Oregon Prescription Drug
Affordability Board

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Tresiba & Tresiba FlexTouch Affordability Review[1]

Version 1

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

Table of Contents

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 2,356[2] (Tresiba 77, Tresiba FlexTouch 2,279) 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	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 cost for payers[3]	APAC	$9,148,039 (Tresiba $217,616, Tresiba FlexTouch $8,930,423)
Average annual cost for payers per enrollee[4]	APAC	Tresiba: $2,826.18 Tresiba FlexTouch: $3,918.57
Annual drug gross cost per enrollee	Data call[5]	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[6]	OSU Drug Research Management Utilization Reports 2022[7]	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 excluding Medicaid and Medicare. For more information regarding APAC data visit: https://www.oregon.gov/oha/HPA/ANALYTICS/Pages/All-Payer-All-Claims.aspx

[3] Excludes Medicaid and Medicare

[4] Ibid

[5] 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.

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

[7] 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): **Tresiba, Tresiba FlexTouch**

Non-proprietary name: **Insulin Degludec**

FDA approval

Tresiba was first approved by the FDA on 9/25/2015.[8]

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

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

[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.

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

- 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 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.

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[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

[15] Ibid.

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.

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)*	• T1DM • T2DM	~24 hours	Once daily at the same time	• U-100 vial • U-100 pen • U-300 pen	• Semglee • Rezvoglar
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.*

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

[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.

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).
- 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.

[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.

[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 1 Tresiba WAC over time

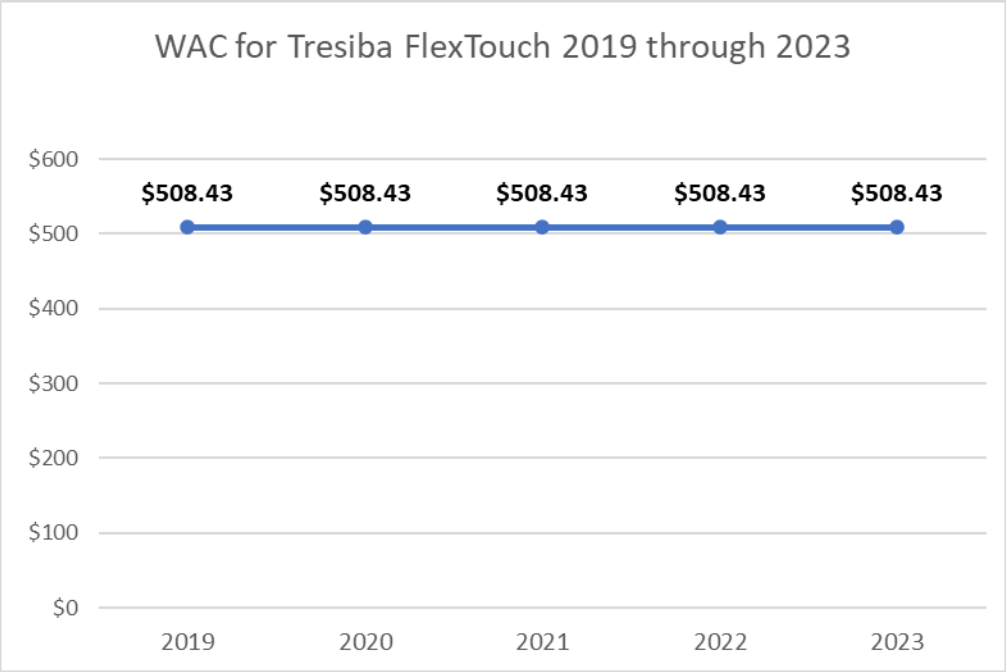

Figure 2 Tresiba FlexTouch WAC over time

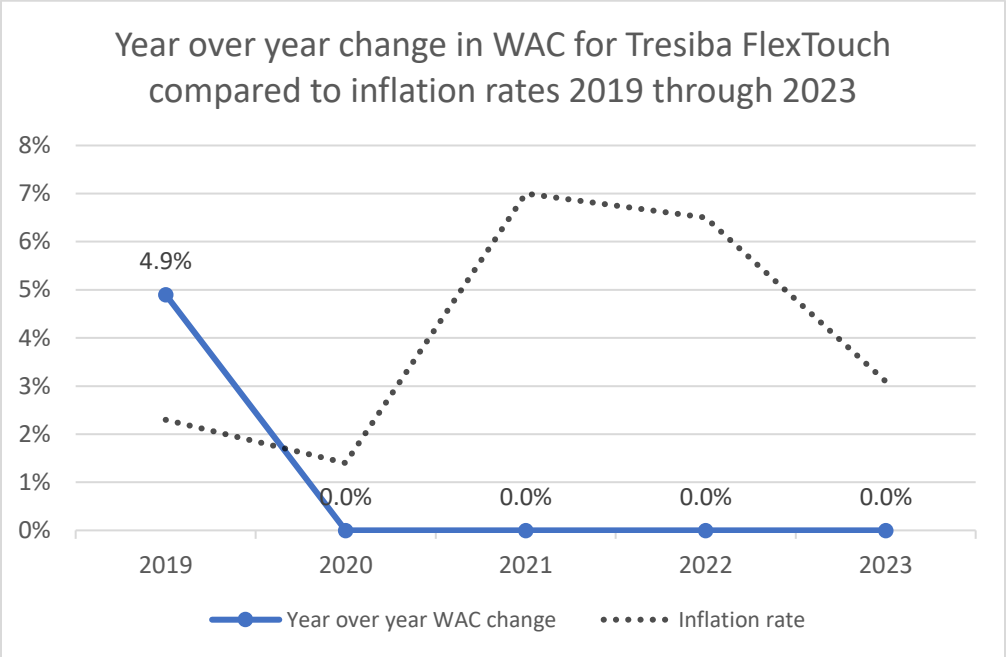

Figure 3 Year over year change in WAC for Tresiba compared to inflation rates[25]

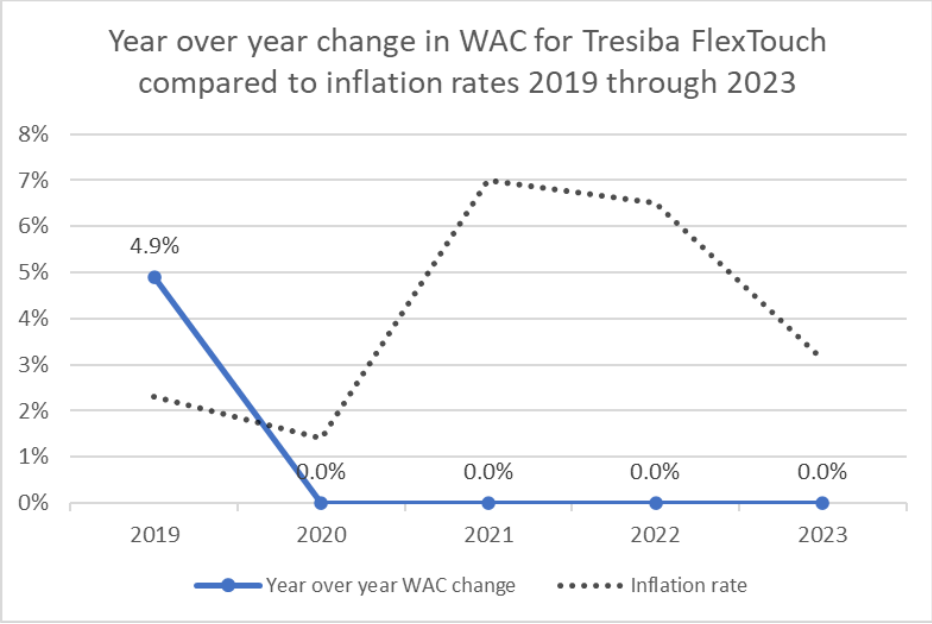

Figure 4 Year over year change in WAC for Tresiba FlexTouch compared to inflation rates [26]

[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.
[26] Ibid.

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] was analyzed to determine the average patient copayment or other cost-sharing for the prescription drugs.

Table 4 Out of Pocket Costs

2022 Average annual patient out of pocket costs[28]			
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[29]	**$150.92**	**$169.64**	Drugs not on data call

Cost to health benefit plans

The APAC database[30] was analyzed to determine both the total annual spend and cost per patient for health insurance benefit plans.

[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] Medicaid and Medicare were excluded from cost information.
[29] For patients who used the drug at least once in the 2022 calendar year.
[30] 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 5 2022 Annual costs to health plans

2022 Annual costs to health plans[31]		
Value	**APAC[32]**	**Data Call[33]**
Total Annual Spend	$9,148,039 (Tresiba $217,616, Tresiba FlexTouch $8,930,423)	Drugs not on data call
Total Annual Spend per Patient	Tresiba: $2,826.18 Tresiba FlexTouch: $3,918.57	Drugs not on data call

Cost to the state medical assistance program[34]

Table 7 Gross amount paid by Medicaid CCOs

Gross amount paid fee for Medicaid CCO			
Drug	**Amount paid**	**Claim count**	**Average paid per claim**
Tresiba	$121,307.03	291	$416.86
Tresiba FlexTouch	$4,378,996.65	6,642	$659.29

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.

[31] Medicaid and Medicare were excluded from cost information.
[32] APAC total cost may include a dispensing fee and physician administration fees.
[33] 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.
[34] Source: Oregon State University Drug Use and Research Management DUR utilization reports 2022. DUR Reports | College of Pharmacy | Oregon State University.

Cost of Therapeutic Alternatives

Table 8 Therapeutic alternative (TA) comparison

	NDC	Drug Name	Package size	2022 WAC package size	Package strength	2022 WAC unit price	AAAC[35] unit price	NADAC[36] unit price	Percent difference of NADAC from review Rx & TA
Subject drug	00169-2662-11	Tresiba	1 vial	$338.95	10 mL	$33.90	$32.66	$32.32	
Therapeutic alternative	00955-1729-01	Insulin glargine	1 vial	$113.42	10 mL	$11.34	$10.96	$10.89	196.8%
Subject drug	00169-2660-15	Tresiba FlexTouch	5 cartridges per box	$508.43	3 mL	$33.90	$32.66	$33.89	
Therapeutic alternative	00955-1728-05	Solostar	5 cartridges per box	$170.12	3 mL	$11.34	N/A	$10.90	196.5%

Tresiba was compared to a single therapeutic alternative. 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 therapeutic alternative to Tresiba vial is 196.8% less expensive. Additionally, the therapeutic alternative Solostar is 196.5% less expensive than the Tresiba pen.

[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.

Access profile

Utilization and Health Equity

Impact of Diabetes in the Community

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]

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.

[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
[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.

Oregon Counties Social Vulnerability Map[43]

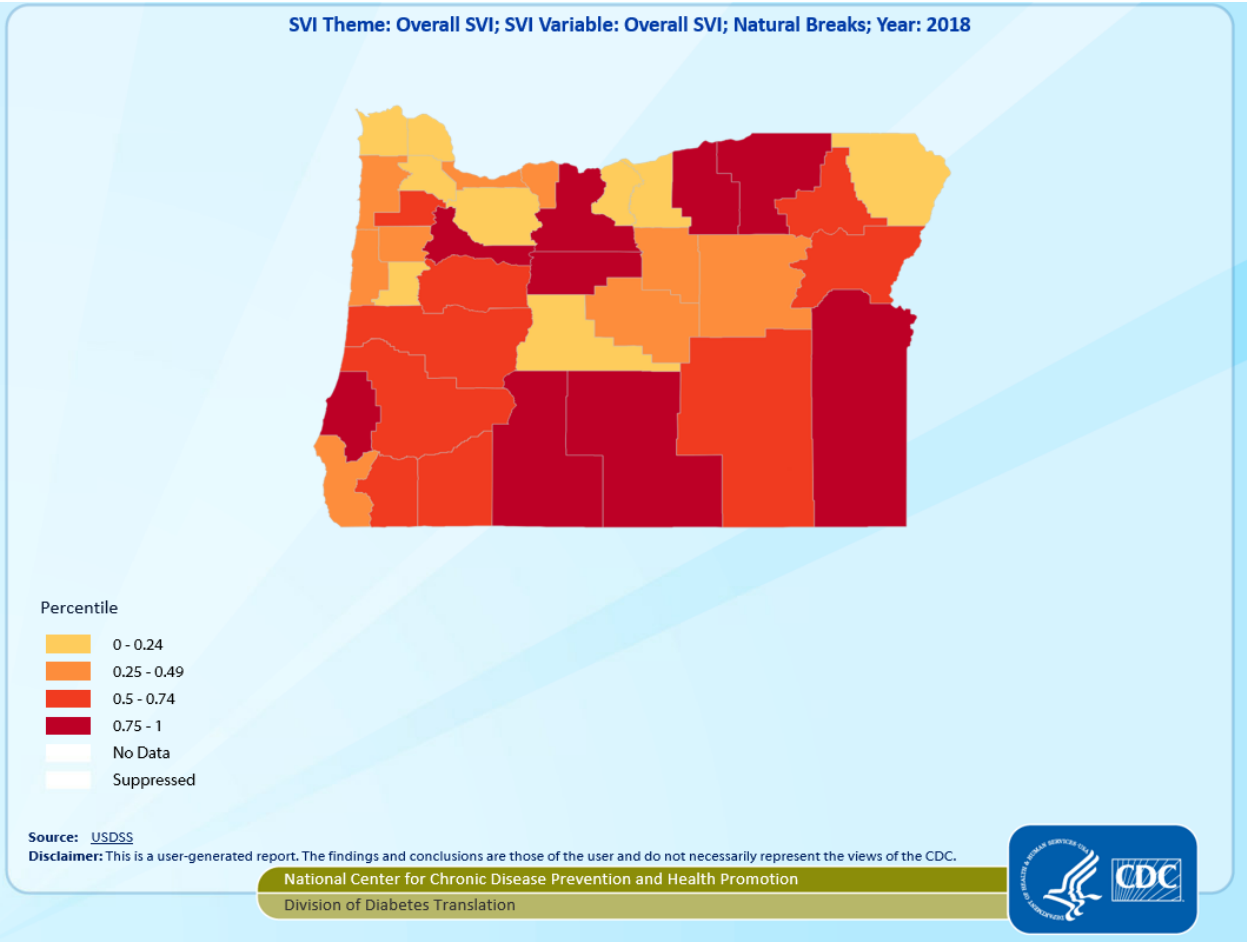

Figure 5 Oregon Counties Social Vulnerability Map

[43] 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[44]

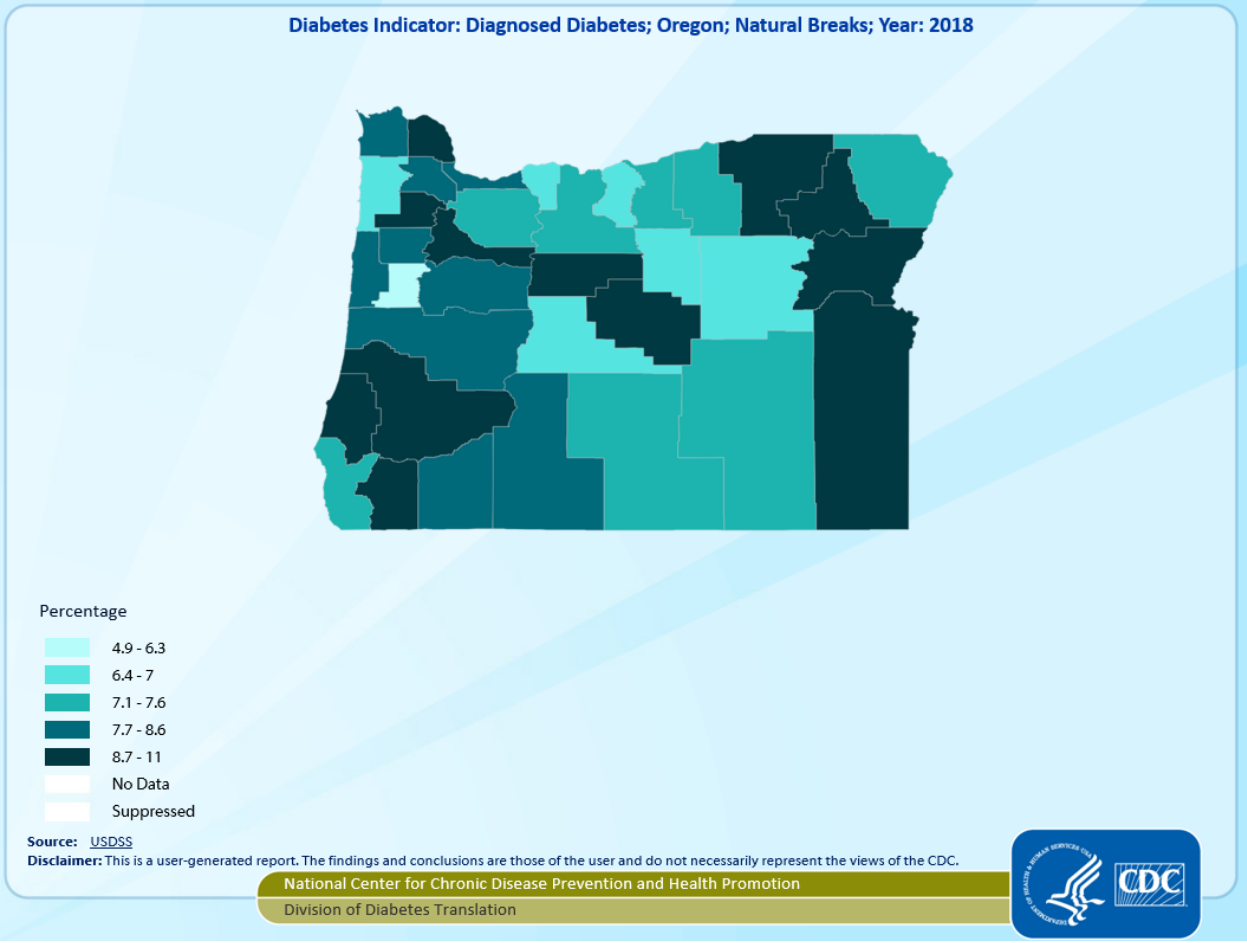

Figure 6 Oregon Counties Diagnosed Diabetes Map

[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%

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

[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.

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 Noro 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

Appendix A: Novo Nordisk

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.

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