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Analysis of California Senate Bill 621 Biosimilar Drugs

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Abbreviated Analysis

California Senate Bill 621 Biosimilar Drugs

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SUMMARY

The California Senate Committee on Health requested that the California Health Benefits Review Program (CHBRP)¹ conduct an evidence-based assessment of California Senate Bill (SB) 621, Biosimilar Drugs. SB 621 would specify that a plan, insurer, or utilization review organization is not prohibited from requiring an enrollee to try a biosimilar before providing coverage for the reference biologic (i.e., step therapy).

SB 621 would not require a change in benefit coverage or a change in terms and conditions of covered medications.

Relevant Populations

If enacted, SB 621 would apply to the health insurance of approximately 14,025,000 enrollees (36% of all Californians).² This includes commercial and CalPERS enrollees and excludes Medi-Cal beneficiaries.

Context

Step therapy is “a type of protocol that specifies the sequence in which different prescription drugs for a given medical condition and medically appropriate for a particular patient are to be prescribed.”³

Biologics have significantly improved the management of high-burden diseases, such as autoimmune disorders, cancers, chronic renal failure, and diabetes. Many of these medications filled a gap in available treatments, providing improved outcomes over existing medications.

Biologics, or biological products, are preparations made from living organisms used to prevent, diagnose, treat, and cure a wide range of diseases and medical conditions. They are typically large, complex molecules and may be composed of biomolecules, including carbohydrates, proteins, and nucleic acids, or whole cells and tissues.

Biologics are regulated by the Food and Drug Administration (FDA). Unlike most small

molecule medications, which are chemically synthesized and therefore have well-defined structures that are easy to characterize, biologics have natural variations that make them difficult to characterize and lead to differences between manufactured lots.

A biosimilar, or follow-on biologic, is a biologic with a highly similar structure and function to a reference biologic that does not demonstrate clinically meaningful differences in purity, chemical identity, and bioactivity. While biosimilars are versions of brand-name products, they are not the same as generic medications because they are not exact replicas of the reference biologic.

As of 2023, there are six biologics that have biosimilars licensed by the FDA. However, not all licensed biosimilars are available in the United States.

Medical Effectiveness

CHBRP did not identify any studies that assessed the effect of step therapy requirements that require trying a biosimilar before receiving a reference biologic on utilization of these medications, health outcomes, utilization of other health care services, or timeliness of treatment. Because there was no literature that addressed any of the research questions, there is *insufficient evidence*⁴ that step therapy affects these outcomes.

¹ Refer to CHBRP’s full report for full citations and references.

² For this analysis, CHBRP has assumed that mandates that reference plans and policies that cover prescription drugs are relevant to pharmacy benefit coverage.

³ INS 10123.201

⁴ *Insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

Step Therapy Protocols in Health Insurance

CHBRP estimates approximately 40% of commercial and CalPERS enrollees are enrolled in a plan or policy with a step therapy protocol requirement for biologics for which there are biosimilars. This could require trying a biosimilar before receiving coverage for a reference biologic.

Utilization of Biologics and Biosimilars

For this analysis, CHBRP summarized utilization of biosimilar and biologic drugs typically covered under an outpatient pharmacy benefit using 2021 claims data. In 2021, there were six biologics that had licensed biosimilars. The reference biologics Humira and Enbrel had no biosimilars on the market in the United States in 2021 (thus no utilization) despite having FDA-licensed biosimilars, and were therefore excluded from the below estimates. There are several new biosimilars that have come to market since 2021, and utilization of biosimilars is likely to be notably higher now. With the arrival of more biosimilar products to market, health plans and policies have also begun to apply step therapy to require the use of a biosimilar before the reference biologic. Thus, while these data from 2021 are informative, CHBRP expects current utilization estimates of biosimilars are higher than what is presented here.

In 2021, about 0.15% of all commercial/CalPERS enrollees (21,000 enrollees) received a prescription for a reference **biologic** drug for which there was a biosimilar available. For these biologics, utilization was 9.71 prescriptions per 1,000 enrollees (prescriptions for a 30-day drug supply). The average cost per prescription for a 30-day supply was \$2,124. The cost per all enrollees per month for these biologics was about \$1.72.

In 2021, about 0.02% of all commercial/CalPERS enrollees (2,400 enrollees) received a prescription for a **biosimilar** product. For these biosimilars, utilization was 0.55 prescriptions per 1,000 enrollees (prescriptions for a 30-day drug supply). The average cost per prescription for a

30-day supply was \$1,582. The cost per all enrollees per month for these biologics was about \$0.07.

Impacts

CHBRP expects no coverage or utilization change due to the bill, thus no impacts are expected as a result of SB 621 in the short term.

In the long term, utilization of biosimilars will likely continue to grow considering their potential for cost savings when compared to reference biologic products. There have been some federal efforts to reduce barriers to entry for new biosimilars on the market, signaling a possible future increase in the entry of and subsequent utilization of these products (Dabrowska, 2019). With a greater number of biosimilars on the market, the costs of reference biologics and biosimilars are likely to decrease and stabilize over time (Mulcahy et al., 2022). Additionally, insurers may continue to adopt step therapy protocols that require use of biosimilars before the reference biologic.

BACKGROUND ON BIOLOGICS AND BIOSIMILARS

What Are Biologics and Biosimilars?

Biologics

Biologics have significantly improved the management of high-burden diseases, such as autoimmune disorders, cancers, chronic renal failure, and diabetes (Ingrasciotta et al., 2018; Janjigian et al., 2018). Many of these medications filled a gap in available treatments, providing improved outcomes over existing medications.

Biologics, or biological products, are preparations made from living organisms used to prevent, diagnose, treat, and cure a wide range of diseases and medical conditions. They are typically large, complex molecules (~50,000 kilodaltons⁵) and may be composed of biomolecules, including carbohydrates, proteins, and nucleic acids, or whole cells and tissues (Dabrowska, 2019). Common examples include Humira to treat rheumatoid arthritis, and Lantus, which is an insulin. Most biologics are administered through intravenous infusion or subcutaneous or intramuscular injection. Biologics that require intravenous infusion are administered by a health professional and may be covered under an enrollee's medical benefit. Subcutaneous biologic injections may be self-administered by the patient with approval from a clinician. Newer biologics are also self-administered through inhalers. Self-administered biologics are typically covered under the pharmacy benefit.

Biologics are regulated by the U.S. Food and Drug Administration (FDA). Most small molecule medications (<1,000 kilodaltons) are chemically synthesized and therefore have well-defined structures that are easy to characterize, which also lends themselves to the creation of a generic version.⁶ In contrast, biologics have natural variations that make them difficult to characterize and lead to differences between manufactured lots, meaning the characteristics of biologics only allow for biosimilars. During its review of a biologic, the FDA examines the manufacturer's protocols and strategies to minimize product variations to ensure the biologic demonstrates consistent clinical performance (FDA, 2020). Biologics that are licensed by the FDA for safety and effectiveness can become reference biologics, or comparisons, for biosimilars.

Biosimilars and Interchangeable Products

A biosimilar, or follow-on biologic, is a biologic with a highly similar structure and function to a reference biologic that does not demonstrate clinically meaningful differences in purity, chemical identity, and bioactivity. The FDA licensed the first biosimilar in March 2015. While biosimilars are versions of brand-name products, they are not the same as generic medications because they are not exact replicas of the reference biologic. FDA-licensed self-administered biosimilars and their associated reference biologics that may be covered under the pharmacy benefit are shown in Table 2. Reference biologics with biosimilars that are usually covered under the pharmacy benefit include Enbrel, Humira, Lantus, Neulasta, and Neupogen and their biosimilars.⁷ Other reference biologics with biosimilars, such as Avastin and Herceptin, are usually covered under the medical benefit because they are administered through an intravenous infusion.

Interchangeable products are biosimilars that meet additional requirements outlined in the federal Biologics Price Competition and Innovation Act (BPCIA). To be considered interchangeable, the BPCIA requires a biosimilar to produce the same clinical result as the reference biologic in any given patient. In

⁵ A kilodalton is a unit of molecular mass or molecular weight. One kilodalton is equal to one kilogram per mole.

⁶ Drug characterization is the determination of the chemical and physical properties of the product, including the molecule's size, shape, optimal conditions to maintain function, toxicity (Parr et al., 2016).

⁷ Some biologics or biosimilars may also be covered under the medical benefit, depending on how the medication is administered.

addition, the biosimilar must be able to be substituted for the reference biologic without the need for intervention by the provider who prescribed the reference product. The FDA approved the guidelines for biosimilar interchangeability in May 2019 (FDA, 2019). Interchangeable products have been licensed for Humira (Cyltezo) and Lantus (Rezvoglar and Semglee) (FDA, 2023).

Step Therapy

Step therapy or “fail-first” protocols may be applied to prescription medications by health plans and insurers to control costs, ensure medication compatibility, and manage safety. Step therapy protocols require an enrollee to try and fail on one or more medications prior to receiving coverage for the initially prescribed medication. These protocols usually recommend starting with a medication that is less expensive (e.g., generics) and/or has more “post-marketing safety experience” (PBMI, 2015). In addition, they sometimes require starting with a less potent medication or dosage, perhaps with fewer side effects, and graduating to more potent medications as necessary (e.g., from prescription Motrin to OxyContin to treat pain). Step therapy protocols are also used to apply clinical guidelines established by professional societies and other recognized organizations to treatment plans. Generally, more expensive or more potent medications are covered when the patient fails to respond to the step therapy–required medication (PBMI, 2018). Step therapy policies vary between plans and insurers.

In the case of biologics, a patient may be required to try a biosimilar medication prior to accessing coverage for an initially prescribed reference biologic medication. For example, a patient may be required to try Semglee before receiving coverage for the reference biologic Lantus. If coverage for the initially prescribed medication is declined under the step therapy protocol, the prescriber may either reissue the prescription for the step therapy–required medication or appeal the decision directly to the health plan or insurer (requesting approval for a step therapy override). A patient always has the option to purchase the initially prescribed medication by paying the full cost out of pocket. In the case of SB 621, plans and policies would be able to require use of a biosimilar before providing coverage for the reference biologic. Because biosimilars are highly similar to reference biologics in structure and function, most patients would be expected to respond in a similar manner to both medications.

Preferred and Nonpreferred Medications

Separate from step therapy, insurers may designate medications as “preferred” or “nonpreferred.” These medications are typically listed on different formulary tiers and cost sharing for the preferred medication is lower. However, if an enrollee chooses to obtain the nonpreferred medication, the insurer would grant coverage for the medication at the designated cost sharing.

Prevalence of Diseases Treated by Biologics and Biosimilars in California

Biologics and biosimilars treat a wide range of conditions. The prevalence of their use depends on the ailment that is being treated. Rheumatoid arthritis, Crohn’s disease, and numerous types of cancers are some of the more common conditions treated with biologics, as indicated in Table 1. Rheumatoid arthritis is an autoimmune and inflammatory disease that affects 1.3 million people nationally (CDPH, 2017). Crohn’s disease and ulcerative colitis are inflammatory bowel diseases that impact about 3 million people nationwide. In California, breast and colorectal cancers are the second and third leading causes of cancer death in women, occurring in 121.23 and 31.03 per 100,000 persons, respectively. Colorectal cancer is also the third leading cause of cancer death in men in California, with an incidence rate of 39.25 per 100,000 males (CCR, 2017). Non-Hodgkin lymphoma occurs in 21.4 per 100,000 persons in California (Movsisyan et al., 2019). About 12% of the adult population in California has been diagnosed with diabetes mellitus, although only a subset use insulin to help manage their diabetes (America’s Health Rankings, 2022; CHBRP. 2023).

Table 1. Self-Administered Reference Biologics and Biosimilars Available and Conditions for Which They Are Used

Reference Biologic Medication	Biosimilar(s)	Year Biosimilar Licensed	FDA-Approved Indications for all Reference Biologics and Biosimilars*	How Medication Is Administered	Biosimilar Market Availability in 2023
Enbrel (etanercept)	Eticovo (etanercept-ykro)	2019	Rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, chronic severe plaque psoriasis	Subcutaneous injection	Not available in U.S.
	Erelzi (etanercept-szsz)	2016			
Epogen (epoetin-alfa)	Retacrit (epoetin alfa-epbx)	2018	anemia	Subcutaneous injection or intravenously	Available
Humira (adalimumab)	Idacio (adalimumab-aacf)	2022	Rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, chronic severe plaque psoriasis, Crohn's disease, ulcerative colitis	Subcutaneous injection	Only Amjevita is available in the U.S.
	Yusimry (adalimumab-aqvh)	2021			
	Hulio (adalimumab-fkjp)	2020			
	Abrilada (adalimumab-afzb)	2019			
	Hadlima (adalimumab-bwwd)	2019			
	Hyrimoz (adalimumab-adaz)	2018			
	Cyltezo (adalimumab-adbm)	2017			
	Amjevita (adalimumab -atto)	2016			
	Lantus (insulin glargine)	Rezvoglar (insulin glargine-aglr)			
Semglee (insulin glargine-yfgn)		2021			

Reference Biologic Medication	Biosimilar(s)	Year Biosimilar Licensed	FDA-Approved Indications for all Reference Biologics and Biosimilars*	How Medication Is Administered	Biosimilar Market Availability in 2023
Neulasta (pegfilgrastim)	Fylnetra (pegfilgrastim-pbbk)	2022	Febrile neutropenia in patients with non-myeloid cancer	Subcutaneous injection or intravenously; administered by health professional or patient	All available in the U.S.
	Stimufend (pegfilgrastim-fpgk)	2022			
	Nyvepria (pegfilgrastim-apgf)	2020			
	Ziextenzo (pegfilgrastim-bmez)	2019			
	Fulphila (pegfilgrastim-jmdb)	2018			
	Udenyca (pegfilgrastim-cbqv)	2018			
Neupogen (filgrastim)	Releuko (filgrastim-ayow)	2022	Severe neutropenia in patients with congenital, cyclic, or idiopathic neutropenia; febrile neutropenia in patients with non-myeloid cancer; reduce time to neutrophil recovery for patients with acute myeloid leukemia receiving treatment	Subcutaneous injection or intravenously; administered by health professional or patient	All available in the U.S.
	Nivestym (filgrastim-aafi)	2018			
	Zarxio (filgrastim-sndz)	2015			

Source: California Health Benefits Review Program, 2023.

Note: *Unless otherwise indicated.

Key: FDA = U.S. Food and Drug Administration

Factors that Promote or Restrict Utilization of Biosimilars

There are a variety of factors that influence utilization of biosimilars, including placement on insurers' formularies, pricing, and financial incentives including rebates.

As of 2019, fewer than 2% of people in the United States used biologics, yet it was estimated these drugs account for around 40% of all pharmaceutical spending (Mulcahy et al., 2018; Zhai et al., 2019). From 2014 to 2018, spending on biologic drugs increased 50% to \$125 billion (Brill and Ippolito, 2019). Research suggests that the increase in spending is driven primarily by the increase in prices of these products, not simply due to increased utilization (Chen et al., 2018; Hernandez et al., 2020; Mulcahy et al., 2018; Nabhan et al., 2018). In 2021, three biologics listed in Table 1 were ranked in the number 1 (adalimumab), 6 (insulin glargine), and 9 (etanercept) spots among the top 25 drugs by expenditures (Tichy et al., 2022).

In 2021, the shift from reference biologics to biosimilars as the preferred medication on insurers' formularies was significant and rapid, largely due to new biosimilars being licensed and available in the United States (Tichy et al., 2022). Utilization of and expenditures for biologics and biosimilars continued to increase in 2021; and use of biosimilars is one of the main forces restraining drug expenditures in the United States. Additionally, market share of biosimilars continued to increase in 2022. As more biosimilars are licensed by the FDA, this market shift will likely continue to occur.

Biosimilars are often listed at a discounted price in comparison to reference biologics. Lower price biosimilars can decrease the cost of treating patients, and there is significant market pressure to reduce list prices for biosimilars (Falit et al., 2015; Rompas et al., 2015). Researchers have estimated the potential cost savings from biosimilars would be \$44.2 billion dollars between 2017 to 2026 (Mulcahy et al., 2018). However, in reality, substantial barriers have prevented widespread adoption of biosimilars (Chen et al., 2018; Crespi-Lofton and Skelton, 2017; Prasad et al., 2017; Zhai et al., 2019). These obstacles include gaps in acceptance and knowledge regarding biosimilars among patients and providers and potential financial incentives for the payer to cover reference biologics instead of biosimilars.

For example, research on the uptake of infliximab biosimilars (which are typically covered under the medical benefit) shows an example of the impact financial incentives have on biosimilar uptake. Research found that despite the availability of biosimilars for the reference biologic and the offering of these biosimilars at discounts of between 15% and 40% off the list price for the reference biologic, most major payers in the United States continue to name the reference biologic (infliximab) the preferred medication as of 2018 (Nabhan et al., 2018). In a published commentary by hospital system administrators regarding their experience with transitioning patients to a biosimilar (infliximab-dybb) for new infusions, they found the biggest obstacle to making the transition was third-party payer preference for the reference biologic over its biosimilar (Rossmann and Cross, 2020).

Manufacturers' rebates can play a significant role in controlling costs for health plans and insurers. However, there is debate about whether these rebates are limiting the uptake of biosimilars (Falit et al., 2015; Hakim and Ross, 2017). Some biosimilar manufacturers argue that the rebates and exclusive agreements are anticompetitive and prevent new biosimilars from being added to a health plan or insurer's list of covered drugs, even if the cost of the biosimilar is lower than the reference biologic. With rebates in place, the reference biologic may end up being cheaper than the biosimilar for the plan, thus there can be a financial benefit to having the biologic as the preferred drug (Kim et al., 2020; Yazdany, 2020; Yazdany et al., 2018). As previously mentioned, some biosimilar manufacturers have fought back legally by arguing that rebates and exclusive agreements are anticompetitive and prevent new biosimilars from being used.

For enrollees who have a coinsurance for medications covered under the pharmacy benefit, this means an enrollee could have higher cost sharing if they are being prescribed a reference biologic over a biosimilar.

POLICY CONTEXT

The California Senate Committee on Health has requested that the California Health Benefits Review Program (CHBRP)⁸ conduct an evidence-based assessment of the impacts of SB 621, Biosimilar Drugs. However, because SB 621 would not require a change in benefit coverage, CHBRP has provided background information on biologics and biosimilars, as well as information about step therapy policies and utilization of biologics and biosimilars.

Bill-Specific Analysis of SB 621, Biosimilar Drugs

Bill Language

SB 621 would specify that a plan, insurer, or utilization review organization is not prohibited from requiring an enrollee to try a biosimilar before providing coverage for the reference biologic (i.e., step therapy).

SB 621 would not require a change in benefit coverage or a change in terms and conditions of covered medications.

See Appendix A for the full text of SB 621.

Relevant Populations

If enacted, SB 621 would apply to the health insurance of approximately 14,025,000 enrollees (36% of all Californians). This represents 61% of the 22.8 million Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law, which includes health insurance regulated by the Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI). If enacted, the law would apply to the health insurance of enrollees in DMHC-regulated plans and/or CDI-regulated policies, exempting beneficiaries enrolled in DMHC-regulated Medi-Cal managed care plans.

Analytic Approach and Key Assumptions

CHBRP previously analyzed related bill language, AB 2144 Step Therapy and Prior Authorization in 2020 and SB 1452 Biological Products in 2020. Where applicable, this analysis builds off those previous analyses.

For this analysis, CHBRP has assumed that mandates that reference plans and policies that cover prescription drugs apply to pharmacy benefit coverage. Drugs that are clinician-ordered and administered under the supervision of a physician (generally in a hospital, a provider's office, infusion center, or similar medical facility) during a hospital stay or office visit are generally covered through a medical benefit. Pharmacy benefits cover prescriptions that are generally filled at a retail pharmacy, a mail-order pharmacy, or a specialty pharmacy. Some clinician-administered medications that would typically be covered under the medical benefit may be covered under the pharmacy benefit due a process called "white bagging," where a patient obtains a clinician-administered medication from a pharmacy and brings it with them to a clinician to administer. CHBRP has excluded claims for infusion-only medications from this analysis.

Should SB 621 be interpreted to apply to medications covered under the medical benefit as well, protections for plans and policies would be extended to additional medications. As mentioned previously, SB 621 does not result in changes in benefit coverage.

⁸ CHBRP's authorizing statute is available at www.chbrp.org/about_chbrp/faqs/index.php.

Interaction with Existing State and Federal Requirements

Health benefit mandates may interact and align with the following state and federal mandates or provisions.

California Policy Landscape

California law and regulations

Step therapy

Existing California law⁹ states that “if there is more than one drug that is clinically appropriate for the treatment of a medical condition, a [plan or policy] that provides coverage for prescription drugs may require step therapy.” Current law also outlines the requirements and process for exceptions to the step therapy requirement, and states that a plan, insurer, or utilization review organization is not prohibited from requiring an enrollee to try a generic or interchangeable biological product before providing coverage for the equivalent branded prescription. SB 621 adds to this statute that biosimilars can also be required before providing coverage for the branded prescription (i.e., reference biologic).

California has an existing law regarding biologics and substitution of biosimilars if they have been designated as “interchangeable.”¹⁰ If biosimilars have been designated as such, a pharmacist can substitute a biosimilar for a prescribed biologic as long as the patient’s cost sharing is the same or lower than it would be for the prescribed biologic and the prescribing provider has not indicated substitution is not allowed.

Similar requirements in other states

Several states have introduced or recently passed similar legislation.¹¹ Arkansas’s Governor signed legislation in February 2023 and Colorado passed legislation in 2022 almost identical to SB 621. Kentucky and Washington introduced similar legislation in 2023. Iowa introduced a bill in 2023 that states plans are not prevented from requiring step therapy for interchangeable biosimilars prior to providing coverage for the reference biologic.

Federal Policy Landscape

Advancing Education on Biosimilars Act of 2021¹²

Federal law requires the FDA to “advance education and awareness among health care providers about biological products as appropriate, including by developing or improving continuing education programs that address the prescribing of biological products and biosimilars.”

Affordable Care Act

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how SB 621 may interact with requirements of the ACA as presently

⁹ HSC 1367.206; INS 10123.201.

¹⁰ Business and Professions Code 4073.5.

¹¹ Search of other states’ legislation via Legiscan on March 15, 2023.

¹² S. 164 - 117th Congress (2021-2022).

exist in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).^{13,14}

The Biologics Price Competition and Innovation Act¹⁵

The Biologics Price Competition and Innovation Act (BPCIA) — a provision in the ACA signed into law in 2010 — amends Section 351 of the Public Health Service Act to include an abbreviated process for the FDA to approve biosimilars. Additionally, the BPCIA details the information required for a biological product to be deemed a biosimilar, introduces standards for determining interchangeability of a biosimilar and its reference product, establishes a 12-year period of exclusivity for the initial reference product (i.e., before any biosimilar may be licensed) as well as an exclusivity period for the first biosimilar determined to be interchangeable with a particular reference product.

Essential health benefits

In California, nongrandfathered¹⁶ individual and small-group health insurance is generally required to cover essential health benefits (EHBs).¹⁷ In 2024, approximately 12.1% of all Californians will be enrolled in a plan or policy that must cover EHBs.¹⁸ SB 621 would not require coverage for a new state benefit mandate and would not exceed the definition of EHBs in California.

MEDICAL EFFECTIVENESS

The medical effectiveness review summarizes findings from evidence on the impact of step therapy on utilization of reference biologics and biosimilars, health outcomes, utilization of other health care services, and timeliness of treatment. The medical effectiveness review does not address the safety or effectiveness of reference biologics because all have been licensed by the FDA, which examines the manufacturer's protocols and strategies to minimize product variations or ensure the biologic demonstrates consistent clinical performance. The FDA assesses the safety and effectiveness of biosimilars and determines which biosimilars are interchangeable products. Because all biologics and biosimilars discussed in this analysis are FDA licensed, CHBRP considers them to be safe and effective.

Research Approach and Methods

The search was limited to abstracts of studies published in English and from 2015 to present, as 2015 was the year that the first biosimilar was licensed by the FDA. A more thorough description of the

¹³ The ACA requires nongrandfathered small-group and individual market health insurance — including but not limited to qualified health plans sold in Covered California — to cover 10 specified categories of EHBs. Policy and issue briefs on EHBs and other ACA impacts are available on the CHBRP website:

www.chbrp.org/other_publications/index.php.

¹⁴ Although many provisions of the ACA have been codified in California law, the ACA was established by the federal government, and therefore, CHBRP generally discusses the ACA as a federal law.

¹⁵ ACA Section 7001-7003.

¹⁶ A grandfathered health plan is “a group health plan that was created – or an individual health insurance policy that was purchased – on or before March 23, 2010. Plans or policies may lose their ‘grandfathered’ status if they make certain significant changes that reduce benefits or increase costs to consumers.” Available at: www.healthcare.gov/glossary/grandfathered-health-plan.

¹⁷ For more detail, see CHBRP's issue brief *California State Benefit Mandates and the Affordable Care Act's Essential Health Benefits*, available at https://chbrp.org/other_publications/index.php.

¹⁸ See CHBRP's resource *Sources of Health Insurance in California for 2024* and CHBRP's issue brief *California State Benefit Mandates and the Affordable Care Act's Essential Health Benefits*, both available at https://chbrp.org/other_publications/index.php.

methods used to conduct the medical effectiveness review and the process used to grade the evidence is presented in Appendix B.

Key Questions

1. Compared to people whose coverage is not subject to a step therapy protocol, for people who require the use of self-administered biological products or biosimilars, does a step therapy protocol that requires an enrollee to try a biosimilar before receiving coverage for its reference biologic affect:
 - a. Health outcomes?
 - b. Utilization of either biologics or biosimilars?
 - c. Utilization of other health care services (e.g., ED visits)?
 - d. The timeliness of treatment?

Findings Regarding Impact of Step Therapy

CHBRP did not identify any studies that assessed the effect of step therapy requirements on utilization of reference biologics and biosimilars, health outcomes, utilization of other health care services, or timeliness of treatment. Because there was no literature that addressed any of the research questions, there is *insufficient evidence* that step therapy affects utilization of reference biologics and their biosimilar, the health outcomes of people who use biologics/biosimilars, the use of other health care services, or timeliness of treatment.

Figure 1. Effect of Step Therapy on Utilization of Biologics/Biosimilars, Health Outcomes, Utilization of Other Services, or Time to Treatment

NOT EFFECTIVE		INSUFFICIENT EVIDENCE				EFFECTIVE	
Clear and Convincing	Preponderance	Limited	Inconclusive	Limited	Preponderance	Clear and Convincing	

BENEFIT COVERAGE AND UTILIZATION

If enacted, SB 621 would apply to the health insurance of approximately 14,025,000 million enrollees (36% of all Californians). This represents about 61% of the 22.8 million Californians who have health insurance regulated by the state that may be subject to any state health benefit mandate law, which includes health insurance regulated by DMHC or CDI. If enacted, the law would apply to the health insurance of enrollees in DMHC- regulated plans and CDI-regulated policies.

Analytic Approach and Key Assumptions

- SB 621 does not prohibit health plans, insurers, and utilization review organizations from requiring an enrollee to try a biosimilar before providing coverage for the reference biologic (i.e., step therapy). **As it is a not a mandate, CHBRP estimates no fiscal impact due to the enactment of this bill.**
- Below, CHBRP presents discussion of the share of enrollees with health insurance that includes step-therapy protocols for biosimilars or biologics and a qualitative discussion of utilization of biosimilars and biologics based on 2021 claims data.

- CHBRP makes no estimates or assumptions regarding change in utilization in the first year post-enactment because CHBRP expects no coverage or utilization change due to the bill (thus, no fiscal impact).

For further details on the underlying data sources and methods used in this analysis, please see Appendix C.

Enrollees in Plans or Policies with Step Therapy Protocols of Biosimilars and Biologics

CHBRP estimates approximately 40% of commercial and CalPERS enrollees are enrolled in a plan or policy with a formal step therapy requirement for biologics for which there are biosimilars.

Baseline Utilization and Cost of Biologics and Biosimilars

Using Milliman's 2021 Consolidated Health Care Guidelines Sources Database (CHSD), CHBRP summarized utilization of biosimilar and biologic drugs typically covered under an outpatient pharmacy benefit (Table 2). This analysis excludes biologic drugs for which there was no biosimilar alternative in 2021. The reference biologics Humira and Enbrel had no biosimilars on the market in the United States in 2021 (thus no utilization) despite having FDA-licensed biosimilars. Overall, there are several new biosimilars that have come to market since 2021, and utilization of biosimilars is likely to be notably higher now. With the arrival of more biosimilar products to market, health plans and policies have also begun to apply step therapy to require the use of a biosimilar before the reference biologic. Thus, while these data from 2021 are informative, CHBRP expects current utilization estimates of biosimilars are higher than what is presented here.

Biologics

In 2021, about 0.15% of all commercial/CalPERS enrollees (21,000 enrollees) received a prescription for a reference biologic drug for which there was a biosimilar available. For these biologics, utilization was 9.71 prescriptions per 1,000 enrollees (prescriptions for a 30-day drug supply). The average cost per prescription for a 30-day supply was \$2,124. The cost per all enrollees per month for these biologics was about \$1.72.

Biosimilars

In 2021, about 0.02% of all commercial/CalPERS enrollees (2,400 enrollees) received a prescription for a biosimilar product. For these biosimilars, utilization was 0.55 prescriptions per 1,000 enrollees (prescriptions for a 30-day drug supply). The average cost per prescription for a 30-day supply was \$1,582. The cost per all enrollees per month for these biologics was about \$0.07.

Table 2. Utilization and Cost of Biologics and Biosimilars in 2021 Among Commercial and CalPERS Enrollees

	Biologic (b)	Biosimilar (c)
Enrollees		
Total estimated commercial enrollees (a)	14,025,000	14,025,000
Proportion of enrollees taking a biologic or biosimilar	0.15%	0.02%
Estimated # enrollees taking a biologic or biosimilar	21,000	2,400
Utilization and cost		
Utilization of biologic or biosimilar drug per 1,000 enrollees (# of prescriptions with a 30-day supply)	9.71	0.55
Average cost per prescription for 30-day supply (d)	\$2,124	\$1,582
Cost per all enrollees per month (d)	\$1.72	\$0.07

Source: California Health Benefits Review Program, 2023.

Note: (a) Enrollees in plans and policies regulated by DMHC or CDI. Includes those associated with Covered California and CalPERS, but excludes members enrolled in Medi-Cal.

(b) Includes only reference biologics for biosimilars covered under the pharmacy benefit. Includes the biologic drugs: Epogen, Lantus, Neulasta, and Neupogen. The average cost and per enrollee per month cost in this column is mix-adjusted using current biosimilar utilization.

(c) Includes the biosimilar drugs covered under the pharmacy benefit: Fulphila, Nivestym, Retacrit, Semglee, Udenyca, Zarxio, and Ziextenzo.

(d) The listed costs do not include rebate payments received from pharmaceutical manufacturers, and therefore, may not reflect the true cost of the medication.

SHORT- AND LONG-TERM IMPACTS

CHBRP expects no coverage or utilization change due to the bill, thus no impacts on cost or utilization are expected due to this bill in the short term.

In the long term, CHBRP expects utilization of biosimilars may likely continue to grow considering their potential for cost savings when compared to reference biologic products. There have been some federal efforts to reduce barriers to entry for new biosimilars on the market, signaling a possible future increase in the entry of and subsequent utilization of these products (Dabrowska, 2019). With a greater number of biosimilars on the market, the costs of reference biologics and biosimilars are likely to decrease and stabilize over time (Mulcahy et al., 2022). Additionally, insurers may continue to adopt step therapy protocols that require use of biosimilars before the reference biologic.

APPENDIX A TEXT OF BILL ANALYZED

On February 16, 2023, the California Senate Committee on Health requested that CHBRP analyze SB 621, as introduced on February 15, 2023.

SENATE BILL

NO. 621

Introduced by Senator Caballero

February 15, 2023

An act to amend Section 1367.206 of the Health and Safety Code, and to amend Section 10123.201 of the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

SB 621, as introduced, Caballero. Health care coverage: biosimilar drugs.

Existing law, the Knox-Keene Health Care Service Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care. Existing law provides for the regulation of health insurers by the Department of Insurance. Existing law authorizes a health care service plan or health insurer that provides coverage for prescription drugs to require step therapy if there is more than one drug that is clinically appropriate for the treatment of a medical condition. Existing law does not prohibit a plan, insurer, or utilization review organization from requiring an enrollee or insured to try an AB-rated generic equivalent or interchangeable biological product before providing coverage for the equivalent branded prescription drug.

This bill would specify that a plan, insurer, or utilization review organization is also not prohibited from requiring an enrollee or insured to try a biosimilar before providing coverage for the equivalent branded prescription drug.

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: no

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. Section 1367.206 of the Health and Safety Code is amended to read:

1367.206. (a) If there is more than one drug that is clinically appropriate for the treatment of a medical condition, a health care service plan that provides coverage for prescription drugs may require step therapy.

(b) A health care service plan shall expeditiously grant a request for a step therapy exception within the applicable time limit required by Section 1367.241 if a prescribing provider submits necessary justification and supporting clinical documentation supporting the provider's determination that the required prescription drug is inconsistent with good professional practice for provision of medically necessary covered services to the enrollee, taking into consideration the enrollee's needs and medical history, along with the professional judgment of the enrollee's provider. The basis of the provider's determination may include, but is not limited to, any of the following criteria:

(1) The required prescription drug is contraindicated or is likely, or expected, to cause an adverse reaction or physical or mental harm to the enrollee in comparison to the requested prescription drug, based on the known clinical characteristics of the enrollee and the known characteristics and history of the enrollee's prescription drug regimen.

(2) The required prescription drug is expected to be ineffective based on the known clinical characteristics of the enrollee and the known characteristics and history of the enrollee's prescription drug regimen.

(3) The enrollee has tried the required prescription drug while covered by their current or previous health coverage or Medicaid, and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse reaction. The health care service plan may require the submission of documentation demonstrating that the enrollee tried the required prescription drug before it was discontinued.

(4) The required prescription drug is not clinically appropriate for the enrollee because the required drug is expected to do any of the following, as determined by the enrollee's prescribing provider:

(A) Worsen a comorbid condition.

(B) Decrease the capacity to maintain a reasonable functional ability in performing daily activities.

(C) Pose a significant barrier to adherence to, or compliance with, the enrollee's drug regimen or plan of care.

(5) The enrollee is stable on a prescription drug selected by the enrollee's prescribing provider for the medical condition under consideration while covered by their current or previous health coverage or Medicaid.

(c) A health care provider or prescribing provider may appeal a denial of an exception request for coverage of a nonformulary drug, prior authorization request, or step therapy exception request consistent with the health care service plan's current utilization management processes.

(d) An enrollee or the enrollee's designee or guardian may appeal a denial of an exception request for coverage of a nonformulary drug, prior authorization request, or step therapy exception request by filing a grievance under Section 1368.

(e) This section does not prohibit either of the following:

(1) A health care service plan or utilization review organization from requiring an enrollee to try an AB-rated generic ~~equivalent~~ *equivalent, biosimilar, as defined in Section 262(i)(2) of Title 42*

of the United States Code, or interchangeable biological product product, as defined in Section 262(i)(3) of Title 42 of the United States Code, before providing coverage for the equivalent branded prescription drug.

(2) A health care provider from prescribing a prescription drug that is clinically appropriate.

(f) This section does not require or authorize a health care service plan that contracts with the State Department of Health Care Services to provide services to Medi-Cal beneficiaries to provide coverage for prescription drugs that are not required pursuant to those programs or contracts, or to limit or exclude any prescription drugs that are required by those programs or contracts.

(g) For purposes of this section, “step therapy exception” means a decision to override a generally applicable step therapy protocol in favor of coverage of the prescription drug prescribed by a health care provider for an individual enrollee.

(h) Commencing January 1, 2022, a health care service plan contract with a utilization review organization, medical group, or other contracted entity that performs utilization review or utilization management functions on a health care service plan’s behalf shall include terms that require the contracted entity to comply with this section and Section 1367.241.

SEC. 2. Section 10123.201 of the Insurance Code is amended to read:

10123.201. (a) A policy of health insurance that covers outpatient prescription drugs shall cover medically necessary drugs. The policy may provide for step therapy and prior authorization consistent with Section 1342.7 of the Health and Safety Code and any regulations adopted pursuant to that section.

(b) (1) Commencing January 1, 2017, an insurer shall maintain a pharmacy and therapeutics committee that shall be responsible for developing, maintaining, and overseeing any drug formulary list. If the insurer delegates responsibility for the formulary to any entity, the obligation of the insurer to comply with this part shall not be waived.

(2) The pharmacy and therapeutics committee board membership shall conform with both of the following:

(A) Represent a sufficient number of clinical specialties to adequately meet the needs of insureds.

(B) Consist of a majority of individuals who are practicing physicians, practicing pharmacists, and other practicing health professionals who are licensed to prescribe drugs.

(3) Members of the board shall abstain from voting on any issue in which the member has a conflict of interest with respect to the issuer or a pharmaceutical manufacturer.

(4) At least 20 percent of the board membership shall not have a conflict of interest with respect to the issuer or any pharmaceutical manufacturer.

(5) The pharmacy and therapeutics committee shall meet at least quarterly and shall maintain written documentation of the rationale for its decisions regarding the development of, or revisions to, the formulary drug list.

(6) The pharmacy and therapeutics committee shall do all of the following:

(A) Develop and document procedures to ensure appropriate drug review and inclusion.

(B) Base clinical decisions on the strength of the scientific evidence and standards of practice, including assessing peer-reviewed medical literature, pharmacoeconomic studies, outcomes research data, and other related information.

(C) Consider the therapeutic advantages of drugs in terms of safety and efficacy when selecting formulary drugs.

(D) Review policies that guide exceptions and other utilization management processes, including drug utilization review, quantity limits, and therapeutic interchange.

(E) Evaluate and analyze treatment protocols and procedures related to the insurer's formulary at least annually.

(F) Review and approve all clinical prior authorization criteria, step therapy protocols, and quantity limit restrictions applied to each covered drug.

(G) Review new United States Food and Drug Administration-approved drugs and new uses for existing drugs.

(H) Ensure the insurer's formulary drug list or lists cover a range of drugs across a broad distribution of therapeutic categories and classes and recommended drug treatment regimens that treat all disease states and does not discourage enrollment by any group of insureds.

(I) Ensure the insurer's formulary drug list or lists provide appropriate access to drugs that are included in broadly accepted treatment guidelines and that are indicative of general best practices at the time.

(7) This subdivision shall be interpreted consistent with federal guidance issued under paragraph (3) of subdivision (a) of Section 156.122 of Title 45 of the Code of Federal Regulations. This subdivision shall apply to the individual, small group, and large group markets.

(c) (1) A health insurer may impose prior authorization requirements on prescription drug benefits, consistent with the requirements of this part.

(2) (A) If there is more than one drug that is clinically appropriate for the treatment of a medical condition, a health insurer may require step therapy.

(B) A health insurer shall expeditiously grant a request for a step therapy exception within the applicable time limit required by Section 10123.191 if a prescribing provider submits necessary justification and supporting clinical documentation supporting the provider's determination that the required prescription drug is inconsistent with good professional practice for provision of medically necessary covered services to the insured, taking into consideration the insured's needs and medical history, along with the professional judgment of the insured's provider. The basis of the provider's determination may include, but is not limited to, any of the following criteria:

(i) The required prescription drug is contraindicated or is likely, or expected, to cause an adverse reaction or physical or mental harm to the insured in comparison to the requested prescription drug, based on the known clinical characteristics of the insured and the known characteristics and history of the insured's prescription drug regimen.

(ii) The required prescription drug is expected to be ineffective based on the known clinical characteristics of the insured and the known characteristics and history of the insured's prescription drug regimen.

(iii) The insured has tried the required prescription drug while covered by their current or previous health coverage or Medicaid, and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse reaction. The health insurer may require the submission of documentation demonstrating that the insured tried the required prescription drug before it was discontinued.

(iv) The required prescription drug is not clinically appropriate for the insured because the required drug is expected to do any of the following, as determined by the insured's prescribing provider:

(I) Worsen a comorbid condition.

(II) Decrease the capacity to maintain a reasonable functional ability in performing daily activities.

(III) Pose a significant barrier to adherence to, or compliance with, the insured's drug regimen or plan of care.

(v) The insured is stable on a prescription drug selected by the insured's prescribing provider for the medical condition under consideration while covered by their current or previous health coverage or Medicaid.

(C) This section does not prohibit either of the following:

(i) An insurer or utilization review organization from requiring an insured to try an AB-rated generic ~~equivalent~~ *equivalent, biosimilar, as defined in Section 262(i)(2) of Title 42 of the United States Code*, or interchangeable biological ~~product~~ *product, as defined in Section 262(i)(3) of Title 42 of the United States Code*, before providing coverage for the equivalent branded prescription drug.

(ii) A health care provider from prescribing a prescription drug that is clinically appropriate.

(3) An insurer shall provide coverage for the medically necessary dosage and quantity of the drug prescribed for the treatment of a medical condition consistent with professionally recognized standards of practice.

(4) For plan years commencing on or after January 1, 2017, an insurer that provides essential health benefits shall allow an insured to access prescription drug benefits at an in-network retail pharmacy unless the prescription drug is subject to restricted distribution by the United States Food and Drug Administration or requires special handling, provider coordination, or patient education that cannot be provided by a retail pharmacy. A nongrandfathered individual or small

group health insurer may charge an insured a different cost sharing for obtaining a covered drug at a retail pharmacy, but all cost sharing shall count toward the policy's annual limitation on cost sharing consistent with Section 10112.28.

(d) A health care provider or prescribing provider may file an internal appeal of a denial of an exception request for coverage of a nonformulary drug, prior authorization request, or step therapy exception request consistent with the health insurer's current utilization management processes.

(e) An insured or the insured's designee or guardian may appeal a denial of an exception request for coverage of a nonformulary drug, prior authorization request, or step therapy exception request by filing an internal appeal with the health insurer pursuant to Section 2719 of the federal Public Health Service Act (42 U.S.C. Sec. 300gg-19) and any subsequent rules or regulations issued thereunder.

(f) Every health insurer that provides prescription drug benefits shall maintain all of the following information, which shall be made available to the commissioner upon request:

(1) The complete drug formulary or formularies of the insurer, if the insurer maintains a formulary, including a list of the prescription drugs on the formulary of the insurer by major therapeutic category with an indication of whether any drugs are preferred over other drugs.

(2) Records developed by the pharmacy and therapeutics committee of the insurer, or by others responsible for developing, modifying, and overseeing formularies, including medical groups, individual practice associations, and contracting pharmaceutical benefit management companies, used to guide the drugs prescribed for the insureds of the insurer, that fully describe the reasoning behind formulary decisions.

(3) Any insurer arrangements with prescribing providers, medical groups, individual practice associations, pharmacists, contracting pharmaceutical benefit management companies, or other entities that are associated with activities of the insurer to encourage formulary compliance or otherwise manage prescription drug benefits.

(g) If an insurer provides prescription drug benefits, the commissioner shall, as part of its market conduct examination, review the performance of the insurer in providing those benefits, including, but not limited to, a review of the procedures and information maintained pursuant to this section, and describe the performance of the insurer as part of its report issued as part of its market conduct examination.

(h) The commissioner shall not publicly disclose any information reviewed pursuant to this section that is determined by the commissioner to be confidential pursuant to state law.

(i) For purposes of this section, the following definitions shall apply:

(1) "Authorization" means approval by the health insurer to provide payment for the prescription drug.

(2) "Step therapy" means a type of protocol that specifies the sequence in which different prescription drugs for a given medical condition and medically appropriate for a particular patient are to be prescribed.

(3) "Step therapy exception" means a decision to override a generally applicable step therapy protocol in favor of coverage of the prescription drug prescribed by a health care provider for an individual insured.

(4) “Utilization review organization” means an entity that conducts utilization review, other than a health insurer performing its own utilization review.

(j) Nonformulary prescription drugs shall include any drug for which an insured’s copayment or out-of-pocket costs are different than the copayment for a formulary prescription drug, except as otherwise provided by law or regulation.

(k) This section does not affect an insured’s or policyholder’s eligibility to submit a complaint to the department for review or to apply to the department for an independent medical review under Article 3.5 (commencing with Section 10169).

(l) This section does not restrict or impair the application of any other provision of this part.

(m) This section and Section 10123.191 apply to both the health insurer and a utilization review organization that performs utilization review or utilization management functions on the insurer’s behalf. Commencing January 1, 2022, a contract between a health insurer and a utilization review organization that performs utilization review or utilization management functions on the insurer’s behalf shall include terms that require the utilization review organization to comply with this section and Section 10123.191.

APPENDIX B LITERATURE REVIEW SPECIFICATIONS

This appendix describes methods used in the literature review conducted for this report. A discussion of CHBRP's system for medical effectiveness grading evidence.

Studies assessing the impact of step therapy requirements on utilization of self-administered biologics/biosimilars, health outcomes, utilization of other health care services, and timeliness of treatment were identified through searches of PubMed, the Cochrane Library, Web of Science, Embase, and Scopus. Websites maintained by the following organizations were also searched: PubMed Health, the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), PubMed Health, the World Health Organization (WHO), and the Scottish Intercollegiate Guideline Network (SIGN). The search was limited to abstracts of studies published in English and from 2015 to present, as 2015 was the year that the first biosimilar was licensed by the FDA.

CHBRP excluded studies of biologics or biosimilars that health plans and policies typically cover under the medical benefit because SB 621 only applies to reference biologics and biosimilars covered under the pharmacy benefit. Refer to Table 2 for included biologics/biosimilars.

Reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria.

Medical Effectiveness Review

The literature review returned abstracts for 262 articles, of which 17 were reviewed for inclusion in this report and 0 were included in this report. Most articles were eliminated because they did not focus on reference biologics and their biosimilars covered under the pharmacy benefit; study the safety, effectiveness, and/or efficacy of particular reference biologics or biosimilars; or study the cost-effectiveness of reference biologics or biosimilars. Two studies (Boytssov et al., 2020; Kozma et al., 2015), also identified during CHBRP's analysis of SB 1452 in 2020, assessed the impact of step therapy requirements on biologic utilization and treatment effectiveness among multiple reference biologics, but did not compare differences in utilization or health outcomes between reference biologics and their biosimilars. Because these studies did not directly address the research questions, they were excluded. CHBRP also identified some studies where health centers or insurers instituted a mandatory switch from a biologic to a biosimilar (Bhat et al., 2020; Fisher et al., 2022; Glintborg et al., 2019) and one study that discussed non-medical switching in the United States generally (Dolinar et al., 2019). However, these articles were also excluded because step therapy was not directly addressed.

Medical Effectiveness Evidence Grading System

In making a "call" for each outcome measure, the medical effectiveness lead and the content expert consider the number of studies as well the strength of the evidence. Further information about the criteria CHBRP uses to evaluate evidence of medical effectiveness can be found in CHBRP's *Medical Effectiveness Analysis Research Approach*.¹⁹ To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design;
- Statistical significance;
- Direction of effect;

¹⁹ Available at: <https://www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis>.

- Size of effect; and
- Generalizability of findings.

The grading system also contains an overall conclusion that encompasses findings in these five domains. The conclusion is a statement that captures the strength and consistency of the evidence of an intervention's effect on an outcome. The following terms are used to characterize the body of evidence regarding an outcome:

- *Clear and convincing evidence*;
- *Preponderance of evidence*;
- *Limited evidence*;
- *Inconclusive evidence*; and
- *Insufficient evidence*.

A grade of *clear and convincing evidence* indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

A grade of *preponderance of evidence* indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

A grade of *limited evidence* indicates that the studies had limited generalizability to the population of interest and/or the studies had a fatal flaw in research design or implementation.

A grade of *inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

A grade of *insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

APPENDIX C COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

With the assistance of CHBRP's contracted actuarial firm, Milliman, Inc, the cost analysis presented in this report was prepared by the faculty and researchers connected to CHBRP's Task Force with expertise in health economics.²⁰

Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.²¹

This appendix describes analysis-specific data sources, estimation methods, caveats, and assumptions used in preparing this cost impact analysis.

Analysis-Specific Caveats and Assumptions

This subsection discusses the caveats and assumptions relevant specifically to the abbreviated analysis of SB 621.

- National Drug Codes (NDCs) for biosimilar drugs and biologic drugs for which there are biosimilars were identified using the MediSpan® Master Drug Data Base v2.5.
- Once identified, these NDCs were used to extract cost and utilization data from Milliman's 2021 Consolidated Health Cost Guidelines Sources Database (CHSD). CHBRP limited its data pull to California only. These data were used to develop prevalence, utilization, and baseline allowed cost. Notably, CHBRP made the following adjustments to the data:
 - CHBRP adjusted the average cost for biologic drugs with a biosimilar counterpart to reflect the same utilization mix as biosimilar drugs in 2021.
 - CHBRP's estimates of allowed cost represent the costs paid to pharmacies but do not reflect rebate payments that pharmaceutical manufacturers may pay to health plans. Member cost sharing is typically assessed on the allowed costs paid to pharmacy before rebates.
 - As mentioned elsewhere in this report, CHBRP does not expect that SB 621 would require a change in benefit coverage or a change in terms and conditions of covered medications. Therefore, CHBRP did not apply utilization or trend to the data and instead presents them as descriptive statistics for 2021.

While the utilization and cost estimates from 2021 are informative, CHBRP expects that future utilization and cost of biosimilar and biologic drugs may change from what is presented in this report with the introduction of new biosimilars to the market.

²⁰ CHBRP's authorizing statute, available at https://chbrp.org/about_chbrp/index.php, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.

²¹ See method documents posted at http://chbrp.com/analysis_methodology/cost_impact_analysis.php; in particular, see 2023 Cost Analyses: Data Sources, Caveats, and Assumptions.

REFERENCES

- America's Health Rankings. Annual Report, Diabetes, California, United States. 2022 edition. Available at <https://www.americashealthrankings.org/explore/annual/measure/Diabetes/state/CA>. Accessed on February 20, 2022.
- Bhat S, Altajar S, Shankar D, et al. Process and clinical outcomes of a biosimilar adoption program with infliximad-dyyb. *Journal of Managed Care & Specialty Pharmacy*. 2020;26(4):410-416.
- Boytsov N, Zhang X, Evans KA, Johnson BH. Impact of Plan-Level Access Restrictions on Effectiveness of Biologics Among Patients with Rheumatoid or Psoriatic Arthritis. *PharmacoEconomics-Open*. 2020;4(1):105-117.
- Brill A, Ippolito B. The Economics Of Biologic Drugs: A Further Response To Bach et al. *Health Affairs Blog*. 2019; August 8.
- California Cancer Registry (CCR). 2017. Available at: <https://www.cancer-rates.info/ca/>. Accessed April 25, 2020.
- California Department of Public Health (CDPH). Arthritis-Related Conditions. 2017. Available at: <https://www.cdph.ca.gov/Programs/CCDCDPH/DCDIC/CDCB/Pages/ArthritisRelatedConditions.aspx#>. Accessed on April 25, 2020.
- California Health Benefits Review Program (CHBRP). *Analysis of California Senate Bill 90 Health Care Coverage: Insulin Affordability*. Berkeley, CA; 2023.
- Chen BK, Yang YT, Bennett CL. Why Biologics and Biosimilars Remain So Expensive: Despite Two Wins for Biosimilars, the Supreme Court's Recent Rulings do not Solve Fundamental Barriers to Competition. *Drugs*. 2018;78(17):1777-1781.
- Crespi-Lofton J, Skelton JB. The growing role of biologics and biosimilars in the United States: Perspectives from the APhA Biologics and Biosimilars Stakeholder Conference. *Journal of the American Pharmacists Association*. 2017;57(5):e15-e27.
- Dabrowska A. *Biologics and Biosimilars: Background and Key Issues*. Congressional Research Service; 2019.
- Dolinar R, et al. The non-medical switching of prescription medications. *Postgraduate Medical Journal*. 2019;131(5):335-341.
- Falit BP, Singh SC, Brennan TA. Biosimilar competition in the United States: statutory incentives, payers, and pharmacy benefit managers. *Health Affairs (Millwood)*. 2015;34(2):294-301.
- Fisher A, Kim J, Dormuth CR. Mandatory nonmedical switching from originator to biosimilar infliximad in patients with inflammatory arthritis and psoriasis in British Columbia: a cohort study. *CMAJ Open*. 2022;10(1):E109-E118.
- Glintborg B, Ibsen R, Bilbo REQ, Lund Hetland M, Kjellberg J. Does a mandatory non-medical switch from originator to biosimilar etanercept lead to increase in healthcare use and costs? A Danish register-based study of patients with inflammatory arthritis. *RMD Open*. 2019;5(2):e001016.
- Hakim A, Ross JS. Obstacles to the Adoption of Biosimilars for Chronic Diseases. *Jama*. 2017;317(21):2163-2164.

- Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US, 2007-2018. *Jama*. 2020;323(9):854-862.
- Ingrasciotta Y, Cutroneo PM, Marcianò I, Giezen T, Atzeni F, Trifirò G. Safety of Biologics, Including Biosimilars: Perspectives on Current Status and Future Direction. *Drug Safety*. 2018;41:1013-1022.
- Janjigian YY et al. Talking to patients about biosimilars. *Future Oncology*. 2018;14(23):2403-2414.
- Kim H, Alten R, Avedano L, et al. The Future of Biosimilars: Maximizing Benefits Across Immune-Mediated Inflammatory Diseases. *Drugs*. 2020;80(2):99-113.
- Kozma CM, Ingham M, Paris A, Ellis L. Effectiveness of step therapy policies for specialty pharmaceuticals in immune disorders. *Journal of Medical Economics*. 2015;18(8):646-653.
- Mulcahy A, Buttorff C, Finegold K, El-Kilani Z, Oliver JF, Murphy S, Jessup A. Projected US savings from biosimilars, 2021-2025. *American Journal of Managed Care*. 2022;28(7):329-335. doi: 10.37765/ajmc.2022.88809. PMID: 35852882.
- Mulcahy AW, Hlavka JP, Case SR. Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. *Rand Health Q*. 2018;7(4):3.
- Nabhan C, Parsad S, Mato AR, Feinberg BA. Biosimilars in Oncology in the United States: A Review. *JAMA Oncology*. 2018;4(2):241-247.
- Parr MK, Montacir O, Montacir H. Physicochemical characterization of biopharmaceuticals. *Journal of Pharmaceutical and Biomedical Analysis*. 2016;130:366-389.
- Pharmacy Benefits Management Institute (PBMI). *2014-2015 Prescription Drug Benefit Cost and Plan Design Report*. Plano, TX: PBMI; 2015.
- Pharmacy Benefits Management Institute (PBMI). *2018 Trends in Specialty Drug Benefits Report*. Plano, TX: PBMI; 2018.
- Prasad V, De Jesús K, Mailankody S. The high price of anticancer drugs: Origins, implications, barriers, solutions. *Nature Reviews. Clinical Oncology*. 2017;14(6):381-390.
- Rompas S, Goss T, Amanuel S, et al. Demonstrating Value for Biosimilars: A Conceptual Framework. *Am Health Drug Benefits*. 2015;8(3):129-139.
- Rossmann L, Cross RK. Just Say No...to the Nocebo Effect. *Inflammatory Bowel Diseases*. 2020;26(5):669.
- Tichy EM et al. National trends in prescription drug expenditures and projections for 2022. *American Journal of Health Systems Pharmacists*. 2022;79(14):1158-1172.
- U.S. Food and Drug Administration (FDA). *Biological Product Definitions Factsheet*. Washington, DC: FDA. Available at <https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf>. Accessed April 15, 2020.
- U.S. Food and Drug Administration (FDA). *Considerations in Demonstrating Interchangeability With a Reference Product Guidance for Industry*. 2019. Available at <https://www.fda.gov/media/124907/download>. Accessed on April 25, 2020.

U.S. Food and Drug Administration (FDA). *Purple book database of licensed biological products*. 2023. Available at: <https://purplebooksearch.fda.gov/>. Accessed on April 3, 2023.

Yazdany J, Dudley RA, Lin GA, Chen R, Tseng CW. Out-of-Pocket Costs for Infliximab and Its Biosimilar for Rheumatoid Arthritis Under Medicare Part D. *Jama*. 2018;320(9):931-933.

Yazdany J. Failure to Launch: Biosimilar Sales Continue to Fall Flat in the United States. *Arthritis & Rheumatology*. 2020; Jan 10 [Epub ahead of print].

Zhai MZ, Sarpatwari A, Kesselheim AS. Why Are Biosimilars Not Living up to Their Promise in the US? *AMA Journal of Ethics*. 2019;21(8):E668-678.

ABOUT CHBRP

The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP **Faculty Task Force** comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct much of the analysis. The **CHBRP staff** works with Task Force members in preparing parts of the analysis, and manages external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **Milliman**, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit. The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. Information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.

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CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

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Please direct any questions concerning this document to: California Health Benefits Review Program; MC 3116; Berkeley, CA 94720-3116, info@chbrp.org, or www.chbrp.org