



# STRATEGIES TO ADVANCE INSULIN AFFORDABILITY IN THE UNITED STATES

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September 2020

## Preface

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This study was funded by the National Institute for Health Care Reform.

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## Summary and Recommendations

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US insulin prices are the highest in the world and have increased multifold in recent decades. A vial of insulin that sold for less than \$30 twenty years ago retails for more than \$300 dollars today. In addition to insulin, patients spend as much or more each year on related supplies such as syringes, pens, and glucose monitors.<sup>1</sup> Combined with high deductibles and lack of universal health care coverage, the cost of insulin therapy has made control of diabetes unaffordable for millions of Americans. One in four diabetic patients reports using less insulin than prescribed due to cost, and such rationing has led to preventable complications and even death.<sup>2</sup>

Rising prices and higher prevalence of diabetes have also made insulin a growing component of spending for public and private payers. Plans are reporting that insulin in its various forms has become one of the highest drug spending categories.<sup>3</sup> Payer costs, of course, are ultimately a societal cost reflected in premiums and in the burden of health care spending on employers, states, and the federal government.

The issue of insulin affordability is emblematic of broader drug pricing and affordability issues in the US and our complex and fragmented systems of health care financing and payment. While there is no single solution or policy lever to solve these issues, we examined multiple strategies for achieving the following three objectives:

1. Make insulin affordable to patients, so they can maintain access to treatment, prevent adverse health outcomes, and avoid financial insecurity;
2. Reduce prices of the current generation of insulins through increased market competition; and
3. Maintain affordability and address systemic issues through more direct action to constrain US drug prices and price increases.

For each of these objectives, we assessed a range of policies for their likely impact and feasibility. Clearly, our three objectives overlap – reducing prices would make insulin more affordable to patients and would lower the price tag for covering insulin costs – and all can be pursued simultaneously. However, recognizing that patients' lives and financial stability are at stake today, especially amid the health and economic consequences of a global pandemic, we urge that action be taken immediately to address patient affordability through provisions strengthening public and private coverage of insulin and related supplies. At the same time, policies should be pursued to lower prices through increased market competition for insulin and, when the political opportunity arises, to implement systemic changes to better rationalize US drug prices and price increases.

### 1. Ensure insulin is affordable to patients

For patients with insurance, insulin therapy should be considered high-value care and should be covered with no cost-sharing. Studies have shown that doing so would help patients with high out-of-pocket drug costs and improve medication adherence while adding only modestly to premiums, especially for the privately insured.<sup>4</sup> While either no cost-sharing or modest copay caps could be considered affordable for most people, we favor first dollar coverage because of the importance of incentivizing adherence to insulin therapy. There is little need to discourage overuse of insulin by imposing a copayment. The impact



on payer costs and premiums can be minimized. There will be some cost offset from patients paying out-of-pocket for expenses other than insulin that now fall under their deductible. Consistent with principles of value-based insurance design, additional cost offsets could be generated by reducing coverage of non-value-added services. (If, instead, copays are reduced through insulin copay caps rather than first dollar coverage, per prescription or monthly caps better support patient affordability than annual caps).<sup>5</sup>

Implementation of such a coverage policy for all Americans is complicated by the patchwork of public and private sources of health care coverage in the US and the combination of federal and state laws and regulations that govern them. At a minimum, the actions that follow will be needed.

- 1.1. Pass federal legislation that modifies Medicare Part D to establish no or low-cost sharing for at least one insulin of each type across all phases of coverage. Making at least one insulin product per type available at low cost, rather than all insulins, supports patient affordability while maintaining the ability of the pharmacy benefit manager (PBM) or payer to negotiate rebates based on the ability to direct patients to preferred products. Without Congressional action, the Centers for Medicare & Medicaid Services (CMS) Innovation Center has the authority to implement programs such as the new Part D Senior Savings Model,<sup>6</sup> an enhanced Part D plan with a \$35 per month insulin copay cap, after the model has been tested and meets criteria for system implementation.
- 1.2. Reduce insulin cost sharing to \$0 for all Medicaid and low-income subsidized (LIS) Medicare beneficiaries. As more biosimilar insulins become available, this approach is consistent with the Medicare Payment Advisory Commission (MedPAC) recommendation to eliminate co-payments on Medicaid-covered generics and biosimilars to incentivize use of lower-cost drugs.<sup>7</sup>
- 1.3. Require that private insurers provide no or low-cost sharing for at least one insulin of each type. The most straightforward way to accomplish this is to pass federal legislation adding insulins and associated medical supplies to the list of preventive services required under Section 2713 of the Public Health Service (PHS) Act to be covered with no cost sharing in all group and individual non-grandfathered plans (42 U.S.C. Section 18022).<sup>8</sup> Absent this federal action, a more piecemeal approach would need to be implemented to legislate federal requirements for ERISA-exempted self-insured plans and pass state laws to cover individual market and fully-insured group plans. Colorado offers an example of a state law capping insulin co-payments.<sup>9</sup>
- 1.4. For the uninsured, once insulin is covered with no or low cost-sharing under all types of insurance, the real solution to making insulin therapy affordable is through universal coverage. Until then, clinicians must consider both the clinical and economic appropriateness of the insulin regimen prescribed, including use of non-branded analog or traditional human insulins where appropriate or helping patients access the patient assistance programs currently offered by each of the three insulin manufacturers in the US market.

## 2. Lower insulin prices by accelerating competition in the insulin market

Manufactured human insulins are biologics, which cannot be duplicated precisely as generics but can be very closely reproduced as “biosimilars.” The US currently has one of the most competitive generic drug markets in the world, with more than 90% of retail pharmaceutical prescriptions dispensed as generics, but similar success has not yet been achieved with biosimilars.



Many of the policies that should be pursued to reduce insulin prices are systemic changes to improve the functioning of the US market for biologics, whether in the patent process or in the path to biosimilar market entry and impact. Implementing these policies will be important not only for insulin prices but for US health spending more broadly, as most of the growth in drug spending is in specialty biologic drugs.

Nearly all the most popular modern branded insulins have either recently come off patent or will lose patent protection over the next few years, opening the door to competition from lower-priced biosimilar insulins. Biosimilar insulins do not yet have a meaningful presence in the US market. The non-branded alternatives (follow-on products, “authorized generic” insulins from the existing brand manufacturers, and one biosimilar) available in the US today are priced about 15% to 50% lower than the reference product, but do not yet have significant uptake. Researchers have estimated that biosimilar insulins could be manufactured and brought to market (including a reasonable margin) at prices under \$10 a vial, showing that biosimilar insulins have at least the potential to be economically viable at the price reductions of 80% or more achieved by small-molecule generics.

The US Food and Drug Administration (FDA) has been making progress over the past year in better defining the regulatory pathway for biosimilar approval. As of March 2020, insulin was officially transferred to this new pathway.<sup>10</sup> As successful experience is demonstrated with this process, drug makers will have more confidence in making the investment to bring a biosimilar to market.

Unfortunately, approval of a biosimilar does not guarantee it will penetrate the market, even at a lower price. Unlike generics, which are automatically substitutable for the brand name drug at the pharmacy, approved biosimilars must also be designated by the FDA as “interchangeable” to be substituted without a new prescription. State regulations also govern the ability of pharmacists to substitute a generic or biosimilar drug. Interchangeability and substitutability have been important in driving the widespread shift to generics. The FDA has not yet deemed any biosimilar drug to be interchangeable; however recent draft FDA guidance defines an easier path to interchangeability for insulin specifically, as insulin is less complex and better studied than most newer biologics.

Another barrier to competition for insulins and other drugs is the way drug manufacturers can leverage the current systems of patents and market exclusivity to make the development and approval of biosimilar drugs longer and more burdensome. In a practice known as “evergreening,” manufacturers have extended patent protection periods through strategic incremental patenting of both product formulations and methods of administration. The creation of a “patent thicket” of many overlapping patents on a single drug also creates lengthy and expensive legal hurdle for potential competitors and can delay market entry of even approved biosimilars. Changes to drug patent laws and processes are needed to both curb overuse of patents and reform the reporting and rules around patent litigation to less heavily advantage the patent holder over the competitors.

Competition will also be enhanced if new sources enter the market beyond the three firms – Eli Lilly, Novo Nordisk, and Sanofi – that supply virtually all insulin sold in the US. FDA research has found that price reductions for a drug increase as the number of generic competitors increases.<sup>11</sup> New domestic drug manufacturing could also serve US security interests by reducing our reliance on foreign drug component and final product manufacturing for essential medicines such as insulin and antibiotics.



In summary, the current generation of insulin products appears poised to face greater market competition from biosimilars and new domestic manufacturing capacity. These trends that should be accelerated through the actions that follow.

- 2.1. Strongly commit FDA resources to continue to define, implement, and refine the regulatory pathway for biosimilars. Finalize the 2019 FDA guidance making it easier for biosimilar insulins to obtain an interchangeability designation from the FDA.
- 2.2. Pass federal legislation to modify the patent system for pharmaceuticals to curb patent thickets and evergreening. A recent bill defines such practices as antitrust violations, an approach that has potential for curbing excess patenting since antitrust penalties can be significant, but does require resources to implement and enforce.<sup>12</sup> Another option is to limit the number of patents that a brand manufacturer could assert against a biosimilar competitor (a recent bill sets a limit of 20),<sup>13</sup> a less strict approach but one that has the advantage of being straightforward to enforce.
- 2.3. Pass federal legislation to modify the process of biosimilar approval with respect to patents to better encourage competition. Again, two recent bills define example modifications. The first would flip the burden of proof from the biosimilar developer to the brand manufacturer in establishing that a patent is still valid, a change that seems consistent with the spirit of patent law and better promotes competition.<sup>14</sup> Another would increase the reporting requirements for patents on biologics so that biosimilar developers would have advance knowledge of the portfolio of patents around a brand biologic, comparable to the information available to generic drug developers.<sup>15</sup>
- 2.4. As more biosimilars are approved and deemed interchangeable, advocate at the state level in any state that has not yet legislated extension of substitutability at the pharmacy to biosimilars.
- 2.5. As more biosimilar insulins are approved and deemed interchangeable, track market share, PBM formulary placements, and pharmacy availability of biosimilars relative to reference biologics to assess and address any remaining barriers to biosimilar penetration.
- 2.6. Support the creation of additional manufacturing capability in the US for critical off-patent drugs, including insulin, to include both base ingredients and final products and possibly related medical supplies. This will both lower prices through increased competition (especially when the manufacturing is created explicitly to offer a new, low-priced source) and strengthen the security of the US drug supply, which is currently highly dependent on manufacturers outside the US. The Association for American Medicines blueprint for enhancing US supply chain security<sup>16</sup> and World Health Organization actions to increase access to insulin globally should also be noted and leveraged.

### 3. Allow more direct government action on US drug prices and price increases

Until the current insulin market becomes more competitive, and for future innovations in insulin therapy that produce new patents and market exclusivity periods, a more active and data-driven approach to drug pricing will be required to achieve societal affordability. Market prices for drugs in the US are high relative to the rest of the world, vary wildly across supplier and formulation, are subject to unpredictable





increases, and are difficult if not impossible to observe in net form. PBMs have proven they can negotiate large rebates in exchange for formulary placement where there is brand competition, but they have little influence on launch prices or rates of increase, especially as manufacturers tend to move prices together.

There has been a great deal of public discourse and proposed legislative action around tackling high insulin prices. Both political parties express concern about high drug prices, but none of the proposals to enable the government to take direct action to lower or limit prices appear to be likely to pass in the current political environment. For example, the Lower Drug Costs Now Act, which would allow the Department of Health and Human Services (HHS) to negotiate a maximum price for insulin (among other things), passed the House but was viewed as “dead on arrival” in the Senate.<sup>17</sup>

As the political opportunity arises, we present the following policies as longer-term, more systematic reforms to advance drug affordability. Examples of language to implement these policies can be found in many of the drug pricing bills introduced over the past two years.<sup>18</sup> The policies are listed from most impactful but politically challenging, to less disruptive and so likely more politically feasible.

- 3.1. Allow the federal government to set prices for prescription drugs purchased with public funding. This would be analogous to current rate setting for Medicare reimbursement of inpatient stays, outpatient visits, and other health care services. Prices could be set by HHS or a newly created pricing commission.
- 3.2. Allow the federal government to negotiate prices for some or all drugs directly with the manufacturer. This policy would leverage the outsized US share of the global market for pharmaceuticals. And, unlike proposals to index prices to those in other countries, it would allow the US to negotiate our own prices based on our own priorities and would not be subject to countermoves in international pricing by the manufacturers or other countries.
- 3.3. Allow the federal government to set reasonable upper bounds or criteria for launch prices and for price increases.
- 3.4. Take a step toward greater transparency in drug pricing by requiring manufacturers to submit as part of the drug approval process an accounting of research and development (R&D) costs associated with the drug and an estimate of manufacturing costs, much as hospitals who receive public payer funding must submit a Medicare Cost Report.

Insulin therapy and active disease management has greatly improved life with diabetes, but the disease is still a daily burden to patients and can lead to disability and premature death. The millions of Americans with diabetes, and our society overall, will be well served by continued innovation in the treatment of this disease. Still, drug pricing and policy debates in the US tend to be framed as if we alone are responsible for the profitability and incentives for innovation of the pharmaceutical industry. The US is a large drug market but not the only market. Nor is all drug R&D done in the US. In the case of insulin, only one of the three dominant drug makers, Eli Lilly, is an American company. In taking the action needed to rationalize US drug prices in the long run, we must consider the impact on new drug development, but recognize that the rest of the world has a significant stake in pharmaceutical innovation as well.



# 1 The Problem of Insulin Affordability

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According to the most recent estimates from the Centers for Disease Control and Prevention (CDC), 26.9 million people in the US have been diagnosed with diabetes, including 26.7 million adults and 210,000 children and adolescents under age 20.<sup>19</sup> About 5% of this total, or about 1.4 million adults and 187,000 children and adolescents, have Type 1 diabetes.

All children and adults with Type 1 diabetes need to administer insulin daily to survive. Some individuals with Type 2 diabetes are also insulin-dependent and some use insulin along with other medications to manage their condition. In total, about 8 million Americans rely on insulin.<sup>20</sup>

Insulin prices in the US are the highest in the world and have increased dramatically over the past two decades. For example, the list price of the insulin *Humalog* rose from \$21 a vial in 1999 to \$332 a vial in 2019, an increase of more than 1,000%.<sup>21</sup> Net prices appear to have risen more slowly than list prices; however, even after accounting for large, estimated discounts and rebates, US prices are many times higher than in other countries. Combined with high deductibles and lack of universal health care coverage, the cost of insulin has made management of diabetes unaffordable for many American patients and their families. A study published in *JAMA Internal Medicine* found that one in four people with diabetes uses less insulin than prescribed due to cost.<sup>22</sup> Several well-publicized deaths caused by people rationing their insulin have raised public awareness of the dangers and the daily challenges faced by those struggling to afford insulin therapy.

In addition to concerns about patient out-of-pocket costs, insulin therapy is a growing component of health care spending by public and private health care payers, affecting premiums and tax expenditures. Some plans are reporting that insulin and insulin-combined drugs are now among the top drug spending categories.<sup>23</sup> With high rates of obesity and an aging population, this societal cost burden is projected to steadily rise. The CDC estimates that in addition to the 27 million people diagnosed with diabetes today, another 7 million people are undiagnosed and 88 million are pre-diabetic, making 40% of the adult population in the US either diabetic or pre-diabetic.<sup>24</sup> Already, one in three Medicare beneficiaries is being treated for diabetes<sup>25</sup> and Medicare spending on insulin products has grown from \$1.4 billion in 2007 to \$13.3 billion in 2017, an increase of 840%.<sup>26</sup>

The objective of this study was to identify and assess policies to improve insulin affordability for patients and payers. We first provide a short primer on insulin that is important to understanding the rest of the discussion. Next, we examine insulin prices and trends and identify major market and policy drivers of high US prices. Finally, we describe a variety of policy options for addressing patient affordability and prices. Insulin costs are emblematic of larger issues in the US drug market. To the extent that approaches to insulin affordability address systemic issues, they also present an opportunity to better rationalize US drug prices now and in the future.



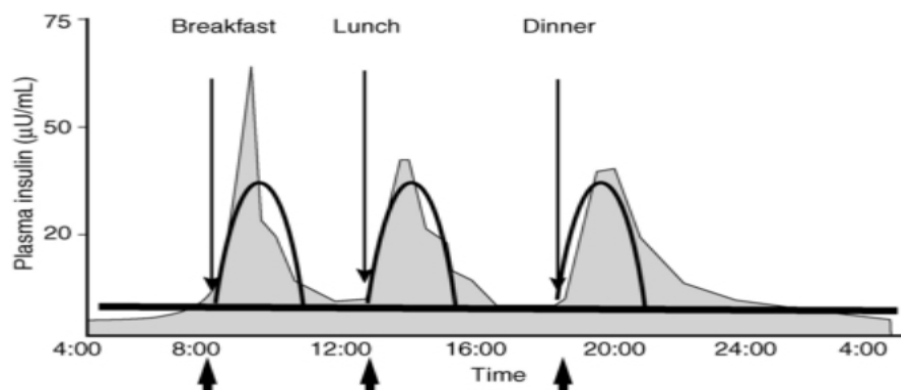
## 2 The Basics of Insulin

Insulin is a hormone used by the body to convert glucose (sugars) from food into fuel. Insulin released by the pancreas allows cells to either use or store glucose. With insufficient insulin, not only are cells deprived of energy, but the build-up of glucose in the blood can damage organs and cause other harmful reactions in the body. With no insulin at all, death can occur in hours or days.

In a person with Type 1 diabetes, the pancreas is unable to produce insulin. Until a century ago, this condition led to early death. The development of supplemental insulin treatment transformed Type 1 diabetes from an acute to a chronic condition. To avoid the dangerous effects of blood sugar levels that are either too low or too high, patients must monitor their glucose levels and take account of their food intake and activities to administer the correct type and dose of insulin throughout the day.

Lifestyle habits and rising obesity have dramatically increased the prevalence of Type 2 diabetes in recent decades. In Type 2 diabetes, the body uses insulin less effectively and the pancreas must produce higher and higher levels of insulin to process glucose. Type 2 diabetes can be treated and sometimes reversed with diet and exercise, but many Type 2 diabetics will require supplemental insulin or other types of drugs to manage blood sugar. While Type 2 diabetes does not become Type 1 diabetes, Type 2 diabetes can progress to the point of insulin-dependence.

Living with diabetes is fundamentally about managing blood sugar. People are at risk if their blood sugar (blood glucose level) is either too low or too high. Being too low, or *hypoglycemic*, can cause seizures, unconsciousness, or death if untreated. Being too high, or *hyperglycemic*, can lead to diabetic ketoacidosis, a dangerous excess of acidic ketones in the blood that can cause coma or death. Blood sugar naturally fluctuates during the day, especially after eating, and a healthy pancreas releases insulin in response to these fluctuations. A simplified illustration of the body's natural insulin levels looks like this:



Source: Adapted from White RD. Insulin Pump Therapy (Continuous Subcutaneous Insulin Infusion). *Primary Care Clinics in Office Practice* 2007;34:845-71.



As shown, the body produces a low baseline level of insulin with spikes at mealtimes to process the glucose in consumed food. Many of the advances in insulin formulations over the past 40 years seek to more closely imitate this pattern.

## 2.1 THE EVOLUTION OF MODERN INSULINS

To understand insulin prices and strategies to improve affordability, it is necessary to understand something of the evolution of insulin therapy and the wide variety of insulins available today. The original insulin developed to treat diabetes in the 1920s was extracted from animals, typically cows or pigs.<sup>27</sup> In the decades that followed, *neutral protamine Hagedorn* (NPH) insulins were created when additives such as zinc were combined with insulin to prolong the duration of action and reduce the number of injections needed per day. Regular and NPH animal insulins were the standard of care for treating diabetes for more than 50 years.

A major development occurred in the 1980s when genomic technology was used to create the first manufactured human insulin, Eli Lilly's *Humulin*. Use of manufactured human insulin was said to be associated with lower anti-insulin antibody levels and better absorption than animal insulins. Soon most diabetic patients had switched to human insulin, and today only one to two percent of patients in the US use animal insulin, although systematic reviews of the science years later show it is less clear that human insulins offer a meaningful clinical advantage.<sup>28</sup>

*Humulin* and all the human insulins that have followed are biologics, meaning they are large molecule drugs grown from living organisms in a lab.<sup>29</sup> As a biologic, the manufacturing process is complex and expensive, creating a barrier to market entry. Since it is created from live material, another manufacturer cannot produce a truly identical "generic" replica of a branded insulin in the way that a small molecule drug can be duplicated. However, a "biosimilar" may be produced that meets criteria for showing no clinically meaningful difference from the reference drug.

Regular human insulins, those that have not been combined with additives, are "short-acting," taking effect in 30 minutes and lasting three to six hours. Human insulins have also been formulated to prolong duration as "intermediate-acting" insulins, taking effect in one to two hours and lasting up to 12 hours. In the 1980s and 1990s, most patients began to use a combination of a short-acting regular insulin such as *Humulin R* with an intermediate acting version, such as *Humulin N*. Premixed combinations of these two types of insulins were also developed.

The traditional human insulins – short-acting, intermediate-acting, and pre-mixed – are still in use today and are at the lower end of insulin prices. The most affordable insulin available in the US is a version of Novo Nordisk's traditional human insulin *Novolin* produced for Walmart under the private label brand name *ReliOn*.



In the 2000s, evolving DNA technology made it possible to make minor modifications to the insulin genome to create what are called insulin analogs. Insulin analogs such as *lispro* or *aspart* worked faster than regular human insulin and were termed “rapid-acting,” taking effect in 15 minutes and lasting two to four hours. Insulin analogs such as *detemir* or *glargine* lasted longer than the intermediate-acting regular insulins and were termed “long-acting,” taking effect in two to four hours and lasting up to 24 hours. These formulations required less advanced planning for every meal and better glycemic control overnight.

Today, more than 20 types of insulin are available in the US, in a variety of formulations and prices. Both traditional insulins and analog insulins require that patients on intensive insulin therapy combine an intermediate- or long-acting insulin with a short- or rapid-acting insulin to process daily fluctuations in blood sugar levels. Insulins from the same manufacturer are usually combined, although there is some evidence that products from different companies can be combined with no change in efficacy or safety.<sup>30</sup> Clinicians prescribe the types, dosage, and schedule for administering insulin and work with patients to calibrate treatment until blood sugar levels are well controlled. The clinical expertise required, the variation in responses to a drug, and the time it can take to find the optimal regimen create strong barriers to switching insulins. Type 1 diabetics are likely to be particularly concerned about the medical risk in changing a regimen that is working.

## 2.2 USING INSULIN

Insulin products vary not only in formulation but in method of administration. Both regular and analog insulins are available in traditional vials, which require syringes to inject, and in pre-filled or reusable injection pens, which are more portable and have dials used to set the desired dosage. Insulin pens are usually more expensive than vials – on the order of one-third more expensive – although the comparison is less clear when all factors are considered, including costs of syringes to use with vials, needles to use with pens, replacement cartridges for long-lasting reusable pens, the amount of insulin wasted in administering the drug, maintaining proper storage and refrigeration, and aligning dosages to the quantity of insulin packaged.

In the 1990s, external insulin pumps were developed to dispense both basal, or baseline insulin, and bolus, or rapid-acting insulin around mealtimes. About the size of a cell phone, the digital pump connects to a port that allows direct release of insulin into the body. Using a pump makes it faster and easier to adjust insulin levels throughout the day, but it still requires human operation.

Regardless of the method of administering insulin, a critical component of diabetes management is the monitoring of blood sugar levels. The traditional method still used today is to use a lancet to lightly prick the skin, usually in the fingertip, to obtain a small amount of blood. The blood is transferred to a test strip which is read by a portable blood glucose meter, called a glucometer.



An innovation that improved the accuracy and convenience of glucose monitoring is the continuous glucose monitor (CGM), introduced in 1999. The CGM is a small device with a thin sensor wire inserted under the skin and held in place with adhesive patch to give an instant, digital blood sugar reading when paired with a cell phone or other device. While more expensive, for Type 1 diabetics, especially children or those having difficulty with glycemic control, the ease with which glucose can be checked frequently with a CGM can greatly improve lifestyle and outcomes. CGMs can also be cost-effective to the extent that they improve glycemic control and reduce the risk of expensive complications.<sup>31</sup>

## 2.3 THE FUTURE OF INSULIN THERAPY

Drug makers are continuing to invest in the development of new insulin formulations and methods of administration. New products under development include a once-weekly long-lasting basal insulin, and a mealtime insulin taken in pill form.<sup>32</sup>

Another ongoing area of innovation is the electronic connection of CGMs to insulin pumps, to automatically dispense insulin under programmed conditions. There is a large support network of individuals and families around the world that have created do-it-yourself versions of these automated monitoring and dispensing systems, sometimes called an artificial pancreas.<sup>33</sup> The Medtronic MiniMed 670g, approved by the FDA in 2016, is the first commercial version of such a “closed loop” glucose monitor and insulin pump system, although online reviews are mixed. It appears likely that there will be more closed loop insulin pumps in the market over the next several years. These commercial devices are not yet fully automated and require significant patient attention and participation.

Outside of improvements to supplemental insulin therapy, other innovations on the horizon include improved pancreas transplant surgery and the possibility of regenerating or stimulating pancreatic tissue to restart insulin production.

Diabetes remains a disease that requires constant daily monitoring and management. Poor management of blood sugar levels has serious consequences, from limb amputation to vision loss to early death. There is much room for innovation to more seamlessly and reliably manage insulin and blood sugar levels, and even the possibility of a cure. While the focus of this study is to address the problem of high insulin costs, we also recognize the importance of continuing to develop these new and potentially life-changing innovations.



## 3 US Insulin Prices

### 3.1 INSULIN PRICE LEVELS, TRENDS, AND COMPARISONS

Insulin prices in the US are unaccountably high when compared to prices paid in peer countries. US prices, especially list prices, have also increased dramatically over the past 15 years.

#### 3.1.1 International price comparisons

A report prepared for the US House of Representatives, Committee on Ways and Means in 2019 found that average insulin prices in the US were more than three times the international average, about \$35 per dose compared to the international average of less than \$11 per dose.<sup>34</sup>

We also compiled US and international data on drug prices to compare two top-selling modern analog products: the Lantus Solostar Pen and the Novolog Flexpen.

Table 1 displays prices for these products as of late 2019 in the US by payer, and in a dozen peer countries.<sup>35</sup>

The lowest price for these insulin products (and other drugs) in the US are paid by the Department of Veterans Affairs (VA). The prices reported in the VA Federal Supply Schedule are 30-40% of the average retail price as reported by GoodRx.

Yet even the US VA prices are markedly higher than the prices paid in other countries. For the Lantus Solostar Pen, international prices range from \$1 to \$28, compared to the US VA price of \$46 and the average US retail price of \$115. For the Novolog Flexpen, international prices ranged from \$2 to \$13 compared to the US VA price of \$69 and the average US retail price of \$225.

The big picture view of the global insulin market reinforces the higher US prices seen in comparisons of specific insulin products: the US represents about 7% of the global diabetes population, but about 40% of global insulin revenues.<sup>36</sup>

**Table 1: US and global prices for two popular insulins**

Country	Lantus Solostar Pen	Novolog Flexpen
<b>United States</b>		
<b>Average Wholesale Price</b>	\$204	\$268
<b>VA (Federal Supply Schedule)</b>	\$46	\$69
<b>Medicare Part D</b>	\$149	\$211
<b>Average Retail Price (GoodRx)</b>	\$115	\$225
<b>Sweden</b>	\$22	\$12
<b>New Zealand</b>	\$24	\$13
<b>Australia</b>	\$13	\$11
<b>Denmark</b>	\$2	\$2
<b>Iceland</b>	\$6	\$5
<b>Lebanon</b>	\$5	\$3
<b>Czech Republic</b>	\$1	\$9
<b>Norway</b>	\$5	\$4
<b>France</b>	\$17	\$2
<b>Canada</b>	\$28	n/a
<b>Portugal</b>	n/a	\$3
<b>Netherlands</b>	n/a	\$3



### 3.1.2 Growth in US insulin prices

Insulin prices in the US have not always been hundreds of dollars per pen or vial. Prices have increased significantly over the past 20 years, despite only incremental changes to formulations or methods of administration. From the early 2000s through the mid-2010s insulin prices roughly tripled for all formulations, including both regular and analog insulins.<sup>37,38</sup> And the rapid growth in prices did not end in the mid-2010s. According to an analysis of private health insurance claims by the Health Care Cost Institute, annual insulin costs for a person with Type 1 diabetes averaged \$2,864 in 2012. Four years later, the cost had doubled, to \$5,705 in 2016.<sup>39</sup>

The USC Schaeffer Center analyzed recent trends in various measures of insulin costs for the [Insulin Access and Affordability Working Group](#) of the American Diabetes Association.<sup>40</sup> Schaeffer Center researchers analyzed data on 30 insulin products including short-acting (regular), rapid-acting (analog), and long-acting (analog) insulins, finding double-digit annual growth rates during a period when overall annual inflation was only 2.2%. The study found:

- ▲ The average list price, or wholesale acquisition cost (WAC) for these insulins increased 15% to 17% per year from 2012 to 2016.
- ▲ The price pharmacies paid to purchase the insulins, or the National Average Drug Acquisition Cost (NADAC), also increased about 15% per year from 2012 to 2016.
- ▲ Average out-of-pocket costs per insulin user under Medicare Part D increased by 10% per year for all insulin types from 2006 to 2013.

In addition to high price levels and growth rates, the complexity and opacity of the US drug supply chain result in extreme variation in the prices charged to patients. In 2019, researchers called more than 250 pharmacies around the country asking for the cash price for 12 common drugs.<sup>41</sup> These were the prices that patients without insurance would need to pay at the pharmacy counter to fill the prescription. The study found that the price patients would be asked to pay for a Lantus Solostar Insulin Injector Pen 5-pack ranged from \$96 to \$1,759, with a median price of \$445. If one package per month were needed, patients paying the median cash price would pay more than \$4,000 per year more than if they paid the lowest cash price. The difference between paying the highest and lowest price for Lantus for the same patient without insurance would add up to \$20,000 per year! It is hard to name a functioning consumer market with that kind of price variation on the same product, especially one that represents a critical daily need.

Finally, it is useful to try to understand some of the components of current insulin prices. The price charged should be expected to cover the cost of manufacturing the insulin and bringing it to market. During the period the drug is protected from competition, manufacturers can also recover research and development (R&D) costs for the drug and offset a portion of the costs for failed trials that are part of the R&D process. Manufacturing costs are not readily available for most drugs. However, a 2018 study published in the medical journal *BMJ* developed detailed, bottom-up estimates of the cost of





manufacturing a vial of both traditional and analog insulin. The study estimated that traditional human insulin could be brought to market as a biosimilar for between \$2.28 and \$3.42 per vial. For an analog insulin, the cost would be only slightly higher, between \$3.69 and \$6.16 per vial.<sup>42</sup> These estimates include all active ingredients, additional raw materials, costs of the development and product approval process, and assume a 20% margin.

Using the high end of the manufacturing cost ranges, assuming some inflation since 2018, and even rounding up, produces production cost estimates of \$4 a vial for traditional insulin and \$7 a vial for analog insulin. These estimates bring to light two observations. First, despite the large price differences, analog insulins are not much more expensive to manufacture than traditional insulins. Second, at less than \$10 a vial to manufacture and bring to market, current US insulin prices are at least 10 times higher than what would appear to be a cost-based price, even assuming very large hidden rebates. A better accounting of R&D costs to be recovered during the market exclusivity period is needed to assess these branded prices.

### 3.1.3 Costs of supplies for insulin therapy

Unlike medications taken orally, the cost of insulin therapy includes more than the drug itself, it includes the supplies needed to administer the insulin and those to monitor glucose levels to determine the appropriate timing and dosage. Whether the patient uses vials and syringes, pens and needles, pumps and cartridges, lancets and glucometers or CGMs, these supplies are used daily, often many times a day, and represent an ongoing expense that is required for the insulin to be delivered effectively.

New research in *JAMA* finds that for commercial patients with Type 1 diabetes, average out-of-pocket costs for the supplies and equipment associated with administering insulin and monitoring glucose levels are greater than out-of-pocket costs for the insulin itself.<sup>43</sup> The study found that for adults, the amount spent out-of-pocket on supplies each year was comparable to that spent on insulin. For children, who are more likely to use insulin pumps and CGMs, annual out-of-pocket supply costs far exceeded the insulin costs (on average, more than \$800 per year for supplies versus about \$500 for insulin).

These findings underscore the importance of considering all needed components of insulin therapy to ensure affordability: the insulin, the means to administer the insulin, and the glucose monitoring needed to determine when and how much insulin to deliver.

## 3.2 DRIVERS OF HIGH INSULIN PRICES

Why are insulin prices in the US higher than the rest of the world? Why have list prices been rising so rapidly over the past 15 years in the absence of breakthrough innovations? Characteristics of the US insulin market, our legal and regulatory systems, and our health care financing system are among the drivers of high and rising prices. We explore these drivers to better identify and assess policies to lower US insulin prices.



### 3.2.1 Lack of competition in the US insulin market

Three manufacturers produce nearly all insulins sold in the US and 90% of the world's insulin.<sup>44</sup> Novo Nordisk, a Danish company, is a merger of the two firms that produced the first insulin in the 1920s. Eli Lilly, a US company, and Sanofi, a French company, are the other major players in the insulin market. Table 2 characterizes the size and overall financial performance of these companies. These three manufacturers produce competing insulins in many of the same categories, including traditional human insulins (short-acting, intermediate-acting, and premixed) and modern analog insulins (rapid-acting, long-acting).

**Table 2: Financial Indicators for the Big 3 Insulin Companies**

	Novo Nordisk	Eli Lilly	Sanofi
<b>Market Cap (5/1/2020)</b>	\$148.6	\$147.0	\$121.3
<b>2019 Total Revenues</b>	\$18.3	\$22.3	\$41.4
<b>2019 Net Income</b>	\$5.8	\$8.3	\$3.1
<b>2019 EBITDA</b>	\$8.2	\$6.9	\$11.8
<b>Net Margin</b>	32.0%	24.0%	8.2%
<b>2019 Research Development</b>	\$2.1	\$5.8	\$6.6

Source: Yahoo Finance and CNBC. All numbers except Net Margin are \$billions.

Having three competitors offering similar insulin products in each category (e.g., rapid-acting, intermediate-acting, long-acting, pre-mixed) would be expected to bring down insulin prices. In practice, the companies have tended to follow one another in the timing and magnitude of list price increases.<sup>45</sup> In fact, even the traditional human insulins produced by these companies, while more affordable, have increased in list price at about the same pace as the analog insulins.

The competition for market share among the three companies happens behind closed doors through the rebates offered to pharmacy benefit managers (PBMs) in exchange for formulary placement. There are three PBMs in the US that together represent about three-quarters of all prescription drug claims.<sup>46</sup> PBMs use formulary placement to incentivize patients to use one insulin over another in each category. For example, a PBM formulary that includes Novolog will exclude Humalog. This creates pressure for manufacturers to offer favorable terms to at least one of the major PBMs, so their drug will not be largely shut out of the US commercial and Medicare Advantage markets. Rebates on individual insulins are proprietary but there is evidence that with three brand competitors, rebates on insulin products are higher than average and may be 50% or more.

The US market-based system of drug pricing relies on the introduction of generics to bring real downward pressure on prices once a drug is off patent. For small molecule drugs, the US now has one of the most competitive generic markets in the world. While decades ago there was skepticism about generics, the public has become more familiar with them and use has increased dramatically. Today, more than 90% of retail pharmaceutical drug prescriptions in the US are dispensed as generics. A robust pathway for generic competition has been critical to expanding drug access and promoting public health. Part of the reason



generic drugs can be offered at much lower prices is that the safety and efficacy of the drug has already been established so the pathway to approval can be faster and less costly. The FDA has worked hard to encourage generic entry after patents and exclusivities on branded drugs have lapsed.

Not all parts of the US pharmaceutical market have been open to competition from more affordable products. This is especially true for biologic medicines, which are complex molecules produced by living cells, and are increasingly the backbone of modern drug therapy.<sup>47</sup> Until recently, biologics lacked effective competition because there was no abbreviated pathway for bringing biosimilars to market like there was for generic versions of small molecule drugs.

In 2010, Congress, through the Biologics Price Competition and Innovation Act (BPCIA), gave the FDA the authority to implement a pathway for approval of biosimilar and interchangeable products to open biologics to competition. Although progress has been much slower than stakeholders might wish, the FDA has made significant progress in the past few years on developing guidelines for allowing biosimilars – specifically for insulin – to be approved and substitutable for their reference biologics.<sup>48</sup>

In May 2019, the FDA issued final guidance on how biosimilars can achieve interchangeable status, meaning they may be substituted for the reference biologic without a prescriber intervening.<sup>49</sup> This guidance provides pharmaceutical companies with more certainty on how to develop interchangeable products and details data and study design requirements that allow flexibility and the use of global comparator products to support applications. In November 2019, the FDA released draft guidance specific to insulin to help pharmaceutical companies bring biosimilars to the US market more quickly.<sup>50</sup> Previously, the agency had taken the position that data from a comparative clinical immunogenicity study would likely be needed to evaluate the potential risk and clinical impact of immunogenicity of proposed biosimilar insulins. In the updated draft guidance, FDA argued that if a comparative analytical assessment based on state-of-the-art technology supports a demonstration of ‘highly similar’ for a proposed biosimilar or interchangeable insulin product, a comparative clinical immunogenicity study generally would be unnecessary, reducing the time and resources required.<sup>51</sup> As of March 23, 2020, approved new drug applications for insulin products will be “deemed to be licenses” and can then serve as reference products for proposed biosimilar and interchangeable insulin products.<sup>52</sup>

Another step in easing the path to biosimilar entry was the passage of the Creating and Restoring Equal Access to Equivalent Samples (CREATES) act in December 2019, as part of the [2020 consolidated appropriations package](#). CREATES strengthens the ability of biosimilar developers to obtain samples of the branded products needed to support their applications. CREATES allows a path for developers to sue companies that refuse to sell them product samples required for testing their products prior to approval. In 2019, the FDA identified 55 products for which companies had been unable to obtain samples.<sup>53</sup> Under the new legislation, if the developer wins the suit establishing that samples were inappropriately withheld, the brand company must pay all legal fees and potential additional penalties.



Some competitive action has begun in the market for rapid-acting insulin analogs. The two major formulations of rapid-acting insulin sold in the US are *insulin lispro* (Eli Lilly brand *Humalog*) and *insulin aspart* (Novo Nordisk brand *Novolog*). In 2017, Sanofi's *Admelog* containing *insulin lispro* was approved as the first "follow on" biologic using the 505(b)(2) pathway of the FDCA. This pathway allows some reliance on past research establishing safety and effectiveness of a previously-approved drug, in this case *Humalog*. *Admelog* was introduced at a lower price than *Humalog* and has since seen further price reductions. In Spring 2019, Eli Lilly launched a lower priced, exact copy "authorized generic" of *Humalog*.<sup>54</sup> The product is called *Insulin Lispro* and is available in similar preparations (vial and pen options) as *Humalog*. Novo Nordisk also launched authorized generic versions of their insulin products at reduced prices, including an *Insulin Aspart* generic of *Novolog*, and has continued to innovate in this space.<sup>55</sup>

Unfortunately, approval of a lower priced alternative, even an authorized generic that is the same drug from the same manufacturer with a different label, does not guarantee sales will shift from the branded drug. As of March 2020, after more than a year on the market, authorized generic *Insulin Lispro* represents about one-third of the Lilly's rapid-acting prescription insulin fills, while about two-thirds of Lilly's fills remain as *Humalog*.<sup>56</sup> For Novo Nordisk, after several months on the market, their authorized generic *Insulin Aspart* represents 12% of their rapid-acting insulin fills, while 88% remain as *Novolog*.

An investigation by Sens. Elizabeth Warren (D-MA) and Richard Blumenthal (D-CT) released in December 2019 examined this issue by exploring the availability of Lilly's generic *Insulin Lispro*.<sup>57</sup> In a phone survey of close to 400 pharmacies, both independents and chain stores across all 50 states, the study found that *Insulin Lispro* was not available at 83% of pharmacies. Even for patients willing to wait, the generic *Insulin Lispro* could not be ordered by 69% of pharmacies. It is not clear whether this is a pharmacy supply or prescription demand issue, so this should be revisited as soon as a biosimilar insulin earns interchangeability.

The market for long-acting analog insulins tells a slightly more encouraging story. After the patent for Sanofi's best-selling, long-acting insulin *Lantus* expired in 2015, Eli Lilly pursued approval of *Basaglar*, containing *insulin glargine*, the same active ingredient as *Lantus*. *Basaglar* was finally approved in the US in December 2016 as the first biosimilar insulin in the US market.<sup>58</sup> *Basaglar* is priced about 15%-20% lower than *Lantus*. *Basaglar* is not considered interchangeable so cannot be automatically substituted for *Lantus* at the pharmacy; however, *Basaglar* is now 34% of the market for long-acting insulins, while *Lantus* has dropped from 80% of the market to 42%.<sup>59</sup>

An important factor in the speed of biosimilar uptake is the placement of products in PBM formularies. The three dominant PBMs in the country are ExpressScripts, CVS Health/Caremark, and Optum. According to each of the recently-released 2020 formulary specifications, [Express Scripts](#) does not cover generics *Insulin Lispro* and *Insulin Aspart*, or the lower-priced Sanofi lispro product *Admelog*, and instead covers branded *Humalog*. The 2020 [CVS Health](#) formulary does not cover generic *Insulin Aspart* and



instead covers brand name *Novolog* but is covering the biosimilar *Basaglar* over branded *Lantus*. The 2020 [OptumRx](#) formulary does not cover *Insulin Lispro* or *Basaglar* and instead covers *Humalog* and *Lantus*. Because the prices and the rebates negotiated by each PBM are proprietary, as are the provisions of the contracts between the PBMs and payers, it is impossible to know whether the branded drugs on the preferred formulary list were offered at net prices less than the generics, or whether PBMs preferred higher rebates over lower generic list prices.

Another key factor is interchangeability, allowing the pharmacists to substitute the lower priced generic version at the pharmacy, without requiring a new prescription from the clinician. Once generic drugs are approved, they may be substituted at the pharmacy, as regulated by the state. For biologics, the FDA designation of biosimilarity allows the drug to enter the market, but the FDA must separately designate the biosimilar as interchangeable. State laws then specify when and how pharmacists may substitute biosimilars for the reference biologic and the extent to which the prescriber or the patient must be informed. As of April 2020, all but one state (Oklahoma) and the District of Columbia have passed legislation addressing biosimilar interchangeability, and legislation is pending in those two locations.<sup>60</sup>

### 3.2.2 Rapid adoption of new technologies without weighing benefit versus cost

Since their development in the early 2000s, analog insulins have rapidly become the predominant type of insulin used in the US. An analysis of privately insured adults with Type 2 diabetes found that from 2003 to 2010, the share using analog insulins rose from 18% to 91%.<sup>61</sup>

The rapid transition from animal insulins to manufactured human insulins, and then to analog insulins, is characteristic of the rapid adoption of new technologies in US health care. Each of these innovations in insulin offered improvements, but there was little formal assessment of the tradeoffs between clinically meaningful impact and higher cost for different types of patients before most were transitioned.

Prices of analog insulins are much higher than traditional human insulins. The average retail price of a 10ml vial of an analog insulin is about \$360, more than 2.5 times more expensive than the average \$138 per vial for traditional human insulin.<sup>62</sup> When compared to the least expensive human insulin available, Novo Nordisk's *Novolin* sold under the Walmart private label *ReliOn*, the average analog price of \$360 is 14 times more expensive than the \$25 per vial *ReliOn* price. Patients with Type 1 diabetes usually need from two to six vials per month; at four vials per month, the cost would be \$100 per month for *ReliOn*, \$552 per month at the average retail price for traditional insulin, and \$1,440 per month at the average retail price for analog insulin.

Some experts believe that analog insulins have demonstrated better performance, particularly at avoiding overnight hypoglycemia, and that the more predictable glucose management may be associated with lower rates of adverse events and so actually lower overall health care spending.<sup>63</sup> The glycemic stability and control offered with analog insulins are especially important for those living with Type 1 diabetes.



Evidence from other studies, including official guidance from WHO, finds that regular insulins can be used effectively to manage blood sugar levels for some patients with Type 2 diabetes, at much less cost.<sup>64,65,66</sup> Insulin users with Type 2 diabetes are the larger group, at about 6.5 million in the US versus 1.5 million with Type 1 diabetes, and, again, nearly all are currently being treated with analog insulins.

In addition to a reluctance to accept explicit use of cost-effectiveness criteria for determining coverage, drug company marketing to physicians and direct-to-consumer advertising in the US also contribute to rapid shifts to new technologies and preferences for branded products, even when cheaper alternatives are available. The US and New Zealand are the only two countries that permit direct-to-consumer drug advertising. Spending on US drug marketing and advertising has been estimated at more than \$26 billion per year, with about \$20 billion targeting physicians and about \$6 billion (and growing) targeting consumers.<sup>67</sup> To put these figures in perspective, the total marketing and advertising budget represents about 5% of annual retail plus non-retail drug spending in the US, while the consumer marketing represents about 2% of retail prescription drug spending.<sup>68</sup> Given these small percentages, while drug prices presumably need to cover these expenses, the impact of marketing on physician behavior and consumer preferences for branded drugs is probably more important in supporting higher prices.

### 3.2.3 Patents and market exclusivity

Pharmaceuticals are granted two different types of protections from competition – patents and market exclusivity periods. Patents are granted by the US Patent and Trademark Office (USPTO) to all types of inventions, including drugs, that are new, not obvious, and useful. Patent protection from competition is 20 years from the filing date of the application, which is usually early in the drug development process.

Market exclusivity is granted by the FDA upon approval of a new drug and represents a period during which no other applications for the same active ingredient can be accepted or approved. Biologics are granted 4 years of filing exclusivity, during which other manufacturers are prohibited from filing an application for a biosimilar drug, and 12 years of approval exclusivity, during which the FDA is prohibited from approving any biosimilar.<sup>69</sup> Both patent protections and market exclusivities are intended to incentivize investment in the long process of pharmaceutical research and testing by granting temporary monopoly status to the manufacturer, allowing early pricing to cover not only manufacturing costs but recovery of R&D costs.<sup>70</sup>

The current patent system is being leveraged to extend protections and discourage competition in at least two ways. In a practice sometimes called “evergreening,” drug makers systematically add new patents on a drug for incremental changes such as reformulating the drug for children or improving the drug delivery system. While these may be real and beneficial improvements in the product offering, the investment required is not comparable to that required for invention of a new drug. Strategic use of patenting can extend protections around a single drug for decades beyond the original protection period intended for this original invention.<sup>71</sup>



Another way in which the layering of many patents around a drug – sometimes called a “patent thicket” – discourages competition is by increasing the cost and risk associated with patent litigation. This is especially true since the burden of proof is currently on the potential competitor to establish that no patents are being violated.

### 3.2.4 Lack of government negotiation of drug prices

The US represents on the order of 40% of the global market for insulin. Government programs represent about three-quarters of US insulin spending. Yet the federal government is prohibited from leveraging this market power to negotiate drug prices with manufacturers, and the Centers for Medicare & Medicaid Services (CMS) has interpreted current statute as prohibiting the Medicare program from considering price in coverage decisions for drugs or any other therapies.<sup>72</sup> While formulary placement has been used successfully by payers or their PBMs to negotiate rebates of 50% or more off the list price of drugs where there is brand competition, the PBM has no influence on the launch price or subsequent price increases, especially as manufacturers have tended to move together on prices. Put another way, the US represents a much larger publicly-funded market for insulin than any North American or European peer country, yet those countries negotiate prices that are a fraction of the US price for the same insulin product.

### 3.2.5 The rebate system and its impact on list prices

The private sector negotiation that characterizes most prescription drug coverage in the US has created a system where list prices are high, and discounts are offered in the form of proprietary rebates paid to insurers, or their PBMs, that are outside the consumer’s drug purchase transaction. This system has created wide gaps between list prices and net prices and made it very difficult to see and track true prices, especially for branded drugs. It also creates incentives for higher list prices to the extent that PBMs, wholesalers, and others in the supply chain are paid according to the list price or the size of the rebate. Tying a portion of PBM fees to rebate amounts does reward the PBM for negotiating greater price reductions, but that success does not really represent a constraint on prices if a larger discount is simply a reflection of an artificially higher list price.

The proprietary nature of rebates also blocks visibility into insulin prices. In response to criticism over high insulin prices, drug manufacturers argue that the net price after rebates that they receive for insulin and other drugs is not only much lower than the list price but has not been growing nearly as rapidly. Recent analyses leveraging information published in company quarterly financial reports have corroborated this assertion. A 2020 *JAMA* study found that from 2007 to 2018, list prices of the insulins examined increased by 262% while estimated net prices increased by 51%.<sup>73</sup> Similarly, a 2020 National Bureau of Economic Research paper found that from 2012 to 2017, list prices for the insulins examined grew by 16% while estimated net prices grew by only 2%.<sup>74</sup> Sanofi recently reported that from 2012 to 2019, list prices for its insulins grew by 140% while the company’s net prices fell by 41%, and have been falling for five years in a row.<sup>75</sup> Nevertheless, despite having to bear criticism for price increases that do not accrue to





them, drug manufacturers may be reluctant to move to a system that allows more transparency into prices by product and payer.

Rebates do significantly lower the effective cost of insulin to the payer and so lower premiums. Yet patients with cost exposure face the artificially high list price, either as a basis for cost sharing calculations or as the cash price for those without insurance. By paying rebates directly to the insurer rather than having them reflected in the price paid at the pharmacy, patients using insulin are in effect subsidizing lower premiums for their fellow health plan beneficiaries. This system also places undue burden on the uninsured, who prices that may be more than double the typical net price on a branded insulin.

### 3.2.6 Distortions in the market for health insurance

Most Americans are shielded from paying for the full value of their health insurance, resulting in coverage that is more generous than they might otherwise choose. Employer-sponsored insurance, which provides drug coverage for about half of Americans, is paid for by employers using pre-tax dollars, giving consumers insurance that is 20 to 30 percent less costly than the premium they would pay out of earnings. Medicare Part D, another major source of drug coverage, is funded largely by general revenues, not from past payroll taxes contributed by today's beneficiaries. The result is coverage and health care spending at levels higher than Americans would choose if these distortions did not exist, allowing for higher prices.





## 4 Assessment of Policies to Reduce Patient Cost Burden

In this brief, we examine policies to make insulin affordable to:

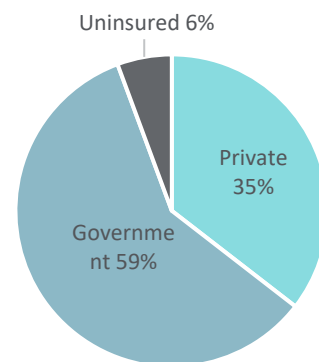
- ▲ patients, so they can maintain access to treatment, prevent adverse health outcomes, and avoid financial insecurity; and
- ▲ payers, who should be paying fair prices with respect to manufacturer costs and the prices paid by peer countries. Payer costs, of course, are ultimately reflected in premiums and the burden of health care spending on employers, states, and the federal government.

Clearly, there is overlap between patient affordability and insulin prices. If US insulin prices were magically lowered to those paid in most peer countries, it would eliminate much of the patient affordability problem. While long-term patient affordability may be achieved through bringing down insulin prices, patients’ lives and financial stability are at stake today. Action needs to be taken immediately to address out-of-pocket costs at the same time longer term policies are pursued to lower US insulin prices.

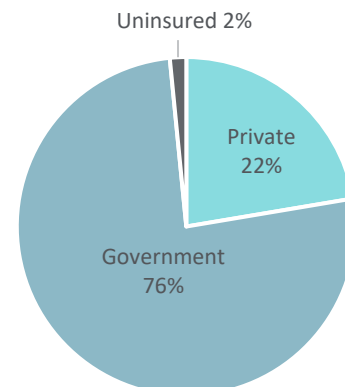
A patient’s out-of-pocket costs for insulin depend on that patient’s health insurance. Under the patchwork system of public and private health care coverage in the US, different sources of coverage are governed by different sets of federal and state laws and regulations, offering different policy levers to make changes. We therefore assess approaches to addressing the patient cost burden under each major type of drug coverage – Medicare Part D, Medicare Advantage, Medicaid, private health insurance, and the uninsured – with the goal of ensuring insulin is affordable under all types of coverage.

Most people being treated for diabetes in the US are covered by Medicare or Medicaid. The American Diabetes Association (ADA) estimated that in 2017, of the roughly 24 million people being treated for diabetes, 59% were covered under Medicare, Medicaid, or other public sources, another 35% were covered under private insurance, and 6% were uninsured.<sup>76</sup> The same study found that insulin spending is even more heavily weighted toward the publicly insured, highlighting the importance of addressing insulin affordability under Medicare and other government programs.

**US diabetes patients by payer type, 2017**



**US insulin spending by payer type, 2017**





## 4.1 INSULIN AFFORDABILITY UNDER MEDICARE PART D

To assess proposals for ensuring insulin is affordable for patients covered under Medicare Part D, it is necessary to understand the complicated structure of the benefit and the ways cost-sharing may vary over the plan year. The Medicare Part D benefit has four phases that a beneficiary may move through during a plan year as their spending on drugs increases: the deductible, the initial cost-sharing phase, the coverage gap, and the catastrophic phase. The patient's cost sharing varies by phase.

At the beginning of the plan year, patients pay the full cost of their prescriptions, at list price, up to the deductible, which plans can set up to \$435.<sup>77</sup> After the deductible is met, the initial cost-sharing phase begins, requiring either a copayment amount (a dollar amount per prescription fill) or a coinsurance share (a percentage of the price of the fill), depending on the plan. The amount of the copayment or coinsurance may also vary depending on the formulary tier in which the prescribed drug has been placed. In 2019, nearly 90% of Part D plans were found to offer long-acting insulins with copayments of about \$45 per monthly fill.<sup>78</sup>

Once a patient's total drug spending reaches the 2020 limit of \$4,020, patients enter the coverage gap, during which most plans require 25% coinsurance, computed based on the list price of the drug. Finally, if a patient's drug spending reaches \$6,350, they enter the catastrophic phase, where they pay a small cost-sharing rate such as 5%.

### 4.1.1 Capping out-of-pocket costs under Medicare Part D

There is emerging bipartisan support for policies that would relieve the high out-of-pocket cost burden that many seniors enrolled in Medicare Part D face for their medications.<sup>79,80</sup> In Congress, both the US Senate's Prescription Drug Pricing Reduction Act (PDPRA) bill and the US House's Elijah E. Cummings Lower Drug Costs Now Act (HR3) bill include provisions that would cap annual out-of-pocket beneficiary costs, as part of a larger strategy to restructure the Part D benefit. Studies have found that these proposals would benefit Part D beneficiaries using insulin with very high drug spending, but that the impact on patients' costs would depend on each Part D plan's benefit design. Current bills, consistent with the current Part D program, allow plans to impose either beneficiary copayments (a flat dollar amount) or coinsurance (a percentage share) on prescription drug costs. Studies of the proposed cost sharing caps find that if Part D plans require flat copayments on insulin until patients reach the out-of-pocket spending limit (which is what most plans do now), insulin patients under the proposed changes would save \$589 from what they would expect to spend under a typical Part D plan. However, if plans require a 25% coinsurance rate instead, as is allowed, patients would pay \$704 more than they do now under a typical plan.<sup>81</sup>



Annual caps are easier for budgeting purposes but are harder to operationalize and they create a burden for patients in the months before the annual cap is reached. Capping the amount of cost sharing per prescription, rather than annually, would smooth beneficiary cost sharing and make it more predictable to budget every month, provide more generous coverage, and improve the affordability of drugs for beneficiaries. A per prescription cap might also improve patient medication adherence, making it more likely patients will initiate a prescribed medication regimen and less likely they will abandon it. The policy would also protect drug users from the cost-sharing implications of price increases; inflation caps on Part D spending would also accomplish this goal.

The disadvantages of capping out-of-pocket costs for Part D beneficiaries at the per prescription level is the modest cost increase. It would provide more insurance coverage to seniors and therefore cost more money than the annual cap from the perspective of Medicare payments. The Medicare Payment Advisory Commission (MedPAC) estimated this policy would raise premiums for all seniors enrolled in Part D by about \$4 per month if all prescriptions were covered (not limited to insulin products).

In March 2020, CMS announced the launch of the [Part D Senior Savings Model](#), a voluntary pilot program to reduce out-of-pocket insulin costs for beneficiaries under standalone Medicare Part D plans and Medicare Advantage plans that provide Part D drug coverage. Under participating enhanced plans, insulin copays would be capped at \$35 per 30-day prescription in all phases of the annual Part D benefit until the beneficiary reached the catastrophic phase, when cost sharing would be 5%. The model aims to make cost sharing for insulin both lower and more predictable to improve medication adherence and outcomes. CMS estimates that beneficiaries who take insulin and enroll in a participating plan should save an average of \$446 in annual out-of-pocket costs on insulin, reducing cost-sharing by more than 60% compared to average costs today. The program is scheduled to begin in January 2021 for insurers and drug manufacturers who agree to participate. All three insulin manufacturers have expressed interest in participating.<sup>82</sup>

#### 4.1.2 Passing drug rebates through to Part D patients

The Medicare Part D program explicitly prohibits federal government negotiation of Part D prices. Health plans or their PBMs, who can negotiate prices, have successfully achieved discounts off the list prices of branded drugs in exchange for preferential formulary placement; however, these discounts have primarily taken the form of rebates paid by manufacturers directly to the plans or PBMs, and lie outside the retail drug transaction. Under Part D, a portion of rebates also flows to the federal government. While the rebate percentages can be substantial (more than half off the price of some branded drugs) and therefore do reduce Part D premiums, they do so at the expense of drug-purchasing Part D patients whose cost-sharing percentage is based on the list price, not the net price after rebate.<sup>83</sup>

Researchers at the USC Schaefer Center recently modeled a Part D policy change that would base beneficiary cost-sharing on net, rather than list, price for patients who do not receive low-income



subsidies.<sup>84</sup> They found that such a policy change would reduce out-of-pocket spending for about 47% of these beneficiaries, with 20% saving more than \$100 per year and 1% saving more than \$1,000 per year. They also found that many fewer of these beneficiaries would reach catastrophic coverage, resulting in federal reinsurance savings of about 19%. Study results were computed across all Part D drugs, but among the data presented on a few selected drugs, the study found that annual patient out-of-pocket costs for users of the analog insulin Humalog in pen form would fall 16%, from \$4,684 to \$4,029 per year if cost-sharing was based on net rather than list price.

Another solution that was considered in 2018 by the Trump administration would be to eliminate rebates altogether by removing the safe harbor currently protecting drug companies and payers from liability under anti-kickback law, which prohibits payments to induce use of services reimbursable under federal health care programs.<sup>85</sup> The Congressional Budget Office (CBO) analyzed the legislative removal of the safe harbor and found that federal spending would increase over the decade.<sup>86</sup> A key assumption was that new manufacturer drug discounts would be 85% of the current rebates, based on the prohibition of discounts in exchange for higher sales volume, the major PBM bargaining tool. CBO projected that beneficiary utilization of prescriptions drugs would increase 2% due to lower cost sharing, but that spending on hospitalizations and other care would decrease due to greater medication adherence, for a net savings to the government of \$10 million. Nevertheless, with lower discounts, on balance federal spending under Medicare and Medicaid was projected to increase \$177 billion for the ten-year period from 2019 to 2029, likely contributing to this solution not being pursued.

We conclude that under the current system of private sector PBM and payer drug price negotiation, the safe harbor allowing the volume discount should remain. Implementation of first dollar coverage for insulin (or, at a minimum, copay caps) as recommended in our discussion of patient affordability, would alleviate the burden of coinsurance percentages being computed on list price rather than net price for patients with insurance.

## 4.2 INSULIN AFFORDABILITY UNDER MEDICAID

For individuals with Medicaid drug coverage, co-payments are generally modest (\$1 to \$5) for drugs on the preferred drug list. Although there is some variation in Medicaid drug coverage by state, all states include some insulins on their preferred lists. However, for some publicly insured low income patients, even a small co-payment requirement may be a barrier to prescription drug access.<sup>87,88</sup>

Given the importance of glycemic control and the unlikelihood of unnecessary utilization of insulin, insulin should be exempt from cost sharing for all Medicaid and low-income subsidized (LIS) Medicare beneficiaries. MedPAC has proposed eliminating co-payments on all generic and biosimilar drugs covered under Medicaid, and for LIS beneficiaries in Medicare.<sup>89,90</sup> The proposal entails capping out of pocket payments at \$0 for generics and biosimilars.



## 4.3 INSULIN AFFORDABILITY FOR PRIVATELY INSURED PATIENTS

### 4.3.1 Encouraging high-deductible plans to cover insulin as preventive care

For the large and growing number of Americans insured under high deductible health plans (HDHPs), there has already been some positive action around insulin affordability. A little-reported Internal Revenue Service (IRS) rule change (notice 2019-45<sup>91</sup>) expanded the list of covered preventive care to include prescription drugs and some diagnostic tests used to manage selected chronic conditions, effective July 19, 2019.<sup>92</sup> The conditions targeted include heart disease, diabetes, asthma, depression and liver disease.

One notable feature of the rule change is that drugs are included, as are services that largely complement drug-based treatment adherence and are effective in sustaining health (including glucose testing strips and monitors). Specifically, the notice expanded the list of preventive care benefits permitted to be provided by a HDHP under section 223(c)(2) of the Internal Revenue Code without meeting the minimum deductible for a HDHP. HDHPs must satisfy certain requirements with respect to minimum deductibles and maximum out-of-pocket expenses and may not provide benefits for any year until the minimum deductible for that year is satisfied. Section 223(c)(2)(A) provides a safe harbor for the absence of a deductible for preventive care, which was used to expand qualified prevention services in the current notice.<sup>93</sup>

### 4.3.2 Extending the definition of preventive service benefits to include insulin

The change in the definition of preventive services covered by HDHPs might have wider implications for Americans insured by non-grandfathered group health plans and health insurance issuers offering insurance in the group and individual health markets.<sup>94</sup> Section 2713 of the PHS Act created the list of ten essential health benefits that all individual and small-group plans must cover. The same section also required insurance plans to provide access to preventive interventions with no cost-sharing.<sup>95</sup> Although this latter benefit primarily includes preventive services (such as blood pressure screenings, colonoscopies, or mammograms), it also includes many drug products, including immunizations, statins, and prescription contraceptive methods for most health plans.

Following the precedent of the IRS rule change for HDHPs, preventive services defined under Section 2713 of the PHS Act for individual and group plans could be expanded to include care for select chronic conditions, including insulin and related medical supplies. This change would likely require legislation, but it would have the advantage of pertaining to all types of private health plans – individual, small group, large group, and self-insured (ERISA) plans.<sup>96</sup> In a single stroke, nearly all plans would be required to provide first dollar coverage for insulin and related supplies, essentially solving the insulin unaffordability problem for most privately insured.<sup>97</sup>

There are tradeoffs to consider in extending the definition of preventive service benefits. The first tradeoff is related to the criteria for service inclusion. Too broad and the plans might lose negotiating



power with pharmaceutical companies, too narrow and the policy may not help enough patients. The recent HDHP notice does articulate some criteria for considering medical care services that could be classified as preventive care for someone with a chronic condition in the future, consistent with the structure and purposes of section 223(c)(2). The notice also suggests that the current list might be revisited and revised with these criteria in mind. The criteria for inclusion in the safe harbor entails that each medical service or product, when prescribed for an individual with the related chronic condition, must demonstrate three characteristics: (1) the service or item is low-cost; (2) there is medical evidence supporting high cost-efficiency (a large expected impact) of preventing exacerbation of the chronic condition or the development of a secondary condition; and (3) there is a strong likelihood, documented by clinical evidence, that with respect to the class of individuals prescribed the item or service, the specific service or use of the item will prevent the exacerbation of the chronic condition or the development of a secondary condition that requires significantly higher cost treatments. A good case could be made that insulin therapy for diabetic patients satisfies these criteria.

The second tradeoff is that payers may face increases in expenditures due to the absence of any patient cost sharing and potential increased utilization. A study modeling a policy of zero cost-sharing for enrollees in high-deductible commercial plans found that patient out-of-pocket savings on insulin spending were partially offset by other health care spending during the year that then went to meet the deductible. Beneficiaries with high insulin costs saved significantly on their insulin while average premiums per member were estimated to rise only about \$5 per year.<sup>98</sup>

#### 4.3.3 Addressing insulin coverage directly through state or federal law

State laws cover individual market and fully-insured group plans, while federal law covers self-insured, or ERISA-exempted, plans. Many states already mandate benefits for specific conditions that include prescription drug coverage. According to the National Conference of State Legislatures, 46 states and DC have some form of mandated coverage for diabetes treatment.<sup>99</sup> Going further, a state could choose to implement mandates for coverage and cost sharing for selected drug-based care including insulin. Seven states currently set caps on patient cost sharing for diabetes. Comparable federal law would also be needed to mandate requirements for low or now cost sharing under ERISA-exempted self-insured plans.

### 4.4 INSULIN AFFORDABILITY FOR UNINSURED PATIENTS

The real solution to affordability for those without insurance is to move further toward a system of universal health care coverage so there are no Americans without insurance. Until that time, those who must pay out-of-pocket for all their insulin products face the high list price at the pharmacy counter.

It would be preferable for the uninsured to be facing prices closer to the net price that insurers pay, especially since there is evidence that much of the growth in insulin list prices in recent years is due to the rebate system. However, allowing or requiring that the uninsured pay prices net of rebates will affect the



ability of insurers (or their PBMs) to negotiate those rebates in exchange for higher sales volume. If the cash price for an insulin is closer to the discounted price rather than the full list price, then that discounted price will be available to all patients, and PBMs will have much less leverage to direct patients to one product over another. In addition, any discounts offered will likely be much lower since manufacturers will know that they are reducing prices paid by the uninsured as well as those represented by the PBM.

For the uninsured, each of the three insulin manufacturers is currently providing patient assistance to limit or eliminate out-of-pocket costs. The [Novo Nordisk Patient Assistance Program](#) provides most Novo insulin products, including analogs, and a supply of pens and needles, free of charge for those with household incomes up to 400% of federal poverty level (FPL). The application for acceptance into the program is submitted through the provider, who indicates the insulins prescribed. If approved, the insulin products are sent to the provider in 120-day supply increments for distribution to the patient. For patients with incomes above 400% FPL, Novo Nordisk began the [My99insulin](#) program in January 2020, offering any patient without insurance a monthly supply of 3 insulin vials or 2 packs of insulin pens for \$99.

Similarly, the [Sanofi Patient Assistance Connection](#) offers uninsured patients with household incomes up to 400% FPL a free supply of Sanofi insulin sent to their provider in 90-day increments. For uninsured patients above the income threshold, Sanofi's [Insulins Valyou Savings Program](#) offers vial insulins for \$99 per month.

Eli Lilly's [Lilly Cares](#) program similarly offers free insulins to those without insurance and incomes at or below 400% FPL. As of April 2020, Lilly has also launched the [Lilly Insulin Value Program](#), offering anyone who is uninsured or who has commercial insurance a payment card to receive any Lilly insulin for a copayment of only \$35 per month.

For patients to fully benefit, it is critical that prescribing physicians are familiar with current programs, introduce them to patients who may need assistance, and engage in the process of applying for and distributing the products as needed.

Some states have passed requirements for drug manufacturers to cap out-of-pocket costs for insulin. In April 2020, Minnesota passed the Alec Smith Insulin Affordability Act, providing for emergency access to a 30-day supply of insulin with a maximum \$35 co-pay, and providing for longer-term insulin access by requiring manufacturers to offer a patient assistance program to Minnesotans earning under 400% of the federal poverty level who do not have access to affordable insulin, with limits on co-payments.<sup>100</sup> The law imposes financial penalties to insulin drug makers who do not offer this patient assistance. The current patient assistance programs offered by all three manufacturers appear consistent with Minnesota's requirements.



While these programs can provide relief to many patients, they can change or be discontinued at any time, especially if only a small number of states require them. In fact, some of the programs that are currently offered did not exist until 2020. Additionally, as biosimilars become more available, low or no cost-sharing programs can also be used to steer patients to branded drugs that are more expensive overall, raising drug spending and premiums. Nevertheless, without insurance coverage, these programs may be the best option for maintaining insulin access. While the spate of recent legislative proposals around insulin are evidence of enough political will to consider modifying public and private coverage or benefit rules to expand coverage of insulin, there is less evidence of a willingness to have the federal government invest in making insulin universally available.





## 5 Assessment of Strategies to Reduce Insulin Prices

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Insulin prices in the US are much higher than estimated manufacturing and distribution costs. US insulin prices are also much higher than prices in the rest of the world, even assuming large rebates off US list prices. Lower prices would make it easier for patients in the US to afford insulin and would lower the impact on insurance premiums (or tax expenditures) of policies to lower or remove the patient cost burden altogether.

Both increased market competition, and public-sector safeguards on excessive prices where competition is not yet possible, are needed. We assess strategies under both approaches, citing proposed legislation as examples where relevant. Many of the policies that will reduce insulin prices are systemic changes to improve the functioning of the market for biologics in general, whether in the patent process or in the path to biosimilar market entry. Implementing these types of policies will have an important impact on future US health spending more broadly, as most of the growth in drug spending is in specialty drugs. Policies such as requiring more information on manufacturer costs and setting reasonable upper bounds on initial pricing and annual price increases will better rationalize US prices for insulin and all drugs.

### 5.1 POLICIES TO INCREASE COMPETITION IN THE INSULIN MARKET

One impactful route to improving insulin affordability is through enhanced competition,<sup>101,102</sup> including policies that encourage insulin biosimilar entry into the US market, the substitution of biosimilars for more expensive brand-name products, and increased insulin product competition.

FDA analyses of price impacts of generic drug entry show that the greater the number of generic competitors, the greater the reduction in prices.<sup>103</sup> To increase competition, in addition to more biosimilar products, we would like to see new manufacturers enter the market beyond the three dominant players. Increased domestic insulin manufacturing capability could also serve US security interests in reducing our reliance on foreign drug manufacturing for essential medicines.

Most branded analog insulins will lose patent protection over the next few years, opening the door to competition from lower-priced biosimilar insulins.<sup>104</sup> The FDA has made important progress in defining a new regulatory pathway for biosimilar market entry, which officially took effect in March 2020. To date, the US market has two “authorized generic” rapid-acting insulin analogs, which are branded insulins sold by their manufacturers without the brand label; one biosimilar long-acting insulin analog by Eli Lilly based on Sanofi’s best-selling Lantus; and one “follow-on” rapid-acting insulin analog by Sanofi.

Researchers have estimated that biosimilar insulins could be manufactured and brought to market at prices well under \$10 a vial.<sup>105</sup> These findings show that biosimilars have the potential to be economically viable at prices much lower than current analog insulins, comparable to the 80% or more savings seen for small molecule generics. These potential reductions are much greater than either the previously modeled



estimates of potential biosimilar price reductions<sup>106</sup> or the 50% list price reductions currently offered on follow-on authorized generic insulins in the US market.

### 5.1.1 Accelerating the introduction of biosimilar insulins to the market

Many of the policies that should be pursued to reduce insulin prices are systemic changes to improve the functioning of the US market for biologics and biosimilars, whether in the patent process or in the path to biosimilar market entry and impact. Implementing these policies will be important not only for insulin prices but for US health spending more broadly, as most of the growth in drug spending is in specialty biologic drugs.

Nearly all the most popular modern branded insulins have either recently come off patent or will lose patent protection over the next few years, opening the door to competition from lower-priced biosimilar insulins. As we have noted, biosimilar insulins do not yet have a meaningful presence in the US market. The non-branded alternatives (follow-on products, “authorized generic” insulins from the existing brand manufacturers, and one biosimilar) available in the US today are priced from 15% to 50% lower than the branded reference product, but do not yet have significant uptake. With estimates that biosimilar insulins, both traditional and analog, could be manufactured and brought to market at prices under \$10 a vial, biosimilar insulins have the potential to provide significant pricing pressure.

As discussed earlier in this report, the FDA has been making important progress in better defining a new regulatory pathway for biosimilar approval and interchangeability. A continued commitment of resources must be made to maintain and even accelerate this process. As successful experience with biosimilar approval and interchangeability is demonstrated, drug makers will have more confidence in making the investment to bring a biosimilar to market.

### 5.1.2 Expanding the US supply of insulin beyond the current three suppliers

All authorized generic, follow-on, or biosimilar insulins currently in the US market are produced by one of the big three insulin manufacturers. The entrance of new competitors and more biosimilar alternatives are likely to increase downward pressure on insulin prices. Research by the FDA shows that large price reductions occur when there are three or more generic alternatives to a drug, and that reductions increase as the number of competitors increases.<sup>107</sup>

Increasing domestic drug manufacturing capacity in the US could also have national security benefits. The US today is highly dependent on foreign drug manufacturing. The [Government Accountability Office \(GAO\) reported](#) that in 2018, more than 80% of the active pharmaceutical ingredients (APIs) used in drugs sold in the US, and more than 40% of finished drugs, were manufactured outside the US.<sup>108</sup> Greater US drug manufacturing capacity could protect and stabilize the supply of essential products such as insulin or antibiotics, as health crises become increasingly global.



In the past year, several new initiatives have been launched to create new generic drug manufacturing enterprises, with the potential to include generic insulin production. [Civica Rx](#) is a non-profit partnering with more than 20 health systems to address chronic shortages and artificially high prices for essential, generic, hospital-based drugs. Civica Rx will enter into long-term contracts to manufacture or procure generic drugs prioritized by their health system partners to create a stable, affordable supply. Civica Rx has [already](#) begun to supply hospitals with needed antibiotics and sterile injectables, and has indicated they would consider taking on generic insulin, but it is not obvious that this would be a top priority among hospital-based drugs. However, this model is clearly disruptive, and payers have taken notice.

[EQRx, Inc.](#) launched in 2020 with the goal of developing and bringing new drugs to market at more affordable prices. The company has assembled an experienced team of drug industry-savvy executives and advisors, as well as investors. According to co-founder Dr. Peter Bach, “EQRx aims to create affordable new medicines that are priced for access, and accessibility is the critical attribute for every medicine if it is going to improve people’s health.”<sup>109</sup> EQRx is targeting development of 10 new drugs over the next decade.

A more direct approach to increasing manufacturing capacity for drugs that are in short supply or are subject to pricing failures would be to pass legislation calling for states or the federal government to commission new manufacturing activities. California recently introduced a bill calling for a state run or sponsored generic drug manufacturing capability to provide lower cost prescription drugs to Californians. At a national level, a bill introduced in 2018 and reintroduced in December 2019, the *Affordable Drug Manufacturing Act*, calls for the government to build or contract for the manufacturing of generic drugs to provide them at lower prices. Drugs that are targeted would need to be off patent and regulatory exclusivity or with patents claimed by the government. In its current form, the legislation specifies criteria such as lack of competition, for drugs that may be considered, but it also specifically calls out insulin and requires that the government begin the process to manufacture generic insulin in the first year. Finally, while focused now on drugs to treat COVID-19, the Trump administration through the Biomedical Advanced Research and Development Authority has contracted with the newly formed Phlow Corp. to domestically manufacture generic drugs and pharmaceutical ingredients.<sup>110</sup>

### 5.1.3 Allowing importation of lower cost insulin from other countries

The FDA must approve all drugs for sale in the US, including those manufactured outside the US. In general, if a drug has been approved in the US and a supply is available, importation or reimportation of a drug, even by individuals for their own use, is prohibited. Under current FDA guidance, the agency can allow importation of small amounts of drugs for personal use on a case-by-case basis, but only if no existing treatment exists in the US. While prohibited, some Americans do take their chances and make periodic trips to Canada and Mexico or use internet sites to purchase their insulin at lower cost, and the FDA has generally been lenient about this individual practice.<sup>111</sup>



FFDCA Sections 801 and 804 give the Department of Health and Human Services (HHS) authority to allow importation or reimportation of drugs in emergency circumstances such as a drug shortage. HHS also has authority to allow importation from Canada if the Secretary of HHS certifies that doing so would not pose additional risk to health and safety and would offer a significant cost reduction.<sup>112</sup> To date, HHS authority has been used to allow temporary importation of drugs during emergencies such as Hurricane Maria, but no Secretary has ever approved importation from Canada to lower cost.

In recent years, there have been several state and federal proposals to expand authorization of drug importation under specified conditions such as large domestic price increases for sole-source, off-patent drugs. Industry groups and others have opposed these proposals on drug safety grounds. In December 2019, the [administration proposed new rules](#) under FFDCA Section 804 laying out a process for HHS to approve applications from states or other non-federal entities to import drugs from Canada. Applicants must establish that safety can be assured, and costs reduced. Even if these proposed rules withstand pushback, drugs that are not covered statutorily by Section 804, including insulin and other biologics, would not be included.

While purchase from other countries such as Canada can provide relief for a subset of consumers who need a short-term solution to affording their insulin, it is unlikely to solve the US affordability problem in the long term. The processes required to ensure the safety and efficacy of imported drugs are burdensome, given that the US does not really need to import the insulin itself, only the price. Further, the US represents about 40% of the entire global insulin market, dwarfing most other country's insulin markets. In Canada specifically, there are about 3 million Canadians with diabetes. The *entire* insulin supply in Canada would cover only 10% of the US diabetic population, even supposing the Canadians were willing to give it up. Canadian health officials have already examined options for protecting their drug supply in response to various US proposals, including passing legislation to ban drug exports to the US.<sup>113</sup> Finally, any significant disruption of the US market such as wide scale importation would prompt a response from a drug industry that has proven adept at navigating global laws and regulations, and maintaining margins through sophisticated differential pricing.

#### 5.1.4 Revising US patent law to reduce excessive barriers to competition

The current systems of patents and market exclusivity have been leveraged to make the process for development and approval of biosimilar drugs longer and more burdensome for potential competitors. The global organization [I-MAK](#) seeks to increase access to medicines through improving global patent systems, advocating raising standards for what is deserving of a patent, examining incentives, increasing transparency, and expanding monitoring of patent systems.

In the US, approaches have been proposed to address excessive use of patents and to change aspects of the legal process that currently favor brand manufacturers.<sup>114</sup> All of these approaches, individually or in combination, can improve competition while still offering reasonable periods of R&D cost recovery.



**Reduce the practice of continual patent extensions for incremental changes.** The [Affordable Prescriptions for Patients Act of 2019](#) targets patent thickets and evergreening by defining certain practices currently used to accumulate and extend drug patents as antitrust violations; for example, obtaining patents for the use, formulation, or manufacturing of a drug after the expiration of the original patent on the active ingredient, or replacing a branded drug with a “follow-on” reformulation of the product to maintain patent protection against generic or biosimilar entry. The threat of antitrust enforcement has the potential to be an effective deterrent, as antitrust penalties can be significant. The brand manufacturer would have the burden of proof to establish that the benefits of its activities to patients or others outweigh the anticompetitive effects. The [Affordable Prescriptions for Patients Through Improvements to Patent Litigation Act](#) would set a limit of 20 patents that a brand manufacturer could assert against a biosimilar competitor. This bill seeks to simplify and shorten patent suits since currently hundreds of patents may be brought to bear, representing a significant time and cost barrier for biosimilars to gain market entry.

**Reduce barriers to getting past expired patent protections for biosimilar competitors.** For example, the [Terminating the Extension of Rights Misappropriated \(TERM\) Act](#) of 2019 would flip the burden of proof from the biosimilar developer to the brand manufacturer in establishing that a patent is still valid. Currently, manufacturers pursuing the practice of making minor changes to the product to establish “follow-on” patents and extend patent protection has little cost. Under the TERM Act, patent protection would be assumed to expire at the end date of the earliest-expiring patent on the drug unless the manufacturer could prove that any subsequent patents represented genuine innovations over the first patent.

Another approach is to bring transparency around patents for biologics in line with that of small molecule drugs. For example, the [Biologic Patent Transparency Act](#) of 2019 would increase the reporting requirements for patents on biologics so that biosimilar developers would have advance knowledge of the portfolio of patents around a brand drug. Currently, this information is required for small molecule drugs and publicly recorded by the FDA in the “Orange Book.” This bill would require similar detail in the comparable record of biosimilar drugs, the “Purple Book.” Any patent not listed by the manufacturer in the Purple Book could not be brought to bear against a biosimilar competitor.

**Shorten the market exclusivity period for biologics.** The [Price Relief, Innovation, and Competition for Essential Drugs Act](#) proposes to shorten the market exclusivity period granted by the FDA for biologics from 12 years to five years, consistent with the exclusivity period for small molecule drugs. Alternatively, the exclusivity period could be shortened to somewhere between five and 12 years, based on an analysis of how often and how long the market exclusivity period is the limiting factor to competition.



## 5.2 GOVERNMENT PRICE SETTING OR NEGOTIATION

It appears that the market for the current best-selling analog insulins is poised to become more competitive with the entry of biosimilars, especially if public and private actions to accelerate the process continue. Until the market competition puts more downward pressure on prices, and for future innovations that produce new patents and market exclusivity periods, the federal government should take a more direct role in reviewing and potentially limiting unreasonably high initial prices or rates of price growth. We cite several current examples of proposed legislation to set or limit prices or price growth.

Over the past several years, there has been much public discourse and proposed legislative action around tackling high insulin prices from both Congress and the administration. Both political parties are publicly in favor of addressing high drug prices, but none of the bills proposing to use federal authority to achieve this are likely to receive the bipartisan support needed to become law under the current Congress.

We support greater federal government participation in drug prices for several reasons. The US is one of the largest consumers of insulin in the world, with public programs funding three-quarters of insulin spending in the US, yet we do not fully leverage that market power to lower the cost to the US taxpayer. PBMs have demonstrated that they can negotiate large rebates when there is brand competition, but the size of the rebate can be an artifact of the list price, which we know has been rising faster than net prices for insulin. PBMs also have no impact on setting launch prices or on price increases, especially when manufacturers tend to move together.

We observe that the federal government already sets prices under publicly funded programs for health care services. Negotiated or specified drug prices would be analogous to the Medicare physician fee schedule or the hospital prospective payment rates that are set annually.

Of course, legislation could be passed to set or negotiate the price of insulins alone. Insulin affordability has popular appeal and this action could be counted as a win for drug price relief, while being limited enough in scope that it might be acceptable to drug manufacturers. This might represent spending a lot of political capital on changing the system for one drug, or it might establish insulin as a test case for broader reforms.

### 5.2.1 Allowing government negotiation of drug prices

There are numerous White House and Congressional proposals to allow the federal government to negotiate on behalf of people covered by Medicare.<sup>115</sup> All of these proposals would specifically replace subsection (i) of 42 U.S.C.A. § 1395w-111 governing Medicare negotiations, which currently provides that HHS, the agency that administers the Medicare program, “may not interfere with the negotiations between drug manufacturers and pharmacies and [prescription drug plan] sponsors” and “may not require a particular formulary or institute a price structure for the reimbursement of covered part D drugs.” In



place of this prohibition, these proposals would explicitly grant the Secretary of HHS the right to negotiate with pharmaceutical companies over the prices of drugs covered by Part D.

In most of these proposals, the negotiated rates would be available to other public plans, including Medicaid, and to private plans. All proposals include criteria for negotiating prices, the number of drugs that will be negotiated for annually and penalties for non-cooperation.

HR 3, the [Lower Drug Costs Now Act](#), would grant the Secretary of HHS the authority to negotiate the price of up to 250 drugs per year that are high cost and that do not have at least one generic or biosimilar competitor.<sup>116</sup> The negotiated rate would be available to the commercial market in addition to Medicare. The legislation creates a maximum price for any negotiated drug with an international price index, to be called the Average International Market price. While, as noted above, the government does not have the ability to refuse to cover any drug that has been proven effective, HR 3 gives significant leverage to the government by imposing non-compliance fees starting at 65% of the gross sales of the drug and increasing over time to 95% if the manufacturer refuses to participate or to reach an agreement.<sup>117</sup>

An approach used by other countries in assessing drug prices is value-based pricing, using cost-effectiveness analysis to compare the additional benefits offered by the drug to the additional cost. The work of the Institute for Clinical Evaluation and Research (ICER) provides cost-effectiveness analyses for many major pharmaceutical therapies in the US. HR3 incorporates a flavor of value-based pricing into the criteria for negotiating prices, which would include: (1) the therapeutic gain offered by the drug, (2) the cost of bringing the therapeutic class of drugs to market, (3) the current costs of treating the indicated disease, and (4) international prices charged for these drugs.<sup>118</sup>

One other Congressional proposal, the [‘Medicare Negotiation and Competitive Licensing Act’](#), introduced into the U.S. House of Representatives in February 2019 and sponsored by Lloyd Doggett and Sherrod Brown (HR 1046), is unique among current proposals in the penalties proposed. Under HR 1046, in the event the Secretary of HHS is “unable to successfully negotiate an appropriate price” for the drug, the bill authorizes the Secretary to grant a competitive license to another company to manufacture and sell the drug. This license would allow the other company the use of “any patent, clinical trial data, or other exclusivity granted by the federal government” to the innovator company. The license holder would also get priority review of its drug application by the FDA. In exchange for the license, the holder would have to provide “reasonable compensation [to the innovator company], as determined by the Secretary.”

The potential for government cost savings is substantial if Medicare could set drug prices as it sets annual payment rates and fee schedules for services like hospital stays and physician office visits. For insulin alone, a cost analysis found that in 2017, simply setting Medicare prices equal to the prices negotiated by the VA would have reduced spending on insulin from \$7.8 billion to \$5 billion, a savings of nearly \$3 billion.<sup>119</sup>





A simpler solution in the short run is to link the US price for a drug to an international index of prices for that drug in comparator countries.<sup>120</sup> This strategy allows the US to leverage other countries' discipline in assessing value and using national market power to negotiate prices, while not having to explicitly grant the US government the authority to negotiate. There would be complications, of course, including the inability to compare prices of drugs that are released first in the US, and, more importantly, the actions to counter this strategy that would undoubtedly follow from other countries and from drug manufacturers. Longer term, we believe it would be cleaner and better aligned with US culture and preferences to do our own negotiation.

### 5.2.2 Setting bounds on initial pricing or price increases

Two examples of proposed legislation to expand government authority over drug prices are the Prescription Drug Price Relief Act (PDPRA) of 2019 and the FLAT Prices Act. These bills and others being proposed are unlikely to pass in current form, but they are indicative of continued interest in legislative action on drug prices.<sup>121</sup>

The [PDPRA](#), among other things, would give the Secretary of Health and Human Services the authority to review the pricing of all brand-name drugs and biologics to determine whether such prices are “excessive,” and to take strong action if excessive pricing is found. The Secretary would be required to consider the value of the drug to patients, detailed manufacturing and research costs, and a comparison of the US price with the median price for the product in five comparator countries. Drug makers would be required to report annually on brand-name drug pricing, costs, revenues, R&D costs, and international prices. If the Secretary determined that the price of a brand-name drug was excessive, they would be authorized to “waive or void any government-granted exclusivities” and to issue “open, non-exclusive [compulsory] licenses” that allow competitors to “make, use, offer to sell or sell, and import [the brand-name drug] and to rely upon the regulatory test data.”

HR 1188, the [Forcing Limits on Abusive and Tumultuous \(FLAT\) Prices Act](#) would target high drug price increases by establishing consequences to major price hikes in the form of reductions to the drug's market exclusivity period.<sup>122</sup> Current FLAT Prices Act provisions state that price increases of more than 10% in one year, 18% in two years, or 25% over a three-year period would be subject to a reduction in the drug's market exclusivity period of up to 180 days.

### 5.2.3 Nationalizing ownership of insulin

HR 1046, discussed previously, shares similarities with [other existing](#) ‘compulsory licensing’ rules already enacted in the US. Perhaps the most important existing rule is [28 U.S. Code § 1498 \(“Section 1498”\)](#). Under Section 1498, the federal government has the power to use or manufacture any patented product including those related to administration devices if the government pays the patent owner a reasonable price. Section 1498 is a tool that the government once wielded with some frequency to tame high drug





prices. It was used routinely by federal agencies in the 1960s and early 1970s to obtain cheaper generic drugs, but its use waned as the pharmaceutical industry's power grew amid an altered political dynamic.<sup>123</sup>

In 1965, the pharmaceutical lobby tried and failed to amend Section 1498 to limit the law only to instances that implicated “national security.” Government officials strongly opposed any change that would “forgo one of the valuable powers which the Government has to assure fair prices” and to remedy “exorbitant pricing.” The rule remains intact today and was threatened to be invoked as late as 2017 by policymakers interested in increasing access and affordability to drugs to treat hepatitis C. Section 1498 is also used today in areas outside of prescription drugs. For example, the US Army Corps of Engineers relied on Section 1498 in the past decade to use patented methods to clean up hazardous waste.

Government compensation to companies for use of patented technologies has typically been settled at 10% of the company's sales of that technology. With sales in the billions of dollars, a 10% royalty on an insulin product could represent a large government expenditure. Drug companies strenuously argue that using Section 1498 to sidestep patent law and market pricing would reduce incentives to invest in innovation. Importantly, most of the commonly used analog insulins are coming off patent in the next few years. Perhaps the optimal strategy is using this power as a bargaining tool, as in 2001, when Secretary of Health and Human Services Tommy Thompson pressured Bayer to reduce the price of an antibiotic to treat anthrax by 50% simply by threatening to invoke Section 1498.

### 5.3 PROTECTING FUTURE AFFORDABILITY AND INNOVATION

Insulin therapy and active disease management has greatly improved life with diabetes, but the disease is still a daily burden to patients and can lead to disability and premature death. The millions of Americans with diabetes, and our society overall, will be well served by continued innovation in the treatment of this disease. There are promising paths to better-automated blood sugar control and even potential cures through replacing or rejuvenating the pancreas. But new innovations will mean new patents and pricing power, countering our efforts to ensure widespread affordability.

The private sector currently funds about three-quarters of medical R&D.<sup>124</sup> The current US system allows for recovery of R&D investments through market protection periods and relatively unrestricted drug pricing with no public understanding of the underlying cost basis. To increase transparency and get more specific about threats to innovation from various drug pricing policies, the federal government could require manufacturers to submit as part of the drug approval process an accounting of R&D costs associated with the drug and an estimate of manufacturing costs, much as hospitals who receive public payer funding must submit annual Medicare Cost Reports.

A more disruptive option would be to separate the costs of R&D from the market price of the drug by increasing federal funding for pharmaceutical R&D, at the same time requiring prices for approved drugs to be more closely related to manufacturing costs. While unlikely to be politically palatable in the near



term, this strategy would have the advantage of allowing research funding to be prioritized according to an assessment of societal need rather than being motivated by market or profitability potential.

Finally, we note that drug pricing and policy debates in the US tend to be framed as if we alone are responsible for the profitability and incentives for innovation of the pharmaceutical industry. The US is a large drug market but not the only market. Nor is all drug R&D done in the US. Again, in the case of insulin, only one of the three dominant drug makers, Eli Lilly, is an American company. In taking the action needed to rationalize US drug prices in the long run, we must consider the impact on new drug development, but recognize that the rest of the world has a significant stake and presence in pharmaceutical innovation as well.

#### 5.4 ADDENDUM: COVID-19 AND INSULIN AFFORDABILITY

With the world turned upside down due to the COVID-19 pandemic, it was important to reflect on what this might mean for insulin affordability and US drug policy. There are several emerging themes following the passage of the [Coronavirus Aid, Relief, and Economic Security \(CARES\) Act](#).

First, this pandemic created an affordability imperative for all essential health care goods and services. Legislation was developed and passed with extraordinary speed to ensure first-dollar coverage of COVID-19 testing and costs across all payers (though there are outstanding issues about surprise bills). Clearly, then, it can be done. Lessons from this success could be applied to legislatively address the patient cost burden for insulin and diabetic supplies. Insulin affordability is less time-critical for the nation than responding to a pandemic, but it is a life or death issue nonetheless for millions of people.

Second, with passage of three COVID-19 legislative actions – including the single highest cost legislation in US history – and a fourth under discussion, we are in a period where federal spending that increases the debt must be made to protect the health of Americans and save our economy. Again, the timing may be right for aggressive policy to make insulin therapy more affordable with less focus on short-term fiscal restraint.

Finally, this pandemic has highlighted the interconnected global drug supply chain and the strong US dependence on foreign pharmaceutical manufacturing. It seems an appropriate time to pursue increasing domestic drug manufacturing capability both to increase competition and from a national security perspective, to better ensure a stable supply of critical prescription drugs like insulin and antibiotics, as well as new vaccines and therapies.



## Acronyms

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ACA	[Patient Protection and] Affordable Care Act
API	Active Pharmaceutical Ingredient
BPCIA	Biologics Price Competition and Innovation Act
CARES	Coronavirus Aid, Relief, and Economic Security
CBO	Congressional Budget Office
CDC	Centers for Disease Control and Prevention
CGM	Continuous glucose monitor
CMS	Centers for Medicare & Medicaid Services
COVID-19	<u>C</u> oronavirus <u>D</u> isease (pandemic) caused by the novel SARS-CoV-2 coronavirus
CRS	Congressional Research Service
DOD	Department of Defense
ERISA	Employee Retirement Income Security Act
FDA	Food and Drug Administration
FLAT	Forcing Limits on Abusive and Tumultuous [Prices Act]
FFDCA	Federal Food, Drug, and Cosmetic Act
GAO	Government Accountability Office
HDHP	High-deductible health plan
HHS	[Department of] Health and Human Services
HR	House Resolution
IRS	Internal Revenue Service
JAMA	Journal of the American Medical Association
LIS	Low-income subsidy
MedPAC	Medicare Payment Advisory Commission
NDA	New drug application
PBM	Pharmacy Benefit Manager
PDPRA	Prescription Drug Pricing Reduction Act



PHS	Public Health Service
R&D	Research and development
TERM	Terminating the Extension of Rights Misappropriated [Act]
USPTO	United States Patent and Trademark Office
VA	Veterans Affairs



## Endnotes

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<sup>81</sup> Dusetzina S, Huskamp H, Keohane L & N Keating, “Medicare Part D and Insulin Affordability – The Devil Is in the Details,” New England Journal of Medicine, April 1, 2020. DOI: 10.1056/NEJMp2001649 <https://www.nejm.org/doi/full/10.1056/NEJMp2001649>

<sup>82</sup> Thomas, Katie. “Insulin Costs May Be Capped in a Medicare Program” The New York Times. March 11, 2020. <https://www.65incorporated.com/topics/medicare-part-d-prescription-drug-plans/medicare-announces-2014-part-d-costs/>

<sup>83</sup> Patients covered by plans with fixed copayments on prescription drugs, rather than coinsurance percentages, would not be impacted by a “pass through” of rebates as their payment is not dependent on the drug price.

<sup>84</sup> Trish E, Kaiser K, and J Geoffrey. “How Would Sharing Rebates at the Point of Sale Affect Beneficiary Cost-Sharing in Medicare Part D?” USC Schaeffer Center, March 2020. Available at [https://healthpolicy.usc.edu/wp-content/uploads/2020/03/Sharing\\_Rebates\\_at\\_POS\\_Beneficiary\\_Cost-Sharing\\_Medicare\\_PartD\\_WhitePaper.pdf](https://healthpolicy.usc.edu/wp-content/uploads/2020/03/Sharing_Rebates_at_POS_Beneficiary_Cost-Sharing_Medicare_PartD_WhitePaper.pdf)

<sup>85</sup> Health and Human Services. 42 CFR Part 1001. Fraud and Abuse; Removal of Safe Harbor Protection for Rebates Involving Prescription Pharmaceuticals and Creation of New Safe Harbor Protection for Certain Point-of-Sale Reductions in Price on Prescription Pharmaceuticals and Certain Pharmacy Benefit Manager Service Fees. February 6, 2019. Available at: <https://www.regulations.gov/contentStreamer?documentId=HHSIG-2019-0001-0001&contentType=pdf>

<sup>86</sup> Congressional Budget Office. “Incorporating the Effects of the Proposed Rule on Safe Harbors for Pharmaceutical Rebates in CBO’s Budget Projections—Supplemental Material for Updated Budget Projections: 2019 to 2029,” May 2019, available at: <https://www.cbo.gov/system/files/2019-05/55151-SupplementalMaterial.pdf>

<sup>87</sup> DiGrande, Samantha. “[Insurance Guidelines Lead to Greater Out-of-Pocket Costs for Patients With MS.](#)” American Journal of Managed Care. February 9, 2019.

<sup>88</sup> Recent Medicaid Prescription Drug Laws and Strategies. “[National Conference of State Legislatures.](#)” August 8, 2018.

<sup>89</sup> Dusetzina, Stacie, Shelly Jazowski, Ashley Cole, Joehl Nguyen. “[Sending the wrong price signal: why do some brand name drugs cost Medicare beneficiaries less than generics?](#)” Health Affairs. July 2019.

<sup>90</sup> Avalere. “[Medicare Part D Generic Drug Tiering Request for Comment: Implications for Patient Out-of-Pocket Spending and Part D Plan Costs.](#)” February 2019.

<sup>91</sup> <https://www.irs.gov/pub/irs-drop/n-19-45.pdf>

<sup>92</sup> On June 24, 2019, President Trump issued Executive Order 13877,3 “Improving Price and Quality Transparency in American Healthcare to Put Patients First.” In this executive order the President directed the Internal Revenue Service and the department of the Treasury to consider ways to expand the use and flexibility of Health savings Accounts (HSAs) and high deductible health plans (HDHPs).

<sup>93</sup> Under section 223(c)(2)(C), “[a] plan shall not fail to be treated as a high deductible health plan by reason of failing to have a deductible for preventive care (within the meaning of section 1861 of the Social Security Act, except as otherwise provided by the Secretary).” Therefore, an HDHP may provide preventive care benefits without a deductible or, subject to any applicable requirements under section 2713 of the Public Health Service Act (PHS Act), with a deductible below the minimum annual deductible otherwise required by section 223(c)(2)(A).



<sup>94</sup> Notice 2004-23 (2004-1 C.B. 725), and Q&As 26 and 27 of Notice 2004-50 (2004-2 C.B. 196), provide guidance on preventive care benefits allowed to be provided by an HDHP without regard to the minimum deductible requirement of section 223(c)(2)(A). Notice 2004-23 clarifies that preventive care generally does not include any service or benefit intended to treat an existing illness, injury, or condition.

<sup>95</sup> Specifically, Notice 2013-57 (2013-40 I.R.B. 293) released in 2013 provides that any item that is a preventive service under section 2713 of the Public Health Service (PHS) Act will also be treated as preventive care under section 223(c)(2)(C) by the IRS. Section 2713 of the PHS Act was added by the ACA, which also added section 715(a)(1) to the Employee Retirement Income Security Act (ERISA) of 1974.

<sup>96</sup> Fernandez B, Forsberg V & R Rosso, “Federal Requirements on Private Health Insurance Plans,” Congressional Research Service, August 28, 2018. <https://fas.org/sqp/crs/misc/R45146.pdf>

<sup>97</sup> Grandfathered plans are a small category exempted from these requirements.

<sup>98</sup> Berman M, Lain S & L Metz, “Mitigating out-of-pocket costs for insulin users,” Milliman, commissioned by Eli Lilly. May 2019. Available at: <https://milliman-cdn.azureedge.net/-/media/milliman/importedfiles/ektron/mitigating-costs-insulin-users.ashx>

<sup>99</sup> <https://www.ncsl.org/research/health/diabetes-pharmaceuticals-state-mandates.aspx>

<sup>100</sup> <https://www.revisor.mn.gov/laws/2020/0/Session+Law/Chapter/73/>

<sup>101</sup> <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-agencys-continued-efforts-bring-competition-insulin>

<sup>102</sup> <https://www.healthaffairs.org/doi/10.1377/hblog20191212.286621/full/>

<sup>103</sup> Conrad R & R Lutter, “Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition to Lower Generic Drug Prices,” US Food and Drug Administration, December 2019. <https://www.fda.gov/media/133509/download>.

<sup>104</sup> Kaplan W & R Beall, “The global intellectual property ecosystem for insulin and its public health implications: an observational study.” J Pharm Policy Pract. 2017; 10: 3. Published online 2016 Jul 19. doi: 10.1186/s40545-016-0072-8 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4955122/>

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<sup>106</sup> Mulcahy A, Predmore Z & S Mattke, “The Cost Savings Potential of Biosimilar Drugs in the United States,” RAND Corporation 2014 (see Table 1).

<sup>107</sup> Conrad R and R Lutter, Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices, US Food and Drug Administration, December 2019. Available at <https://www.fda.gov/media/133509/download>

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<sup>109</sup> <https://www.eqr.com/press-release/eqrx-launches-to-create-innovative-medicines-at-dramatically-lower-prices-for-people-healthcare-systems-and-society/>

<sup>110</sup> Stolberg S & K Thomas, “Trump to Tap New Company to Make Covid-19 Drugs in the U.S.” The New York Times, May 18, 2020. <https://www.nytimes.com/2020/05/18/us/politics/trump-coronavirus-drug-manufacturing.html>



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