data for a large, multi-payer retiree population. See Appendix A for a full list of biologic drugs represented in this study.

The $24.09 per member per month (PMPM) represents the historical 2013 cost of biologic drugs provided in a hospital outpatient setting, physician's office, home health, retail pharmacy, mail pharmacy, or specialty drug pharmacy. **Note that the $6.84 medical benefit drug component only represents 20% of the total cost since Medicare would pay about 80% for these Medicare Part B services. So the total drug cost, including Medicare coverage, is $51.44 PMPM, or more than double the cost of the commercial population in the absence of coordination of benefits with Medicare.**

Table 4 shows the 2013 biologic cost of $24.09 PMPM incrementally as exclusivity expires.

Table 4
12 Year Exclusivity Expiration for
2013 Historical Biologic Drug Cost of $24.09 PMPM

	2014	2015	2016	2017	2018	2019
2013 PMPM distributed by year drugs 12 year exclusivity expires	$17.60	$0.40	$0.68	$1.30	$0.64	$0.22
2013 % of PMPM distributed by year drugs 12 year exclusivity expires	73.1%	1.7%	2.8%	5.4%	2.7%	0.9%
Cumulative %	73.1%	74.8%	77.6%	83.0%	85.6%	86.6%

Source: Milliman 2013 proprietary data for an Ages 65 and Older retiree population. See Appendix A for a full list of biologic drugs represented in this study.

More than 70% of the cost for biologics is represented by drugs whose twelve year exclusivity has come to an end.

IV. DRIVERS OF BIOSIMILAR COST SAVINGS

The estimated savings impact of biosimilar drugs on employer healthcare costs will depend upon many key cost drivers, such as the following:

- The comprehensive list of generally recognized biologic drugs currently on the market. New biologic product patents would preclude analysis of biosimilar counterparts until well beyond the study period (2013 to 2019) of this paper.
- The FDA approval process (as is the case for all drugs).
- The degree to which physicians accept and choose to dispense the biosimilar product in lieu of the original biologic, which may vary for newly treated patients versus patients with ongoing or grandfathered treatment.
- The degree to which newly treated patients, as opposed to grandfathered patients, accept the physician-recommended biosimilar product.
- The price differential between biosimilar and biologic at point of market entry and over ensuing years.
- Potential reductions in manufacturing cost leading to lower drug pricing especially for manufacturers that are second or third to market a product.
- Future trends in specialty and biosimilar drug utilization and cost per prescription.
- Shift in biologic / biosimilar drug dispensing from the medical benefit to the pharmacy benefit or vice versa. Since this assumption would impact the biologic and biosimilar in a positively correlated manner, any impact it may have has not been included in this paper due to the subjectivity of determining dosing differences.
- Potential increased / decreased drug and medical utilization due to increased / decreased side effects of biosimilars above and beyond the known side effects of the original biologic counterpart. Because of the subjective and clinical nature of this assumption, it has not been included in determining the potential impact on cost savings or increases in this paper.
- Employer benefit changes (e.g., copay differential) to incentivize the use of biosimilars.
- The extent to which a biosimilar represents a new therapeutic alternative, such as a biosimilar to Lantus®, which will affect other insulin products. This so called therapeutic interchange or indication creep was beyond the scope of this analysis.
- Differences in manufacturer rebates for biologics and corresponding biosimilars.
- The indication for which the biosimilar is approved compared to the indications for the biologic counterpart. Some biosimilars may be approved for all indications, while others may only be approved for subset of indications that the biologic drug can treat. This impact was beyond the scope of this analysis.

Future savings will be sensitive to each of these cost drivers to a different extent, with patient/physician behavior, biosimilar penetration rate, and price differential (including the impact of rebates) playing the most significant part in the savings outcome. The patient/physician behavior is strongly correlated with market penetration. Because of this, sensitivity analysis for these two primary cost savings drivers is provided in Table 7 of this paper.

The remainder of this section discusses each cost driver.

FDA APPROVAL PROCESS & DATA EXCLUSIVITY PERIOD

In February 2012, the FDA provided their first set of draft guidance on the abbreviated approval pathway for biosimilar drugs. Since that time, additional sets of draft guidance were released, and then the first three draft guidances were finalized in 2015. Some drug manufacturers are currently working on biosimilars in anticipation of entering the FDA queue, and others have waited to watch the Zarxio® process be completed.

There are a few different dates to consider when trying to anticipate the release of biosimilars, including the FDA patent expiration date and the data exclusivity date expiration. Because of the complexity of the manufacturing process, the underlying data knowledge is very important. However, many biologic products have expired data exclusivity dates with no biosimilar expected on the horizon.

Various sources including the FDA website[4] were utilized to estimate the time at which a biosimilar might enter the market for each biologic product in this study. Some biosimilars are expected to be approved within the next one to two years, though many may take longer to reach market even though the data exclusivity for the biologic has already expired. In this study, we used current market intelligence to infer likely upcoming biosimilar release dates, such as for Zarxio® as well as biosimilar versions of Avastin, Humira, et al. In all other cases, we assumed the biosimilar would be released in the year of the biologic's data exclusivity expiration, or in 2017 if exclusivity has already expired.

PATIENT / PHYSICIAN BEHAVIOR

Market penetration for any drug depends upon the patient and physician. Factors that can influence patient and physician behavior may include product cost, benefit design, prior authorization, formulary requirements, physician payment incentives, drug side effects and drug effectiveness.

One would expect that cost is certainly an important factor with biologics and biosimilars for the employer but the healthcare benefit design may insulate the patient from high out-of-pocket expenditures. The patient should be concerned foremost about outcomes and follow a drug selection path that results in the best health outcome. However, the patient typically relies on the attending physician to help make decisions regarding their healthcare treatments that may not be well understood.

It is likely because of personal habits that newly diagnosed patients for high cost healthcare conditions, with a choice between a biologic and biosimilar alternative, will be more accepting of biosimilar drugs since they will have no prior treatment success (or failure) for comparison. Patients currently being treated successfully with an original biologic may be less apt to take the risk of switching to a potentially less costly alternative that may result in a worse, equivalent or better health outcome. Affordability might increase patient acceptance of risk though, and patients may be more accepting of a biosimilar with both biosimilarity and interchangeability status compared to a biosimilar that only has biosimilarity status.

Biologic drugs whose patient populations have a high percentage of new patients and less sensitivity to treatment change risk may produce higher biosimilar market penetration than those provided in Tables 5 and 6. The sensitivity of these assumptions are provided in Table 7 of this paper. It is apparent that there is a higher percentage of new biologic drug patients for most cancer related conditions but this may be somewhat offset by relatively fewer new patients for other conditions.

BIOSIMILAR / ORIGINATOR PRICING DIFFERENCE

The price differences between generic and brand versions of small molecular drugs has been well documented from historical data. The first generic manufacturer often has a six-month marketing exclusivity period and thus the price differential to the brand tends to be lower during this period, typically 10% – 20% below the brand. After the six-month exclusivity period and depending upon the generic competition, the price differential to the brand typically drops to 50% or more compared to the brand price and over time may approach as much as a 90%+ differential. Much of the price differential is in relation to the number of manufacturers producing the product. Biosimilars have been on the market for many years in Europe, but there has been limited evidence of such pricing in looking broadly at biosimilars there. For the U.S., using the European experience as a benchmark, pricing at a 30% discount might be considered somewhat aggressive at the time of launch with perhaps price improvement over time as additional manufacturers create additional biosimilars. A price differential assumption of 10% – 30%, used in this paper, is largely based on what can be discerned from the global market to date, in particular within the European Union where biosimilars have been available for many years. Looking at the market in Europe for Eprex®, Neupogen® and Genotropin®, the average price difference was 18% – 30% based on 2013 Procentric™ data.

One important driver of price in the biosimilar discussion is the Medicare Part D Coverage Gap Discount Program (CGDP). Beginning in 2011, brand drug manufacturers who want their drugs included under Medicare Part D coverage, must participate in the 50% discount program for drugs in the Part D benefit coverage gap (i.e., annual costs between $3,310 and approximately $7,515.22). **CMS issued guidance in April 2015 indicating that biosimilar drugs will not participate in the 50% discount in the coverage gap**. As a result, a Medicare patient subject to the coverage gap may find the biologic price to be lower than that of the biosimilar.

DRUG TRENDS

Milliman Inc., performs extensive research (e.g., Milliman *HCGs*) each year to quantify the cost for prescription drugs in various markets and the key drivers of cost. During that annual research, we perform drug price analysis from quarter to quarter, analyze changes in drug mix, and project drug cost for developing insurance premiums for future periods. An important part of the biosimilar cost modeling process is the projection of historical per capita costs for biologic drugs to future years. Table 5 shows the 2013 and 2014 fourth quarter AWP prices and the annual changes for fifteen of the top biologic drugs in this study.

Table 5 Biologic Drug Price Trends Top 15 Biologics by Dollars Spent			
Biologic Product®	**AWP Cost 4Q 2013[1]**	**AWP Cost 4Q 2014[1]**	**Price Trend**
Humira Pen	$1,404.65	$1,689.53	1.203
Remicade	1,012.26	1,113.89	1.100
Enbrel Sureclick	723.50	826.78	1.143
Neulasta	7,642.63	8,011.13	1.048
Avastin	190.46	199.13	1.046
Herceptin	4,091.74	4,330.38	1.058
Rituxan	80.13	84.60	1.056
Enbrel	538.39	601.67	1.118
Rebif	967.28	1,034.99	1.070
Tysabri	353.12	374.15	1.060
Stelara	14,949.42	15,710.92	1.051
Humira	1,186.97	1,403.04	1.182
Avonex	2,607.00	2,709.15	1.039
Advate	1.68	1.72	1.024
Other	N/A	N/A	N/A
Total			**1.102**

[1]AWP for the most prevalent NDC for the product listed based on MediSpan.

Publically available drug trend studies performed by leaders in the industry have been used to project costs from 2013 to 2019. The 2013 and 2014 Express Scripts Drug Trend Reports[5], and in particular the section of the reports addressing specialty cost trends, provide extensive detail on observed and projected trends for specialty therapeutic classes. Specialty trends were extremely high in 2014, primarily due to the release of new, very high-cost treatments for the Hepatitis C Virus (however, these treatments are *not* biologics), and are projected to be about 21% to 23% in 2015 through 2017. The trend assumptions in this paper vary by drug therapeutic class and composite to approximately 21% per year through 2019.

Projecting trends for more than two years is very subjective, given the constant change in the availability of drug products and market conditions. Since trends in drug utilization and cost vary substantially from year to year, for simplicity this analysis used uniform trends by drug therapy class over the entire six-year projection period, based on the average forecasted trends in the 2013 and 2014 ESI reports.

EMPLOYER BENEFIT CHANGES

Prescription drugs may be dispensed and/or administered in many different healthcare settings. If prescription drugs are dispensed from a pharmacy, then these drugs are typically covered under the terms of the employers prescription drug benefit. Prescription drugs dispensed from an institutional or physician's office setting are covered under the employer's medical benefit. This analysis of biosimilar savings excludes drugs provided from a hospital inpatient or nursing home stay because reimbursement is generally bundled with all other hospital ancillary charges or a nursing home daily rate and not possible to isolate.

When drugs are provided through the employer's medical benefit, the member cost sharing is commonly subject to one or more of the following: deductible, coinsurance (e.g., 20%), and out-of-pocket limit (e.g., $2,500). Based on a review of actual medical benefit claim data used in this analysis, patients covered under an employer sponsored insurance plan typically pay 0% – 15% of the cost for specialty drugs when they are covered under the medical benefit.

When drugs are provided through the employer's drug benefit, the member cost sharing is commonly subject to a brand or specialty brand copayment or coinsurance, and in some cases subject to an out-of-pocket limit. It is becoming much more common in recent years for employers to have specialty drugs on a separate cost sharing tier with either a high dollar copayment or coinsurance to help control the cost of these drugs.

According to the 2015 Specialty Drug Benefit Report released by the Pharmacy Benefit Management Institute (PBMI)[6], the following information reflects the average employer's position on specialty drug benefits administered under the drug benefit:

- 62% of employers surveyed charged a separate drug tier copayment/coinsurance for specialty drugs in 2014. This is up over 20% in just the one year from 2013 to 2014, and has been increasing significantly compared to several years ago when this practice was not common. This was only about 19% four years ago.

- The average copayment charged for specialty drugs was $69.06 for preferred specialty medications and $129.21 for non-preferred specialty medications, assuming a 30-day fill. Splitting out specialty medications into separate cost sharing tiers is a very new strategy for employers, and one which may become increasingly common as biosimilars begin to emerge.

- The average coinsurance charged for specialty drugs under the pharmacy benefit was 47% in 2014. This is up from 33% in 2013 and has been growing steadily in recent years. Some plans utilizing coinsurance include a maximum out of pocket cost per prescription or in aggregate.

To simplify the analysis, an assumption of a $0 or $50 difference between the biologic and biosimilar member cost sharing when provided under the prescription drug benefit was used.

BIOSIMILAR MARKET PENETRATION

At this time, it is difficult to determine the degree to which biosimilar drugs will take market share from the corresponding biologic or biologics within the same drug therapy class. Most discussions seem to indicate that the market share change will be more like the relationship between two brand drugs used to treat the same condition rather than a small molecular brand to generic comparison. 2013 European market penetration results available through IMS Health Research[7] for three drug therapy classes' (erythropoietin, human growth hormone and granulocyte colony-stimulating factor) shows very inconsistent penetration rates from country to country and class to class. The median penetration rate for biosimilars in these classes alone was 27%.

Given all the biologic drug classes, a market penetration of 30% across all biologics with a biosimilar counterpart might be considered to be somewhat aggressive for the U.S. initially like Europe five or six years ago. This is not a market where generic penetration rates of 80% or even higher are expected over the short term, or potentially long term. Biosimilar drugs will most likely not approach the pricing differences that current small molecular generic drugs have compared to the original brand drug and thus penetration may be dampened. This price difference contributes a large part to the penetration rate for generic products. In addition, if biosimilars are not considered interchangeable, some patients may not be willing to use them. Further, if biosimilars are not interchangeable, pharmacists will not be allowed to automatically substitute a biosimilar for the biologic counterpart.

COST SHIFTING BETWEEN EMPLOYER BENEFITS

There are important differences between providing prescription drugs through the medical benefit versus the drug benefit that need to be recognized when reviewing employer benefits for employees or retirees and their dependents.

The cost to the employer for specialty drugs will be higher under the medical benefit than the pharmacy benefit for like medications if provider contracting is not well defined for drugs and supplies. The cost to the member will typically be lower under the medical benefit due to the out-of-pocket limit which applies to all medical services. It would not be commonplace but, if the provider contracting for specialty drugs is reimbursed at Medicare allowed levels (i.e., Average Sales Price (ASP) + 6%), then it will be cheaper for the employer to dispense specialty drugs through the medical benefit because pricing based on ASP is cheaper than pricing based on Average Wholesale Price (AWP). Beyond the price paid for drugs, there may also be some cost management opportunities and manufacturer rebates through the Pharmacy Benefit Manager (PBM).

It had been a common practice for specialists such as oncologists to charge considerably more than AWP for specialty drug products until Medicare instituted the ASP pricing requirement on January 1, 2005. However, ASP pricing has not gained acceptance in the Commercial provider marketplace at this time.

Without appropriate drug cost management, there is little incentive to substitute generic drugs for multi-source brand drugs when provided through the medical benefit. In most cases, the patient is unaware of or concerned about administered medication choices, which is not the case when a patient visits the retail pharmacy and has an opportunity to see the price at point-of-service.

As a result of these factors, employers have been performing cost analyses on drug coverage under the medical versus pharmacy benefit, and some employers have begun shifting coverage away from the medical benefit in recent years.

PERCENTAGE OF NEW PATIENTS

Patient and physician behavior are not expected to be consistent for newly diagnosed and treated patients versus previously diagnosed and currently treated patients. Newly diagnosed and treated patients make drug choices without first-hand experience with biologics and rely heavily on the physician for guidance. This group of patients is more likely to view biosimilars as a viable treatment option. Previously diagnosed patients currently being treated with a biologic may be less receptive to switching to a biosimilar if their outcomes to date have been successful, even though outcomes may not differ if they did. The latter patient has an element of risk to consider having existing outcomes for comparison.

The existing patient treatment decision bias exists if the current treatment is working. The primary factor that could overcome that bias is lower patient out-of-pocket cost or the FDA deeming a biosimilar is interchangeable. If the patient out-of-pocket cost difference is immaterial, it is more unlikely that a patient would switch to a biosimilar. For purposes of this study, we assumed 90% of patients treated for a condition utilizing a biologic course of treatment, are existing patients and only 10% are new patients. New patients would be patients that are selecting treatment for the first time for conditions that can be treated using a biologic drug. These percentages were based on drug utilization trend analysis and condition onset or new condition prevalence.

V. PROJECTED SAVINGS BASED ON HISTORICAL CLAIM DATA

Each year since 1954, Milliman has performed research to estimate the loosely managed nationwide average healthcare cost for a commercially active population, published in the *HCGs.*

In 2013, the commercial population (employees and their dependents covered under an employer-sponsored health benefits plan) spent about $22.28 on biologic drugs per member per month (PMPM). So, for an employer insuring 10,000 lives (roughly 5,000 employees plus dependents), this translates to $2.67 million in annual covered expenditures for biologics before member cost sharing, which represents 5.2% of total covered healthcare costs (assuming a healthcare spend of $428 PMPM or $51.4 million, based on Milliman's 2013 *HCGs*).

If a biosimilar had been introduced for every biologic drug immediately and all patients used a biosimilar product which was 30% cheaper, the total covered healthcare costs would have decreased by 1.6% (5.2% x 30%) in 2013. This would obviously represent close to a "best case" scenario, i.e., immediate and complete biosimilar availability across the entire biologic spectrum and all current biologic drug users switching to biosimilars with an average price savings of 30%. Clearly this scenario did not materialize, given that the first biosimilar was not approved until March 2015 and has not yet been released at the time of publication due to litigation. So there is clearly some delay between the opportunity for a biosimilar in the market and the actual approval and marketing of the product. Achieving a 1.6% savings would require more time, better pricing than a 30% discount or higher market penetration.

PROJECTED EMPLOYER SAVINGS SCENARIOS

Actual employer savings will depend upon many factors but certain groups of assumptions or scenarios help to quantify the biosimilar impact to employers. Although a seemingly infinite combination of scenarios can be modeled, three benchmark scenarios were used to project the biosimilar savings from 2014 to 2019. The three benchmark scenarios are:

- Scenario 1: Aggressive, for United States, biosimilar market penetration of 30%, with 100% acceptance from both physician and patient, at a 30% biosimilar price discount and $50 copay differential (i.e., $100 biologic and $50 biosimilar). Market penetration not beginning until late 2015, using expected approval dates for known pipeline biosimilars and allowing others with expired exclusivity to reach the market beginning in 2017.

- Scenario 2: Less aggressive, for United States, biosimilar market penetration of 15%, with 50% acceptance from both physician and patient, at a 20% biosimilar price discount and $50 copay differential. Market penetration not beginning until late 2015, using expected approval dates for known pipeline biosimilars and allowing others with expired exclusivity to reach the market beginning in 2017.

- Scenario 3: Moderate, for United States, biosimilar market penetration between 15% and 25%, with market penetration and biosimilar price discount (20% – 30%) increasing gradually over the next five years. Market penetration not beginning until late 2015, using expected approval dates for known pipeline biosimilars and allowing others with expired exclusivity to reach the market beginning in 2017.

The key differences in the assumptions for the three benchmark scenarios are provided in Table 6.

Table 6
Summary of Benchmark Scenario 1-3 Assumptions

Assumption	Scenario 1	Scenario 2	Scenario 3
Biosimilar Market Penetration	30%	15%	15% – 25%
New Patient %	10%	10%	10%
New Patient Acceptance	100%	50%	67% – 100%
Existing Patient Acceptance	100%	50%	50% – 80%
Price Difference	30%	20%	20% – 30%
Biosimilar Copay	$50	$50	$50
Biologic Copay	$100	$100	$100
12 Yr. Exclusivity Basis[1]	Most Likely Date	Most Likely Date	Most Likely Date

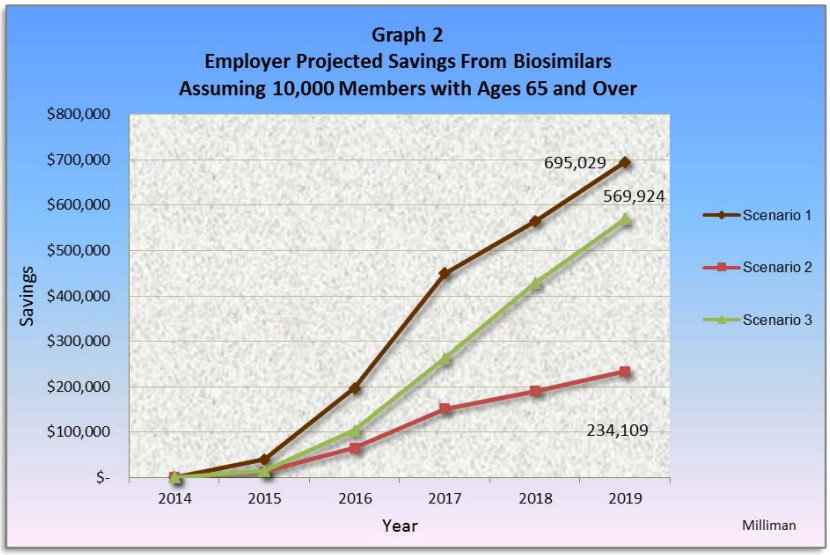
[1]*The most likely date is the expected 2016 introduction of certain biosimilar products, 2017 for any biologics whose data exclusivity has already expired and the data exclusivity expiration date for all others.*

Each of these assumptions is described in greater detail in Section IV of the paper.

Graph 1 depicts the biosimilar savings for each scenario starting with the commercial active employee market.

The savings under the various scenarios range from 2.6% – 7.6% of 2019 total drug spend and 0.3% – 0.8% of 2019 total healthcare spend. As can be seen by the graph, 2014 – 2018 show lower but increasing savings.

The corresponding savings for the Medicare eligible retiree or age 65 and older population are provided in the Graph 2 below.



The savings under the three scenarios for retirees range from 2.5% – 7.4% of 2019 total drug spend and 0.4% – 1.1% of 2019 total healthcare spend. These results are not significantly different from the commercial population results, primarily because of the Medicare primary benefit that reduces the cost for biologics under the medical benefit by approximately 80%.

PRICE AND MARKET PENETRATION SENSITIVITY

Although there are a number of variables that will contribute to the magnitude of the savings for employers, it eventually comes down to just two: price and market penetration. The other variables impact these two variables.

Table 7 shows the range of savings for the commercial population in 2019 dollar terms as the price and market penetration assumptions change. All costs have been trended and a larger percentage of biologic drugs have lost exclusivity protection by 2019.

Table 7
2019 Biosimilar Employer Projected Savings Matrix
Based on 10,000 Commercial Lives

Biosimilar Market Penetration	Price Difference				
	10%	20%	30%	40%	50%
10%	$77,736 (0.095%)	$144,856 (0.178%)	$211,975 (0.260%)	$279,095 (0.342%)	$346,214 (0.424%)
20%	$155,472 (0.191%)	$289,711 (0.355%)	$423,950 (0.520%)	$558,189 (0.684%)	$692,428 (0.849%)
30%	$233,208 (0.286%)	$434,567 (0.533%)	$635,925 (0.780%)	$837,284 (1.026%)	$1,038,642 (1.273%)
40%	$310,944 (0.381%)	$579,422 (0.710%)	$847,900 (1.039%)	$1,116,378 (1.369%)	$1,384,856 (1.698%)
50%	$388,680 (0.476%)	$724,278 (0.888%)	$1,059,87 (1.299%)	$1,395,473 (1.711%)	$1,731,070 (2.122%)

The $635,925 (30% Price, 30% Market Penetration) is reflective of the aggressive Scenario 1, year 2019 in the earlier Commercial graph. The aggressive scenario is used in Table 7 because the full penetration rate above each column is realized (i.e., 100% physician and patient acceptance of biosimilar option). This number represents total dollar savings for a single employer with 10,000 insured memebers. Table 7 shows that biosimilar savings grows with greater biosimilar market penetration and also with a greater price differential compared to the original product, as would be expected, though the maximum savings is just over 2%. Penetration plays a slightly greater role than price in savings when looking at a comparison of 50% to 10%. This savings ratio is 5 times for price vs. 4.5 times for price. The high end of the table is based on 50% ultimate market penetration and a 50% discount, both of which are aggressive assumptions. The 50% penetration is particularly aggressive, considering the length of time it has taken for a single biosimilar product to be approved. The 50% price difference is a larger ratio than that experienced in Europe, but could be achievable if large rebates are introduced to maintain competitiveness. On the other hand, the low end of Table 7 represents 10% market penetration and a 10% price difference, resulting in only 0.1% savings to employers. This scenario seems quite pessimistic and well below the three scenarios used to depict employer savings.

Over time, as more information becomes available, the matrix provided in Table 7 may become more focused on a specific price differential and market penetration rate. Based on the current FDA process and Zarxio®, the study range is more narrowly defined within the shaded region of the table. The U.S. trails Europe by six to nine years when it comes to biosimilars and the market penetration for biosimilars outside the U.S. has been increasing since inception, just like what is expected in the U.S.

VII. WHAT IMPACT WILL BENEFIT DESIGN PLAY?

Current employer drug benefit design does little to incentivize members to utilize generics for drugs covered under the medical benefit. This contrasts from the pharmacy benefit, where the implementation of drug tiers has played a pivotal role in maximizing the generic dispensing rate.

Typically, the greater the copay difference between a generic and corresponding multi-source brand drug, the greater the incentive for the member to seek the generic alternative. The demand for generics is often based on out-of-pocket cost with less concern about drug effectiveness. With biologic drugs, the drug effectiveness may be the driving force behind the physicians and indirectly the members' decision making and copay differential is secondary. If lowering the copayment for biosimilars does not increase the biosimilar market penetration, then the employer bears the cost for the lower copayment charged.

The savings analysis in this paper used a $50 copay differential for biosimilars, which is similar to the average differential between preferred and non-preferred specialty medication copayments in 2014. The utilization was not changed to reflect greater demand for lower priced biosimilars. It was assumed that the patient demand is nearly inelastic compared to the non-biologic drug environment where as the patient out-of pocket increases, drugs considered discretionary are forgone and the utilization is lower overall.

Another consideration when discussing drug tiers that may be relevant is rebates. If formulary management associated with selective drug tiers were to induce current biologic manufacturers to begin to pay a rebate, then there would be savings, even if the biosimilar was not used. In addition, the biosimilar manufacturer could pay a rebate. In recent months, the introduction of multiple Hepatitis C drugs from various manufacturers resulted in a sudden marked increase in rebates for these high cost drugs, in order to maintain market share. While Hepatitis C drugs are not biologics and thus excluded from this study, a similar situation could take place with the introduction of biosimilars as competition for products that have otherwise maintained longstanding exclusivity. Biologic manufacturers may be forced to provide a large rebate in order to incentivize plans to still cover their drug rather than the biosimilar, particularly if interchangeability is permitted, and biosimilars may also provide rebates to compete. It remains to be seen what the ending relationship will be between the cost of the biosimilar versus the biologic after accounting for rebates, though Table 7 shows how savings would increase if there is a large cost differential between the biologic and biosimilar. Savings could be greater if both the biologic and biosimilar introduce large rebates, causing net costs to decrease regardless of which drug is used by patients.

VIII. METHODOLOGY AND ASSUMPTIONS

We took historical pharmacy claim data, isolated a select list of biologic drug products, and projected the future cost to employers and resulting cost savings due to the introduction of biosimilar drug products.

The study period was calendar years 2013 through 2019. The first year of the study represents the known drug cost composition in that year, and each subsequent year represents a projected estimate of drug costs, even though for example 2014 is now historical. The base year data is based on actual employer fully-insured and self-insured 2013 prescription drug experience obtained from the Truven Health MarketScan® database. We applied a series of data filters to remove unreliable data from contributors with large gaps in data or anomalous claim patterns. We summarized the data at an NDC level and selected 282 biologic drug products to include in the study (see Appendix A). This list includes drugs filled in both the medical and pharmacy setting; we used both medical and pharmacy claims for the same group of members. Medical drug claims were identified by the HCPCS codes associated with the products in this analysis.

Total employer healthcare spend for all medical and pharmacy costs in the base year were estimated using Milliman's 2013 *Health Cost Guidelines* for Commercial and Ages 65 and Over populations. For the ages 65 and over population, total costs were reduced by the expected portion of coverage provided by Medicare, assuming that Medicare is the primary payer for retirees. In subsequent years (2014 – 2019), a combined 8% annual utilization and cost trend was applied to project total healthcare costs.

The projected biosimilar savings is dependent on a large number of assumptions, many of which are described in detail in Section IV and throughout this paper. The most relevant assumptions in our analysis are listed below, along with the values assumed in the three scenarios:

- Maximum Biosimilar Penetration: This assumption reflects the maximum degree to which biosimilar drugs can take market share from the corresponding biologic or other biologics within the same therapeutic class. Each of the three scenarios assumes 30% maximum penetration. The maximum market penetration is reduced by one minus the combined physician and patient acceptance rate for biosimilars across newly treated and currently treated patients.

- Biosimilar Price Relative to Biologic Price: In Scenario 1, we assumed the biosimilar would cost 30% less than the corresponding biologic. In Scenario 2, we assumed the biosimilar would cost 20% less and in Scenario 3, the discount would start at 20% in 2015 and increase to 30% in 2018 and 2019.

- Percentage of New Patients (i.e., newly diagnosed for treatment using either a biologic or biosimilar product): We assumed 10% in all scenarios.

- New Patient Acceptance of Biosimilars:

  – The patient acceptance rate acts as a factor to reduce the maximum biosimilar penetration mentioned above. The combination of these two components results in the ultimate biosimilar market penetration expected, considering both the degree to which biosimilars will be able to saturate the market and the proportion of patients and physicians willing to try them.

  – Scenario 1, which is the most optimistic view of biosimilar entry and acceptance, assumes 100% acceptance of biosimilar products.

  – Scenario 2 assumes 50% acceptance and Scenario 3 increases the acceptance from 66.7% in 2015 to 100% in 2019.

- Existing Patient Acceptance of Biosimilars:
  - Scenario 1 assumes 100% acceptance. This outcome is aggressive, but reflects the maximum potential savings available if all patients shift to the biosimilar product.
  - Scenario 2 assumes 50% acceptance and Scenario 3 assumes an initial acceptance rate of 50% in 2015, gradually increasing to 80% acceptance by 2019.
- Biosimilar Entry Date: We estimated the data exclusivity expiration date using various sources including the FDA website[4]. In many cases, the data exclusivity has already expired, but no biosimilar has been approved, sometimes due to remaining patent protection. As such, true savings will be delayed. We adjusted the data exclusivity expiration dates based on research for true expected approval dates for anticipated new biosimilars over the next few years, such as expected approvals for biosimilars to Avastin and Humira. If a biologic no longer holds exclusivity but no biosimilar is anticipated in 2015 or 2016, we assumed the biosimilar would be released in 2017 at the earliest.
- Drug Trends: As described in Section IV, we applied projected utilization and cost trends at a therapeutic class level. These trends were the same in all scenarios and averaged about a 20% annual PMPM trend.

IX. CONCLUSIONS

The cost to payers of biologically manufactured products is high and that cost increases future drug spend and drug trends. The savings from biosimilars, though welcomed, appears to be small in the context of total biologic spending and similar savings can be achieved simply by increasing the generic member copayment by one dollar. It should be noted that increasing generic copays takes little to no effort by the employer and brings minimal member disruption.

Savings due to biosimilars for 2014 were zero and projected to be negligible for 2015 with only one approved drug (Zarxio) but no drug sales through May 2015. For a 10,000 lives employer with 2019 annual commercial healthcare expenditures of $81.5 million, the 2019 total estimated savings is just $635,925 or 0.8% of total healthcare spend assuming 30% total market penetration and 30% lower pricing of biosimilars. The estimated savings is much less if not all patients are willing to try biosimilars, which may be the case for existing patients using biologic products.

Based on a review of published articles on biosimilars and this cost modeling analysis of current biologic drug costs, we see biosimilars having a slow, but incremental and increasing impact on overall biologic drug costs over the next five years. We expect that biosimilar drugs will not become prevalent in the market until sometime after 2016, trailing the biosimilar penetration curve in Europe by about six to nine years. Even with the recent FDA biosimilar approval pathway final guidance, more recently approved biologic drugs will have data exclusivity that extends well beyond 2016.

Since per capita specialty drug costs have exhibited such high trends, it may be difficult to notice the impact of biosimilars. By 2019, we expect the per capita spending on specialty drugs, including biologics, may be almost three times the level of 2013. Given that only one product has been approved to date in 2015 and has not yet been released, it still will take several years before there are enough products in the market to generate material savings. Even at peak availability, it may be difficult to gain acceptance from currently treated biologic patients who can afford the medications based on income level or due to ample insurance coverage.

The overall savings as a percentage of total healthcare costs resulting from biosimilars is likely to be small, given the relatively small frequency of members with high-cost conditions. At this level of savings potential, it is questionable that employers change benefit provisions to incent the use of biosimilars over biologics. The demand curve for healthcare services is flatter for patients with high-cost conditions because fewer services are discretionary. That said, with an increasing public focus on specialty drugs and their escalating costs, some employers are already working to better manage their specialty benefit, and thus may incorporate incentives to use biosimilars as one means of managing costs.

Based on the modeled scenarios using the assumptions outlined throughout this paper, we expect biosimilars to produce savings for employers of commercial active lives of 2.6% – 7.6% of total drug spend and 0.3% – 0.8% of total healthcare spend in 2019. Similarly, for employers covering retiree lives, we would expect savings ranging from 2.5% – 7.4% of total drug spend and 0.4% – 1.1% of total healthcare spend in 2019. While these estimates are based on many factors that are still unknown, such as biosimilar price and patient acceptance, it is unlikely that total savings out of all costs for healthcare will be great.

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Milliman is an independent firm of actuaries and healthcare consultants. The content of this study is based on Milliman proprietary data and healthcare consulting experience.

The assumptions in this paper are consistent with information that was available in the spring of 2015. Some of this information may change in the future or new information may become available, which could make the results in this study outdated.

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APPENDIX A

Biologic Drugs Represented in this Study

Appendix A
Milliman, Inc.
Assumed List of Biologic Drug Products

ACTEMRA
ACTHAR HP
ACTIMMUNE
ADAGEN
ADCETRIS
ADRIAMYCIN
ADVATE
ALFERON N
ALIMTA
ALKERAN
ALPHANATE/VON WILLEBRANDFACTOR COMPLEX/HUMAN
ALPHANINE SD
AMEVIVE
AMIFOSTINE
APOKYN
ARALAST NP
ARANESP ALBUMIN FREE
ARCALYST
AVASTIN
AVONEX
AVONEX PEN
BARACLUDE
BEBULIN
BEBULIN VH
BENEFIX
BENLYSTA
BERINERT
BETASERON
BICNU
BLEOMYCIN SULFATE
BOTOX
BRAVELLE
CARBOPLATIN
CARIMUNE NANOFILTERED
CAYSTON
CEREZYME
CERUBIDINE
CETROTIDE
CHORIONIC GONADOTROPIN
CIMZIA
CIMZIA STARTER KIT
CINRYZE
COMETRIQ
COPAXONE
CORIFACT
COSMEGEN
CREON
CYSTARAN
CYTARABINE
CYTOGAM
DACARBAZINE
DACOGEN
DACTINOMYCIN
DAUNORUBICIN HCL
DDAVP
DEFEROXAMINE MESYLATE
DESFERAL
DESMOPRESSIN ACETATE
DOCEFREZ
DOXIL
DOXORUBICIN HCL LIPOSOME
DYSPORT
EGRIFTA
ELAPRASE
ELELYSO
ELIGARD
ELITEK
ELLENCE
ELSPAR
EMTRIVA
ENBREL
ENBREL SURECLICK
EPIVIR
EPIVIR HBV
EPOGEN
ERBITUX
ERWINAZE
ETHYOL
ETOPOPHOS
EUFLEXXA
EXTAVIA
FABRAZYME
FASLODEX
FEIBA NF
FIRAZYR
FIRMAGON
FLOLAN
FLOXURIDINE
FLUDARABINE PHOSPHATE
FLUOROURACIL
FOLLISTIM AQ
FORTEO
FUDR
FUZEON
GABLOFEN
GAMASTAN S/D
GAMMAGARD LIQUID
GAMMAGARD S/D
GAMMAGARD S/D IGA LESS THAN 1MCG/ML
GAMMAKED
GAMUNEX-C
GANIRELIX ACETATE
GATTEX
GEMCITABINE HCL
GEMZAR
GENOTROPIN
GENOTROPIN MINIQUICK
GONAL-F
GONAL-F RFF
GONAL-F RFF PEN
GONAL-F RFF REDIJECT
HELIXATE FS
HEMOFIL M
HEPAGAM B
HERCEPTIN
HIZENTRA
HUMATE-P
HUMATROPE
HUMATROPE COMBO PACK
HUMIRA
HUMIRA PEN
HUMIRA PEN-CROHNS DISEASESTARTER
HUMIRA PEN-PSORIASIS STARTER
HYALGAN
HYCAMTIN
HYPERRHO S/D
IFEX
ILARIS
INCRELEX
INFERGEN
INTRON-A
INTRON-A W/DILUENT
ISTODAX
IXEMPRA KIT
KADCYLA
KALBITOR
KALETRA
KEPIVANCE
KINERET
KOATE-DVI
KOGENATE FS
KOGENATE FS BIO-SET
KYNAMRO
KYPROLIS
LAZANDA
LEUKINE
LEUPROLIDE ACETATE
LIORESAL INTRATHECAL
LIPODOX
LOVENOX
LUCENTIS
LUMIZYME
LUPRON DEPOT
LUPRON DEPOT-PED
MENOPUR
MICRHOGAM ULTRA-FILTEREDPLUS
MIRENA
MITOMYCIN
MONONINE
MOZOBIL
MUSTARGEN
MYLOTARG
MYOBLOC
MYOZYME
NABI-HB
NEULASTA
NEUMEGA
NEUPOGEN
NIPENT
NORDITROPIN FLEXPRO
NORDITROPIN NORDIFLEX PEN
NORVIR
NOVAREL
NOVOSEVEN
NOVOSEVEN RT
NPLATE
NULOJIX
NUTROPIN
NUTROPIN AQ
NUTROPIN AQ NUSPIN 10
NUTROPIN AQ NUSPIN 20
NUTROPIN AQ NUSPIN 5
NUTROPIN AQ PEN
OCTREOTIDE ACETATE
OMNITROPE
ONCASPAR
ORENCIA
ORTHOVISC
OVIDREL
OXALIPLATIN
PAMIDRONATE DISODIUM
PANCREAZE
PANCRELIPASE
PEGASYS
PEGASYS PROCLICK
PEG-INTRON
PEG-INTRON REDIPEN
PEG-INTRON REDIPEN PAK 4
PERTZYE
PHOTOFRIN
PREGNYL W/DILUENT BENZYLALCOHOL/I
PRIALT
PROCRIT
PROLASTIN-C
PROLEUKIN
PROLIA
PULMOZYME
QUTENZA
REBETOL
REBIF
REBIF REBIDOSE
REBIF REBIDOSE TITRATIONPACK
REBIF TITRATION PACK
RECLAST
RECOMBINATE
REMICADE
REMODULIN
REPRONEX
RHOGAM ULTRA-FILTERED PLU
RHOPHYLAC
RITUXAN
RIXUBIS
SAIZEN
SAIZEN CLICK.EASY
SANDOSTATIN
SANDOSTATIN LAR DEPOT
SEROSTIM
SIGNIFOR
SIMPONI
SKYLA
SOLIRIS
SOMATULINE DEPOT
SOMAVERT
STAVUDINE
STELARA
STIMATE
SUCRAID
SUPARTZ
SUPPRELIN LA
SYLATRON
SYNAGIS
SYNAREL
SYNVISC
SYNVISC ONE
TEMODAR
TEV-TROPIN
THERACYS
THIOTEPA
THROMBATE III W/10 ML STE
THYROGEN
TICE BCG
TOPOTECAN HCL
TREANDA
TRETINOIN
TYSABRI
TYVASO
TYVASO REFILL
TYVASO STARTER
ULTRESA
VALSTAR
VANTAS
VELCADE
VELETRI
VENTAVIS
VIDEX
VINBLASTINE SULFATE
VISUDYNE
VIVAGLOBIN
VPRIV
WILATE
WINRHO SDF
XEOMIN
XGEVA
XIAFLEX
XOLAIR
XYNTHA
XYNTHA SOLOFUSE
ZANOSAR
ZEMAIRA
ZENPEP
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APPENDIX B

Glossary of Terminology

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Average Wholesale Price (AWP): A benchmark drug price level commonly used in pharmacy benefit plans. Pharmacy acquisition cost is typically lower than AWP.

Biologic Drug: A drug that is grown using living organisms such as bio-engineered yeast, bacteria, or tissue.

Biosimilar Drug: A biologic drug that is intended to be a copy of an original biologic produced by a different manufacturer.

BPCIA: Biologics Price Competition and Innovation Act of 2009. Component of the Affordable Care Act which introduced an approval pathway for biosimilar biologic products.

Coverage Gap Discount Program: Program instituted under the Affordable Care Act in which pharmaceutical manufacturers provide a 50% discount on their brand products when filled in the coverage gap phase of the Medicare Part D benefit for non-low income members.

Data Exclusivity Date: Date at which a biologic drug loses exclusive status; earliest date at which a biosimilar competitor can enter the market. This is set at 12 years after market entry for most brand biologics, per BPCIA.

Generic Drug: A drug that has the same active ingredients, route of administration, strength and dosage form of a brand-name drug but is available at a lower cost. Generic drugs are available only after the patent protection on a brand-name drug expires.

Health Cost Guidelines: Milliman product that provides medical, dental, and prescription drug benchmarks of healthcare utilization, charge levels, and expected claims costs for both Commercial and Ages 65 and Over populations.

Level II HCPCS: Healthcare Common Procedure Coding System™ (HCPCS) Level II coding for prescription drugs that ordinarily cannot be self-administered, chemotherapy drugs, immunosuppressant drugs, inhalation solutions, and other miscellaneous drugs and solutions.

Medicare Part B: Portion of the standard Medicare benefit that covers many outpatient services, including prescription drugs administered at an outpatient setting.

NDC: National Drug Code used as a universal product identifier for all drugs.

Pharmacy Benefit Manager (PBM): A company specializing in the administration and management of prescription drug benefit plans.

Specialty Drug: Drugs placed on a specialty tier by a payer, typically because of high price or the need for special handling.