CalRx Status Update: Initial Progress Under the California Affordable Drug Manufacturing Act

(Senate Bill 852, Pan, Chapter 207, Statutes of 2020)

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Executive Summary

Far too many Californians feel the pain of skyrocketing drug prices while drug companies and other supply chain actors post record profits. Even those with health insurance struggle to afford their lifesaving medications while seeing their health insurance premiums increase year over year. For these reasons, Governor Newsom's first executive order (Executive Order N-01-19) focused on prescription drug prices. One follow-up from this executive order was a proposal announced by the Governor in the 2020 Budget to establish a state-led generic drug label, "CalRx," which called for increased manufacturing of generic drugs in highly concentrated, low competition drug markets. Later codified into law as the California Affordable Drug Manufacturing Act of 2020 (SB 852 (Pan), Chapter 207, Statutes of 2020), CalRx empowers the State of California to develop, produce, and distribute generic drugs and sell them at low cost.

Because of the market failure in access to a low-cost insulin, CalRx's first drug project will focus on supporting the development of a generic version or "biosimilar" insulin. Referred to as the CalRx Biosimilar Insulin Initiative, this project will lay the groundwork for future drug projects addressing pain point medications that have become a financial burden for Californians. To implement the CalRx Biosimilar Insulin Initiative, the Department of Health Care Access and Information (HCAI) secured in the 2022 Budget Act a one-time appropriation of $100 million General Fund. Of these funds, $50 million will be used to work with a partner to develop and bring to market interchangeable biosimilar insulin products in both vial and pen form at a fraction of existing cash prices for insulin and $50 million towards the standing up of a California-based manufacturing facility.

HCAI has selected the nonprofit generic drug company, Civica Rx, as the partner, and the State's investment will enable Civica Rx to bring to market the three most popular insulin products (glargine, aspart, and lispro) under a CalRx branded label within the next 2-3 years. CalRx insulin prices are estimated to be about 90% lower than existing branded products and save patients using insulin between $2,000 and $4,000 annually. This will provide much needed financial relief for persons living with diabetes, especially those who are uninsured or underinsured and need insulin to maintain their health and quality of life.

Introduction

Millions of Americans have difficulty paying for their prescription drugs. When markets work well, generic drugs offer a cost-savings relief and can drive down prices to a fraction of the branded drug's price. According to the FDA, approved generic medications now account for 90 percent of the prescriptions dispensed in the U.S. and can cost, on average, 80 to 85 percent less than the brand-name equivalents.[1] However, not all generic drug markets experience price reductions.[2] Pharmaceutical markets are susceptible to market failures, pricing fixing and other problems. In recent years, over 20% of the generic drugs sold in the U.S. market experienced price increases of 100% or more. High generic drug prices compromise patient affordability – both in cost sharing and when increased payer costs are passed on to patients.

In response to certain drugs being increasingly unaffordable, Governor Gavin Newsom announced in the 2020 Budget the intent to create a state-led generic drug label. The program, called the CalRx Initiative (CalRx), empowers the State to become a backstop for markets that fail to deliver affordable medications for Californians by promoting increased generic manufacturing to address such market failures as low competition, drug shortages, and fragile supply chains. CalRx was codified into state law via the California Affordable Drug Manufacturing Act (Senate Bill 852, Pan, Chapter 207, Statutes of 2020), officially becoming part of California's policy strategy to address the high cost of prescription drugs.

[1] Janet Woodcock, MD. *Safety, Efficacy, and Quality Remain Top Priorities as We Continue Our Work to Expand Access to Cost-Saving Generic Drugs for the American Public*, US Food and Drug Administration, May 13, 2019.
[2] Tessema FA, Kesselheim AS, Sinha MS. *Generic but Expensive: Why Prices Can Remain High for Off-Patent Drugs*. Hastings Law Journal. 2019;71:1019

SB 852 sets guidelines for how the California Health and Human Services Agency (CHHSA) should choose which drugs to prioritize and sets up timelines for reporting progress in forming partnerships with manufacturers to produce or distribute generic prescription drugs and at least one form of insulin, provided that a viable pathway for manufacturing a more affordable form of insulin exists at a price that results in savings.

This legislative report meets SB 852's requirements to provide:

> (1) A description of the status of all drugs targeted under this chapter.
>
> (2) An analysis of how the activities of CalHHS may impact competition, access to targeted drugs, the costs of those drugs, and the costs of generic prescription drugs to public and private purchasers.

Diabetes in California

The estimated prevalence of prediabetes and diabetes among California adults has significantly increased since 2013, with higher rates among communities of color and older adults.[3] In 2019, nearly 3.2 million (10.5%) of California adults reported having diabetes, and an additional 884,000 people in California have diabetes but do not know it yet. Every year an estimated 272,800 people in California are newly diagnosed with diabetes.[4] It is estimated that roughly 31% of diabetics use insulin.[5]

Approximately 95,500 uninsured Californians are diagnosed as diabetic and use insulin.[6] It is also estimated that 14% of diabetics who use insulin spend at least 40% of their income, after paying for food and housing, on insulin.[7]

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[3] Taylor CW, Downie C, Mercado V. (2019). *Burden of Diabetes in California*. California Department of Public Health. Sacramento, California, June 2019

[4] American Diabetes Association, *The Burden of Diabetes in California Fact Sheet*, January 2022

[5] Centers for Disease Control and Prevention *Age-adjusted percentage of adults with diabetes using diabetes medication, by type of medication*, U.S., 1997–2011. May 5, 2015.

[6] This figure was estimated by HCAI using data from the American Diabetes Association and the Kaiser Family Foundation, Statistica Research Department, *Health Insurance Status of the Population of California 2021*, November 7, 2022

[7] Mallory Locklear, *Insulin is an Extreme Financial Burden for Over 14% of Americans who Use It*, July 5, 2022

Serious complications from untreated diabetes include heart disease, stroke, limb amputation, end-stage kidney disease, blindness, and death. Diabetes was the nation's eighth leading cause of death in 2020.

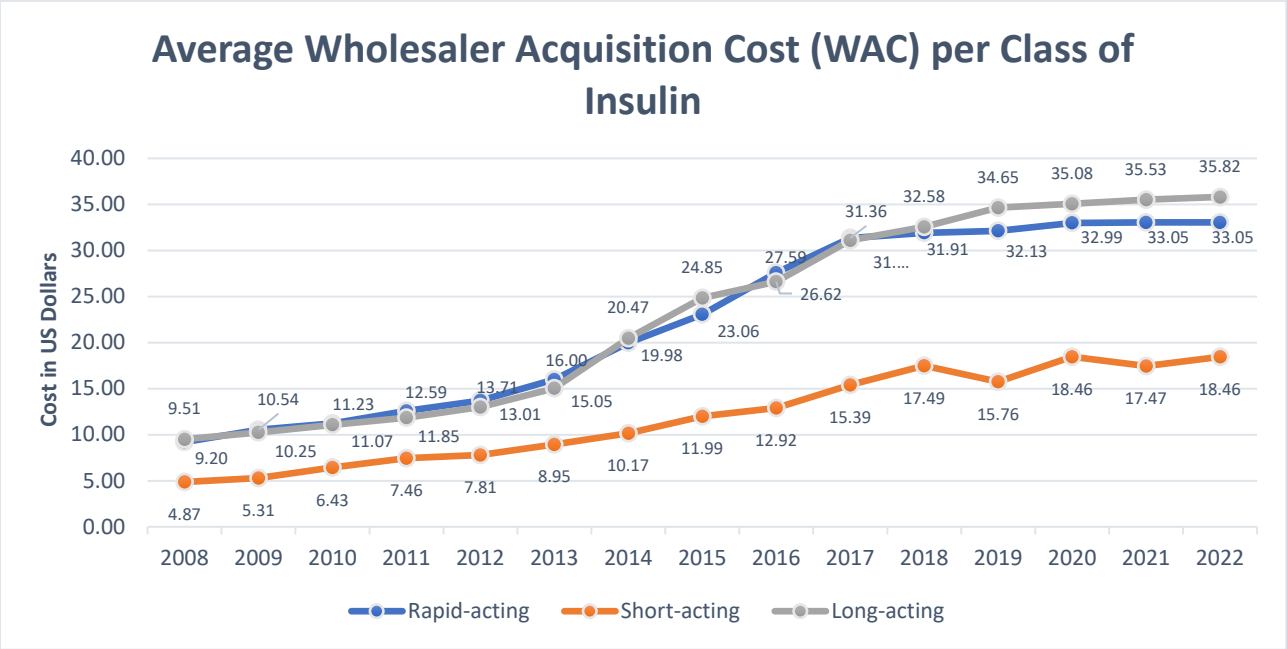
The Insulin Market

Despite insulin being first introduced over 100 years ago, insulin prices have not followed the traditional trend of lowered prices once generic and biosimilar insulins are introduced into the market. Currently in the U.S., three main companies have dominated the insulin market for several years: Eli Lilly, Sanofi, and Novo Nordisk. These companies, commonly known as the "Big Three," control over 90 percent of the global insulin market today for four types of insulin products – rapid-acting, short acting, intermediate acting, and long-acting insulins.[8]

Insulin prices in the U.S. are, on average, five to ten times higher than in other industrialized countries.[9] Since 2008, growth in insulin prices has been accelerating, with a reprieve only in recent years. The list price of insulin per milliliter (mL) in the U.S. increased, on average, 10.5 percent annually from 2008-2012, 17.6 percent annually from 2013-2017, 4.3 percent annually between 2018-2020, and 0.4 percent annually from 2021-2022.[10]

[8] Judith A. Johnson, *Insulin Products and the Cost of Diabetes Treatment,* Congressional Research Service, November 19, 2018
[9] *Cost of Insulin by Country 2023*, World Population Review, January 2023
[10] SSR Health US Prescription Brand Pricing Data Tool. *https://www.ssrhealth.com/*

Figure 1 - Average Wholesaler Acquisition Cost per Class of Insulin 2008 – 2022



Newer versions of insulin retail for between $90 and $300 per 10 mL vial.[11] Most patients with diabetes need two to three vials per month, and some patients require more. Current prices are especially challenging for uninsured patients and patients with high deductible plans, who often pay cash for their insulin.

While patients with more generous health coverage may pay very little for their insulin due to their relatively low out-of-pocket cost sharing responsibilities, many diabetics do not fall into this category or are at risk of paying high out-of-pocket costs during coverage disruptions, such as unemployment or aging out of dependent coverage.

[11] Benita Lee, Diane Li, *How Much Does Insulin Cost? Here's How 28 Brands and Generics Compare*, GoodRx Health, January 2022

Uninsured and underinsured[12] diabetics typically must pay the list price for their insulin, spending thousands of dollars per year to afford their lifesaving medications. Even diabetics with moderate deductible plans still spend substantial sums for their insulin. Based on national data, as many as 1 in 4 diabetics cannot afford their insulin, and thus ration or have ceased taking insulin altogether.[13] Those not adhering to insulin therapy have worse diabetes control and are at higher risk for diabetes exacerbations, long-term complications, and death.

Therefore, CalRx prioritized targeting insulin as its first drug given the longstanding and significant market failures that prevent consumers from access to affordable insulin.

Prior Efforts to Reform the Insulin Market

Prior efforts to reform insulin pricing have been limited in their effectiveness in addressing structural issues in the market for insulins. For example, In March 2010, Congress passed the Biologics Price Competition and Innovation Act of 2009 (BPCIA). This law established a statutory pathway for approval of "biosimilars", follow-on versions of innovative biological products. However, under the framework, biosimilar insulins are treated like branded products, which has resulted in manufacturers engaging in the same tactics of charging high list prices and participation in high rebates to lock-in market share.

[12] According to the *Commonwealth Foundation*, underinsured means persons who reported high yearly out-of-pocket costs or deductibles (not including premiums) relative to their income, as follows:

- Out-of-pocket costs, excluding premiums, over the prior 12 months are equal to 10 percent or more of household income; or
- Out-of-pocket costs, excluding premiums, are equal to 5 percent or more of household income if income is under 200 percent of the federal poverty level ($22,980 for an individual and $47,100 for a family of four); or
- Deductible is 5 percent or more of household income.

[13] Darby Herkert, Pavithra Vijayakumar, Jing Luo, MD., *Cost-Related Insulin Underuse Among Patients with Diabetes*, JAMA Intern Med. 2019;179(1):112-114. doi:10.1001/jamainternmed.2018.5008

Most recently, on August 16, 2022, President Biden signed into law the Inflation Reduction Act, giving the Medicare program the power to negotiate the prices of qualifying prescription drugs, including small molecular drugs and biologics, and to implement the negotiated prices starting in 2026:

Year	Drugs Selected	Spending Reference Period
2026	10 Part D (retail prescription) drugs with the highest Medicare spending exceeding $200 million/year	Jun 1, 2022 – May 31, 2023
2027	15 additional Part D drugs	Nov. 1, 2023 – Oct. 31, 2024
2028	15 additional Part B (drugs administered by physicians) or Part D drugs	Nov. 1, 2024 – Oct. 31, 2025
2029	20 additional Part B or Part D drugs	Nov. 1, 2025 – Oct. 31, 2026
2030	20 additional Part B or Part D drugs	Nov. 1, 2026 – Oct. 31, 2027

Also starting in 2023, the Inflation Reduction Act will impose a $35 monthly cap on out-of-pocket costs for insulin for Medicare beneficiaries. The $35 monthly cap was originally drafted to apply to the entire private insurance market but was removed due to the Senate parliamentarian ruling that it would violate budget reconciliation rules. It is important to note that while the $35 monthly cap for insulin will help Medicare beneficiaries by limiting what they pay for cost-sharing, it does not address the underlying price of insulin. Thus, insulin affordability remains a challenge for millions of uninsured and underinsured Americans who typically pay the full retail price (or cash price) for their insulin.

A bipartisan U.S. Senate Finance Committee investigation into insulin pricing found that insulin manufacturers and pharmacy benefits managers (PBMs) work in tandem and respond to incentives to keep insulin prices high and rising.

The Committee's report described the dynamic between the two industries as follows:

> "Higher list price increases the dollar value of rebates, discounts, and other fees that a manufacturer can offer to a PBM and health plans, which are based on a percentage of the list price… PBMs have an incentive for manufacturers to keep list prices high, since the rebates, discounts, and fees PBMs negotiate are based on a percentage of a drug's list price—and PBMs retain at least a portion of what they negotiate… [T]he investigation found instances in which insulin manufacturers were dissuaded from setting lower list prices for their products, which would have likely lowered out-of-pocket costs for patients, due to concerns that PBMs and health plans would react negatively." [14]

As the U.S. Senate Finance Committee's report found, hyper-consolidation along the insulin supply chain and dysfunctional incentive structures have constrained true competition within the insulin market. As a result, both list (also known as wholesale acquisition cost or WAC) and net prices for insulin have risen dramatically over the last decade.[15]

To remedy the crisis of insulin affordability, CalRx's first priority – the CalRx Biosimilar Insulin Initiative – intends to work with a partner to develop, manufacture, and distribute low-cost biosimilar insulins.

Investments in the 2022 Budget Act

The 2022 Budget Act included a one-time appropriation of $100 million General Fund for the Department of Health Care Access and Information (HCAI) to implement the CalRx Biosimilar Insulin Act.

[14] Charles E. Grassley, Ron Wyden, *Insulin: Examining the Factors Driving the Rising Cost of a Century Old Drug*, Staff Report to the United States Senate Finance Committee, January 19, 2021
[15] Ibid. Grassley-Wyden Insulin Report

This budget appropriation includes $50 million to work with a partner to develop and bring to market interchangeable biosimilar insulin products in both vial and pen form at a fraction of existing cash prices for insulin.

The remaining $50 million is for the construction of an insulin manufacturing facility based in California to strengthen the supply chain for insulin and have the added benefit of economic development through job creation in the state.

Many Californians, especially the uninsured and underinsured, are exposed to high list prices, and would benefit enormously from broadly available low-cost insulin. In the long run, all consumers would benefit if the branded insulin manufacturers lowered their prices in response to the entry of a low-cost option.

The experience and lessons learned from the CalRx Biosimilar Insulin Initiative will also inform future drug projects.

Selected Partner

A key goal of the CalRx Biosimilar Insulin Initiative, and a requirement of SB 852, is to focus on low-cost, transparent pricing without the use of coupons, discount programs or rebates (except where federally mandated). With that in mind, HCAI issued a Request for Information (RFI CBII-001) in August 2022 to seek information about approaches for drug development and the capabilities of potential partners to support the development of the three biosimilar insulin products. The State evaluated respondents based on the following criteria:

1. Ability to meet legislative requirements including:
    a. California-branded insulin products are brought to market to demonstrate the State's commitment to lowering the cost of insulin prices;
    b. Insulin products are available at transparent prices without the use of coupons or rebates, except where federally mandated;
    c. Payments are based on defined milestones;
    d. The State has representation and involvement with the governance of the contracted entity;

2. The respondent's ability to obtain an FDA approved Biologics License Application (BLA) and manufacture the insulin products;

3. The respondent's willingness to take responsibility for the distribution and commercialization of the CalRx-branded insulin;

4. The respondent contributing their own funds to add to the State's investment to develop, manufacture, and distribute the three biosimilar insulin products; and

5. The respondent demonstrating proven expertise to bring drugs to market.

The nonprofit generic drug company, Civica Rx (Civica), was ultimately selected to partner with the State for drug development due to their close alignment with the State's goals under SB 852.

Prior to the launch of HCAI's RFI, on March 3, 2022, Civica announced their plans to manufacture and distribute insulins that, once approved by the FDA, will be available at a significantly lower price than insulins currently on the market:

> "Civica will produce three insulins – glargine, lispro and aspart (biologics corresponding to, and interchangeable with, Lantus, Humalog and Novolog respectively) – each of which will be available both in vials and prefilled pens. Civica will co-develop and manufacture the drug product, complete the clinical trials, and file the necessary applications for FDA approval. Civica plans to set a recommended price to the consumer of no more than $30 per vial and no more than $55 for a box of five pen cartridges, a significant discount to prices charged to uninsured individuals today."[16]

[16] Civica to Manufacture and Distribute Affordable Insulin. Civica Rx, March 3, 2022

Civica's strategy aligns with the State's goals. In their RFI response, Civica noted the price will be based on the cost of development, production, and distribution, so diabetic patients can purchase their life saving insulin as close as possible to the cost of production:

> "Civica's mission is to provide a reliable supply of essential medications on a cost-plus basis. The Civica Foundation facilitates philanthropic contributions from leaders who are passionate about improving and saving the lives of millions and are committed to building pathways to reliable drug access and affordability. Civica's guiding principle is to "do what is the best interest of patients". To date, Civica has supplied more than 91 million vials of 67 different drugs to its member hospitals, which account for more than one-third of licensed beds in the United States."

Civica also noted the same low-cost insulin would be available for all Californians and nationwide through multiple channels including brick and mortar pharmacies and major online pharmacies. The State's investment in Civica will enable them to bring the three most popular insulin products – glargine, aspart, and lispro – to the market under the CalRx brand in both vial and prefilled pens sooner than their current funding allows. Civica's target prices of $30 per vial and $55 per 5-pack of pens are as close as possible to the cost of production, and with their nonprofit mission, they are committed to further lowering their prices if unit costs could be reduced.

The availability of a low-cost biosimilar insulin would provide much needed relief to patients living with diabetes who need insulin to maintain their health and quality of life. A transparent pricing structure will help send a signal to the market that insulin can be sold at prices that are not distorted by high list prices and high rebates.

Additionally, Civica was the only company that responded to HCAI's RFI that is seeking approval on the fast-acting insulin, lispro, which would allow patients to not have to change their current prescription to the other fast-acting insulin, aspart.

This would allow patients to move to the CalRx product more seamlessly without having to request a new prescription, as well as avoid potential side effects such as altered blood sugar control, which can sometimes be experienced when switching insulin products.

Estimated Savings to Patients

The California Health and Human Services Agency engaged the Drug Access and Affordability Initiative at Johns Hopkins University (JHU) to provide research and data analysis in support of the CalRx Initiative, including the savings associated with the addition of state-led low-cost biosimilar insulins to the market. These estimated savings were published in a commentary in the Annals of Internal Medicine by Dr. Mariana Socal, Vishaal Pegany, and Secretary of Health and Human Services, Dr. Mark Ghaly. The study found that CalRx insulin prices are estimated to be about 90% lower than existing reference products.[17] This will provide much needed financial relief for persons living with diabetes, especially those who are uninsured or underinsured. Uninsured patients do not have a third party negotiating on their behalf. Therefore, typically, uninsured patients are charged the full list price for their insulin.

[17] Mariana P. Socal MD, Vishaal Pegany, Mark Ghaly MD. *When States Step Up: California and the Case for State-Led Insulin Manufacturing*. Ann Intern Med. [Epub 15 November 2022]. doi:10.7326/M22-2339

As shown in Table 1 below, uninsured patients with Type 1 diabetes who currently pay cash prices for one of the reference products could save $2,000 to $4,000 per year if they switched to a CalRx biosimilar insulin product.

Table 1: Savings Estimates for California Patients and Payors Under Projected CalRx Biosimilar Insulin Prices

Payor and Product	Estimated Average Annual Spending on Reference Product, per Person	Estimated Average Annual Spending Under CalRx Prices, per Person	Estimated Average Annual Savings per Person (Percentage of Spending Represented by the Savings)
Patient out-of-pocket costs and potential savings (average per person, per year)			
Uninsured paying cash price			
Insulin lispro	$4,764	$374	$4,391 (92%)
Insulin aspart	$5,216	$374	$4,842 (93%)
Insulin glargine	$2,267	$214	$2,054 (91%)
Uninsured paying GoodRx discounted price			
Insulin lispro	$2,568	$374	$2,194 (85%)
Insulin aspart	$5,145	$374	$4,771 (93%)
Insulin glargine	$1,820	$214	$1,606 (88%)
High-deductible health plan enrollee			
Insulin lispro	$4,602	$374	$4,228 (92%)
Insulin aspart	$4,109	$374	$3,735 (91%)
Insulin glargine	$2,406	$214	$2,192 (91%)
Plan costs and potential savings (average per person, per year)			
Private health insurance plans (prices before rebates)			
Insulin lispro	$1,402	$138	$1,264 (90%)
Insulin aspart	$2,930	$244	$2,686 (92%)
Insulin glargine	$1,974	$194	$1,780 (90%)
Private health insurance plans (net prices after rebates)			
Insulin lispro	$407	$138	$269 (66%)
Insulin aspart	$542	$244	$298 (55%)
Insulin glargine	$341	$194	$147 (43%)

Uninsured patients paying discounted prices, through manufacturer-provided patient assistance programs, would also have saved between 85% and 93% of their out-of-pocket costs if they were to use CalRx products instead, representing savings of up to $4,771 per year.

Patients enrolled in a high-deductible health plan would have saved between 91% and 92% of their out-of-pocket costs if they were to use CalRx products instead, representing savings up to $4,228 per year.

This likely reflects the upper bound of savings, as patients may benefit from discount cards or patient assistance programs that help lower out-of-pocket costs. Savings to fully insured patients will depend on the cost-sharing requirements of their health plan. However, CalRx prices could allow health plans to offer insulins free of cost to beneficiaries and still spend significantly less than they currently do. Although the estimated prices do not account for fees and markups that may be added by supply chain participants, the transparent prices will allow plans and patients to identify such additions and direct their purchasing to outlets selling the product at the publicized price.

Distribution Strategies

Offering a low-cost insulin in the market does not automatically ensure it will be widely available to all Californians due to the current incentive structures in the pharmaceutical supply chain. These incentives continue to play out even with the July 2021 approval by the FDA of the first interchangeable, biosimilar insulin, Semglee, manufactured by Viatris and Biocon Biologics.

When Semglee first launched, it had a list price or wholesale acquisition cost (WAC) price of $99 a vial, which was less expensive than the reference brand product, Lantus, at $284 per vial.[18] However, Semglee experienced challenges in being selected by PBMs and placed on health plan formularies. Industry commentators have noted this is likely because PBMs can increase profits by charging higher fees based on a percentage of the higher list prices of brand name drugs. Due to low take-up by PBMs, Viatris relaunched Semglee with a 300% price increase, from $99 a vial to $279, and was successful in enlisting the PBM Express Scripts to cover the high price, high rebate version.[19]

[18] Bob Herman, *The new generic insulin isn't as cheap as you thought*, Axios, November 21, 2021
[19] Fraiser Kansteiner, *Viatris launched 2 versions of its interchangeable insulin biosimilar. Why?*, Fierce Pharma, November 16, 2021

Many payers also prefer high list price, high-rebate versions of drugs due to plans receiving rebates offered by the manufacturers. Employers then use the rebates to offset non-drug healthcare costs.[20]

The success of CalRx depends on how many beneficiaries learn of and accept the new products. If all CalRx insulins have an interchangeable status, this will allow pharmacies to substitute an approved biosimilar insulin product without requesting approval from the provider. According to an infographic published by the FDA, biosimilars have no clinically meaningful differences from their reference products in terms of safety, purity, and potency.[21] A strong communication strategy engaging patients, providers, health plans, and pharmacists on the high quality of biosimilar insulins will be critical for uptake.

To the extent that existing supply chain actors do not cover CalRx insulin, California may need to consider alternative distribution methods. These may include independent pharmacies, direct-to-consumer (DTC) channels such as online mail order pharmacies, local grocery stores, and community-based clinics that serve patients without fixed addresses. California should also pursue partnerships with health plans in state administered coverage programs, such as California Public Employees' Retirement System (CalPERS) and Covered California, to ensure those members have access to CalRx-branded insulin products.

While the market take-up of CalRx insulin is unknown, it will first and foremost address a significant market failure by ensuring uninsured and underinsured patients have access to insulin at a low, transparent price.

[20] Adam J. Fein, Ph.D. *Why PBMs and Payers are Embracing Insulin Biosimilars with Higher Prices*, Drug Channels Institute. November 9, 2021
[21] U.S. Food & Drug Administration, *Infographic – Biosimilars: Are they the same quality?*, September 16, 2022

Potential Future Drugs to Target

The success of the CalRx Biosimilar Insulin Initiative will lay the groundwork for future drug targets. CalRx will identify drugs that present high costs for California consumers and payers despite having generic versions available on the market, or where generics should exist but do not. Potential candidate drugs under CalRx may include the following:

1. Drugs that are widely used and impact a large population;
2. Drugs that represent a high portion of total spending for health care payers and/or patients;
3. Drugs that treat serious life-threatening diseases or chronic conditions, such as asthma, cancer, multiple sclerosis, hepatitis B, epilepsy, and tuberculosis;
4. Drugs that treat or address the effects of substance use disorders; and
5. Drugs that have a feasible commercial, market, or regulatory pathway for offering a more affordable version.

Conclusion

CalRx's first project will address the affordability crisis for insulin by providing a low-cost, biosimilar insulin to all Californians who need it. The entry of CalRx products into the drug market will likely increase price competition and help shift the industry from obscure, rebate-based pricing towards more transparent, low pricing. Nonetheless, it will be critical for the selected partner, Civica, to distribute CalRx insulin through both the existing supply chain as well as alternative distribution methods, such as sales channels that reach consumers more directly.