Oregon Prescription Drug Affordability Board

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Agenda

This is a rescheduled regular meeting. *Date*: **January 26, 2024** | *Time*: **1:00 p.m.**
This agenda is subject to change.

Meeting name	**Prescription Drug Affordability Board**
Meeting location	Virtual
Zoom link	Register for the meeting

Board Members: Chair Akil Patterson; Vice Chair Shelley Bailey; Daniel Hartung; Amy Burns; Robert Judge; John Murray

Staff: Ralph Magrish, executive director; Cortnee Whitlock, policy analyst; Stephen Kooyman, project manager; Brekke Berg, policy analyst, Melissa Stiles, administrative specialist; Jake Gill, counsel; Pramela Reddi, counsel

Purpose	Subject	Presenter	Estimated Time Allotted
Informational and vote	Call to order, roll call, approval of **12/13/2023 minutes**	Chair Patterson	5 minutes
Informational	Executive director's program update	Ralph Magrish	5 minutes
Discussion and vote	**Affordability review: 1) Tresiba and 2) Tresiba FlexTouch:** drug-specific public comment, board discussion, and potential motion to include product on the list of insulin products that may create affordability challenges for health care systems or high out-of-pocket costs for patients in this state.	Ralph Magrish and Cortnee Whitlock	75 minutes
	5-minute break		5 minutes
Discussion and vote	**Affordability review: 3) Humulin R U-500 KwikPen:** drug-specific public comment, board discussion, and potential motion to include product on the list of insulin products that may create affordability challenges for health care systems or high out-of-pocket costs for patients in this state. Final adoption of list of insulin product(s).	Ralph Magrish and Cortnee Whitlock	40 minutes
Informational	Announcements	Staff	3 minutes
Informational	General public comment	Chair Patterson	10 minutes
Informational	Adjournment	Chair Patterson	2 minutes

Next meeting

Feb. 21, 2024, at 9:30 a.m.

Accessibility

Anyone needing assistance due to a disability can contact Melissa Stiles at least 48 hours ahead of the meeting at pdab@dcbs.oregon.gov or 971-374-3724. advance.

How to submit public comment

Oral testimony
For oral comments, please submit the PDAB public comment form no later than 24 hours before the PDAB meeting. The form is located on the Prescription Drug Affordability Board public comment page.

General written testimony
For written comments, please submit the PDAB public comment form with attachments no later than 72 hours before the PDAB meeting. The form is located on the Prescription Drug Affordability Board public comment page. Written comments will be posted to the PDAB website.

Public comment for drug affordability review
For written comments specific to drugs under review by the board, please submit the PDAB public comment form with attachments by the deadline listed on the public comment page. For oral testimony about drugs under review by the board, please submit the PDAB public comment form no later than 24 hours before the PDAB meeting. The form is located on the Prescription Drug Affordability Board public comment page. Written comments received by the deadline will be included in the board meeting materials and posted to the web.

Open and closed sessions

All board meetings except executive sessions are open to the public. Pursuant to ORS 192.660, executive sessions are closed, with the exception of news media and staff. No final actions will be taken in the executive session. When action is necessary, the board will return to an open session.

Oregon Prescription Drug Affordability Board

Oregon Prescription Drug Affordability Board (PDAB) Regular Meeting
Wednesday, December 13, 2023
Draft Minutes

Web link to the meeting video: https://youtu.be/xdKmkFlTdCQ
Web link to the meeting materials: https://dfr.oregon.gov/pdab/Documents/20231213-PDAB-document-package.pdf
Web link to Excel spreadsheets and data information: https://dfr.oregon.gov/pdab/Pages/data.aspx

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Call to order and roll call: Chair Akil Patterson called the meeting to order at 9:30 am and roll was called.
Board members present: Chair Akil Patterson, Dr. Richard Bruno, Dr. Amy Burns, Dr. Daniel Hartung, Robert Judge, John Murray
Absent: Vice Chair Shelley Bailey

Approval of minutes: Richard Bruno made the motion and Amy Burns provided a second to approve the minutes on Pages 3-6 in the agenda packet. View the approval in the meeting video at minute 00:01:22.
MOTION to approve the minutes.
Board Vote:
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Chair Akil Patterson
No: None
Abstain: Robert Judge, John Murray
Motion passed 4-0

Program update by Executive Director Ralph Magrish. View the executive director's report in the meeting video at minute 00:04:37.

Board discussion and vote to extend meeting time: Robert Judge made the motion and John Murray provided the second to extend board meetings by 30 minutes. View the discussion and vote in the meeting video at minute 00:10:12.
MOTION to extend the meeting by 30 minutes.
Board Vote:
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

Board discussion about filtering prescription drug and insulin lists for biosimilars and generics: Ralph Magrish, executive director, began the discussion about the information on Pages 7-21 of the agenda packet. View the video of the board discussion and votes at minute 00:12:19. Richard Bruno made the motion to approve and Amy Burns provided the second.
MOTION to approve revised prescription drug subset list as shown below in Table 1 and also on the PDAB web page 2023-PDAB-Subset-Drug-list-v3.0.xlsx.
Board Vote:
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

Table 1: Board approved updated subset list of prescription drugs also posted to the PDAB web page: PDAB-2023-Insulin-Subset-List-v2.0.xlsx.

Proprietary name(s)	Non-proprietary name
Cosentyx / Cosentyx Sensoready Pen / Cosentyx Sensoready	Secukinumab
Entyvio	Vedolizumab
Genvoya	Elvitegravir-Cobicistat-Emtricitabine-Tenofovir Alafenamide
Inflectra	Infliximab-dyyb
Ocrevus	Ocrelizumab
Rybelsus / Ozempic	Semaglutide
Shingrix	Zoster Vaccine Recombinant Adjuvanted
Skyrizi / Skyrizi Pen	Risankizumab-rzaa
Tremfya	Guselkumab
Triumeq / Triumeq PD	Abacavir-Dolutegravir-Lamivudine
Trulicity	Dulaglutide
Vyvanse	Lisdexamfetamine Dimesylate

Amy Burns made the motion to approve the revised insulin subset list and Robert Judge provided the second.

MOTION to revised subset insulin list as shown in Table 2 below and also posted to the PDAB web page: PDAB-2023-Insulin-Subset-List-v2.0.xlsx.

Board Vote:

Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson

No: None

Motion passed 6-0

Table 2: Board approved updated subset list of insulin products also posted to the PDAB web page: PDAB-2023-Insulin-Subset-List-v2.0.xlsx.

Insulin type	Proprietary name(s)	Non-proprietary name
Long-Acting	Tresiba	Insulin Degludec
Long-Acting	Tresiba FlexTouch	Insulin Degludec
Short-Acting	Humulin R U-500 KwikPen	Insulin Regular (Human)

Board survey overview for OAR 925-200-0020: Ralph Magrish and Cortnee Whitlock, policy analyst, discussed the board survey shown on Pages 22-31 in the agenda packet. View the discussion in the meeting video at minute 00:38:03.

2024 affordability review work plan, template, and public comment for stakeholder submissions: Ralph Magrish, Amanda Claycomb, and Cortnee Whitlock discussed the affordability review process for 2024 shown on Pages 32-47 in the agenda packet. View the discussion in the meeting video at minute 00:45:42.

Board discussion on policy recommendations and letter for the Oregon Legislature: Cortnee Whitlock discussed the policy recommendations and letter on Pages 48-52 of the agenda packet. View the discussion in the meeting video at minute 01:10:48.

The board voted on recommendations one, two, and three in the letter. Amy Burns moved to include Recommendation 1 Lower insulin co-pay limit to $35 and/or decouple from inflation index. John Murray provided the second.
MOTION to approve and include Recommendation 1 Lower insulin co-pay limit to $35 and/or decouple from inflation index.
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

John Murray moved to include Recommendation 2 with amendments to add the word interchangeable and strike the last two sentences. Robert Judge provided the second.
MOTION to amend Recommendation 2 Change Oregon's statute language regarding substitution requirements for biological products and biosimilars
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

Amy Burns moved to approve Recommendation 2 as amended and Robert provided the second.
MOTION to approve Recommendation 2 as amended
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

Daniel Hartung moved to approve Recommendation 3 Expand PBM reporting requirements for more transparency. Amy Burns provided the second.
MOTION to approve Recommendation 3 Expand PBM reporting requirements for more transparency.
Yes: Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, John Murray, Chair Akil Patterson
No: None
Motion passed 6-0

Executive session: Chair Patterson called for a board adjournment into executive session pursuant to ORS 192.660(2)(f) to consult with legal counsel. The board returned to public session after six minutes and took a roll call. Board members present were Chair Akil Patterson, Richard Bruno, Amy Burns, Daniel Hartung, Robert Judge, and John Murray. View this portion of the meeting video at minute 02:01:50.

Board discussion and vote on policy recommendations and letter for the Oregon Legislature continued. View this portion of the discussion in the meeting video at minute 02:09:22.

Public comment: Chair Patterson called on those who signed up to speak to the board. There were eight requests to provide oral testimony and 10 written comments, which are posted to the PDAB website. View the public comments in the meeting video at minute 02:14:07.

The meeting was adjourned at 12:06 pm. View the adjournment in the meeting video at minute 02:33:30.

Oregon Prescription Drug
Affordability Board

Email: pdab@dcbs.oregon.gov Phone: 971-374-3724 Website: dfr.oregon.gov/pdab

Tresiba & Tresiba FlexTouch Affordability Review[1]

Version 2

[1] Image. https://www.novomedlink.com/diabetes/products/treatments/tresiba/. Accessed 01/08/2024.

Table of Contents

Revisions Made

- Page 3: Updated summary section and tables.
- Page 4: Added information regarding ORS 743A.069 and added name of manufacturer.
- Page 5: Additional information added to clinical profile section.
- Page 7: Updated Table 3 Alternative long-acting insulin analogues.
- Pages 8 & 9: Updated graphs to include therapeutic alternative WAC from 2019-2023.
- Pages 11: Updated the cost to health benefit plans section. Removed commercial and Medicaid tables. Added a new table for all health coverage cost profiles.
- Page 13: Expanded information in the therapeutic alternative tables and updated information statement.

Review Summary

The Prescription Drug Affordability Board (PDAB) conducted affordability reviews for Tresiba and Tresiba FlexTouch. The Oregon All Payer All Claims (APAC) reporting program indicated the drugs were prescribed to 6068 [2] (Tresiba 220, Tresiba FlexTouch 5,848) Oregonians in 2022 with a prescription drug benefit from an Oregon health insurance carrier.

Table 1 Summary of costs to the patient

Costs to the patient		
	Source	**Amount**
Average annual out of pocket cost per commercially insured enrollee	APAC	Tresiba: $150.92 Tresiba FlexTouch: $169.64

Table 2 Summary of costs to the healthcare system

Costs to the healthcare system		
	Source	**Amount**
Total annual gross spends for payers[3]	APAC	$25,879,188.21 (Tresiba $696,955.57, Tresiba FlexTouch $25,182,232.64)
Average annual gross spends for payers per enrollee	APAC	Tresiba: $3,167.98 Tresiba FlexTouch: $4,306.13
Annual drug gross cost per enrollee	Data call[4]	Drugs not on data call
Average annual drug net cost	Data call	Drugs not on data call
Percentage of drug price concessions	Data call	Drugs not on data call
Average Quarterly Medicaid fee for service cost[5]	OSU Drug Research Management Utilization Reports 2022[6]	Tresiba and Tresiba FlexTouch not among the top drugs listed for 2022

[2] Number of 2022 unique enrollees from Oregon's All Payers All Claims (APAC) data. For more information regarding APAC data visit: https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx

[3] 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.

[4] 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.

[5] Quarterly metric used in lieu of annual as the drug may not have been on the 2022 reports for all four quarters.

[6] 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.

Enacted in 2021, ORS 743A.069 provides that health benefit plans offered in Oregon may not require enrollees in their plans to incur cost-sharing or other out-of-pocket costs above certain inflation-adjusted limits for insulin prescribed for the treatment of diabetes. Plans covered by this provision insure approximately 1 million Oregonians. For 2024, the out-of-pocket cost limits are $85 for each 30-day supply or $255 for each 90-day supply.[7] These limits reflect an increase of 13.3% from 2021.

In addition to information provided by the Department of Consumer and Business Services (DCBS) pursuant to ORS 646A.694, this review reflects information from various sources, including 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): **Tresiba, Tresiba FlexTouch**

Non-proprietary name: **Insulin Degludec**

Manufacturer: **Novo Nordisk**

FDA approval

Tresiba and Tresiba FlexTouch were first approved by the FDA on 9/25/2015.[8]

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

[7] OAR 836-053-0025 (*available at* https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=303523). ORS 743A.069 requires the Department of Consumer and Business Services, by rule, to annually adjust the cost limits based on changes to the Consumer Price Index for All Urban Consumers, West Region (All Items).

[8] 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.

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

Clinical profile

Drug indications[9]

- FDA Approved: To improve glycemic control in patients 1 year of age and older with diabetes mellitus (type 1 or type 2)
- Off Label Uses: None

Clinical Efficacy

- Insulin degludec is a long-acting insulin analog with a duration of action exceeding 42 hours.
- FDA approval of insulin degludec was based on 3 trials evaluating it as part of a basal-bolus regimen in type 1 diabetes mellitus (T1DM) and 6 studies in type 2 diabetes mellitus (T2DM).[10] Most of these studies were non-inferiority studies designed to test the non-inferiority of long-acting insulin degludec to another long-acting insulin analogue, most often being insulin glargine. These studies were randomized, open label, and ranged from 26-52 weeks.[11] Basal insulin dose was adjusted weekly to achieve a fasting morning glucose level between 70 and 90 mg/dl.
- In T1DM, insulin degludec was shown to be non-inferior to insulin detemir and glargine on the primary endpoint of change from hemoglobin A1c (HbA1c) from baseline and resulted in an average change from baseline of -0.36 to -0.70.[12] None of the 3 studies showed insulin degludec was statistically superior to the long-acting comparator.[13]
- In T2DM, insulin degludec was found to be non-inferior to insulin glargine in 5 studies with the upper bound of the 95% confidence interval below the 0.4 non-inferiority margin. The average change from baseline in HbA1c was from -1.07 to -1.53.[14] This larger reduction in HbA1c in T2DM was likely due to higher levels at baseline (8%-9%). The treatment difference between insulin degludec and insulin glargine always favored glargine and quality of life outcomes did not differ between groups. One additional study

[9] Tresiba Prescribing Information. Novo Nordisk Inc. Plainsboro, NJ: 2022.
[10] Food and Drug Administration Center for Drug Evaluation and Research. Application Number: 203313Orig1s000 203314 and Orig1s000 Summary Reviews. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/203313Orig1s000_203314Orig1s000SumR.pdf
[11] Ibid.
[12] Ibid.
[13] Ibid.
[14] Ibid.

found insulin degludec to be superior in reducing HgA1c compared to sitagliptin, an oral DPP4-inhibitor (-1.53 vs. -1.09; treatment difference -0.44; 95% CI -0.62 and -0.25).[15]

- At the time of FDA approval, there was no evidence to conclude that insulin degludec has effects on mortality, microvascular outcomes, or macrovascular outcomes.

Clinical Safety[16]

- FDA safety warnings:
  - Hypoglycemia
  - Hyperglycemia due to medication errors or changes in insulin products
  - Hypersensitivity reactions
  - Hypokalemia
- Common side effects:
  - Hypoglycemia (5-18%), injection site reactions (4%), weight gain (~2 kg)
- Safety advantages or disadvantages
  - In 7 out of the 8 studies, hypoglycemia rates were similar with degludec and insulin glargine. One study showed insulin degludec to be superior to glargine regarding hypoglycemia.
  - Longer acting insulin analogues may result in lower risks of nocturnal hypoglycemia and severe hypoglycemia than alternatives.
  - Rates of other adverse events are similar between insulin degludec and insulin glargine.
  - Insulin degludec has a longer duration of action over other basal insulin analogues that can allow for more flexibility in once daily dosing regimens.

[15] Food and Drug Administration Center for Drug Evaluation and Research. Application Number: 203313Orig1s000 203314 and Orig1s000 Summary Reviews. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/203313Orig1s000_203314Orig1s000SumR.pdf

[16] Tresiba Prescribing Information. Novo Nordisk Inc. Plainsboro, NJ: 2022.

Therapeutic alternatives[17]

Table 3 Alternative long-acting insulin analogues

Drug	FDA Approved Indications	Duration	Frequency	Formulations	Biosimilars Available
Insulin degludec *(subject drugs)*	• T1DM • T2DM	≥ 42 hours	Once daily (flexible timing)	• U-100 vial • U-100 pen • U-200 pen	No
Insulin glargine *(therapeutic alternative)* Basaglar, Lantus, Toujeo	• T1DM • T2DM	~24 hours	Once daily at the same time	• U-100 vial • U-100 pen • U-300 pen	• Semglee (Lantus) • Rezvoglar (Lantus)
Insulin detemir* *(therapeutic alternative)*	• T1DM • T2DM	7 to > 24 hours	Once or twice daily	• U-100 vial • U-100 pen	No

**Will be discontinued by end of 2024 due to manufacturing constraints.*

Comparative effectiveness to therapeutic alternatives:

- Clinical guidelines do not give preference to one long-acting insulin over another.[18]
- One randomized, double-blind, multicenter, cardiovascular outcomes trial compared insulin degludec to insulin glargine in patients with T2DM at high risk of cardiovascular events (n=7637).[19] Overall, insulin degludec was non-inferior to insulin glargine in the primary outcome of major cardiovascular events (8.5% vs. 9.3%; hazard ratio [HR] 0.91; 95% CI 0.78 to 1.06; p<0.001 for noninferiority).[20] There was a higher rate of severe hypoglycemic events in the insulin glargine group (6.25 events per 100 patient-years) compared to the insulin degludec group (3.70 events per 100 patient-years) (rate ratio [RR] 0.60; 95% CI 0.48 to 0.76; p<0.001).[21] There was also a lower rate of nocturnal severe hypoglycemia in the degludec group compared to glargine (0.65 vs. 1.40 events per 100 patient-years).

[17] 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.

[18] American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178

[19] Marso SP, McGuire DK, Zinman B, et al.; DEVOTE Study Group. Efficacy and Safety of Degludec versus Glargine in Type 2 Diabetes. N Engl J Med. 2017 Aug 24;377(8):723-732.

[20] Ibid.

[21] Ibid.

- There is not a clinically meaningful difference in HbA1c reduction between insulin degludec and insulin glargine in T2DM or T1DM based on high quality evidence in T2DM and moderate in T1DM.[22]

Cost profile

Pricing information

The package wholesale acquisition cost (WAC) for Tresiba (NDC 00169266211) was $338.95 and Tresiba FlexTouch (NDC 00169266015) was $508.43 as of 01/08/2024.[23]

The WAC for the drugs 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 1%. This historical change in the package WAC is displayed in Figure 1 for Tresiba and in Figure 2 for Tresiba FlexTouch. The comparison of the year over year change in WAC and the 2019-2023 inflation rates[24] is shown in Figure 3 for Tresiba and Figure 4 for Tresiba FlexTouch.

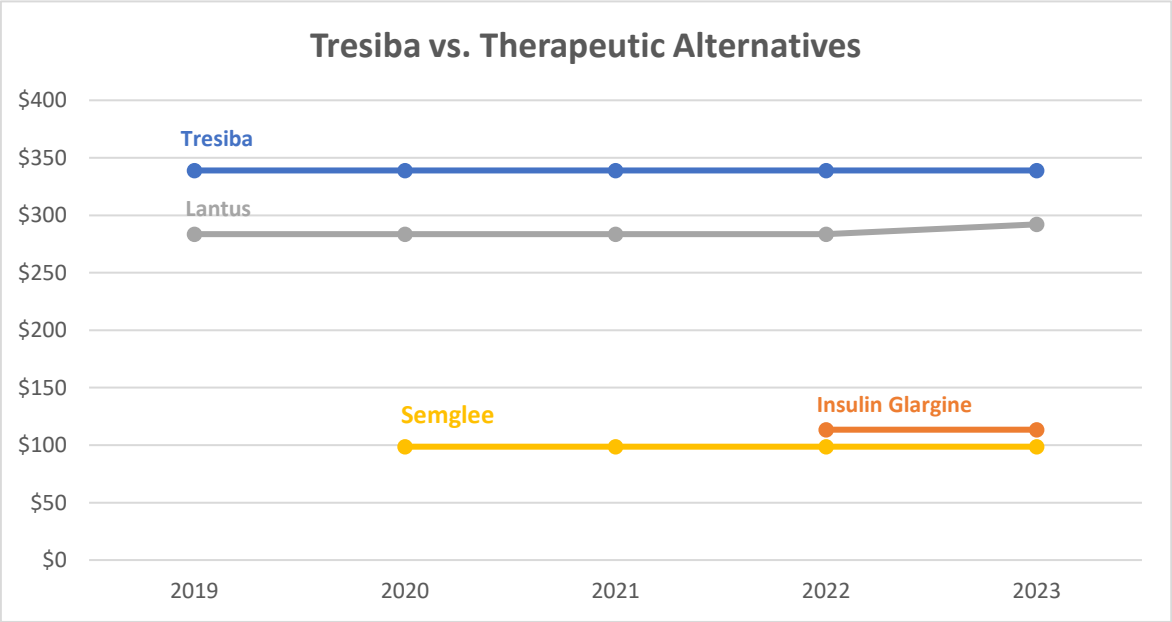

Figure 1 Tresiba and therapeutic alternative WAC from 2019-2023

[22] Holmes RS, Crabtree E, McDonagh MS. Comparative effectiveness and harms of long-acting insulins for type 1 and type 2 diabetes: A systematic review and meta-analysis. Diabetes Obes Metab. 2019 Apr;21(4):984-992.
[23] 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.
[24] 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.

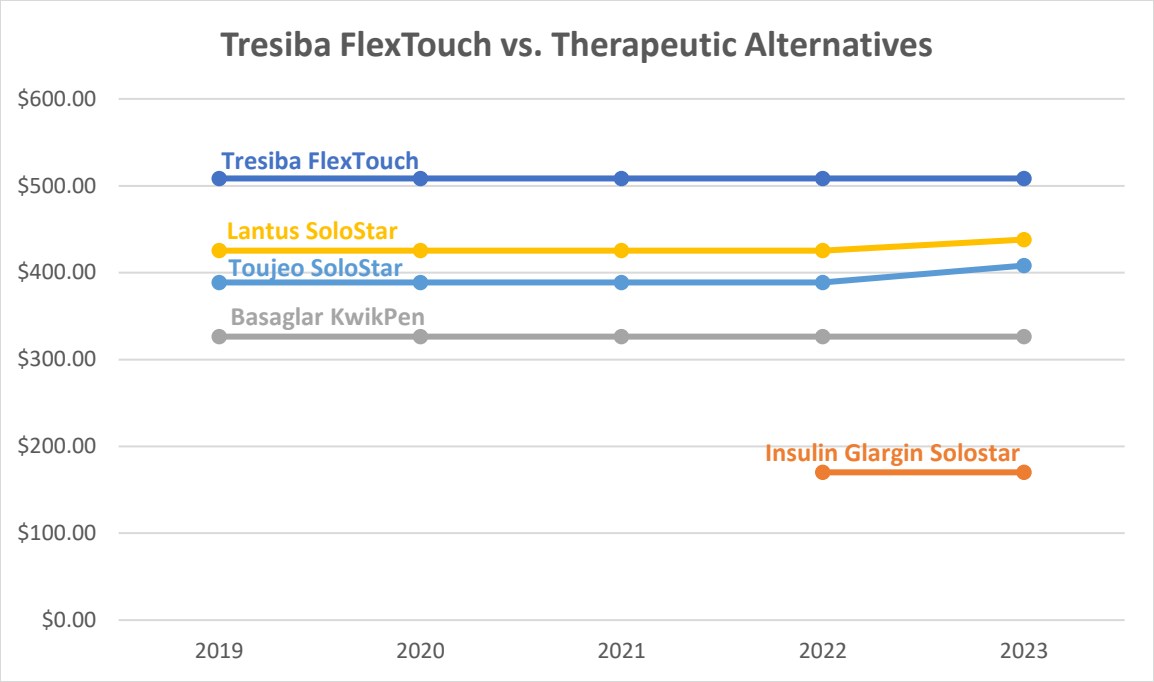

Figure 2 Tresiba FlexTouch and therapeutic alternative WAC from 2019-2023

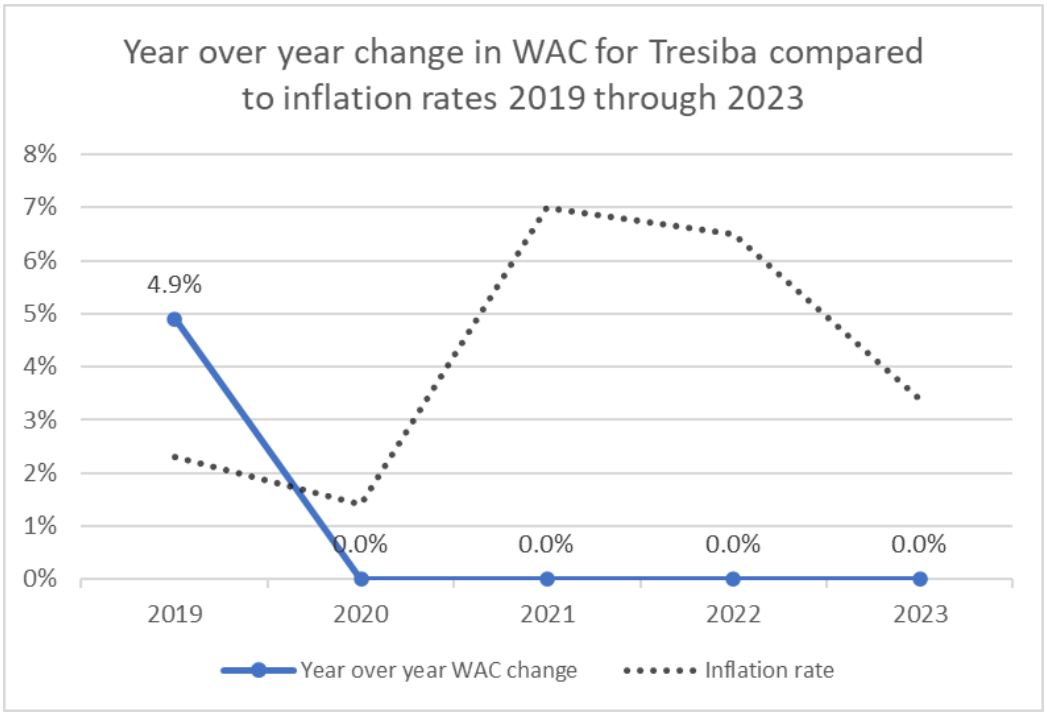

Figure 3 Year over year change in WAC for Tresiba compared to inflation rates[25]

[25] 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.

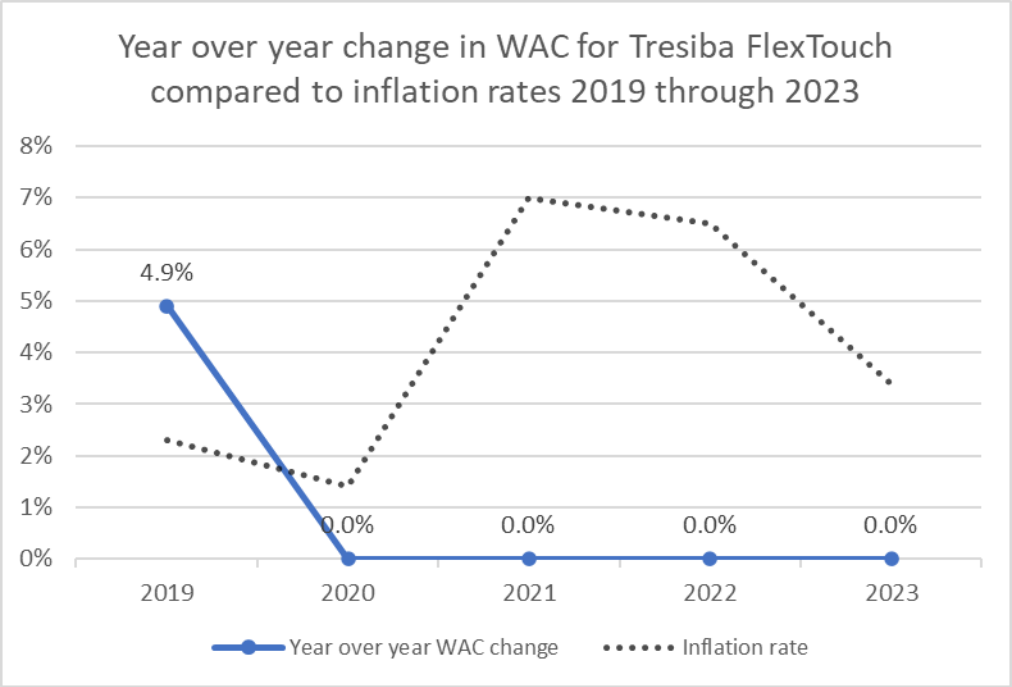

Figure 4 Year over year change in WAC for Tresiba FlexTouch compared to inflation rates [26]

Package WAC was reviewed as an indication of historic price trends for the drugs. 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 drugs 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 drugs price offset.

Cost to stakeholders

Cost to patients

The APAC database[27,28] was analyzed to determine the average copayment for commercially insured enrollees or other cost-sharing for the prescription drugs.

[26] 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.
[27] 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.
[28] APAC total cost may include a dispensing fee and physician administration fees.

Table 4 Out of Pocket Costs

2022 Average annual patient out of pocket costs[29,30]			
Value	APAC		Data Call
	Tresiba	Tresiba FlexTouch	
Average Co-Pay	$93.20	$120.93	Drugs not on data call
Average Deductible	$43.12	$16.49	Drugs not on data call
Average Coinsurance	$14.61	$32.22	Drugs not on data call
Other Cost Sharing	$0	$0	Drugs not on data call
Total Out-of-Pocket Costs for Patients	**$150.92**	**$169.64**	Drugs not on data call

Cost to health benefit services

The APAC database[31],[32] was analyzed to determine the total gross paid amount, total number of enrollees and claims, and the average paid per claim and per enrollee for all Oregon health benefit services.

Table 5 2022 Annual costs to health benefit services

Tresiba	Gross paid amount	Total unique claims	Total unique patients	Average paid per claim	Average paid per patient
Commercial	$217,615.99	419	78	$519.37	$2,789.95
Medicaid[33]	$139,115.02	339	47	$410.37	$2,959.89
Medicare	$340,224.56	410	95	$829.82	$3,581.31
Total	**$696,955.57**	**1168**	**220**	**$596.71**	**$3,167.98**

Tresiba FlexTouch	Gross paid amount	Total unique claims	Total unique patients	Average paid per claim	Average paid per patient
Commercial	$8,930,940.87	12280	2281	$727.28	$3,915.36
Medicaid[34]	$4,853,176.53	7385	1214	$657.17	$3,997.67
Medicare	$11,398,115.24	12164	2353	$937.04	$4,844.08
Total	**$25,182,232.64**	**31829**	**5848**	**$791.17**	**$4,306.13**

[29] Medicaid and Medicare were excluded from cost information.
[30] For patients who used the drug at least once in the 2022 calendar year.
[31] 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.
[32] APAC total cost may include a dispensing fee and physician administration fees.
[33] Medicaid costs include care coordination organization (CCO) and fee for service (FFS). Amount paid on the claim = 1) Ingredient Cost ([AAAC/NADAC/WAC] x Dispense Quantity) + Dispensing Fee. If billed amount was lower, pay billed amount, minus TPL amount. DUR Reports | College of Pharmacy | Oregon State University.
[34] Ibid.

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 6 Therapeutic alternative (TA) comparison

	NDC	Drug Name	Package size	2022 WAC package size	Price per package	Package strength in mL	2022 WAC unit price	AAAC[35] unit price	NADAC[36] unit price	Percent difference of NADAC from subject Rx & TA
Subject drug	**00169-2662-11**	**Tresiba**	**1 vial**	**$338.95**	**$338.95**	**10 mL**	**$33.90**	**$32.66**	**$32.32**	
Therapeutic alternative	00955-1729-01	Insulin Glargine	1 vial	$113.42	$113.42	10 mL	$11.34	$10.96	$10.89	196.79%
Therapeutic alternative	00088-2220-33	Lantus	1 vial	$283.56	$283.56	10 mL	$28.36	$27.23	$27.23	18.69%
Therapeutic alternative	49502-0195-80	Semglee	1 vial	$98.65	$98.65	10 mL	$9.87	$26.12	$9.44	242.37%
Subject drug	**00169-2660-15**	**Tresiba FlexTouch**	5 prefilled pens	**$508.43**	**$101.69**	**3 mL**	**$33.90**	**$32.66**	**$33.89**	
Therapeutic alternative	00955-1728-05	Insulin Glargin SoloStar	5 prefilled pens	$170.12	$34.02	3 mL	$11.34	N/A	$10.90	210.92%
Therapeutic alternative	0002-7715-59	Basaglar KwikPen	5 prefilled pens	$326.36	$65.27	3 mL	$21.76	N/A	$20.93	61.92%
Therapeutic alternative	49502-0196-75	Semglee pen-injector	5 prefilled pens	$148.00	$29.60	3 mL	$9.87	$26.13	$9.53	255.61%
Therapeutic alternative	00088-2219-05	Lantus SoloStar	5 prefilled pens	$425.30	$85.06	3 mL	$28.35	N/A	$27.23	24.46%
Therapeutic alternative	00024-2869-03	Toujeo SoloStar	3 prefilled pens	$388.72	$129.57	1.5 mL	$86.38	$82.87	$82.93	-59.13%

[35] 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.

[36] 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

Price comparisons were made between the wholesale acquisition cost (WAC), the National Average Drug Acquisition Cost (NADAC), and the Average Actual Acquisition Cost (AAAC). Tresiba was compared to three therapeutic alternatives. The percentage difference between the therapeutic alternative NADAC was compared to the baseline drug's NADAC. The NADAC percentage indicates that the therapeutic alternative Semglee vial is 242.37% less expensive than Tresiba. Semglee was approved by the FDA in 2021 and is an interchangeable insulin with Lantus (insulin glargine).

Tresiba FlexTouch was compared to five therapeutic alternatives. Semglee pen injector showed a 255.61% difference in compared price to Tresiba FlexTouch. Toujeo SolorStar shows to be costlier than the Tresiba FlexTouch.

Access profile

Utilization and Health Equity

According to the CDC, in 2021 8.9% of the US population (all age groups) had diagnosed diabetes.[37] 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.[38]

The prevalence of type 1 and type 2 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.[39] Education also showed a relationship to adults diagnosed with diabetes, with 13.1% of adults with less than a high school level of education diagnosed with diabetes, compared to 6.9% of adults with more than a high school level education.[40] 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.[41]

[37] 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
[38] 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.
[39] 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.
[40] Ibid.
[41] Ibid.

To review how the prevalence of diabetes ranges throughout Oregon, Figures 5 and 6 show 2018 rates of diabetes by county from the CDC website.[42] In addition to the rate of diabetes, the data included the Social Vulnerability Index (SVI) scores for each county.

Oregon Counties Social Vulnerability Map[43]

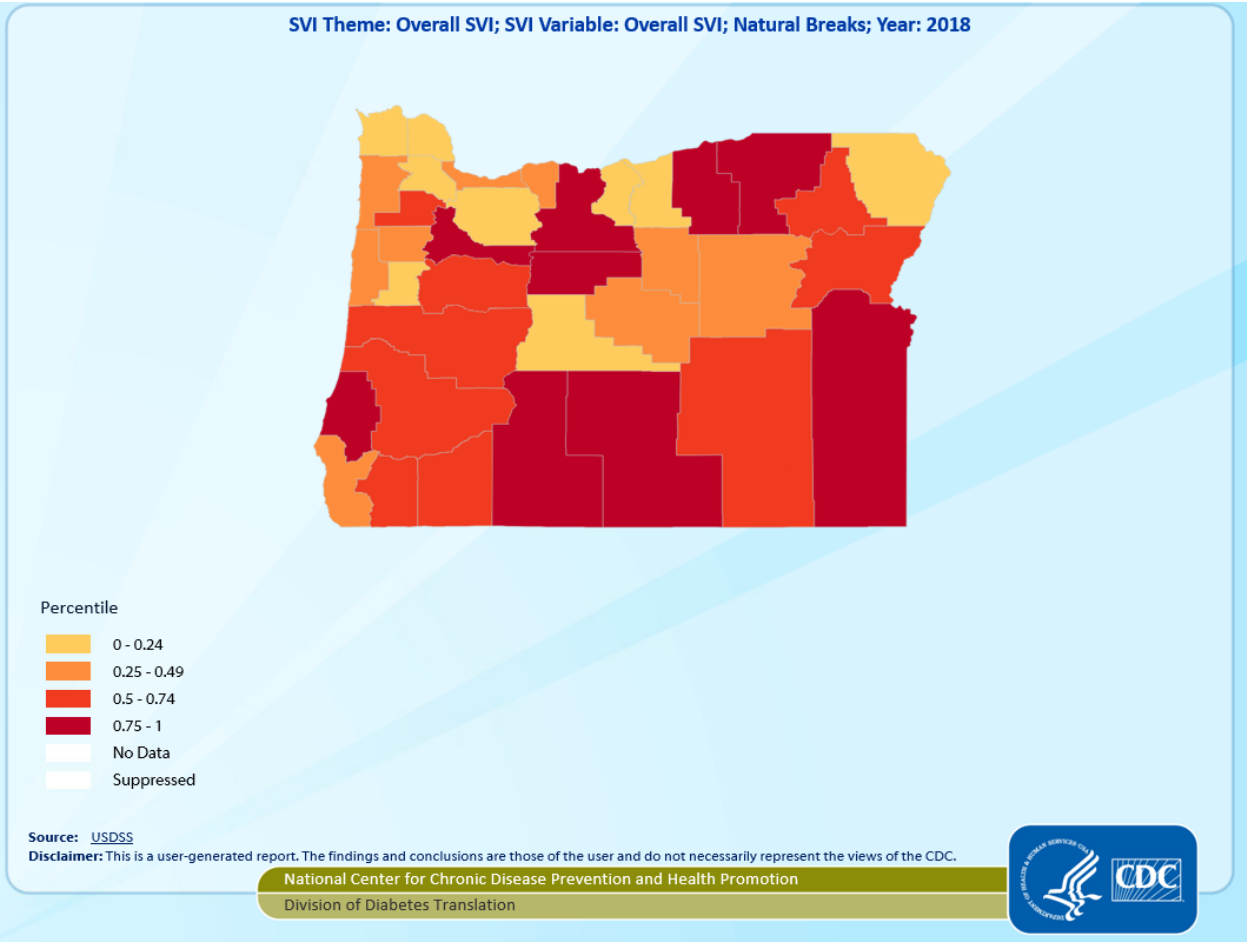

Figure 5 Oregon Counties Social Vulnerability Map

[42] 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.
[43] Ibid.

Oregon Counties Diagnosed Diabetes Map[44]

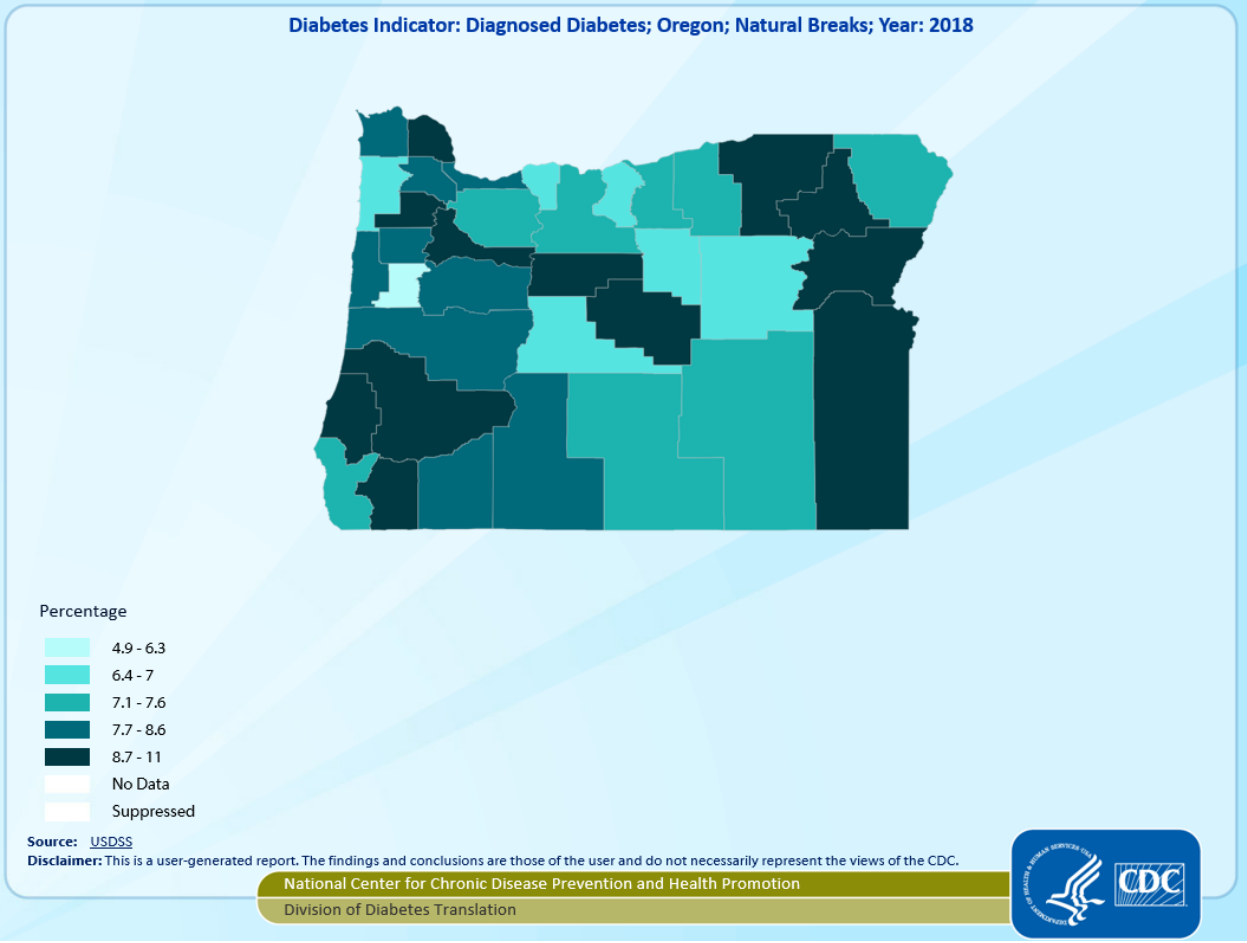

Figure 6 Oregon Counties Diagnosed Diabetes Map

[44] 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[45]

Table 3 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%

[45] 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, indicating these counties may 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

- Kelsey Lovell, Associate Director, with Novo Nordisk submitted information January 5, 2024. Information submitted can be reviewed under Appendix A.

Patient feedback and additional stakeholder feedback

- No information was provided by additional stakeholders.

Appendix A

January 5, 2024

VIA ELECTRONIC FILING

Oregon Division of Financial Regulation
ATTN: Oregon Prescription Drug Affordability Review Board (PDAB)
350 Winter St. NE
Room 410
Salem, OR 97309-0405

RE: January 17th, 2024 Oregon Prescription Drug Affordability Board Meeting and Review of Tresiba®

Dear Members of the Oregon Prescription Drug Affordability Board:

Novo Nordisk appreciates the opportunity to submit written comments to the Oregon Prescription Drug Affordability Board regarding Tresiba®, one of the selected prescription insulin drugs under review by the Board.

Novo Nordisk is a global healthcare company committed to improving the lives of those living with serious chronic conditions, including diabetes, hemophilia, growth disorders and obesity. The Novo Nordisk Foundation, our majority shareholder, is among the top five largest charitable foundations in the world. Accordingly, our company's mission and actions reflect the Foundation's vision to contribute significantly to research and development that improves the lives of people and the sustainability of society.

While we appreciate that part of the Board's purpose is to review prescription drugs that could pose an affordability challenge to Oregonians, we have numerous concerns regarding the Board's information and processes, including:

- the validity of the data upon which the Board has relied, in part because the Board repeatedly revised its product selections as a result of data errors and limitations;
- the Board's methodology for drug selection and lack of insight into the rationale for the Board's decision-making;
- the Board's failure to capture all of the factors necessary to arrive at a more accurate and complete picture of a medication's price;
- an insufficient amount of time allocated towards review, discussion, and a vote on each selected drug; and
- the untenable and undefined standard of whether a drug may create unaffordability challenges.

Given these concerns, we believe that the Board's review will provide an inaccurate picture of Tresiba®'s cost-effectiveness and overall benefit to patients. We also remain concerned that the Board's review will not accurately reflect all the factors and investment required to bring a drug to market. Finally, as a company we have taken numerous actions – through our patient assistance programs and the introduction of an unbranded biologic – to ensure that patients have affordable access to Tresiba. **Taken together, we urge the Board not to move forward with this review.** However, should the Board proceed as planned, below we have provided an

overview of Tresiba®'s clinical benefits and a summary of the measures Novo Nordisk has taken to ensure that Tresiba® is affordable to patients.

Tresiba Clinical Overview

Tresiba® is a long-acting insulin used to control high blood sugar in adults and children who are 1 year of age and older with diabetes. According to the Centers for Disease Control, diabetes mellitus is a chronic health condition that affects how the body turns food into energy. In healthy individuals, beta cells in the pancreas release the hormone insulin to help regulate glucose levels in the blood.

Most patients living with diabetes have either Type 1 diabetes (T1D), an autoimmune disease where beta cells have been destroyed by the body's own immune system yielding insufficient and/or total loss of insulin production by the pancreas, or Type 2 diabetes (T2D), where the body suffers from a combination of disorders involving glucose metabolism, including inadequate insulin secretion, insulin resistance, and metabolic syndrome. Thus, the cornerstone of diabetes management is ensuring that treatment approaches are tailored to the individual patient needs, particularly when insulin therapy is necessary. Furthermore, landmark clinical data in patients with both T1D and T2D have shown that targeting appropriate overall blood sugar control reduces the risk of developing microvascular complications directly associated with diabetes, including vision impairment (or even blindness), loss of kidney function, nerve damage which can increase the risk of amputations, as well as macrovascular, or cardiovascular complications, including myocardial infarction, stroke, heart failure, and peripheral arterial disease.

Insulin dosing is a complex process that requires the consideration of multiple factors on an individual basis. For patients with T1D and the subset of patients with T2D who require insulin, insulin coverage is necessary throughout the day. This 24-hour insulin coverage is provided through a basal insulin component and a mealtime insulin component, both of which are intended to maintain blood sugar levels in the desired target range. The basal insulin works in the background to keep blood sugar levels in the desired target range between meals and while the individual is not eating. The mealtime insulin works to keep blood sugar levels after meals, known as PPG, from rising too high. Since insulin dictates how much sugar cells in the body will absorb, individualizing insulin dosing based on the patient's needs is critical. For instance, too much insulin can cause hypoglycemia, or low blood sugar, while too little insulin can result in hyperglycemia, or too high of blood sugar levels in the blood.

Increased hypoglycemia increases the risk of complications, including decreased sensitivity to hypoglycemia over time which can lead to hypoglycemic unawareness, and with more hypoglycemic events comes increased risk of impaired cognitive function, heart arrhythmias, and mortality. Fear of hypoglycaemia often results in delayed initiation and intensification of insulin therapy for many patients with type 2 diabetes (1-7). In addition to concerns about hypoglycaemia, surveys have shown that both patients and physicians would like a treatment that could be dosed more flexibly to accommodate patients' needs, making it easier for patients to remain compliant and to achieve their glycemic targets (8). (76).

Tresiba® is a basal insulin with an ultra-long duration of action that exceeds 42 hours, with a half-life of ~25 hours. The pharmacokinetic and pharmacodynamic profiles of degludec are flat and stable and were preserved in patient populations independent of age, ethnicity, or injection site, and in patients with renal or hepatic impairment, and it is also associated with lower day-to-

day variability in glucose levels. Tresiba® is indicated for the treatment of individuals with type 1 or type 2 diabetes from the age of one. Furthermore, in situations when it is not possible for adult patients to take their basal insulin injection at the same time each day, individuals will not suffer from compromised control of blood sugar levels from delays between injections, as long as consecutive injections are separated by at least eight hours. And results from the BEGIN clinical trials performed for regulatory approval from the FDA demonstrated that Tresiba® administered once daily was non-inferior to once-daily insulin glargine U100, as well as significantly reduced the risk of nocturnal hypoglycaemia (9-11) and significantly lowered FPG (10-11) compared with insulin glargine U100.

Novo Nordisk is committed to ensuring patients living with diabetes can afford our insulins, a responsibility we take seriously.

Novo Nordisk remains committed to ensuring affordable access to insulins by reducing the out-of-pocket cost burden, helping to transform the complex pricing system, and fostering better pricing predictability.

Currently, we have a savings offer for Tresiba®, and we recently launched an unbranded biologic for Tresiba®, Insulin Degludec. This unbranded biologic is currently available at 65% off the list price of Tresiba®. In addition, all our insulins, including Tresiba®, are available through our MyInsulinRx program, which provides eligible people living with diabetes a 30-day supply of any combination of our insulin products for $35.

At Novo Nordisk, we strive to develop sustainable affordability options that balance patient affordability, market dynamics, and evolving policy changes. Our commitment to insulin affordability in the U.S. is longstanding, as exemplified by our affordability programs for those living with diabetes.

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Thank you for the opportunity to provide comments and for considering our concerns. Should you have any questions or concerns, please contact Kelsey Lovell, Associate Director, Policy, at KLLV@novonordisk.com with any questions or for further information.

References

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3. Rakel RE. Improving patient acceptance and adherence in diabetes management: a focus on insulin therapy. Adv Ther 2009;26:838–46. Link to PubMed

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11. Zinman B, Philis-Tsimikas A, Cariou B, et al. Insulin degludec versus insulin glargine in insulin-naive patients with type 2 diabetes: A 1-year, randomized, treat-to-target trial (BEGIN Once Long). Diabetes Care. 2012; 35:2464-2471.

Oregon Prescription Drug
Affordability Board

Email: pdab@dcbs.oregon.gov Phone: 971-374-3724 Website: dfr.oregon.gov/pdab

Humulin R U-500 KwikPen[1] Affordability Review

Version 2

[1] Image. https://mydiabetesvillage.com/272-2/ht_160127_humulin_r_u500_pen_800x600/#. ©Lilly USA, LLC. Accessed 1/8/2024.

Table of Contents

Revisions Made

- Page 3: Edited review summary section.
- Page 4: Added information regarding ORS 743A.069 and added name of manufacturer
- Page 5: Additional information added to clinical profile section.
- Page 8: Update graphs to include therapeutic alternative WAC from 2019-2023.
- Page 10: Updated the cost to health benefit coverage section. Removed commercial plans and Medicaid tables. Added new table for all health coverage cost profile.
- Page 11 & 12: Expanded information in therapeutic alternative table and expanded information statement.

Review Summary

The Prescription Drug Affordability Board (PDAB) conducted an affordability review for Humulin R U-500 KwikPen (Insulin Regular, Human). The Oregon All Payer All Claims (APAC) reporting program indicated the drug was prescribed to 550 [2] Oregonians in 2022 with a prescription drug benefit from an Oregon health insurance carrier.

Table 1 Summary of costs to the patient

Costs to the patient		
	Source	**Amount**
Average annual out of pocket cost per commercial insured enrollee	APAC	$164.56

Table 2 Summary of costs to the healthcare system

Costs to the healthcare system		
	Source	**Amount**
Total annual gross spends for payers[3]	APAC	$6,621,244.37
Average annual gross spends for payers per enrollee	APAC	$12,038.63
Annual drug gross cost per enrollee	Data call[4]	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[5]	OSU Drug Research Management Utilization Reports 2022[6]	Drug not on report

[2] Number of 2022 unique enrollees from Oregon's All Payers All Claims (APAC) database. For more information regarding APAC data visit: https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx

[3] 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.

[4] 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.

[5] Quarterly metric used in lieu of annual as the drug may not have been on the 2022 reports for all four quarters.

[6] 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.

Enacted in 2021, ORS 743A.069 provides that health benefit plans offered in Oregon may not require enrollees in their plans to incur cost-sharing or other out-of-pocket costs above certain inflation-adjusted limits for insulin prescribed for the treatment of diabetes. Plans covered by this provision insure approximately 1 million Oregonians. For 2024, the out-of-pocket cost limits are $85 for each 30-day supply or $255 for each 90-day supply.[7] These limits reflect an increase of 13.3% from 2021.

In addition to information provided by the Department of Consumer and Business Services (DCBS) pursuant to ORS 646A.694, this review reflects information from various sources, including 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)**

Manufacturer: **Eli Lilly and Company**

FDA approval

Humulin R U-500 KwikPen was first approved by the FDA on 12/29/2015.[8]

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[7] OAR 836-053-0025 (*available at* https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=303523). ORS 743A.069 requires the Department of Consumer and Business Services, by rule, to annually adjust the cost limits based on changes to the Consumer Price Index for All Urban Consumers, West Region (All Items).

[8] 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.

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.

Clinical profile

Drug indications[9]

- 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[10]

- Humulin R U-500 KwikPen is concentrated formulation (500 units per mL) of human regular insulin. It is most often used for individuals who are severely insulin resistant.
- Humulin R U-500 KwikPen 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).[11] KwikPen is a specific syringe for U-500 insulin that was 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.[12] 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).[13] 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.[14]
- There are no clinical trials with insulin U-500 in combination with other insulin formulations.

[9] Humulin R U-500 Prescribing Information. Eli Lilly and Company. Indianapolis, IN. 2022.
[10] Ibid.
[11] 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.
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[14] Ibid.

Clinical Safety[15]

- FDA safety warnings:
  - Hypoglycemia
  - Hyper- or hypoglycemia due to medication errors or changes in insulin products
  - Hypersensitivity reactions
  - Hypokalemia
  - Do not administer U-500 regular insulin without a dedicated U-500 insulin syringe. Do not 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[16]

Table 3 Alternative short-acting insulin

Drug	FDA Approved Indications	Onset	Duration	Frequency	Formulations
Insulin Regular 500 units/ml *(subject drug)*	Diabetes Mellitus in patients requiring >200 units/day	15 minutes	~21 hours	Two or three times daily before meals	• U-500 vial
Insulin Regular 100 units/ml	Diabetes Mellitus	30 minutes	~8 hours	Two or three times daily before meals	• U-100 vial • U-100 pen
Insulin NPH/ Regular Insulin 70/30	Diabetes Mellitus	30 minutes	~ 23 hours	Twice daily before meals	• 70/30 vial • 70/30 pen

[15] Humulin R U-500 Prescribing Information. Eli Lilly and Company. Indianapolis, IN. 2022.
[16] 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.

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 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.[17]
- 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.[18]

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[19] is displayed in Figure 2.

[17] 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.

[18] 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.

[19] 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.

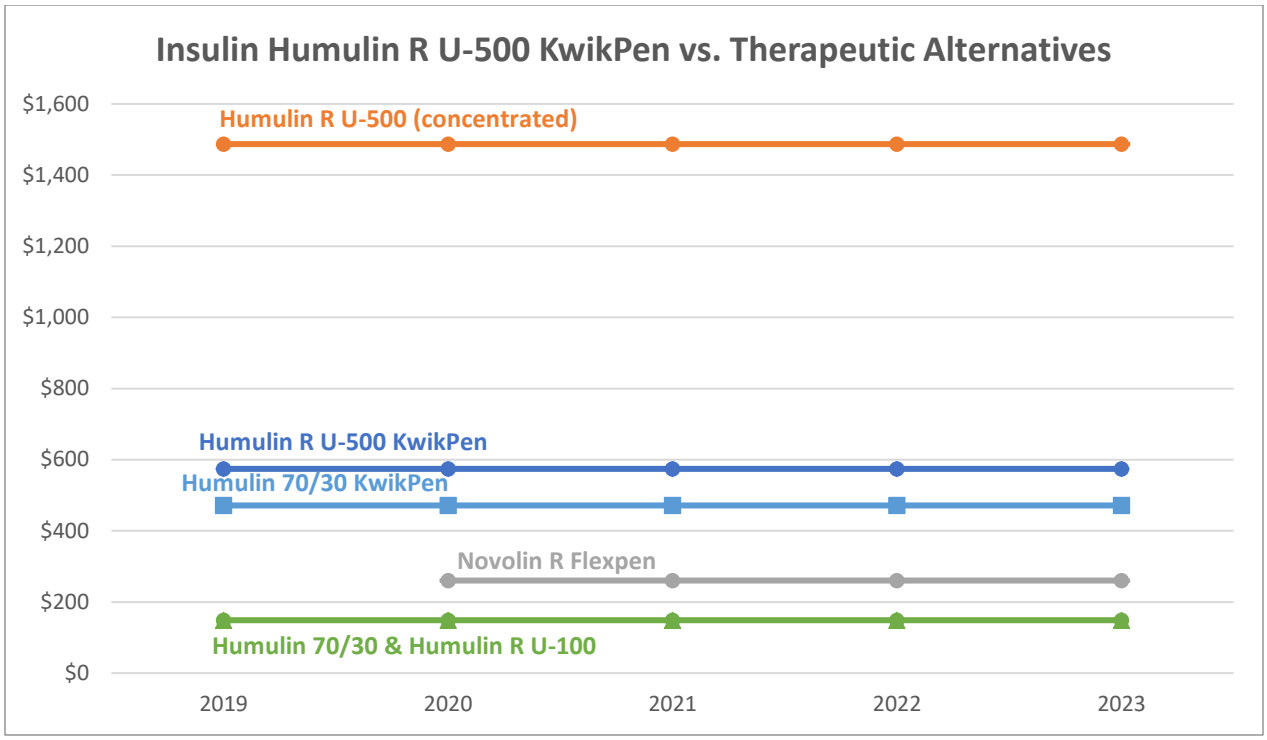

Figure 1 Humulin R-U-500 KwikPen and therapeutic alternative WAC from 2019-2023

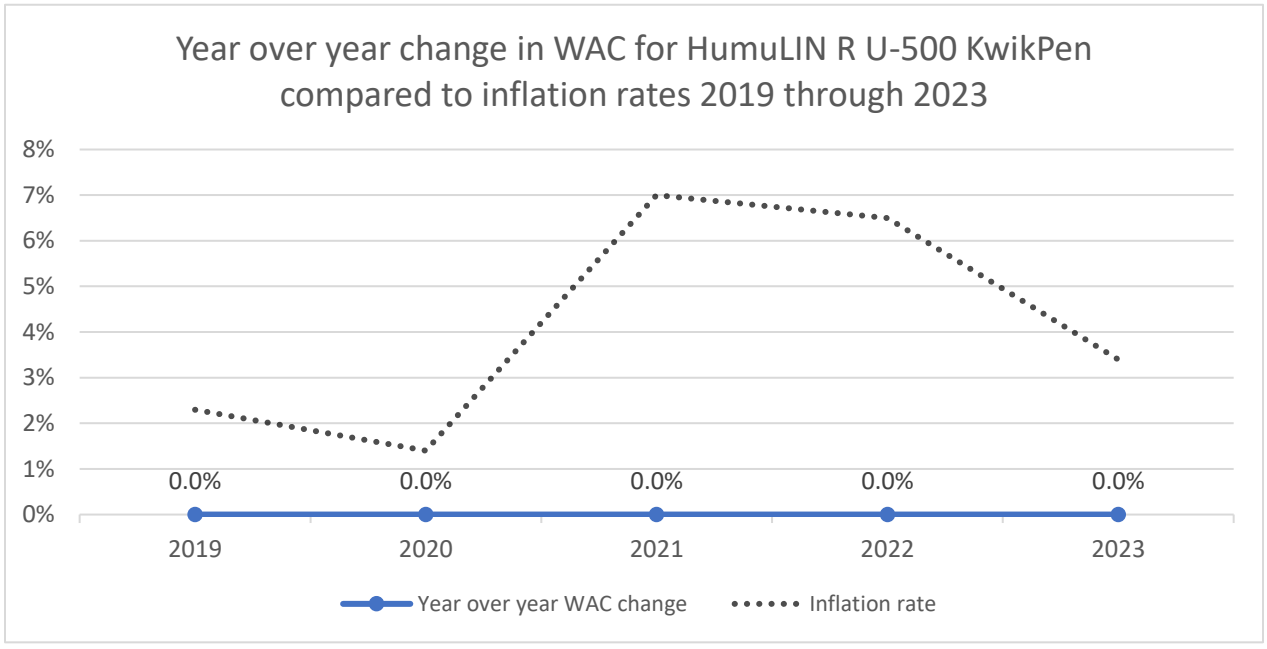

Figure 2 Year over year change in WAC compared to inflation rates[20]

[20] 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.

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[21,22] was analyzed to determine the average copayment for commercially insured enrollees or other cost-sharing for the prescription drug.

Table 4 Out of Pocket Costs

2022 Average annual patient out of pocket costs[23,24]		
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
Total Out-of-Pocket Costs for Patients	**$164.56**	Drug not on data call

[21] 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.
[22] APAC total cost may include a dispensing fee and physician administration fees.
[23] Medicaid and Medicare were excluded from cost information.
[24] For patients who used the drug at least once in the 2022 calendar year.

Cost to health benefit services

The APAC database[25,26] was analyzed to determine the total gross paid amount, total number of enrollees and claims, and the average paid per claim and per enrollee for all Oregon health benefit services.

Table 5 2022 Annual costs to health benefit services

Humulin R U-500 KwikPen	Gross paid amount	Total unique claims	Total unique enrollees	Average paid per claim	Average paid per enrollee
Commercial plans	$1,992,615.97	1,015	167	$1,963.17	$11,931.83
Medicaid[27]	$1,714,340.54	1,123	157	$1,526.57	$10,919.37
Medicare	$2,914,287.86	1,394	226	$2,090.59	$12,895.08
Total	**$6,621,244.37**	**3,532**	**550**	**$1,874.64**	**$12,038.63**

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.

[25] 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.
[26] APAC total cost may include a dispensing fee and physician administration fees.
[27] Medicaid costs include Coordination Care Organizations (CCOs) and fee for service (FFS). Amount paid on the claim = 1) Ingredient Cost ([AAAC/NADAC/WAC] x Dispense Quantity) + Dispensing Fee. If billed amount was lower, pay billed amount, minus TPL amount. DUR Reports | College of Pharmacy | Oregon State University.

Cost of Therapeutic Alternatives

Table 6 Therapeutic alternative (TA) comparison

	NDC	Drug Name	Package size	2022 WAC package size	Pricer per package	Package strength in mL	2022 WAC unit price	AAAC[28] unit price	NADAC[29] unit price	Percent difference of NADAC from subject Rx & TA
Subject drug	**00002-8824-27**	**Humulin R U-500 KwikPen**	**2 prefilled pens**	**$574.20**	**$287.10**	**3 mL**	**$95.70**	**$92.18**	**$91.61**	
Therapeutic alternative	00169-3003-15	Novolin R FlexPen	5 prefilled pens	$260.25	$52.05	3 mL	$17.35	N/A	$16.64	450.5%
Therapeutic alternative	00002-8803-59	Humulin 70/30 KwikPen	5 prefilled pens	$471.30	$94.26	3 mL	$31.42	N/A	$30.15	203.8%
Therapeutic alternative	00002-8501-01	Humulin R U-500 (concentrated)	1 vial	$1,487.00	$1,487.00	20 mL	$74.35	$71.75	$71.06	28.9%
Therapeutic alternative	00002-8715-01	Humulin 70/30	1 vial	$148.70	$29.74	10 mL	$14.87	N/A	$14.28	541.5%
Therapeutic alternative	00002-8215-01	Humulin R U-100	1 vial	$148.70	$29.74	10 mL	$14.87	N/A	$14.28	541.5%

[28] 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.

[29] 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

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. Humulin R U-500 KwikPen was compared to five therapeutic alternatives. Novolin R prefilled pens with a quantity of five pens in each package is 450.5% less expensive per unit price than the subject drug. All therapeutic alternatives reviewed showed a per unit price savings when compared to the subject drug.

Access profile

Utilization and Health Equity

According to the CDC, in 2021 8.9% of the US population (all age groups) had diagnosed diabetes.[30] 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.[31]

The prevalence of type 1 and type 2 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.[32] 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.[33] 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.[34]

[30] 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
[31] 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
[32]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.
[33] Ibid.
[34] 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.

To review how the prevalence of diabetes ranges throughout Oregon, Figure 3 shows 2018 rates of diabetes by county from the CDC website.[35] In addition to the rate of diabetes, the data included the Social Vulnerability Index (SVI) scores for each county.

Oregon Counties Social Vulnerability Map[36]

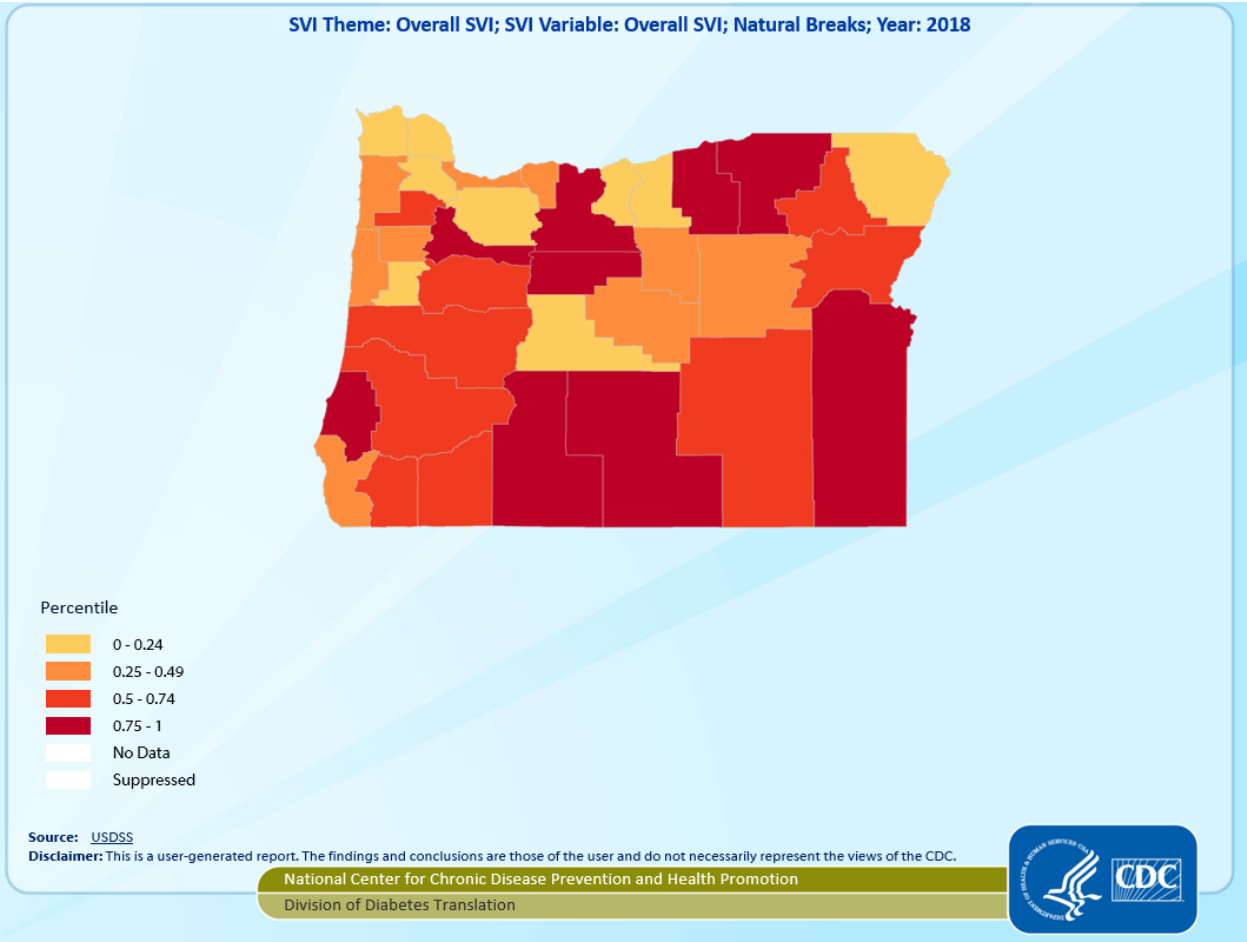

Figure 3 Oregon Counties Social Vulnerability Map

[35] 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.
[36] Ibid.

Oregon Counties Diagnosed Diabetes Map[37]

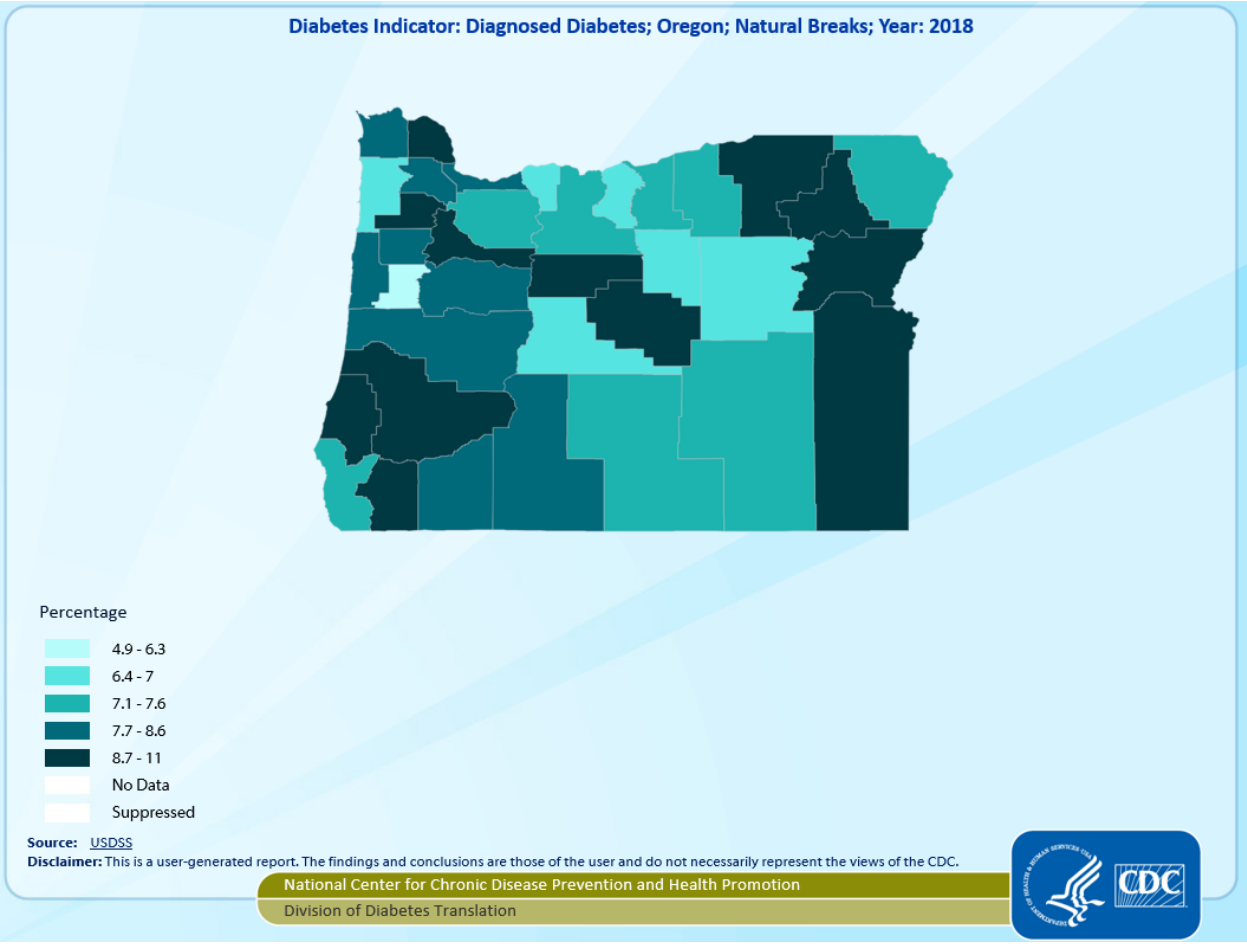

Figure 4 Oregon Counties Diagnosed Diabetes Map

[37] 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[38]

Table 7 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%

[38] 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. Vise 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 A

December 18, 2023

Eli Lilly and Company

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Indianapolis, Indiana 46285
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www.lilly.com

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

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"[1] 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."[2]

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.[3] 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.[4] Clinical trials have shown that Humulin® R U-500 plays a unique and important role in the options physicians have to treat patients. When

[1] Division of Financial Regulation : Prescription drug data : Oregon Prescription Drug Affordability Board : State of Oregon; https://dfr.oregon.gov/pdab/Pages/data.aspx
[2] ORS 646A.694.
[3] For more information, please see Humulin.com and the prescribing information available at: https://pi.lilly.com/us/humulin-r-u500-pi.pdf.
[4] 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.[5]

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.[6]

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, 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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[5] 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 glycymic 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.
[6] For more information about Lilly Cares, including available products and eligibility requirements, see 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.

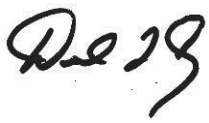
As a cutting-edge pharmaceutical company, innovation is at the heart of what we do, particularly for people with diabetes. In the early 1920s, people with type 1 diabetes had a life expectancy of only a handful of years after diagnosis. With the first animal-derived insulin, Lilly extended life expectancy 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

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,



Derek Asay
Sr. Vice President, Government Strategy & Federal Accounts