



# Humulin R U-500 KwikPen<sup>1</sup> Affordability Review

## Version 1



<sup>1</sup> Image. [https://mydiabetesvillage.com/272-2/ht\\_160127\\_humulin\\_r\\_u500\\_pen\\_800x600/#](https://mydiabetesvillage.com/272-2/ht_160127_humulin_r_u500_pen_800x600/#). ©Lilly USA, LLC. Accessed 1/8/2024.

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## Review Summary

The Prescription Drug Affordability Board (PDAB) conducted an affordability review for Humulin R U-500 KwikPen. The Oregon All Payer All Claims (APAC) reporting program indicated the drug was prescribed to 166<sup>2</sup> Oregonians in 2022 with a prescription drug benefit from a health insurance carrier. Medicaid and Medicare data was excluded from the APAC analysis.

Table 1 Summary of costs to the patient

Costs to the patient		
	Source	Amount
Average annual out of pocket cost per patient	APAC	\$164.56

Table 2 Summary of costs to the healthcare system

Costs to the healthcare system		
	Source	Amount
Total annual cost for payers <sup>3</sup>	APAC	\$1,992,616
Average annual cost for payers per enrollee <sup>4</sup>	APAC	\$12,003.71
Annual drug gross cost per enrollee	Data call <sup>5</sup>	Drug not on data call
Average annual drug net cost	Data call	Drug not on data call
Percentage of drug price concessions	Data call	Drug not on data call
Average Quarterly Medicaid fee for service cost <sup>6</sup>	OSU Drug Research Management Utilization Reports 2022 <sup>7</sup>	Drug not on report

<sup>2</sup> Number of 2022 unique enrollees from Oregon's All Payers All Claims (APAC) data excluding Medicaid and Medicare. For more information regarding APAC data visit:

<https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx>

<sup>3</sup> Excludes Medicaid and Medicare.

<sup>4</sup> Ibid.

<sup>5</sup> Data call refers to cost information collected from the health insurance plans by the Department of Consumer and Business Services on prescription drugs under both pharmacy and medical benefits after price concessions.

<sup>6</sup> Quarterly metric used in lieu of annual as the drug may not have been on the 2022 reports for all four quarters.

<sup>7</sup> Source: Oregon State University Drug Use and Research Management DUR utilization reports 2022. [DUR Reports | College of Pharmacy | Oregon State University.](#)

## Review background

Senate Bill 844 (2021) created the Prescription Drug Affordability Board (PDAB) to evaluate the cost of prescription drugs and protect residents of this state, state and local governments, commercial health plans, health care providers, pharmacies licensed in Oregon and other stakeholders within the health care system from the high costs of prescription drugs.

In accordance with OAR 925-200-0020, the Prescription Drug Affordability Board (PDAB) will conduct an affordability review on the prioritized subset of prescription drugs, selected under OAR 925-200-0010, and identify nine prescription drugs and at least one insulin product that may create affordability challenges for health care systems or high out-of-pocket costs for patients in Oregon.

Information in this report was provided by the Department of Consumer and Business Services (DCBS) for the PDAB to review per ORS 646A.694.

Additional information for this review was gathered from Oregon's All Payers All Claims (APAC) database, state licensed insurance carriers responding to a DCBS data call, Medi-Span, and resources from the U.S. Food and Drug Administration (FDA) such as the Orange Book (small molecule drugs) and the Purple Book (biologics).

## Drug information

Drug proprietary name(s): **Humulin R U-500 KwikPen**

Non-proprietary name: **Insulin Regular (Human)**

### FDA approval

Humulin R U-500 KwikPen was first approved by the FDA on 12/29/2015.<sup>8</sup>

The drug qualified for the following expedited forms of approval: None.

At the time of the review, the drug had no approved indications with designations under the Orphan Drug Act.

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<sup>8</sup> FDA approval date based on the earliest occurring approval dates in the FDA Orange/Purple Book. For drugs with multiple forms/applications, the earliest approval date across all related FDA applications was used.

## Clinical profile

### Drug indications<sup>9</sup>

- FDA Approved:
  - To improve glycemic control in adults and pediatric patients with diabetes mellitus and requiring more than 200 units of insulin per day.
- Off Label Uses:
  - None

### Clinical Efficacy<sup>10</sup>

- The insulin regular U-500 pen was approved by FDA in 2016 to provide an alternative to the U-500 vial and reduce medication errors associated with the concentrated insulin (500 units/ml).<sup>11</sup> A specific syringe for U-500 insulin was also approved to reduce dosing errors.
- There are no controlled, prospective trials evaluating insulin regular U-500 on clinically important outcomes.
- Retrospective data suggests improvements in glycemic control for patients requiring high daily insulin doses when switching from insulin U-100 to U-500.<sup>12</sup> One open-label, 24 week, randomized controlled trial compared twice daily U-500 insulin to three times daily U-500 in patients on at least 200 units of U-100 regular insulin per day (n=325).<sup>13</sup> Both dosing regimens showed similar reductions (>1%) in hemoglobin A1c (HgA1c) with a treatment difference of –0.10% (95% CI (Confidence Interval) –0.33 t 0.12%) and a weight gain of approximately 5 kg in each group.<sup>14</sup>
- There are no clinical trials with insulin U-500 in combination with other insulin formulations.

### Clinical Safety<sup>15</sup>

- FDA safety warnings:
  - Hypoglycemia
  - Hyper- or hypoglycemia due to medication errors or changes in insulin products
  - Hypersensitivity reactions
  - Hypokalemia

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<sup>9</sup> Humulin R U-500 Prescribing Information. Eli Lilly and Company. Indianapolis, IN. 2022.

<sup>10</sup> Ibid.

<sup>11</sup> Institute for Safe Medication Practices. As U-500 insulin safety concerns mount, it's time to rethink safe use of strengths above U-100. Available from [www.ismp.org/newsletters/acutecare/showarticle.aspx?id=62](http://www.ismp.org/newsletters/acutecare/showarticle.aspx?id=62).

<sup>12</sup> Reutrakul S, Wroblewski K, Brown RL. Clinical use of U-500 regular insulin: review and meta-analysis. J Diabetes Sci Technol. 2012 Mar 1;6(2):412-20.

<sup>13</sup> Hood RC, Arakaki RF, Wysham C, et al. Two treatment approaches for human regular u-500 insulin in patients with type 2 diabetes not achieving adequate glycemic control on high-dose u-100 insulin therapy with or without oral agents: a randomized, titration-to-target clinical trial. Endocr Pract. 2015 Jul;21(7):782-93.

<sup>14</sup> Ibid.

<sup>15</sup> Humulin R U-500 Prescribing Information. Eli Lilly and Company. Indianapolis, IN. 2022.

- Do not administer U-500 regular insulin without a dedicated U-500 insulin syringe. Do you mix with other insulin formulations.
- Common side effects:
  - Hypoglycemia, injection site reactions, weight gain, peripheral edema
- Safety advantages or disadvantages
  - Possible lower chance of dosing errors with U-500 Kwikpen compared to U-500 vial. Dosing errors have occurred when the U-500 dose was administered using syringes intended for U-100 insulin.
  - Due to the longer duration of U-500, severe hypoglycemia may develop as long as 18 to 24 hours after a dose.

### Therapeutic alternatives<sup>16</sup>

Table 3 Alternative short-acting insulin

Drug	FDA Approved Indications	Onset	Duration	Frequency	Formulations
<b>Insulin Regular 500 units/ml</b> <i>(subject drug)</i>	Diabetes Mellitus in patients requiring >200 units/day	15 minutes	~21 hours	Two or three times daily before meals	<ul style="list-style-type: none"> <li>● U-500 vial</li> <li>● U-500 Kwik pen</li> </ul>
<b>Insulin Regular 100 units/ml</b>	Diabetes Mellitus	30 minutes	~8 hours	Two or three times daily before meals	<ul style="list-style-type: none"> <li>● U-100 vial</li> <li>● U-100 pen</li> </ul>
<b>Insulin NPH/Regular Insulin 70/30</b>	Diabetes Mellitus	30 minutes	~ 23 hours	Twice daily before meals	<ul style="list-style-type: none"> <li>● 70/30 vial</li> <li>● 70/30 pen</li> </ul>

### Comparative effectiveness to therapeutic alternatives:

- Regular insulin U-500 is concentrated insulin with different pharmacokinetic properties, including a delayed onset and longer duration of action, than traditional U-100 regular insulin. It acts more like an intermediate-acting (NPH) insulin and can be used as insulin monotherapy in select patients, providing both prandial and basal coverage. It allows for

<sup>16</sup> Therapeutic alternative to mean a drug product that contains a different therapeutic agent than the drug in question, but is FDA-approved, compendia-recognized as off-label use for the same indication, or has been recommended as consistent with standard medical practice by medical professional association guidelines to have similar therapeutic effects, safety profile, and expected outcome when administered to patients in a therapeutically equivalent dose. OAR 925-200-0020(2)(c) [PDAB 1-2023: Prescription Drug Affordability Review \(oregon.gov\)](#). Accessed 01/09/2024.

small volume in those requiring high doses (>200 units) of insulin per day, which may result in decreased number of injections, decreased pain, and improved adherence.<sup>17</sup>

- There are no large prospective randomized trials comparing insulin U-500 with other insulins. Clinical guidelines do not give specific recommendations for concentrated U-500 regular insulin.

## Cost profile

### Pricing information

The package wholesale acquisition cost (WAC) for Humulin R U-500 KwikPen (NDC 00002882427) was \$574.20 as of 01/08/2024.<sup>18</sup>

The WAC for the drug was reviewed using Medi-Span's price history tables for the package WAC from 2019 to 2023. From 2019-2023 the average year-over-year change to the package WAC was calculated and determined to be 0%. This historical change in the package WAC is displayed in Figure 1 and the year over year change in WAC for Humulin R U-500 KwikPen compared to inflation rates<sup>19</sup> is displayed in Figure 2.

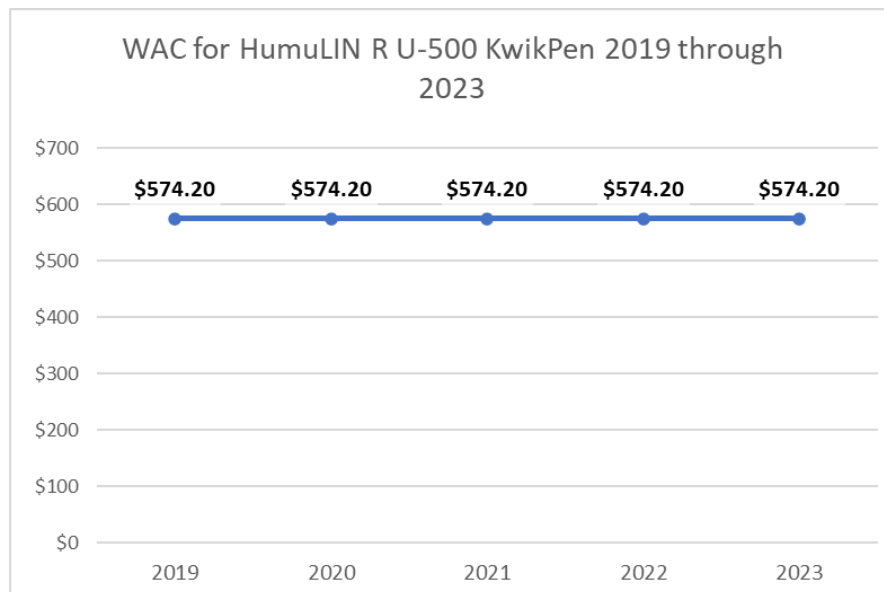


Figure 1 Humulin R-U-500 KwikPen WAC over time

<sup>17</sup> Kabul S, Hood RC, Duan R, DeLozier AM, Settles J. Patient-reported outcomes in transition from high-dose U-100 insulin to human regular U-500 insulin in severely insulin-resistant patients with type 2 diabetes: analysis of a randomized clinical trial. *Health Qual Life Outcomes*. 2016 Sep 30;14(1):139.

<sup>18</sup> To determine which NDC to use for the WAC price history, the available 2022 utilization data was analyzed and the NDC with the highest volume of claims in 2022 was used.

<sup>19</sup> Inflation rates obtained from the US Bureau of Labor Statistics website. Accessed from page <https://www.bls.gov/cpi/tables/supplemental-files/> on 01/08/2024.

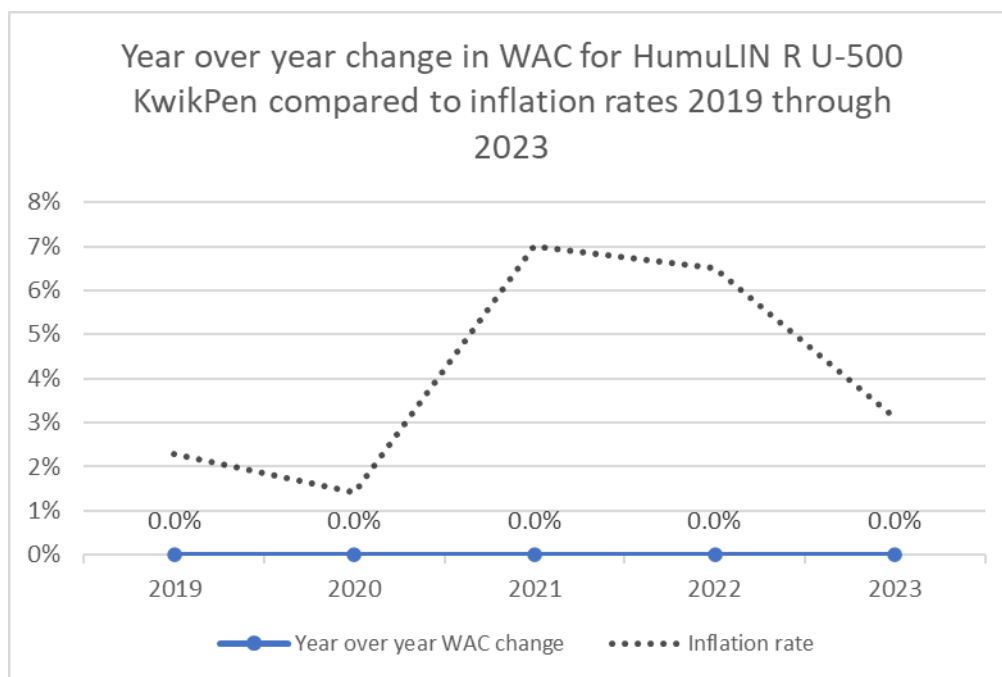


Figure 2 Year over year change in WAC compared to inflation rates<sup>20</sup>

Package WAC was reviewed as an indication of historic price trends for the drug. However, WAC does not account for discounts, rebates, or other changes to the drug’s cost throughout the supply chain.

No additional data or information was found or provided to reflect the relative financial effects of the prescription drug on broader health, medical, or social services costs, compared with therapeutic alternatives or no treatment.

No additional data or information was found or provided to quantify the total cost of the disease and the drug price offset.

### Cost to stakeholders

#### Cost to patients

The APAC database<sup>21</sup> was analyzed to determine the average patient copayment or other cost-sharing for the prescription drug.

<sup>20</sup> Inflation rates obtained from the US Bureau of Labor Statistics website. Accessed from page <https://www.bls.gov/cpi/tables/supplemental-files/> on 01/08/2024.

<sup>21</sup> Costs from the All Payers All Claims (APAC) database are prior to any price concessions such as discounts or coupons. Cost information from the data call is the cost of the drug after price concessions.



Table 4 Out of Pocket Costs

2022 Average annual patient out of pocket costs <sup>22</sup>		
Value	APAC	Data Call
Average Co-Pay	\$122.25	Drug not on data call
Average Deductible	\$7.23	Drug not on data call
Average Coinsurance	\$35.08	Drug not on data call
Other Cost Sharing	\$0	Drug not on data call
<b>Total Out-of-Pocket Costs for Patients<sup>23</sup></b>	<b>\$164.56</b>	Drug not on data call

Cost to health benefit plans

The APAC database<sup>24</sup> was analyzed to determine both the total annual spend and cost per patient for health insurance benefit plans.

Table 5 2022 Annual costs to health plans

2022 Annual costs to health plans <sup>25</sup>		
Value	APAC <sup>26</sup>	Data Call <sup>27</sup>
Total Annual Spend	\$1,992,615.97	Drug not on data call
Total Annual Spend per Patient	\$12,003.71	Drug not on data call

Cost to the state insurance programs<sup>28</sup>

Table 6 Gross amount paid by Medicaid CCOs

Gross amount paid fee for Medicaid CCO			
Drug	Amount paid	Claim count	Average paid per claim
Humulin R U-500 KwikPen	\$1,598,148.87	995	\$1,606.18

<sup>22</sup> Medicaid and Medicare were excluded from cost information.

<sup>23</sup> For patients who used the drug at least once in the 2022 calendar year.

<sup>24</sup> Costs from the All Payers All Claims (APAC) database are prior to any price concessions such as discounts or coupons. Cost information from the data call is the cost of the drug after price concessions.

<sup>25</sup> Medicaid and Medicare were excluded from cost information.

<sup>26</sup> APAC total cost may include a dispensing fee and physician administration fees.

<sup>27</sup> Data call information is only a sample from health insurance carriers and therefore will have a lower total annual spend amount than APAC data. Data call spend information includes discounts, rebates, and other price concessions.

<sup>28</sup> Source: Oregon State University Drug Use and Research Management DUR utilization reports 2022. [DUR Reports | College of Pharmacy | Oregon State University](#)

No additional data or information was found or provided to reflect the relative financial effects on health, medical, or social services costs, compared with therapeutic alternatives or no treatment.

## Cost of Therapeutic Alternatives

Table 7 Therapeutic alternative (TA) comparison

	NDC	Drug Name	Package size	2022 WAC package size	Package strength	2022 WAC unit price	AAAC <sup>29</sup>	NADAC <sup>30</sup>
Subject drug	00002882427	Humulin R U-500 KwikPen	2 cartridges per box	\$574.20	3 mL	\$95.70	\$92.18	\$91.61
Therapeutic alternative	00002850101	Humulin R U-500 (concentrated)	1 vial	\$1,487.00	20 mL	\$74.35	\$71.75	\$71.06
Therapeutic alternative	00002821501	Humulin R U-100	1 vial	\$148.70	10 mL	\$14.87	N/A	\$14.28
Therapeutic alternative	00002871501	Humulin 70/30	1 vial	\$148.70	10 mL	\$14.87	N/A	\$14.28

Humulin R U-500 KwikPen was compared to three therapeutic alternatives. Price comparisons were made between the wholesale acquisition cost (WAC), the National Average Drug Acquisition Cost (NADAC), and the Average Actual Acquisition Cost (AAAC). The percentage difference between the therapeutic alternative NADAC was compared to the baseline drug's NADAC. The NADAC percentage indicates that the Humulin R vial is 541.5% less expensive than the baseline Humulin R U-500 KwikPen.

<sup>29</sup> Oregon Average Actual Acquisition Cost (OR-AAAC) means the rate that is established by the Division or its contractor by rolling surveys of enrolled pharmacies to verify the actual invoice amount paid by the pharmacy or corporate entity to wholesalers, manufacturers, or distribution centers for the product.

<sup>30</sup> National Average Drug Acquisition Cost (NADAC) means the rate that is established by CMS or its contractor by rolling surveys of pharmacies nationwide to verify the actual invoice amount paid by the pharmacy or corporate entity to wholesalers, manufacturers, or distribution centers for the product. [https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=242930#:~:text=\(y\)%20%E2%80%9COregon%20Average%20Actual,distribution%20centers%20for%20the%20product.](https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=242930#:~:text=(y)%20%E2%80%9COregon%20Average%20Actual,distribution%20centers%20for%20the%20product.)

## Access profile

### Utilization and Health Equity

#### Humulin Impact of diabetes in the community

According to the CDC, in 2021 8.9% of the US population (all age groups) had diagnosed diabetes.<sup>31</sup> Of those diagnosed with diabetes, 5.7% of US adults reported using insulin to treat type 1 diabetes. In 2013, 8.3% of Oregon adults aged 18 or older reported being diagnosed with diabetes.<sup>32</sup>

The prevalence of diabetes varies widely by race and ethnicity, education level, and family income level. According to a 2019-2021 national health interview survey, of US adults 18 years or older, 6.9% of people who identified as white, non-Hispanic were diagnosed with diabetes compared to 9.1% of people who identified as Asian, 11.7% of people who identified as Hispanic, 12.1% of those who identified as black, non-Hispanic, and 14.5% of people who identified as American Indian or Alaska Native.<sup>33</sup> Education also showed a relationship to adults diagnosed with diabetes, with 13.1% of adults with less than a high school level of education, compared to 6.9% of adults with more than a high school level education.<sup>34</sup> Family income level also showed a relationship to adults diagnosed with diabetes, 13.1% of adults with a family income level less than 100% of the federal poverty income level were diagnosed with diabetes compared to only 5.1% of adults with a family income level of 500% or more over the federal poverty income level.<sup>35</sup>

To review how the prevalence of diabetes ranges throughout Oregon, Figure 3 shows 2018 rates of diabetes by county from the CDC website.<sup>36</sup> In addition to the rate of diabetes, the data included the Social Vulnerability Index (SVI) scores for each county.

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<sup>31</sup> Centers for Disease Control and Prevention. Estimates of Diabetes and Its Burden in the United States Available at <https://www.cdc.gov/diabetes/data/statistics-report/index.html>. Accessed on 12/11/2023

<sup>32</sup> Centers for Disease Control and Prevention. Diabetes State Burden Toolkit, Oregon Health Burden. Available at: <https://nccd.cdc.gov/Toolkit/DiabetesBurden/Prevalence>. Accessed on 01/04/24

<sup>33</sup>Centers for Disease Control and Prevention. By the Numbers: Diabetes in America. Available at: <https://www.cdc.gov/diabetes/health-equity/diabetes-by-the-numbers.html>. Accessed on 12/11/2023.

<sup>34</sup> Ibid

<sup>35</sup> Centers for Disease Control and Prevention. By the Numbers: Diabetes in America. Available at: <https://www.cdc.gov/diabetes/health-equity/diabetes-by-the-numbers.html>. Accessed on 12/11/2023.

<sup>36</sup> Centers for Disease Control and Prevention. US Diabetes Surveillance System website. Diabetes analysis, Oregon 2018. Available at <https://gis.cdc.gov/grasp/diabetes/diabetesatlas-analysis.html>. Accessed on 12/11/2023.

### Oregon Counties Social Vulnerability Map<sup>37</sup>

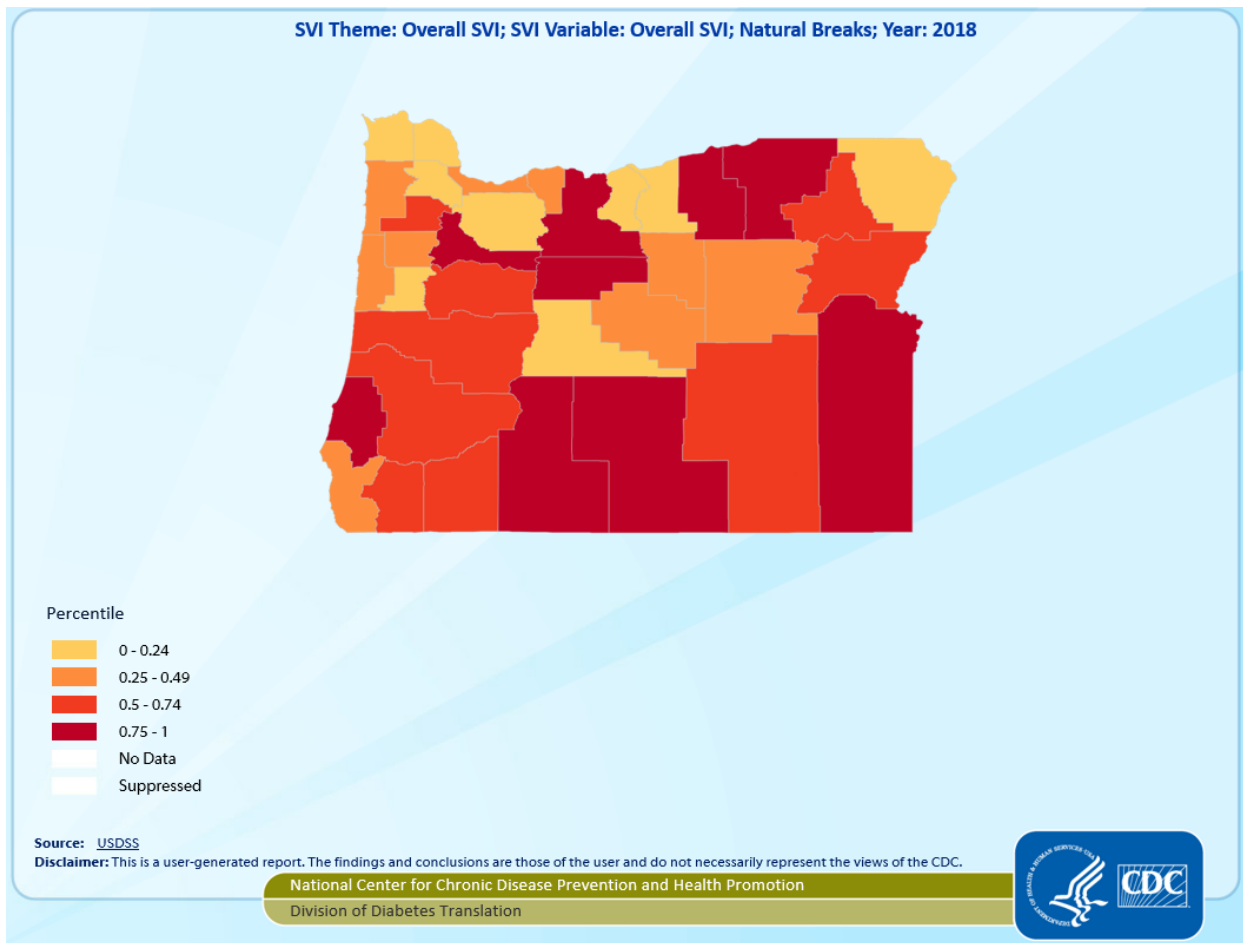


Figure 3 Oregon Counties Social Vulnerability Map

<sup>37</sup> Centers for Disease Control and Prevention. US Diabetes Surveillance System website. Diabetes analysis, Oregon 2018. Available at <https://gis.cdc.gov/grasp/diabetes/diabetesatlas-analysis.html>. Accessed on 12/11/2023.

## Oregon Counties Diagnosed Diabetes Map<sup>38</sup>

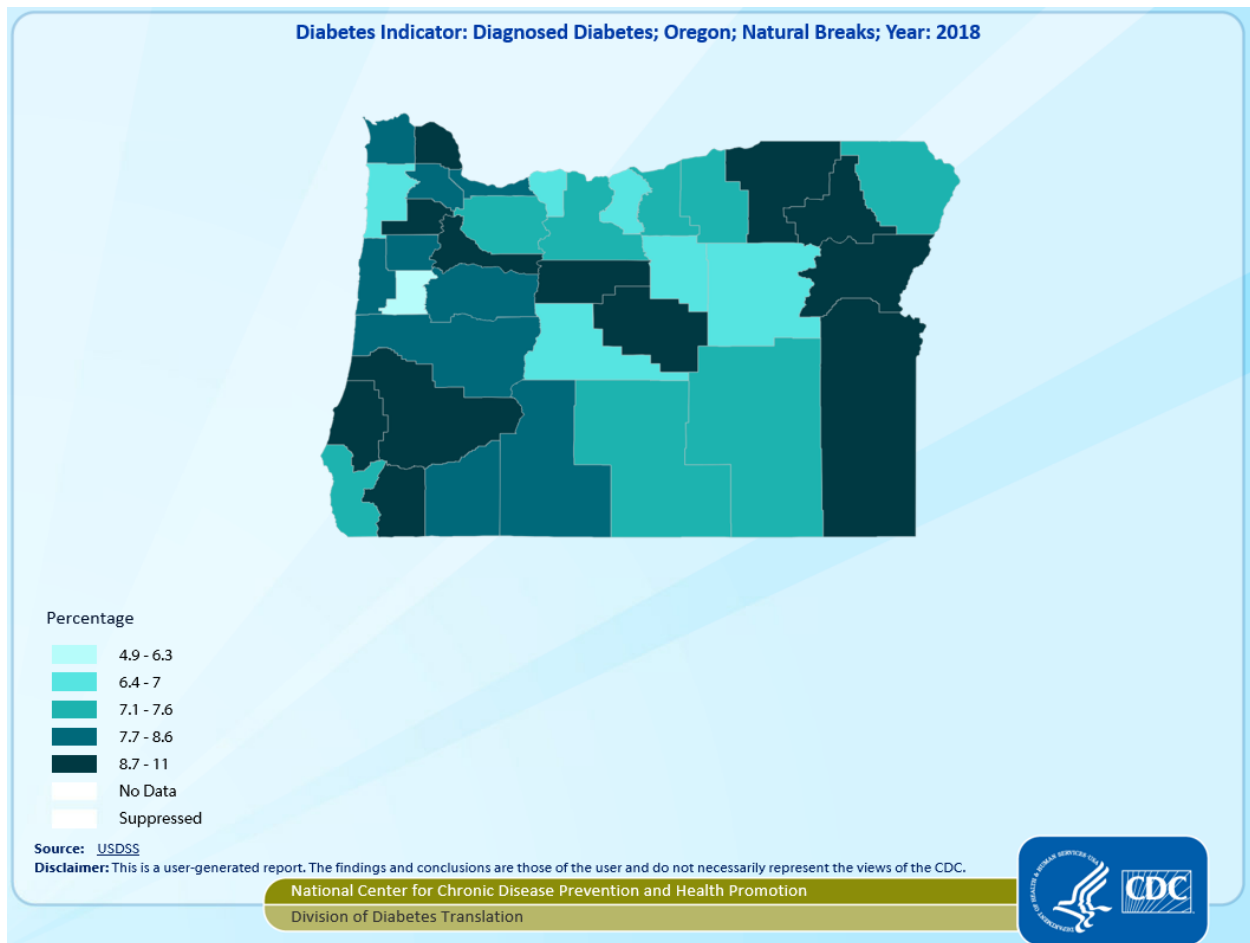


Figure 4 Oregon Counties Diagnosed Diabetes Map

<sup>38</sup> Centers for Disease Control and Prevention. US Diabetes Surveillance System website. Diabetes analysis, Oregon 2018. Available at <https://gis.cdc.gov/grasp/diabetes/diabetesatlas-analysis.html>. Accessed on 12/11/2023.

## 2018 Diabetes rates and social vulnerability by Oregon Counties<sup>39</sup>

Table 9 2018 Diabetes rates and social vulnerability by Oregon Counties

County	Diabetes (diagnosed) rate	Social Vulnerability
Coos County	11.00%	77.1%
Yamhill County	10.40%	65.7%
Marion County	10.30%	88.6%
Crook County	10.30%	45.7%
Umatilla County	9.50%	97.1%
Union County	9.50%	51.4%
Columbia County	9.40%	8.6%
Baker County	9.20%	60.0%
Douglas County	8.90%	68.6%
Josephine County	8.80%	62.9%
Jefferson County	8.70%	94.3%
Malheur County	8.70%	100.0%
Linn County	8.50%	57.1%
Washington County	8.40%	14.3%
Jackson County	8.30%	71.4%
Lincoln County	8.20%	37.1%
Clatsop County	8.10%	20.0%
Multnomah County	8.10%	42.9%
Lane County	8.00%	54.3%
Polk County	7.80%	34.3%
Klamath County	7.70%	91.4%
Clackamas County	7.60%	5.7%
Wallowa County	7.60%	11.4%
Morrow County	7.60%	80.0%
Harney County	7.50%	74.3%
Wasco County	7.40%	85.7%
Curry County	7.30%	31.4%
Gilliam County	7.20%	22.9%
Lake County	7.20%	82.9%
Wheeler County	6.90%	25.7%
Deschutes County	6.90%	0.0%
Tillamook County	6.90%	48.6%
Sherman County	6.80%	2.9%
Hood River County	6.70%	40.0%
Grant County	6.60%	28.6%
Benton County	5.40%	17.1%

<sup>39</sup> Centers for Disease Control and Prevention. US Diabetes US Diabetes Surveillance System website. Diabetes analysis, Oregon 2018. Available at <https://gis.cdc.gov/grasp/diabetes/diabetesatlas-analysis.html>. Accessed on 12/11/2023.

Upon review of the CDC data, Coos County, Yamhill County, and Marion County have the top three highest rates of diabetes in Oregon. Additionally, Coos and Marion counties had high SVI scores, meaning these counties have some of the most vulnerable populations in Oregon. The correlation between the Diabetes (diagnosed) rate and the Social Vulnerability is 0.43 indicating a positive relationship between the two population health measures.

## Stakeholder Feedback

Feedback was submitted from December 20, 2023, to January 5, 2024.

Links to the full feedback documents are included in the sections below.

### Input received from the medical and scientific community

- No information was provided by the medical or scientific community.

### Manufacturer submitted information

- Derek Asay, Sr. Vice President, Government Strategy & Federal Accounts, with Eli Lilly and Company, submitted information on December 18, 2023. Information submitted can be reviewed under Appendix A.

### Patient feedback and additional stakeholder feedback

- No information was provided by additional stakeholders.

## Appendix

### Appendix A: Eli Lilly and Company



Appendix A



December 18, 2023

**Eli Lilly and Company**

**By Email (PDAB@DCBS.oregon.gov)**

Lilly Corporate Center  
Indianapolis, Indiana 46285  
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[www.lilly.com](http://www.lilly.com)

Oregon Department of Consumer and Business Services  
ATTN: Akil Patterson, JD, MLS, PCM, Chair, Oregon Prescription Drug Affordability Board  
(the “Board”)  
P.O. Box 14480  
Salem, OR 97309

*Re: Prescription Drug Affordability Review of Humulin® R U-500*

Dear Chair Patterson,

I write on behalf of Eli Lilly and Company (“Lilly”), the manufacturer of Humulin® R U-500. According to the “[Dec 13, 2013 board revised subset lists](#)”<sup>1</sup> published on the public website for the Oregon Prescription Drug Affordability Board (“Board”), the Board intends to review the insulin class, including Humulin® R U-500, as outlined in [OAR 925.200.0010](#) and [OAR 925.200.0020](#) during the January 17, 2024 Board meeting and determine whether the selected products “may create affordability challenges for health care systems or high out-of-pocket costs for patients.”<sup>2</sup>

Humulin® R U-500 is a concentrated human insulin indicated to improve glycemic control in adults and pediatric patients with diabetes requiring more than 200 units of insulin in a day.<sup>3</sup> Humulin® R U-500 contains 5 times as much insulin (500 units/mL) in 1 mL as Humulin® R U-100 (100 units/mL). Humulin® R U-500 may reduce the number of daily injections compared to standard Humulin® U-100 insulin. In fact, some patients may be able to inject up to 80% less liquid and still get the dose they need. Humulin® R U-500 has both basal and prandial components, meaning it can be used as a monotherapy insulin, covering both basal insulin and some mealtime coverage as well.<sup>4</sup> Clinical trials have shown that Humulin® R U-500 plays a unique and important role in the options physicians have to treat patients. When

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<sup>1</sup> [Division of Financial Regulation : Prescription drug data : Oregon Prescription Drug Affordability Board : State of Oregon](#); <https://dfr.oregon.gov/pdab/Pages/data.aspx>

<sup>2</sup> ORS 646A.694.

<sup>3</sup> For more information, please see Humulin.com and the prescribing information available at: <https://pi.lilly.com/us/humulin-r-u500-pi.pdf>.

<sup>4</sup> The Humulin R U-500 Initiation Trial: <https://www.humulin.com/hcp/efficacy-safety#initiation-trial>

transitioning people uncontrolled on high dose U-100 insulin, U-500 reduced HbA1c by >1% after 24 weeks with low overall rates of documented symptomatic hypoglycemia <50 mg/dL.<sup>5</sup>

We appreciate that you share Lilly's desire to help more Oregonians access lower-cost insulin, including Lilly's Humulin® R U-500, and we are proud to lead the industry in making insulin affordable. Lilly led the way earlier this year by announcing we were reducing the list prices of Lilly's most commonly used insulins by at least 70%, launching a new lower-priced biosimilar, and enhancing our efforts to cap out-of-pocket costs for all our insulins, including Humulin® R U-500, **at \$35 per month, regardless of the number of pens or vials someone needs in a month.**

Our commitment to ensuring people have affordable access to insulin is not new. More than 25 years ago, in 1997, Lilly began donating insulin to a separate charitable organization called the Lilly Cares Foundation, which provides free Lilly medicines to people who qualify. Eligible people with a household annual adjusted gross income of up to 400% of the federal poverty level, which for a family of four means an annual income of about \$120,000, can receive insulin for free.<sup>6</sup>

Lilly has taken the lead in helping those left with high out-of-pocket costs. In early 2020, we introduced the Lilly Insulin Value Program. Under this program, people who have commercial insurance or no insurance at all can visit [InsulinAffordability.com](https://www.lilly.com/insulinaffordability), click two checkboxes, and within seconds receive a savings card to fill their entire monthly prescription of any Lilly insulin for \$35. And those without internet access can get the \$35 card by calling the Lilly Diabetes Solution Center at 1-833-808-1234. Our \$35 program does not require any application, waiting period, identifying information, or income thresholds. We made this solution even easier earlier this year by automating the \$35 cap wherever possible for people with commercial insurance, so they no longer need to present the savings card to their pharmacist or even know the program exists. Whatever their insurance company would have charged them for their monthly supply of Lilly insulin, **the majority of Lilly patients pay \$35 or less per**

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<sup>5</sup> Hood RC, Arakaki RF, Wysham C, Li YG, Settles JA, Jackson JA. Two treatment approaches for human regular U-500 insulin in patients with type 2 diabetes not achieving adequate glycemic control on high-dose U-100 insulin therapy with or without oral agents: a randomized, titration-to-target clinical trial. *Endocr Pract.* 2015; 21: 782-793.

<sup>6</sup> For more information about Lilly Cares, including available products and eligibility requirements, see [LillyCares.com](https://www.LillyCares.com).

**month for their insulin automatically**, with no action needed by the person filling the prescription.

We also partnered with the Centers for Medicare and Medicaid Services several years ago to pioneer the Medicare Part D Senior Savings Model, expanding our \$35 solutions to Medicare. And under the Inflation Reduction Act, Congress made Lilly's \$35 monthly cap permanent for seniors in Medicare Part D, making insulin, including Humulin® R U-500, affordable for seniors.

Our programs work. Last year, our commitment to cap insulin costs saved people with diabetes over \$185 million (which Lilly covers). Because of our efforts over the past few years, in 2022, people paid an average of \$20.48—less than 75 cents per day—for their entire monthly supply of Lilly insulin, and we expect that number to decrease further this year.

As a cutting-edge pharmaceutical company, innovation is at the heart of what we do, particularly for people with diabetes. In the early 1920s, people with type 1 diabetes had a life expectancy of only a handful of years after diagnosis. With the first animal-derived insulin, Lilly extended life expectancy into a person's thirties. Now, following a century of innovation, life expectancy for people with type 1 diabetes is in their sixties. But we're not done. Diabetes still significantly reduces a person's life expectancy. Even with modern insulin and devices, two thirds of people struggle to keep their disease under control. Humulin® R U-500 plays an important role as an innovative option accessible to patients. There's more work to do, not only on diabetes, but also many other diseases like Alzheimer's and cancer.

That's why Lilly consistently invests 25% of our total revenue into research and development—\$7.1 billion last year and \$8.5 billion budgeted this year. That enables us to introduce new medicines—19 in the last decade, including the first Covid antibody therapy, and more medicines in the pipeline. Earlier this year, we shared exciting results from a study on a promising new Alzheimer's medicine, which followed approximately \$8.5 billion in research and development for Alzheimer's and other neurodegenerative afflictions and literally decades of work, including previous late-stage failures of three other potential Alzheimer's medicines.


We appreciate that the Board shares our commitment to insulin affordability. We are proud of the impact that our efforts have had on making insulin more affordable and believe the Board's review of Humulin® R U-500 will demonstrate the meaningful impact our solutions

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have had for patients with diabetes. We will continue to do our part, ensuring that all people have affordable access, regardless of their insurance status.

Sincerely,

A handwritten signature in black ink, appearing to read "Derek Asay". The signature is stylized and cursive.

Derek Asay

Sr. Vice President, Government Strategy & Federal Accounts