April 11, 2024

Oregon Prescription Drug Affordability Board
PO Box 14480
Salem, OR 97309

Re: Removal of Dupixent® as an approved orphan drug from subset list of 2023 prescription drugs for affordability reviews

Dear Members of the Oregon Prescription Drug Affordability Board,

Sanofi appreciates the opportunity to submit comments to the Oregon Prescription Drug Affordability Board ("OR PDAB") regarding its subset list of 2023 prescription drugs for affordability reviews. Our product, Dupixent, was selected by the OR PDAB for inclusion on the subset list at the March 19, 2025 meeting. Dupixent is approved to treat six different indications, including eosinophilic esophagitis – a rare disease for which Dupixent was granted an "orphan drug" approval. Given its approved orphan designation, and the prohibition on including such approved products from affordability reviews under the OR PDAB authorizing statute, we respectfully ask that the Board remove Dupixent from any affordability review.[1]

Dupixent, which Sanofi commercializes with its partner, Regeneron, is a biologic medication that blocks the signaling of two key sources of Type 2 inflammation (IL-4 and IL-13) and is currently indicated in the treatment of six conditions: eczema/atopic dermatitis; asthma; nasal polyps; eosinophilic esophagitis (EoE); prurigo nodularis and chronic obstructive pulmonary disease (COPD).

EoE is a rare type 2 inflammatory disease that damages the esophagus and prevents it from working properly. There are approximately 160,000 patients in the U.S. living with EoE who are currently treated, of whom approximately 48,000 have failed multiple treatments. For people with EoE, swallowing the smallest amount of food can be a painful and worrisome choking experience. This disease can also cause narrowing of the esophagus and dilation (physical expansion) of the esophagus may be needed, which is often painful. In severe cases, a feeding tube is the only option to ensure proper caloric intake and adequate nutrition. People with EoE may have poor quality of life and are more likely to experience depression than people without EoE.

Dupixent was granted an orphan designation by the FDA under 21 U.S.C. 360bb for the potential treatment of EoE in 2017. On May 20, 2022, Sanofi received full approval for the treatment of EoE in adult and pediatric patients aged 12 years and

[1] Sanofi reserves the right to supplement this submission with additional information to inform the OR PDAB's decision-making on this important topic.

older. Last year, this indication was extended to cover the treatment of pediatric patients aged one year and older. Included with this letter is copy of the FDA's Orphan Drug Designations and Approvals database entry for Dupixent confirming the approved orphan drug status.

Under the OR PDAB's authorizing statute, "[a] drug that is designated by the Secretary of the United States Food and Drug Administration, under 21 U.S.C. 360bb, as a drug for a rare disease or condition is not subject to review under subsection (1) of this section."[2] Given that Dupixent is approved by the FDA with an orphan designation for the treatment of a rare disease, it should be excluded from review and removed from the list.

Sanofi remains committed – and devotes significant resources – to exploring all of the potential disease states and patient populations that could benefit from Dupixent. Dupixent was recently approved as the first ever biologic product treatment for COPD.[3] We believe that Dupixent will also benefit future patients with other serious diseases and conditions and are currently in clinical trials to pursue several additional indications. In fact, Dupixent is currently being studied in another rare disease orphan indication – bullous pemphigoid.[4]

Dupixent represents precisely the type of innovation and approach to pricing that should be expected from our industry – pursuing first in class or best in class medicines that have the potential to transform the practice of medicine for patients, and pricing those medicines in a manner that reflects the value they provide to patients and society.

Thank you for the opportunity to provide comments and for considering our concerns. We expect that after considering Dupixent's orphan approval, **the Board will remove Dupixent from the subset list of 2023 prescription drugs for affordability reviews.**

Please feel free to contact me at with any questions at andrea.todd-harlin@sanofi.com or (651) 341-3444.

Sincerely,

Andrea Todd-Harlin
Head, State Government Relations, Sanofi

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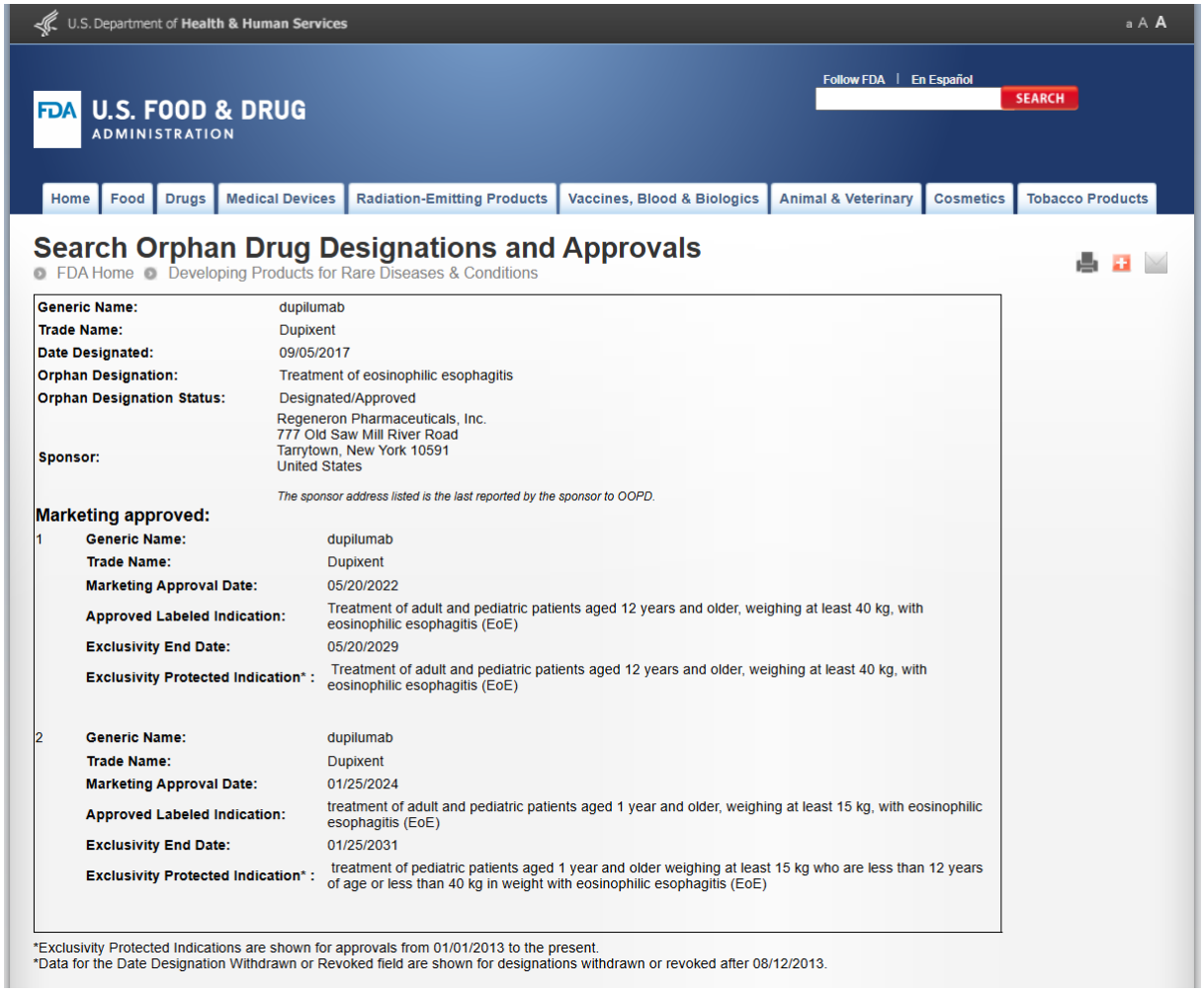
[2] Or. Rev. Stat. § 646A.694(2) (2023).
[3] Sanofi, Press Release, Dupixent Approved in the US as the First-Ever Biologic Medicine for Patients with COPD (Sept. 27, 2024), https://www.sanofi.com/assets/dotcom/pressreleases/2024/2024-09-27-13-35-00-2954551-en.pdf.
[4] Sanofi, Press Release, Dupixent sBLA accepted for FDA priority review for the targeted treatment of bullous pemphigoid, (Feb. 18, 2025), https://www.sanofi.com/en/media-room/press-releases/2025/2025-02-18-06-00-00-3027482.

Attachment A: FDA Orphan Drug Designations and Approvals database entry for Dupixent®



U.S. Department of Health & Human Services

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Generic Name:	dupilumab
Trade Name:	Dupixent
Date Designated:	09/05/2017
Orphan Designation:	Treatment of eosinophilic esophagitis
Orphan Designation Status:	Designated/Approved
Sponsor:	Regeneron Pharmaceuticals, Inc. 777 Old Saw Mill River Road Tarrytown, New York 10591 United States

The sponsor address listed is the last reported by the sponsor to OOPD.

Marketing approved:

1	**Generic Name:**	dupilumab
	Trade Name:	Dupixent
	Marketing Approval Date:	05/20/2022
	Approved Labeled Indication:	Treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE)
	Exclusivity End Date:	05/20/2029
	Exclusivity Protected Indication* :	Treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE)
2	**Generic Name:**	dupilumab
	Trade Name:	Dupixent
	Marketing Approval Date:	01/25/2024
	Approved Labeled Indication:	treatment of adult and pediatric patients aged 1 year and older, weighing at least 15 kg, with eosinophilic esophagitis (EoE)
	Exclusivity End Date:	01/25/2031
	Exclusivity Protected Indication* :	treatment of pediatric patients aged 1 year and older weighing at least 15 kg who are less than 12 years of age or less than 40 kg in weight with eosinophilic esophagitis (EoE)

*Exclusivity Protected Indications are shown for approvals from 01/01/2013 to the present.
*Data for the Date Designation Withdrawn or Revoked field are shown for designations withdrawn or revoked after 08/12/2013.

Bristol Myers Squibb™

April 15, 2025

VIA ELECTRONIC SUBMISSION

Oregon Prescription Drug Affordability Board
350 Winter Street NE
Salem, OR 97309-0405
pdab@dcbs.oregon.gov

Re: Oregon Prescription Drug Subset List

Dear Members of the Oregon Prescription Drug Affordability Board:

Bristol Myers Squibb ("BMS") appreciates the opportunity to submit written comments to the Oregon Prescription Drug Affordability Board (the "Board") on its subset of prescription drugs to prioritize for affordability review. **For the reasons below, we respectfully ask that ELIQUIS® (apixaban) be removed from the prioritized subset and not subject to the affordability review process.** Much of this information was shared previously with the Board in 2023, when ELIQUIS was initially identified for potential review and subsequently removed from consideration after the Board voted to remove prescription drugs based on selection for the Medicare Drug Price Negotiation Program under the Inflation Reduction Act (IRA), which continues to be implemented under the new administration.[1]

Bristol Myers Squibb's Commitment to Oregon Patients

At BMS, we are inspired by a single vision—transforming patients' lives through science. We are in the business of breakthroughs—the kind that transform patients' lives through lifesaving, innovative medicines. We combine the agility of a biotech with the reach and resources of an established pharmaceutical company to create a global leading biopharma company. In oncology, hematology, immunology, cardiovascular disease, and neuroscience—with one of the most diverse and promising pipelines in the industry—we focus on innovations that drive meaningful change. BMS supports public policies that promote patient access to new and effective medical treatments and help ensure patients benefit from the innovation that defines the U.S. health care system, and we have long supported efforts in Oregon to meaningfully enhance patient access and improve affordability by lowering out-of-pocket costs for patients.

Driven by our patient-focused mission, we disagree with the potential application of an "affordability review" process to ELIQUIS. Oregon law states that the Board shall identify prescription drugs "that the [B]oard determines may create affordability challenges for health

[1] Please refer to Table 2 of the Meeting Minutes for the PDAB's November 15, 2023, meeting. Accessible here: https://dfr.oregon.gov/pdab/Documents/20231115-PDAB-approved-minutes.pdf

care systems or high out-of-pocket costs for patients in this state" and instructs the Board to consider multiple factors in determining which prescription drugs to prioritize for affordability review.[2] We are concerned that the current methodology, data sources, and criteria used by the Board to identify prescription drugs for affordability review may not accurately prioritize those prescription drugs that may pose affordability challenges for patients, as the listing of ELIQUIS reflects. We believe that ELIQUIS should be removed from the prioritized subset of prescription drugs as its inclusion is inappropriately based on its volume of use by clinicians and patients in Oregon, rather than its costs to health care systems and patients. Indeed, the statutory affordability review process contemplates many factors beyond volume alone, focusing on products presenting actual affordability issues for patients. Currently, Eliquis is widely available to patients, with over 90% open access among commercial plans and low out-of-pocket costs. On average, non-valvular atrial fibrillation patients with commercial insurance pay only $38 per month for Eliquis, and 5 out of 10 paying $20 per month or less.[3] We also wish to emphasize the clinical attributes of ELIQUIS and evidence of its benefits to patients, the healthcare system, and society.

Background on ELIQUIS

ELIQUIS is a best-in-class direct oral anticoagulant ("DOAC") indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation ("NVAF"), for the treatment and prevention of Deep Vein Thrombosis ("DVT") and pulmonary embolism (PE), and to decrease the risk of DVT blood clots after hip or knee replacement surgery.[4] Atrial fibrillation ("AFib") is the most common type of irregular heartbeat that often causes the heart to beat too quickly and can lead to blood clots, stroke, heart failure and other heart-related complications if left untreated.[5]

As the U.S. population ages, the number of people with AFib is projected to increase to more than 12 million by the year 2030.[6] AFib is associated with an approximately fivefold increased risk of ischemic stroke. The risk of having a stroke is nearly twice as high for non-Hispanic Black adults as for White adults and non-Hispanic Black adults and Pacific Islander adults have the highest rates of death due to stroke.[3] Stroke-related costs in the U.S. came to nearly $56.2 billion between 2019 and 2020 which included the cost of health care services, medicines to treat stroke, and missed days of work.[7] In Oregon, hospitalization costs for adults with stroke totaled $277 million in 2022.[8] Effective treatments to reduce the risk of stroke are important to Oregon's health care system and patients, as stroke-related care commonly leads to costly hospitalizations and extended rehabilitation needs.

[2] Or. Rev. Stat. Ann. § 646A.694(1); Or. Admin. R. 925-200-0010.
[3] Pricing information. AFib Pricing Information for Rx ELIQUIS® (apixaban) | Safety Info (December 2024). https://www.eliquis.bmscustomerconnect.com/afib/price.
[4] ELIQUIS® (apixaban) Package Insert. Bristol-Myers Squibb Company, Princeton, NJ and Pfizer Inc, New York, NY https://packageinserts.bms.com/pi/pi_eliquis.pdf.
[5] Why Atrial Fibrillation Matters. https://www.heart.org/en/health-topics/atrial-fibrillation/why-atrial-fibrillation-af-or-afib-matters.
[6] Centers for Disease Control and Prevention. (2022, October 14). Atrial fibrillation. Centers for Disease Control and Prevention. https://www.cdc.gov/heartdisease/atrial_fibrillation.htm.
[7] Centers for Disease Control and Prevention. (2024, October 24). Stroke Facts. Centers for Disease Control and Prevention. https://www.cdc.gov/stroke/data-research/facts-stats/?CDC_AAref_Val=https://www.cdc.gov/stroke/facts.htm,
[8] 2024 The Oregon Stroke Care Committee Report to the Legislature (2024). State Library of Oregon Digital Collections, accessed 15/04/2025, https://digitalcollections.library.oregon.gov/nodes/view/287173

ELIQUIS's benefits to patients, the healthcare system, and society.

The Board's methodology for selecting prescription drugs to prioritize for affordability review does not reflect the substantial clinical and economic benefits of ELIQUIS. The clinical benefits of ELIQUIS have been demonstrated in both the clinical trial and real-world clinical practice settings. In several U.S. real-world data analyses, ELIQUIS use was associated with a similar or lower risk of stroke-related hospitalizations, as well as a consistently lower risk of bleeding-related hospitalizations, when compared to other oral anticoagulants.[9,10,11,12,13] These findings were consistent across different populations and data sources, including Medicare, Commercial, Veterans Affairs, and Department of Defense.[7-11]

In addition to the clinical benefits of ELIQUIS, the economic benefits were found to be associated with reduced healthcare resource utilization and costs across various populations with NVAF and VTE studied in U.S. real-world data analyses. Specifically, these analyses demonstrated that ELIQUIS was associated with similar or lower all-cause healthcare costs and consistently lower all-cause medical costs—particularly those associated with major bleeding events—when compared to other oral anticoagulants.[14,15,16] Considering the economic burden of NVAF in the U.S. has been predicted to approach $30 billion annually by 2050[17] and is largely driven by costs associated with hospitalization, ELIQUIS provides clinicians and health care systems in Oregon with a less costly approach to reducing the risk of stroke, hospitalizations, and extended rehabilitation needs through treating and preventing blood clots.

Insurer-Reported Data Lacks Transparency and Neglects Patient Cost Realities

We understand that the Board gives decisive weight to Drug Price Transparency ("DPT") carrier data and the so-called "CCO list." We are concerned with this approach given the limitations of the DPT carrier data, the lack of transparency into the Board's methodology for

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[9] Ray WA, Chung CP, Stein CM, et al. Association of Rivaroxaban vs Apixaban With Major Ischemic or Hemorrhagic Events in Patients With Atrial Fibrillation. *JAMA*. 2021;326(23):2395–2404. doi:10.1001/jama.2021.21222

[10] Graham DJ, Baro E, Zhang R, Liao J, Wernecke M, Reichman ME, Hu M, Illoh O, Wei Y, Goulding MR, Chillarige Y, Southworth MR, MaCurdy TE, Kelman JA. Comparative Stroke, Bleeding, and Mortality Risks in Older Medicare Patients Treated with Oral Anticoagulants for Nonvalvular Atrial Fibrillation. Am J Med. 2019 May;132(5):596-604.e11. doi: 10.1016/j.amjmed.2018.12.023. Epub 2019 Jan 9. PMID: 30639551.

[11] Deitelzweig, S, Keshishian, A, Li, X. et al. COMPARISON OF EFFECTIVENESS, SAFETY, AND THE NET CLINICAL OUTCOME BETWEEN DIFFERENT DIRECT ORAL ANTICOAGULANTS IN 162,707 NON-VALVULAR ATRIAL FIBRILLATION PATIENTS TREATED IN US CLINICAL PRACTICE. JACC. 2018 Mar, 71 (11_Supplement) A275.
https://doi.org/10.1016/S0735-1097(18)30816-7

[12] Deitelzweig S, Sah J, Kang A, Russ C, Preib M, Dhamane AD, Ratiu A, Cato M, Alfred T, Levi E, Di Fusco M. Effectiveness and Safety of Apixaban Versus Warfarin in Obese Patients with Nonvalvular Atrial Fibrillation Enrolled in Medicare and Veteran Affairs. Am J Cardiol. 2022 Jan 15;163:43-49. doi: 10.1016/j.amjcard.2021.09.047. PMID: 34930532.

[13] Gupta K, Trocio J, Keshishian A, Zhang Q, Dina O, Mardekian J, Rosenblatt L, Liu X, Hede S, Nadkarni A, Shank T. Real-World Comparative Effectiveness, Safety, and Health Care Costs of Oral Anticoagulants in Nonvalvular Atrial Fibrillation Patients in the U.S. Department of Defense Population. J Manag Care Spec Pharm. 2018 Nov;24(11):1116-1127. doi: 10.18553/jmcp.2018.17488. Epub 2018 Sep 13. PMID: 30212268; PMCID: PMC10398049.

[14] Amin A, Keshishian A, Trocio J, Dina O, Le H, Rosenblatt L, Liu X, Mardekian J, Zhang Q, Baser O, Nadkarni A, Vo L. A real-world observational study of hospitalization and health care costs among nonvalvular atrial fibrillation patients prescribed oral anticoagulants in the U.S. Medicare population. J Manag Care Spec Pharm. 2020 May;26(5):639-51.

[15] Deitelzweig S, Luo X, Gupta K, Trocio J, Mardekian J, Curtice T, Hlavacek P, Lingohr-Smith M, Menges B, Lin J. All-cause, stroke/systemic embolism-, and major bleeding-related health-care costs among elderly patients with nonvalvular atrial fibrillation treated with oral anticoagulants. Clin Appl Thromb Hemost. 2018;24(4):602-11.

[16] Hlavacek P, Guo JD, Rosenblatt L, Keshishian A, Russ C, Mardekian J, Ferri M, Poretta T, Yuce H, McBane R. Safety, effectiveness, and health care cost comparisons among elderly patients with venous thromboembolism prescribed warfarin or apixaban in the United States Medicare population. Curr Med Res Opin. 2019 Dec;35(12):2043-51.

[17] Kim MH, Lin J, Hussein M, et al. Cost of atrial fibrillation in United States managed care organizations. Adv Therapy. 2009;26(9):847–857.

compiling and weighing the data, and manufacturers' inability to independently verify or dispute the accuracy of the data. The Board also has not specified how it has weighed the seven regulatory factors articulated in Or. Admin. R. 925-200-0010.

Continued Implementation of the Medicare Drug Price Negotiation Program

In August 2023, ELIQUIS was included as one of the first ten prescription drugs selected for the Medicare Drug Price Negotiation Program under the Inflation Reduction Act (IRA), with the Maximum Fair Prices (MFPs) for these products set to take effect on January 1, 2026. Within the new presidential administration, both the Centers for Medicare and Medicaid Services (CMS) and key appointees have publicly reaffirmed their commitment to the program:

- On January 29, 2025, CMS stated that it "remains committed to achieving value for beneficiaries and taxpayers" through the program.[18]
- Dr. Mehmet Oz, newly confirmed CMS Administrator, has said of the program: *"It's the law. I'm going to defend it and use it."*[19]
- CMS is hosting a series of public engagement events in April 2025 to "provide an opportunity for patients, beneficiaries, caregivers, consumer and patient organizations, and other interested parties, such as clinicians and researchers, to share input relevant to prescription drugs selected for the second cycle of negotiations."[20]
- CMS has communicated a timeline beginning in June 2025 to pharmacies and other drug dispensing entities to help them prepare for implementation of the program.[21]

These public comments confirm the federal government's intent to continue implementing the Medicare Drug Price Negotiation Program and impose MFPs on selected prescription drugs. Of note, since the IRA's inception, we have expressed serious concerns about the impact government price-setting will have on the development of future medicines that can help patients prevail over serious disease.

ELIQUIS's Limited Remaining Market Exclusivity.

ELIQUIS's patent exclusivity is estimated to expire on April 1, 2028, after which generic competitors are expected to enter the market. This creates a narrow window—just over two years—between the implementation of Medicare's Maximum Fair Price and the arrival of generic alternatives. This substantially limits any potential impacts of the affordability review process, even assuming affordability review was appropriate and could result in positive impacts, which we do not believe to be true.

[18] Centers for Medicare & Medicaid Services. (2025, January 29). *CMS statement on lowering the cost of prescription prescription drugs*. https://www.cms.gov/newsroom/press-releases/cms-statement-lowering-cost-prescription-prescription drugs
[19] Senate Committee on Finance. (2025, March 14). *Hearing to consider the nomination of Mehmet Oz, of Pennsylvania, to be Administrator of the Centers for Medicare and Medicaid Services, vice Chiquita Brooks-LaSure, resigned*. https://www.finance.senate.gov/hearings/hearing-to-consider-the-nomination-of-mehmet-oz-of-pennsylvania-to-be-administrator-of-the-centers-for-medicare-and-medicaid-services-vice-chiquita-brooks-lasure-resigned
[20] Centers for Medicare & Medicaid Services. (2025). 2027 public engagement events. Retrieved from https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation/2027-public-engagement-events
[21] Centers for Medicare & Medicaid Services. *Resources for pharmacies and dispensing entities*. Retrieved from https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation/resources-pharmacies-and-dispensing-entities

Conclusion

BMS is committed to promoting policies that protect Oregonian patients and enable them to better afford their medicines. We encourage meaningful reforms that will help lower the price patients pay for medicines at the pharmacy, such as requiring PBMs to share negotiated savings on medicines with patients. Considering the preceding arguments, **we strongly urge the Board to remove ELIQUIS from the prioritized subset of prescription drugs**.

Thank you for the opportunity to provide comments and for considering our concerns. Should you have any questions or concerns, please contact Richard Meyers, Director, State & Federal Policy at richard.meyers@bms.com and Anne Murray, Director, State & Local Government Affairs, U.S. Policy & Government Affairs at anne.murray@bms.com.

Sincerely,

/s/ Anne Murray

Director, State & Local Government Affairs
Bristol Myers Squibb

Oregon Prescription Drug Affordability Board (PDAB)
Oregon Division of Financial Regulation
P.O. Box 14480
Salem, OR 97309-0405

April 23, 2025

Dear Board Members,

I am writing on behalf of the Multiple Sclerosis Coalition, a group of nine patient advocacy organizations with a shared vision to improve the quality of life for those affected by MS through a collaborative national network of independent MS organizations.

We applaud the diligent efforts of the Oregon PDAB to manage the rising costs of medications. Your commitment to addressing the challenges of prescription drug affordability is commendable and vital for the health and well-being of the community. We would like to specifically express our gratitude for the opportunity to submit our comments ahead of the upcoming review of the MS disease modifying therapy, Ocrevus®. Ocrevus is a high-efficacy medication for people with MS and access directly impacts the lives of many patients who rely on this medication to manage their condition effectively.

Multiple sclerosis is a chronic, incurable disease of the central nervous system with a high likelihood of progressive disability over time. A large body of evidence indicates that early and persistent treatment with an FDA approved MS disease modifying treatment (DMT), reduces the accumulation of damage in the brain and spinal cord thus reducing relapses and disease progression. MS is highly heterogeneous and as such, individualized treatment decisions are needed for highest efficacy, adherence, safety, and long-term benefit. Switching treatment may be necessary based upon effectiveness, side effects and other factors. Thus, access to a wide range of MS DMTs, with differing mechanisms of action and modes of administration is needed for optimal treatment outcomes. While cost is important, it cannot be the only factor in treatment decisions. We believe that the PDAB must consider the heterogeneity of MS that requires individual treatment decisions in their decision-making process to ensure that Oregonians living with MS have access to the MS DMTs that they need.

There is a growing body of evidence indicating that initiation of high-efficacy MS DMTs, which includes Ocrevus, for people diagnosed with a relapsing form of MS provides superior control of the MS disease process through their ability to limit new CNS damage, reduce relapses and reduce disease progression. In MS, "time is brain," and delaying the use of highly effective DMTs can place individuals with MS at high risk for permanent disability. In addition, Ocrevus is the only MS DMT that is FDA approved for the treatment of patients diagnosed with primary progressive MS (those whose symptoms progress from onset of the disease in the absence of well characterized episodes or relapses). No other MS DMT carries the primary progressive MS indication. We strongly recommend the PDAB's consideration of the evidence supporting the use of high-efficacy MS DMTs, the FDA approved drug indication and efficacy in the overall medication decision-making process.

We support the role of the Oregon PDAB and appreciate the opportunity to provide comment ahead of the PDAB review of Ocrevus. We believe that consideration of our recommendations will foster a review and decision-making process that is guided by the principles of equity, affordability, and patient-centered care.

Sincerely,

Kathleen Costello, CRNP, MSCN
President, Multiple Sclerosis Coalition
Email: kcostello@mscare.org
Mobile: 410-652-7822

April 16, 2025

Oral Testimony from Gaby Gardiner – Lead Statewide Engagement Manager, Basic Rights Oregon

- Thank you to the chair and all board members for the opportunity to speak today. My name is **Gaby**, and I am the **Lead Statewide Engagement Manager**, of Basic Rights Oregon (BRO), and BRO is a member of Equality Federation. We are a nonprofit organization dedicated to ensuring that all LGBTQ+ Oregonians experience equality.

- I am here today because I am concerned that including antiviral drugs that treat HIV in the PDAB's affordability review process will only harm patient access to lifesaving medications.

- HIV is a unique disease that requires individualized treatment plans developed in careful consultation with trusted healthcare providers. Often, patients take two or more medications at once to treat HIV, resulting in complex treatment regimens.

- The Oregon PDAB's consideration of a therapeutic alternative when evaluating the cost of a drug fails to consider the nuances of complex diseases such as HIV. There is no one-size-fits-all approach and patients should be able to access the right drug for them at the right time.

- If patients are forced to switch treatment plans for non-medical reasons, they may experience serious side effects, access and affordability challenges, or be burdened with increased travel time or lack of transportation options to seek out different providers or pharmacies for their treatment. This stands to negatively impact treatment adherence and worsen health outcomes for patients living with HIV.

- I also want to highlight that LGBTQ+ adults report living with health conditions or chronic diseases at higher rates. In Oregon, over 7,500 people are estimated to be living with HIV. It's important to remember that by weakening the immune system, HIV makes it easier for patients to get sick with other conditions.

- To be clear, interfering with carefully crafted treatment regimens may lead to virus replication, exposing HIV patients to additional long-term health issues.

- At the same time, this Board's cost review process does not recognize the existing public and private patient assistance programs that support people seeking treatment for HIV, such as state AIDS Drug Assistance Programs. Currently, these programs provide medications to low-income people living with HIV, supporting both access and adherence to treatment.

- The Oregon PDAB has been presented with information on how these existing programs ensure affordability and access to HIV medications and acknowledged the concerns around the potential impact the PDAB may have on the HIV community and care environment.

- Despite this, the Oregon PDAB may disrupt these programs and patient protections, ultimately creating barriers to accessing medications made affordable to patients through existing programs. As the federal government cuts funding for HIV research and prevention, it is even more critical that the Board does not harm the HIV care ecosystem.

- I urge the board to consider the unique needs of patients living with HIV and the many experiences of people dealing with the challenges of chronic conditions. HIV drugs should be excluded from the PDAB cost review process to preserve access to lifesaving medications for patients, providers, and their loved ones.

Best,
Gaby

Gaby Gardiner (they/she/he)
Lead Statewide Engagement Manager, Basic Rights Oregon
www.basicrights.org
Mobile: 503-781-0790

BASIC RIGHTS OREGON

April 28, 2025

Oregon Prescription Drug Affordability Board
350 Winter Street NE
Salem, OR
Via pdab@dcbs.oregon.gov

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to share our thoughts on the Oregon Prescription Drug Affordability Board's list of drugs selected for affordability review. ACS CAN empowers advocates across the country to make their voices heard and influence evidence-based public policy change, as well as legislative and regulatory solutions, which will reduce the cancer burden. As the American Cancer Society's nonprofit, nonpartisan advocacy affiliate, ACS CAN is more determined than ever to end cancer as we know it, for everyone.

Addressing the costs of cancer care is crucial to our mission and ACS CAN has long fought for public policies that support the availability and affordability of prescription drugs. Drug therapies play an integral role in cancer treatment and survival and access to a full range of prescription drug therapies is a key determinant in successful cancer outcomes. Both cancer patients and survivors rely on medications to treat their cancer and prevent recurrence.

While intended to increase affordability, Prescription Drug Affordability Board (PDAB) policies may negatively impact patient access to critical medications if not designed and implemented with careful consideration of the unique needs and complexities inherent in oncology. We urge you to ensure that Oregon PDAB affordability review processes are patient-centered, do not impede equitable access to new and existing cancer therapies, and guarantee a direct reduction in patient out-of-pocket costs.

The Oregon PDAB affordability review list includes three oncology drugs including Ibrance, Verzenio, and Perjeta which are all used to treat breast cancer. ACS CAN wants to ensure cancer patients are not disadvantaged by the affordability review process and that any future actions taken by the Oregon PDAB do not impede access to oncology drugs. Importantly, PDAB policies and processes must ensure that any cost savings directly reach Oregon breast cancer patients taking Ibrance, Verzenio or Perjeta and not just result in overall savings for the state.

In addition to ensuring that patients benefit from cost savings, ACS CAN is concerned about patients being able to access the medications most effective for treatment of their specific cancer. We are concerned about the potential for beneficiaries to be steered towards drugs deemed affordable by the PDAB either through formulary placement or by insurers imposing more rigorous utilization management on drugs deemed unaffordable. Cancer patients require access to the specific drug that works for treating their individual cancer and must not be steered toward other potentially less effective drugs as a consequence of PDAB actions.

ACS CAN conducted a survey of cancer patients taking Ibrance in March 2025. Seventy-nine percent of survey respondents said Ibrance has been very important to their cancer care and treatment and about 1 in 5 say it was *critically important* as the only effective therapy for managing their cancer. Forty-six percent said there was no other alternate therapy they could have considered instead. The survey also found over 85 percent of respondents said Ibrance made their daily of life much better.

While this data is limited to just one of the oncology drugs on the PDAB affordability review list, it's vital to recognize that in oncology there are very few drugs that are truly equivalent with respect to the FDA-approved label indication and the scientific evidence supporting the efficacy of a given drug.

Advances in research have significantly improved our understanding of cancer at the molecular level – leading to the development of more precise detection and diagnostic tools and the corresponding therapies that can attack cancer. However, if patients likely to benefit from these advancements face barriers of affordability or accessibility, the opportunity to reach our goal of eliminating death and suffering from cancer is greatly hindered. We urge you to consider the many unique oncology considerations to ensure access to critical cancer therapies is not impeded.

Thank you for your consideration of our comments. If you have any questions or need additional information, please feel free to contact me at jane.leo@cancer.org.

Sincerely,

Jane M Leo

Jane M Leo
Oregon Government Relations Director
American Cancer Society Cancer Action Network

SUBMITTED ELECTRONICALLY

April 30, 2025

Labor & Industry Building
ATTN: Oregon Prescription Drug Affordability Review Board
350 Winter Street NE
Salem, OR 97309

Re: Request for Information Survey - Odefsey Affordability Review

Dear Members of the Prescription Drug Affordability Review Board ("the Board"):

Gilead Sciences, Inc. (Gilead) is submitting this letter in response to the Board's information survey, concerning the Board's preliminary selection of Odefsey® for an affordability review. Odefsey is affordable and accessible to payers, patients, and healthcare programs operating in Oregon. This is shown by industry standard data sources, which demonstrate that 83% of Odefsey patients paid less than $5 on average per month for their prescription in 2023,[i] and over 99% of insured individuals in Oregon had coverage for Odefsey as of April 2025.[ii] In February, the Board appeared to understand the likely adverse implications of subjecting HIV medicines to affordability reviews; however it proceeded to select Odefsey in a subsequent meeting. The Board should recognize that pursuing price-setting policies specifically for HIV treatments like Odefsey risks disproportionately impacting care for disadvantaged people with the disease, as those individuals are most likely to suffer from disruptions in care. We urge Oregon to maintain uninterrupted access to lifesaving medicines by removing Odefsey from the list of drugs slated for affordability review or finding that it is affordable and accessible for people with HIV in the state.

HIV is an infectious disease and currently not curable. As we have previously described to the Board, it is critical to avoid HIV treatment disruptions because interruptions in access to HIV treatment due to federal and/or state policy action could increase the risk of an individual's illness and death, transmission, and development of resistant forms of the virus. [iii] In Oregon and across the country, our HIV treatment and care infrastructure is under threat from interruptions in federal funding disbursement to states and other disruptions to public health programs supporting people with HIV. We urge the Board not to further compound the abrupt changes confronting our national public health infrastructure and refrain from reducing resources for HIV treatment and prevention. Odefsey is a treatment regimen that some people with HIV have been relying on since its introduction in 2016. We are deeply concerned that if Odefsey is ultimately selected for an affordability review – and should the Board gain the necessary authority and choose to set an upper payment limit ("UPL") on the drug – this would have profound negative implications for access to HIV therapy, clinical outcomes in those living with HIV, and public health in Oregon.

Below we summarize high-level considerations for the Board in support of the position that Odefsey should be removed from the Board's list and no affordability review should proceed with respect to any HIV treatment:

- Odefsey is affordable and accessible for Oregonians with HIV;
- Should the PDAB ultimately impose UPLs, affordability reviews represent a step toward adversely impacting patient access and affordability;
- Disruptions in patient access to lifesaving medicines, leading to interruptions in HIV treatment, will lead to worse clinical outcomes, including death, increased risk of HIV transmission, and costly healthcare resource utilization; and
- Treatment disruptions would disproportionately affect vulnerable populations.

In addition, the process of selecting drugs and conducting affordability reviews should be fair, reasoned, and transparent while allowing for meaningful engagement from Gilead and other stakeholders. Finally, the Board should be aware that any future imposition of a UPL based on a determination of unaffordability would raise legal concerns.

* * *

I. Odefsey is affordable and accessible for Oregonians with HIV

A. Odefsey is affordable to Oregonians and Oregon's health care systems.

For insured Oregonians, industry-standard data sources such as Managed Markets Insight & Technology (MMIT)'s databases show that Odefsey is accessible and affordable to patients: over 99% of Oregonians with insurance have coverage for Odefsey and 83% of Oregonians taking Odefsey paid less than $5 on average per month for their prescription in 2023. This includes the 27% of Oregonians who rely on Odefsey that are enrolled in Medicaid, benefitting from $0 cost-sharing requirements. While data for uninsured Oregonians is limited, affordable access to Odefsey may also be available via clinics participating in the federal 340B Drug Pricing Program, through which eligible covered entities may obtain significant discounts on Odefsey, further reducing cost pressures.

Out-of-pocket costs for people living with HIV are also substantially mitigated through an established network of care assistance programs, including Oregon's CAREAssist Program, which is responsible for the administration of Oregon's AIDS Drug Assistance Program[iv] and manufacturer programs such as Gilead's Advancing Access® Patient Support Program. CAREAssist, which receives federal funding through the Ryan White HIV/AIDS Program, covers a majority of treatment costs for eligible individuals and enables low-income people with HIV (defined as having an income at or below 550% of the federal poverty level) to obtain FDA-approved HIV medications, including Odefsey.[v] In addition, Gilead's Advancing Access supports patient affordability for eligible patients through a co-pay coupon card, which helps with out-of-pocket costs, and a patient assistance program, which provides Gilead HIV treatments for free.[vi] For those who do not benefit from CAREAssist or qualify for Gilead's Advancing Access, other secondary payers, such as third party sources of financial support, may still offer cost sharing assistance.

Industry-standard data sets also show that covered individuals are generally not required to go through utilization management before obtaining Odefsey.[vii] This is important because utilization management policies implemented by insurance plans include burdensome requirements such as prior authorization[viii] and/or step therapy,[ix] which can limit or delay an individual's ability to obtain the medicine they and their doctor determine is best for them.

By relying only on select carrier-reported data, the Board's considerations to date fail to consider important aspects of Odefsey's affordability and accessibility. Importantly, the Board has not reviewed any patient cost-sharing data. The Board also has not considered the role of federally funded public health programs like Ryan White in the state, or federally administered programs such as 340B, both of which are integral to the economic environment of Oregon's state-wide health care programs and systems. Further, any consideration of aggregate costs to health care systems must account for the fact that effective and consistent HIV treatment (through Odefsey, among other treatments) helps prevent onward HIV transmission and the associated substantial healthcare costs associated with this transmission. In fact, there are good reasons to believe that use of Odefsey and other antiretrovirals could ultimately lower long-term public health expenses and be a net benefit to Oregon's health care systems (see Section III).

B. Data limitations in the Board's dashboard prevents the Board from conducting meaningful or accurate analyses about Odefsey.

The Board's dashboard does not include a representative set of payer data for the state and relies on calculated drug costs which reflect plan payments that manufacturers do not control, and which inflate total reported drug spending. As the Board itself recognizes, the carrier-reported information in the dashboard reflects a small subset of payers in the state and only accounts for approximately 25% of Oregonians with insurance coverage.[x] The Board's calculated averages therefore do not reflect an overall Oregonian experience, as analyses are not supported by evidence that the Board's data set is representative of the state's overall population. Critically, the spending experience reported by these carriers do not align with data available from other state-wide health programs. According to the Board's dashboard, coordinated care organizations (CCOs) administering Oregon's Medicaid program did not identify Odefsey as a drug of concern. The dashboard includes an indicator column labeled "Drug also on the CCO list" (which, in prior dashboard iterations, identifies high priority [e.g., most costly] drugs for CCOs); Odefsey's entry for this column reads "No." Therefore, while the Board has previously expressed interest in reviewing indicators of "systemic" concern,[xi] the data on which it relies is neither suitable nor sufficient for such analyses.

The data used by the Board also raise other concerns about data reporting methods, the integrity of subsequent analyses, and potentially questionable carrier practices. For example, Odefsey is one of many drugs on the Board's dashboard with a calculated "average cost per prescription" that exceeds the drug's wholesale acquisition cost (WAC), or list price. These calculated amounts are derived by the Board's analysis and suggest that carriers are sometimes paying pharmacies more than list price per prescription for a drug and, in some cases, appear to be paying up to triple the drug's list price. For such calculated dashboard metrics, the Board may be relying on inappropriately derived figures and drawing conclusions based on inaccurate and misleading information. For example, to calculate the dashboard's metric "Average cost net of rebate per

prescription," the Board divides the "Total annual net of rebate spend" by the "Number of prescriptions." The "Terms" dictionary does not provide a definition for "total annual net of rebate spend" and the dashboard does not specify what remuneration are included in this carrier-reported metric. Therefore, it is unclear whether the numerator considers concessions provided by the manufacturer to the carrier that are not rebates; for example, discounts and fees. If the "Total annual net of rebate spend" fails to account for all types of concessions provided by manufacturers, the reported metric would overstate true net spending amounts. In addition, it is also unclear whether the numerator is inclusive or exclusive of dispensing fees, performance-based payments, and/or other administrative costs paid to pharmacies. If other types of fees and payments are included the numerator, the dashboard may be attributing carrier costs to a drug that are outside the manufacturer's control because they are based on contracts between carriers and pharmacies. As a result of these contracts, carriers may be reimbursing pharmacies and setting patient cost-sharing amounts based reimbursement rates that are several times the price charged by the manufacturer.

Given the available data from industry-standard sources maintained by IQVIA and MMIT on Odefsey's affordability and accessibility to Oregonians living with HIV, it strains credulity to assert that Odefsey creates affordability concerns for patients or Oregon's health systems. We encourage the Board to revisit the dashboard's data limitations and reconsider the extent to which reasonable conclusions may be drawn from such a resource. The Board should affirm the data showing that Odefsey is affordable and accessible for people with HIV in Oregon.

II. Should the PDAB ultimately impose UPLs, affordability reviews represent a step toward adversely impacting patient access and affordability.

Prescription Drug Affordability Review Boards and price setting proposals operate on the false assumption that they improve affordability and access to a drug in a state, despite evidence that government price setting reduces patient access.[xii,xiii] While the Board does not have authority to establish UPLs for drugs at this time, the Board seeks to perform affordability reviews as if it had the ability to effectuate government price setting policies. That would be a profound mistake. Government price setting, by intent and design, would necessarily disrupt a complex health care delivery market and has been shown to reduce access, result in treatment delays, and lead to greater costs for patients. HIV treatment is not a therapeutic area in which such disruptions should be taken lightly, given the significant potential public health impact, as described in Section III.

Unintended consequences resulting from price setting can take many forms. Research shows that UPLs will lead to changes in formulary design and increased utilization management, while there would likely not be decreases in patient premiums, deductibles or maximum out of pocket limits.[xiv,xv] Almost all respondents to a payer study (90%) "said that there would 'definitely' or 'likely' be changes to patient cost sharing for UPL-affected drugs or drug classes…that could increase patient costs." Half of respondents in the same study "indicated their plan would increase utilization management (UM) on the UPL drug." Payers have also stated, "…depending on the formulary design, patients may not be able to get their preferred drugs, and the other alternative drugs may have higher out of pocket costs and require a prior authorization." In extreme cases, it's possible a payer may remove a UPL drug from its formulary altogether, leaving a patient with non-

coverage of the drug. Finally, 57% percent of study respondents "anticipated increasing premiums if a UPL is implemented."

In 2024, the Board performed a series of analyses and other activities to understand whether and to what extent implementing UPLs might address affordability challenges.[xvi] The Board's findings include widespread concern among all stakeholders surveyed about anticipated adverse impacts to patient access due to implementation of a UPL – concerns that should give the Board particular pause when considering whether Odefsey, a drug to treat HIV, is affordable. The Board also found that implementing a UPL could lead to additional costs for patients and taxpayers.[xvii] These findings are consistent with other research in which payers have stated "…UPLs fail to consider the entirety of the drug supply chain that may be altered by a UPL, such as PBMs and distributors. Payers are not going to be the ones to make up the difference."[xviii,xix]

We encourage the Board to reconsider spending time and resources on an affordability review for a drug that has not been identified by either patients or health care programs for any reason of concern. The 538 Oregonians who relied on Odefsey in 2023 have found success in their care plan and continue to benefit from Odefsey, based on the advice of their trusted health care providers. The Board should not interfere with life-saving treatment that is working.

III. Disruptions in patient access to lifesaving medicines, leading to interruptions in HIV treatment, will lead to worse clinical outcomes, including death, increased risk of HIV transmission, and costly healthcare resource utilization.

When medicines to treat HIV, like Odefsey, are taken as prescribed, they work to suppress the virus in the body, preventing progression to AIDS and untimely death. [xx] Achieving and maintaining viral suppression with antiretrovirals restores and preserves immune function, reduces HIV associated morbidity and mortality, and prevents the spread of HIV within the community. [xxi] Researchers at the National Institutes of Health found that keeping HIV levels undetectable for at least six months results in people with HIV having no risk of sexually transmitting HIV to partners.[xxii] This helps reduce healthcare costs. Avoiding just one new HIV infection can reduce lifetime healthcare costs by $850,557 on average. In addition, annual and cumulative healthcare costs were up to seven times higher for people with HIV compared to those without HIV.[xxiii] State actions that delay initiation of HIV treatment, create gaps when an individual switches from one regimen to another, or lead people to drop out of care altogether due to not being able to access a preferred regimen, will not only worsen health outcomes for individuals living with HIV, but it will also increase the spread of HIV and costs to Oregon.

HIV drugs have unique clinical and pharmacological qualities that need to be considered when selecting the most appropriate regimen for a person with HIV to support better patient medication adherence, improve viral suppression, and reduce the risk of transmitting HIV. The fundamental principle of antiretroviral therapy (ART) regimen optimization is to maintain viral suppression without jeopardizing future treatment options. If a regimen switch results in the virus not being suppressed (virologic failure), this can lead to the emergence of new resistance mutations. As a result, the person may require a more complex and/or less tolerated regimen. The Board must acknowledge that HIV is a uniquely challenging virus to treat, making HIV medicines especially poor candidates for the affordability review process. HIV aggressively replicates at a rate of one

billion new viral particles per day, overwhelming and simultaneously destroying the immune system by targeting the CD4+ T cells needed for a proper immune response.[xxiv] Effectively targeting viral replication requires combining multiple drugs with different mechanisms of action, often an approach that can be taken in one pill, such as Odefsey, and this highly individualized approach has been critical to transforming a once-deadly disease into a manageable, chronic condition with minimal impact on life expectancy.[xxv]

Effectively managing HIV infection requires vigilance and careful clinical decision-making to fit a patient's needs. Treating HIV is not one-size-fits-all; rather, to keep someone's HIV viral load suppressed (which, as described above, prevents worsening of HIV-related issues and onward transmission of HIV), they must be given a regimen to which they can successfully adhere, that is effective against their strain of HIV, and is appropriate considering their full health profile. Furthermore, HIV mutations can confer resistance to certain classes of drugs and rule those drugs out for a patient. For this reason, the U.S. Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV states that "selection of a regimen should be individualized" for a particular patient based on factors such as virologic efficacy, toxicity, potential adverse effects, pill burden, dosing frequency, drug–drug interaction potential, resistance-test results, comorbid conditions, and childbearing potential.[xxvi] For example, studies show that, as people with HIV age, they are more likely to develop additional health issues and tend to develop them earlier than people who do not have HIV.[xxvii,xxviii] This often means they must take multiple medications and may be more prone to drug-drug interactions from medications for different conditions, particularly when their HIV medication includes certain components. In addition, some patients may be more successful in adhering to a regimen that requires one daily pill rather than multiple pills a day. People on single-tablet regimens (STRs) like Odefsey, which combines multiple different medications, have higher rates of adherence to HIV treatment.[xxix,xxx,xxxi] This is because some people may have difficulty adhering to complex treatment regimens due to factors such as the number of pills, dosing schedule, and dietary restrictions. As such, though multiple-tablet regimens (MTRs) may exist for a specific individual, this does not mean such options represent the best choice to assure meaningful person and public health outcomes for that individual or the community. By improving treatment adherence and persistence, people on STRs like Odefsey are expected to better control their HIV, resulting in decreased rates of hospitalization and lower overall healthcare costs.[xxxii,xxxiii,xxxiv,xxxv,xxxvi] According to the DHHS Guidelines, Odefsey fills a unique patient profile.

Treatment failures and development of drug-resistant HIV can occur if patients are forced off of regimens fitting their clinical profile and needs, including patients whose access to treatment is disrupted by policy interventions. Development of resistance mutations may create the need for varied combinations of medications, which may require taking more pills or otherwise be more inconvenient to take, leading to worse adherence and more transmission of HIV. Thus, given the possibility that resistance could develop to any single drug or class of drug and given the wide variety of considerations involved in choosing the right regimen for a patient, it is essential to have a diverse artillery of ARTs available for all patients. The importance of adherence, risk of transmission, and HIV drug resistance means that the HIV landscape thus poses unique challenges that make the affordability review and UPL approach particularly inapt.

IV. Treatment disruptions would disproportionately affect vulnerable populations.

In Oregon and across the country, our HIV treatment and care infrastructure is under threat. In recent weeks, the federal government has terminated, suspended, or re-organized personnel, programs, and agencies, which will unravel more than three decades' worth of progress towards ending the HIV epidemic. Whether through blunt approaches, such as federal funding freezes, or targeted cuts to specific contracts and activities, the consequences of these abrupt shifts in policies and programs are life-threatening. These hasty changes to our public health infrastructure, along with the shocking scale of proposed cuts to safety net programs, mean that life-saving services to people living with HIV will likely be harder to access. Unless these changes are reversed, our ability to combat emerging HIV outbreaks will be compromised and our capacity to meet the healthcare needs of people living with HIV will be greatly reduced. Research initiatives to discover more effective care for our communities and lead to breakthroughs in new medications, including any possible future cure, will also likely be severely affected.

The Board should recognize that pursuing price-setting policies specifically for HIV treatments like Odefsey risks disproportionately impacting care for disadvantaged people with HIV, as those individuals are most likely to suffer from disruptions in care. HIV disproportionately impacts socially marginalized and disenfranchised populations, particularly sexual minorities and communities of color.[xxxvii] People with HIV experience disproportionately irrational negative behaviors and judgements (stigma) while seeking care, resulting in more opportunity to avoid care. Additional barriers to patients receiving the treatment they chose with providers could further exacerbate the risk of disconnection from care. Therefore, state actions disrupting care for HIV create additional barriers that would disproportionately harm some of the most vulnerable groups in Oregon who already face barriers that limit their ability to access and adhere to treatment. As an example, Black people represent 1.8% of Oregon's population but accounted for 7.8% of all people with HIV in the state and 7.2% of new HIV diagnoses in 2022.[xxxviii] As another example, Hispanic/Latinx people represent 13.8% of Oregon's population, yet account for 17.2% of all people with HIV in the state and 27.6% of new diagnoses in the same year. As of 2022, 73.3% of Black people with diagnosed HIV in Oregon were virally suppressed compared to 78.9% of Hispanic/Latinx people and 79.2% of White people with HIV.

In part because of these disparities in social determinants of health and the nature of HIV, it is even more important to ensure that individuals can work with their providers to select the treatment that is most appropriate for them. Individualized treatment allows for maximization of clinical benefits, including: increasing the likelihood of adherence and persistence that can improve the opportunity for consistent viral suppression, significantly decreased rates of hospitalization and lower healthcare costs,[xxxix] reduced risk of treatment discontinuation, and avoidance of adverse consequences such as drug resistance and transmission of HIV.[xl] For these reasons, it is critical to reduce or eliminate all manner of barriers to receiving effective treatment and care for HIV, not add new challenges by introducing unnecessary price-setting mechanisms. During a time when access to care for people with HIV is under such heightened threat, the Board should refrain from exacerbating the uncertainty and fear already affecting those worried about maintaining uninterrupted access to their lifesaving medicines.

V. If the Board does ultimately select Odefsey, it should ensure meaningful engagement from people with HIV and manufacturers and facilitate rational and reasonable decisions.

If the Board does move forward with the affordability review for Odefsey, it should provide appropriate procedures for meaningful engagement with patients and other stakeholders, including reasonable efforts to protect privacy and provide feasible commenting opportunities. To do this, the Board should provide its meeting materials with sufficient time for stakeholders to review and develop responses in advance of submission and registration deadlines and adopt best practices for acknowledging and integrating input offered by stakeholders.

While anecdotes should not take precedence over robust affordability data, the PDAB has not established any process for patients or other stakeholders to share their experiences other than through open public comment and non-confidential formats. This process is inadequate for drugs like Odefsey, considering public stigma often associated with HIV and the socioeconomic barriers that confront many people living with HIV. HIV not only impacts those in marginalized communities but remains a marginalizing disease itself. Many people living with HIV have not disclosed their condition to their families or friends; they may be reticent to seek care in HIV-specific settings and may be anxious as they take necessary steps to seek care, even when they present to a pharmacy to pick up their prescription. Stigma and fear of disclosure likely play a role in an individual's decision whether to engage in public comment opportunities where anonymity might not be able to be maintained. Without addressing these potential barriers to providing public input, the Board cannot expect significant engagement from people living with HIV, unless it offers a specific pathway that will ensure anonymity and ease of access.

Moreover, the Board's opportunities for public comment are not conducive to fostering substantive exchanges on complex topics. As the Board acknowledged in its annual review of Board policies, the amount of time provided to the public to respond to posted meeting materials is very short.[xli] For example, extensive agenda materials are often posted only within a few business days of a scheduled meeting, and its contents often change without notice. In updating its annual policies for 2025, the Board extended its comment deadlines to "no later than 48 hours before a board meeting."[xlii] However, instructions to the public remain contradictory, as the PDAB Public Comment Policy currently posted continues to state that written public comments must "be submitted no later than 72 hours before the PDAB meeting."[xliii] In addition, the three-minute limit for spoken public testimony is typically not enough time for stakeholders to offer substantive comments.

When the Board does receive input from the public, many stakeholders' concerns remain unaddressed. Stakeholders have little reason to maintain confidence that the Board will be responsive to concerns and questions for clarification when feedback is submitted. Considering the paucity of meaningful public engagement and notification, such short windows for the stakeholder response, and insufficient response by the Board to stakeholder questions and concerns, the Board may wish to reconsider its current practices for soliciting meaningful engagement with the stakeholders they directly impact.

Finally, manufacturers can offer a unique and valuable perspective to the PDAB. They can correct or clarify outdated or incomplete data, explain technical details, and contextualize information about the drug at issue. In preliminarily selecting 27 non-insulin drugs for affordability reviews, the PDAB failed to provide manufacturers and other stakeholders with a reasonable opportunity

to inform accurate and validated data-driven assessments. Instead, the PDAB made these selections of drugs based on incomplete data that represents a small share of drug utilization in Oregon and unpredictable methodology, and by relying on a dashboard which contains inaccuracies, such as erroneous data about certain drugs' FDA-approved orphan designations.[xliv] The Board's approach deprives manufacturers of a meaningful opportunity to comment on the inclusion of their drugs on the initial drug list. The PDAB should address this issue and ensure that Gilead has an opportunity to meaningfully participate in the selection and (if necessary) the affordability review process going forward. This provides another reason to remove Odefsey from any final list of drugs for affordability review.

VI. Imposition of a UPL based on a determination of unaffordability would raise legal concerns.

Should the Board acquire authority to impose a UPL for drugs it finds unaffordable, setting a UPL for Odefsey would conflict with federal patent law and related federal exclusivity laws designed to encourage the development of new medicines, in violation of the Constitution's Supremacy Clause. These laws establish a comprehensive framework that encourages companies like Gilead to develop innovative therapies like Odefsey by providing them limited periods during which they hold the exclusive right to market their medicines. Setting a UPL that eliminates or reduces the risk-reward that Congress intended to provide would impermissibly second-guess Congress's determination, with unforeseeable effects on future investment—significantly undercutting Congress's goals.

Depending on its implementation, a UPL could also impermissibly regulate out-of-state transactions or interfere with the nationwide market for prescription drugs; undermine the interconnected web of federal drug-purchasing and insurance programs, including those applying specifically to HIV; or impermissibly displace federal standards governing Medicare Part D.

* * *

For these reasons, the Board should remove Odefsey from its current list and not move forward with an affordability review for this drug.

Sincerely,

DocuSigned by:
Kristie Banks
3B4BECBA5AB74F3...

Kristie Banks
Vice President, U.S. Market Access
Gilead Sciences, Inc.

[i] IQVIA's Longitudinal Access and Adjudication Data. Data on file with Gilead.
[ii] MMIT data, April 2025.
[iii] Gilead comment letter, April 12, 2024

[iv] Oregon Health Authority. CAREAssist: Oregon's AIDS Drug Assistance Program. Available at: https://www.oregon.gov/oha/ph/diseasesconditions/hivstdviralhepatitis/hivcaretreatment/careassist/pages/index.aspx
[v] Ibid.
[vi] Gilead, Advancing Access. https://www.gileadadvancingaccess.com/
[vii] MMIT data, April 2025.
[viii] Prior authorization is a requirement imposed by an insurer under which a patient must demonstrate that they need the medicine prior to the insurer providing coverage.
[ix] Step therapy is a requirement imposed by an insurer whereby a patient must try another drug before they can obtain coverage for the medicine their doctor prescribed.
[x] IQVIA's Longitudinal Access and Adjudication Data. Data on file with Gilead.
[xi] Oregon PDAB meeting, February 2025.
[xii] U.S. Chamber of Commerce. How American Patients Will Bear the Cost of Government Price Controls. January 31, 2024.
[xiii] Richard Kane. PhRMA. New global analysis shows patient access challenges around the world. April 12, 2023.
[xiv] Health Plans Predict: Implementing Upper Payment Limits May Alter Formularies and Benefit Design But Won't Reduce Patient Costs, Avalere. April 2024.
[xv] Payer Perspectives Confirm UPLs Will Likely Raise Costs and Hinder Patient Access to Medicines, Avalere. March 2025.
[xvi] Constituent Group Engagement Report, Prepared by Myers and Stauffer. August 2024
[xvii] PDAB Upper Payment Limit (UPL) Analysis: Oregon Educators Benefit Board (OEBB) and the Public Employees' Benefit Board (PEBB); Medicaid FFS and CCO. September 2024.
[xviii] Health Plans Predict: Implementing Upper Payment Limits May Alter Formularies and Benefit Design But Won't Reduce Patient Costs, Avalere. April 2024.
[xix] Payer Perspectives Confirm UPLs Will Likely Raise Costs and Hinder Patient Access to Medicines, Avalere. March 2025.
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[xl] Yager J, et al., Relationship Between Single Tablet Antiretroviral Regimen and Adherence to Antiretroviral and Non-Antiretroviral Medications Among Veterans' Affairs Patients with Human Immunodeficiency Virus, 31 *AIDS Patient Care and STDs* 370-76 (2017); Cohen C, et al.; Association of Partial Adherence (PA) To Antiretroviral Therapy With Hospitalizations and Healthcare Costs in an HIV Population, 15 Journal of the International AIDS Society 18060 (2012); Bangsberg DR, et al., Adherence-Resistance Relationships For Protease And Non-Nucleoside Reverse Transcriptase Inhibitors Explained By Virological Fitness, 20 *AIDS* 223-32 (2006).
[xli] Oregon PDAB Meeting, January 15, 2025.
[xlii] Oregon PDAB Public Comment Form, accessed April 3, 2025. https://dfr.oregon.gov/pdab/Pages/public-comment.aspx
[xliii] Oregon PDAB Policies and Procedures, Policy Number 04. Amendment approved February 19, 2025.
[xliv] Oregon PDAB meeting, March 2025.

Johnson & Johnson

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Via Electronic Submission

April 30, 2025

Shelley Bailey, Board Chair
Oregon Prescription Drug Affordability Board
pdab@dcbs.oregon.gov

Dear Board Chair Bailey:

Johnson & Johnson Innovative Medicines provides the following comments and data on TREMFYA® and XARELTO® to the Oregon Prescription Drug Affordability Board ("PDAB" or "Board") to supplement our "Request for Information: Manufacturers" ("RFI") submissions. We also reiterate our concerns regarding the constitutionality of the statute on which the Board decisions are based. We request that the Board exclude TREMFYA and XARELTO from affordability reviews. Alternatively, should the Board continue with its reviews, we request that the Board find that TREMFYA and XARELTO do not cause affordability challenges for Oregon patients and the state health care system.

A. Supplemental Data on TREMFYA

In addition to our RFI response, we have prepared supplemental data on TREMFYA to allow for references to supporting materials (see "ATTACHMENT" starting on page 5). This data focuses on three key areas:

1. What Matters to Oregon Patients;
2. Clinical and Real-World Evidence Overview for a Broad Range of Patients, Including a Clinical Trial Across All Skin Tones in Psoriasis; and
3. Economic Impact of Treatment.

B. J&J Concerns with the Affordability Review Process and Requests for Exclusions

We share the PDAB's goal of improving affordability and access to lifesaving medicines for Oregon patients. However, we oppose the affordability review process because it may result in negative unintended consequences throughout the supply chain, including increased out-of-pocket costs and decreased access for patients. We reiterate our concerns regarding the RFI and affordability review processes as outlined in our comment letter to the Board, dated April 14, 2025.[1] We express further concern that the issues raised in that letter were not addressed at the PDAB's April 16, 2025 Board meeting.

We ask the Board to 1) exclude both TREMFYA and XARELTO from affordability reviews; or alternatively, 2) find that both TREMFYA and XARELTO do not cause affordability challenges for the following reasons:

[1] Oregon Prescription Drug Affordability Board (OR PDAB), *Public Comments, April 16, 2025* (Page 12), https://dfr.oregon.gov/pdab/Documents/20250416-PDAB-public-comments.pdf (last visited Apr. 22, 2025).

- **Payers determine what patients ultimately pay for their medications.**
- **If insurance benefit design makes it difficult for patients to access or afford TREMFYA or XARELTO, J&J offers multiple programs to help support patient access.**
- **Neither TREMFYA nor XARELTO create affordability challenges for the state health care system.**
- **XARELTO is subject to a "Maximum Fair Price" ("MFP") under the Inflation Reduction Act ("IRA"), a PDAB-recommended factor for exclusion.**

1. Payers determine what patients ultimately pay for their medications.

Even as manufacturers' rebates, discounts, and fees increase and net prices decrease, patients' out-of-pocket costs—as determined by payers—continue to rise. J&J's rebates, discounts, and fees have risen significantly from 2016-2023, particularly for private insurers and pharmacy benefit managers ("PBMs").[2] Between 2016 and 2023, J&J's rebates, discounts and fees to commercial insurers have grown eight times from $1.7B (2016) to $13.4B (2023).[3] Nearly one-third of our discounts, rebates, and fees go to health insurers and PBMs.[4] Our net prices have declined by 20 percent over the past seven years.[5] Yet, patients are not directly benefitting from increased rebates, discounts, and fees or lower net prices. Oregon's 2024 "Report on Pharmacy Benefit Manager Drug Price Transparency," presented to the PDAB at the October 16, 2024 Board meeting supports this assertion.[6] The Report showed PBMs often do not pass the large majority of rebates on to patients.[7] To the extent that the PDAB plans to assess whether a medication creates affordability challenges for Oregon patients, it should examine the role of PBMs and health plans in increasing patients' out-of-pocket costs.

2. If insurance benefit design makes it difficult for patients to access or afford TREMFYA or XARELTO, J&J offers multiple programs to help support patient access.

J&J offers multiple programs to support patient access to TREMFYA and XARELTO. Through the "TREMFYA withMe" Savings Program, eligible patients in Oregon using commercial or private insurance pay as little as $0 per dose.[8] Through the "XARELTO withMe" program, eligible patients in Oregon pay as little as $10 for their medication.[9] Additional affordability support for both TREMFYA and XARELTO is available for eligible Oregon patients through the Johnson &

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[2] Johnson & Johnson, *2023 Johnson & Johnson Innovative Medicine U.S. Pricing Transparency Report*, https://transparencyreport.janssen.com/transparency-report-2023 (last visited April 22, 2025).
[3] *Id.*
[4] *Id.*
[5] *Id.*
[6] OR PDAB, Agenda (Oct. 16, 2024), https://dfr.oregon.gov/pdab/Documents/20241016-PDAB-document-package.pdf (last visited Apr. 22, 2025).
[7] *Id.*
[8] Janssen Carepath, *Tremfya withMe: Cost Support to Help You Get Started and Stay on Track*, https://asset.janssencarepath.com/document/TREMFYA-withMe-Affordability-Chart.pdf (last visited Apr. 22, 2025).
[9] *Xarelto withMe*, https://www.xarelto-us.com/xarelto-cost/en/ (last visited Apr. 2025).

Johnson Patient Assistance Program.[10] Through this program, J&J medicines, such as TREMFYA and XARELTO, "may be provided at no cost to eligible patients who are uninsured or have inadequate coverage through commercial, employer group, or government insurance coverage and are not supported by other offerings from J&J."[11]

3. Neither TREMFYA nor XARELTO create affordability challenges for the state.

Neither TREMFYA nor XARELTO create affordability challenges for the state, as established by data that the PDAB is required to prioritize, and it is unclear why TREMFYA and XARELTO are on the PDAB's initial list of 27s drugs. Per Oregon law, when identifying and selecting drugs for affordability reviews, the Board must consider certain manufacturer- and carrier-reported data collected by the Oregon Drug Price Transparency ("DPT") program.[12] Specifically, the Board must review the following carrier-reported "top 25 lists":[13]

- The top 25 most frequently prescribed drugs;
- The top 25 most costly drugs as a portion of total annual spending; and
- The top 25 drugs that have caused the greatest increase in total plan spend.

The Board must also prioritize drugs that are included in the DPT program's manufacturer new drug report or price increase report.[14] Three spreadsheets containing the required DPT data were shared with the PDAB for the March 19, 2025 and April 16, 2025 Board meetings.[15] **Neither TREMFYA nor XARELTO appeared on these three spreadsheets.**[16] The Oregon PDAB Data Dashboard, which aggregates this data, erroneously states that both TREMYFA and XARELTO appear on the "top 25 greatest increase" and "top 25 most costly" lists.[17] Similarly, the FDA recently approved the first generics of Xarelto (rivaroxaban), which is also not reflected in the Drug Dashboard.[18] First, we request that the PDAB correct the errors in the Dashboard. Second, the Board should exclude both TREMFYA and XARELTO from affordability reviews given the prioritized DPT data does not support a finding that either drug creates an affordability

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[10] Janssen Carepath, *Johnson & Johnson Patient Assistance Program: Quick Reference Guide*, https://www.myjanssencarepath.com/resource/1716902197000/Immunology_Medications_English (last visited Apr. 22, 2025).
[11] *Id.*
[12] OR Rev. Stat. 743.025; OR. Rev. Stat. 646A.689; OR PDAB, *Agenda* (Jan. 15, 2025), https://dfr.oregon.gov/pdab/Documents/20250115-PDAB-document-package.pdf#Page=44 (last visited Apr. 22, 2025) ([hereinafter "OR PDAB Agenda, January 15, 2025 Meeting"]).
[13] OR Admin Reg 925-200-0010; OR Rev. Stat. 743.025; OR. Rev. Stat. 646A.689; *OR PDAB Agenda - January 15, 2025 Meeting*, *supra* note 12.
[14] OR. Rev. Stat. 646A.689; *OR PDAB Agenda - January 15, 2025 Meeting*, *supra* note 12.
[15] OR PDAB, *"April 16 and March 19, 2025 Board Meetings,"* https://dfr.oregon.gov/pdab/Pages/data.aspx (last visited Apr. 22, 2025).
[16] *Id.*
[17] OR PDAB, *2023 Preliminary Aggregated Carrier Data*, https://app.powerbigov.us/view?r=eyJrIjoiOGM2YjhlMWUtNzE2OC00MmU1LTk2MjktYWUzZGMyNTNmZmQ1IiwidCI6ImFhM2Y2OTMyLWZhN2MtNDdiNC1hMGNlLWE1OThjYWQxNjFjZiJ9 (last visited Apr. 22, 2025).
[18] FDA, *FDA News Release: FDA Roundup: March 4, 2025*, https://www.fda.gov/news-events/press-announcements/fda-roundup-march-4-2025 (last visited Apr. 22, 2025).

challenge.

4. XARELTO is subject to the PDAB's exclusion criteria.

Xarelto should be excluded from affordability reviews because it is subject to an "MFP," which goes into effect on January 1, 2026.[19] Last year, drugs subject to an "MFP" were excluded from planned affordability reviews. Likewise, in December 2024, the PDAB published its Final UPL Report to the Legislature, which advised that the Board should continue to exclude "MFP" drugs.[20] PDAB staff continued to include this recommendation in its "Affordability Review Approaches" presentation during the March 19, 2025 Board meeting based on discussions from the February 19, 2025 Board meeting.[21] Yet, Xarelto was nevertheless included on the List.

Initial unintended consequences are already starting to emerge for "MFP" drugs, including constraints on pharmacists and reduced patient access. One study found that the "MFP" could result in 71,000 to 93,000 patients abandoning Xarelto and could also result in an increase in major cardiovascular events and deaths nationally.[22] This is all the more reason why "MFP" drugs like Xarelto should be excluded from PDAB's review.

As one of the nation's leading healthcare companies, J&J has a responsibility to engage with stakeholders in constructive dialogue to address gaps in affordability and access as well as protect our nation's leading role in the global innovation ecosystem. We know that patients are counting on us to develop and bring medicines to market. We live this mission every day and are humbled by the patients who trust us to help them fight their diseases and live healthier lives.

Sincerely,

Michael Valenta
Vice President, Value, Access & Pricing, Strategic Customer Group
Johnson & Johnson Services, Inc.

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[19] CMS, *Medicare Drug Price Negotiation Program: Negotiated Prices for Initial Price Applicability Year 2026*, https://www.cms.gov/files/document/fact-sheet-negotiated-prices-initial-price-applicability-year-2026.pdf (last visited Apr. 22, 2025).
[20] *Prescription Drug Affordability Board (PDAB) Upper Payment Limit (UPL) Report to the Legislature* (Dec. 2024), https://dfr.oregon.gov/pdab/Documents/reports/PDAB-upper-payment-limit-report-2024.pdf (last visited Apr. 8, 2025).
[21] OR PDAB, *Agenda* (March 19, 2025), https://dfr.oregon.gov/pdab/Documents/20250319-PDAB-document-package.pdf (last visited Apr. 22, 2025).
[22] Anne M. Sydor, et al., *Could the Inflation Reduction Act Maximum Fair Price Hurt Patients?* J. Health Econ Outcomes Res. (Nov. 27, 2024) https://pubmed.ncbi.nlm.nih.gov/39629268/ (last visited Apr. 22, 2025).

ATTACHMENT

What Matters to Oregon Patients:

Psoriatic disease, such as plaque psoriasis (PsO) and psoriatic arthritis (PsA), and inflammatory bowel diseases (IBD), such as ulcerative colitis (UC) and Crohn's disease (CD), are types of chronic, debilitating immunologic disorders affecting different areas of the body.[1,2]

PsO is a skin disease where cells build up on the surface of the skin and present as thick, dry, itchy, raised, red, brown, or purple patches of skin referred to as plaques.[1] One in three people with psoriasis may also develop PsA, which is an inflammatory disease impacting the joints and entheses (the site where ligaments or tendons connect to the bones). Joint pain, swelling, and stiffness in 1 or more joints are common symptoms of patients with psoriatic arthritis.[1]

UC and CD are immune-mediated diseases that affect the gastrointestinal (GI) tract. In CD, inflammation can occur anywhere in the GI track (mouth to anus) whereas in UC, inflammation is primarily limited to the large intestine. Common symptoms of IBD (UC/CD) include: rectal bleeding, abdominal cramps and pain, bowel movement urgency, loose stools, persistent diarrhea, fatigue, and weight loss.[2]

To learn more about the clinical presentation and burden of these disease states, please visit the following websites:

- National Psoriasis Foundation (NPF)
- Crohn's Colitis Foundation

TREMFYA®, a fully human IL-23 inhibitor, delivers significant value to Oregon patients, providing a treatment option that is both effective and has a well-established safety profile for adults with: moderate to severe plaque PsO who are candidates for systemic therapy or phototherapy, active PsA, moderately to severely active UC, and moderately to severely active CD.[3] The following factors must be considered in evaluating patient affordability:

Clinical and Real-World Evidence Overview for a Broad Range of Patients, Including A Clinical Trial Across All Skin Tones in Psoriasis

TREMFYA has been characterized across several clinical trials, with five years of clinical data in moderate to severe plaque PsO[abc] and two years in active PsA[def] (*See footnotes for select efficacy and safety data)*.[3-9] Post-hoc analyses have been conducted to characterize the efficacy of TREMFYA for specific patients, taking into account body weight, prior therapy, and patients who have not received a biologic therapy prior to TREMFYA.[10-13 g-j] Across moderate to severe plaque PsO or active PsA, TREMFYA has a robust clinical profile with proven efficacy and well-defined safety.[3]

Psoriasis can look different across skin tones, which is something that is often overlooked when

considering treatment. Further, minority representation has been less than 30% in plaque PsO biologic treatment trials.[14] In 2022, J&J initiated VISIBLE, a first-of-its-kind, phase 3b, multicenter, randomized, double-blind, placebo-controlled study, evaluating the efficacy and safety of TREMFYA for adults with moderate to severe plaque PsO across all skin tones.[15,16k] VISIBLE has generated an extensive collection of PsO clinical images across skin tones to assist providers in discussing the diagnosis and treatment journey with their patients.[17,18]

Additionally, several real-world evidence studies demonstrate that patients with PsO or PsA receiving TREMFYA for 2 years experience significantly better persistence on therapy versus comparators.[18-21lmno] Additionally, TREMFYA was superior to comparators, including Humira® (adalimumab), Taltz® (ixekizumab), Cosentyx® (secukinumab), and STELARA® (ustekinumab), in achieving clear or almost clear skin and patient-reported quality of life improvements through more than 2 years (30 months).[22p] Patients with PsA who were persistent on TREMFYA for 6 months experienced significant improvement in peripheral joint disease, skin disease, and patient-reported pain.[23q]

In addition to the evidence of TREMFYA for the treatment of plaque PsO and active PsA, the efficacy and safety of TREMFYA for adults with moderately to severely active UC or CD has been characterized across multiple clinical trials. Data at 1 year are available for both UC and CD, demonstrating that a significantly greater proportion of patients receiving TREMFYA achieved clinical remission versus placebo. In the UC and CD pivotal clinical trials, patients treated with TREMYFA were observed to have healing of the intestinal lining (as measured by endoscopic remission) versus placebo.[24-27rs] In CD, TREMFYA® was evaluated in two separate clinical programs, including one that evaluated the efficacy and safety versus both placebo and head-to-head versus STELARA® (ustekinumab).[27-29] In the trial that included head-to-head comparisons versus STELARA, TREMFYA demonstrated superiority versus STELARA across all prespecified pooled endoscopic endpoints at 1 year, including the composite clinical and endoscopic endpoints.[27-28t] Results for endoscopic outcomes achieved by TREMFYA align with the long-term treatment goals identified by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) in STRIDE II, a consensus-based recommendation guideline for adult IBD patients using a treat-to-target strategy.[30] TREMFYA also has an established safety profile across pivotal trials (*See footnotes for select efficacy and safety data*).[3u]

J&J continues to invest in ongoing research and development for TREMFYA® (guselkumab). Guselkumab is being investigated to bolster the evidence for existing and additional patient populations with immune-mediated disease across a multitude of J&J-sponsored trials.[31]

For additional clinical efficacy and safety information, please see the full Prescribing Information for TREMFYA available here.

Economic Impact of Treatment

PsO: Clinical studies have demonstrated considerable physical, social, and psychological

burdens associated with psoriatic diseases. The cumulative effects of psoriatic disease can contribute to decrements in patients' self-esteem, daily activities, social relationships, and ability to work.[32-35] Additionally, the incidence of comorbid conditions, such as obesity, heart disease, diabetes mellitus, hypertension, malignancy, hyperlipidemia, anxiety, and depression are increased in patients with PsO.[36-43] By not adequately managing PsO, musculoskeletal symptoms can be exacerbated, increasing disease burden for the patient.[44] In a commercially insured population, PsO patients with treated anxiety and depression incurred a substantial economic burden, primarily driven by greater use of medical services.[45] In a recent systematic review, which showed the cost impact of comorbidities in PsO, the cost of PsO per year in the US was estimated to be $112 billion, with $36 billion due to medical comorbidities.[46] Additionally, annual indirect costs due to total work productivity loss per patient is reported to be $9,591.[47] In a retrospective cohort study, treatment with IL-12/23 inhibitors or IL-23 inhibitors was associated with reduced risk of progression to inflammatory arthritis as compared to treatment with tumor necrosis factor inhibitors.[48]

PsA: Several real-world studies comparing patients with and without psoriatic diagnoses have documented the substantial healthcare costs and high comorbidity burden associated with PsA. Compared with patients without PsA or PsO, patients with PsA incur $20,733 more in annual per patient direct healthcare costs. Another analysis demonstrated that patients with PsA have 3.9x higher total annual direct healthcare costs versus patients without PsA.[49] Patients with PsA have higher rates of non-PsA associated comorbidities than patients free of PsA and PsO.[50] Although indirect cost is generally challenging to estimate, a recently published systematic review and meta-analysis of 8 studies estimated the average annual indirect cost for PsA ranged from $1,694 to $50,271 per patient (in 2013 USD).[51]

UC: Direct healthcare costs for patients with UC in the US were estimated at about $18,198 per UC patient per year. The mean cost per admission of UC-related hospitalization ranged from $7711-$48,530 based on severity of illness subclass .[52] Hospitalization risk for UC within 1 year is 26.5% .[53] The 5-year risk of at least 1 surgery is 10% .[54] Total direct healthcare costs went up substantially to $114,535, $52,903, and $49,191 per patient per year for UC patients with a UC-related surgery, with ≥3 months of opioids use, and with ≥3 months of steroids use, respectively .[55] UC patients experienced increased indirect costs (due to both absenteeism and presenteeism) with worsening disease severity compared with remission patients. Compared with remission patients ($4432), those with mild ($11,633) and moderate/severe ($24,754) disease had 2.6 and 5.6 times more work productivity loss-associated annual costs, respectively.[56] The annual total economic burden of UC in the US is estimated to be between $8.1 and $14.9 billion when both direct and indirect costs are considered.[57]

CD: Direct healthcare costs for patients with CD in the US were estimated at $24,500 per CD patient per year, while the direct healthcare costs for patients with moderate to severe CD were estimated at $44,934 per patient per year. Total direct healthcare costs went up significantly to $101,013, $64,909, and $51,020 per patient per year for patients with CD with CD-related surgery, ≥3 months of opioids use, and ≥3 months of steroids use, respectively .[58] Indirect costs associated with CD are also important from a societal perspective. CD patients

experienced increased indirect costs (due to both absenteeism and presenteeism) with worsening disease severity compared to remission patients. Mild ($18,532) and moderate/severe ($30,096) patients had 2.5 and 4.1 times more in work productivity loss-associated annual costs, respectively compared to patients in remission ($7348) .[59] In adult patients with CD, chronic corticosteroid use with a biologic or conventional therapy is related to higher healthcare resource utilization burden compared with non-chronic corticosteroid users [60] Achieving and maintaining remission in this patient population is important from both a clinical and economic perspective.[61]

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[a] VOYAGE 1 (N=837) and VOYAGE 2 (N=992) were phase 3, multicenter, double-blind, placebo-controlled, active comparator trials evaluating the efficacy and safety of TREMFYA 100 mg subcutaneous injection at Weeks 0, 4, and 12, then q8w in adult patients with moderate to severe plaque PsO who were candidates for phototherapy and/or systemic therapy. Co-primary endpoints in both trials were PASI 90 and IGA 0/1 at Week 16.[3,63,64]

[b] In VOYAGE 1, at Week 16, PASI 90 for TREMFYA® (n=329) versus placebo (n=174): 73% (n=241/329) vs 3% (n=5/174), *P*<0.001, and IGA 0/1 for TREMFYA versus placebo: 85% (n=280/329) vs 7% (n=12/174), *P*<0.001. Results at Week 16 are calculated by non-responder imputation. At Week 252, PASI 90 for TREMFYA® (n=391) was 84%, and IGA 0/1 was 82%. In VOYAGE 2, at Week 16, PASI 90 for TREMFYA (n=496) versus placebo(n=248): 70% (n=347/496) vs 2% (n=6/248), *P*<0.001, and IGA 0/1 for TREMFYA versus placebo: 84% (n=417/496) vs 8% (n=21/248), *P*<0.001. At Week 252, PASI 90 for TREMFYA (n=560) was 82%, and IGA 0/1 (TREMFYA n=559) was 85%. Week 252was during an open-label extension, and results were calculated by treatment failure rules. These data include patients who crossed over from placebo to receive TREMFYA at Week 16.[3,64]

[c] Pooled safety, Week 16, % [events/100 PYs of follow-up], TREMFYA (n=823) vs Placebo (n=422): adverse events: 49.2 [330.1] vs 46.7 [316.9]; serious adverse events: 1.9 [6.3] vs 1.4 [4.7]; infections: 23.2 [97.9] vs 21.3 [86.4]; serious infections: 0.1[0.4] vs 0.2 [0.8]. Pooled safety data from VOYAGE 1 and VOYAGE 2 through 5 Years (Week 264) for TREMFYA, events/100 PYs of follow-up, n=1721: adverse events: 149.4; serious adverse events: 5.0; infections: 60.6; serious infections 0.9. Data at Year 5 include all patients exposed to TREMFYA in VOYAGE 1 and VOYAGE 2.[3,65]

[d] DISCOVER 1 (N=381; bio-naïve population [69%] and bio-experienced population: ≤2 TNFα inhibitors [31%]) and DISCOVER 2 (N=739; bio-naïve population) were phase 3, multicenter, double-blind, placebo-controlled trials evaluating the efficacy and safety of TREMFYA 100 mg subcutaneous injection at Weeks 0, 4, and 12, then q8w in adult patients with active PsA despite standard therapies. The primary endpoint in both trials was ACR20 at Week 24.[3,5-8]

[e] DISCOVER 1 ACR20 results for TREMFYA vs placebo: At Week 24: 52% (66/127) vs 22% (28/126); *P*<0.0001. At Week 52: 60% (76/127) of patients receiving TREMFYA q8w. DISCOVER 2 ACR20 results for TREMFYA® (n=248) vs placebo (n=246): At Week 24: 64%(n=159/248) vs 33% (n=81/246), *P*<0.0001. Patients with missing data were considered nonresponders. At Week 52, ACR20 for TREMFYA: 75% (n=185/248). At Week 100, ACR20 for TREMFYA: 74% (n=183/248). After Week 24, the study was open label with blinded dosing interval, which may have affected results. Prespecified as-observed analysis from Week 24 to Week 100 from DISCOVER 2 and from Week 24 to Week 52 from DISCOVER 1 are not shown.[3,5-8]

[f] Pooled safety, Week 24, % [events/100 PYs of follow-up], TREMFYA (n=375) vs Placebo (n=372): adverse events: 48.5 [257.3] vs 47.3 [220.0]; serious adverse events: 1.9 [4.0] vs 3.2 [9.3]; infections: 19.5 [58.3] vs 20.7 [58.5]; serious infections: 0.3 [0.6] vs 0.8 [4.1]. In DISCOVER 2 only through Week 112 (2 Years) for TREMFYA, events/100 PYs of follow-up, n=248: adverse events: 158.0; serious adverse events: 6.1; infections: 40.5; serious infections 2.2. [10,15,63] Data at Year 2 (Week 112) include patients exposed to TREMFYA in DISCOVER 2 only.[3,7,8,66]

[g] ECLIPSE (N=1048) was a phase 3, multicenter, randomized, double-blind, comparator-controlled study in patients

(≤18 years of age) with moderate to severe plaque psoriasis, defined by an IGA≥3, PASI ≥12, and BSA involvement of at least 10%, who were candidates for or previously received either systemic therapy or phototherapy. 1048 patients were randomized in a 1:1 ratio into parallel TREMFYA (n=534) or active comparator (n=514) treatment groups. The study was conducted at 142 sites in 9 countries. TREMFYA 100mg was administered subcutaneously q8w, after weeks 0 and 4, through week 44, and the active comparator was administered through week 44. The last dosing visit was week 44 and patients were followed for an additional 12 weeks with a final safety visit at week 56.[10-12]

[h] In ECLIPSE, at week 48, PASI 90 for TREMFYA versus secukinumab: 84% (n=451/534) vs 70% (360/514), 14.2 treatment difference 95% CI (9.2-19.2); *P*<0.0001 for noninferiority and superiority. Efficacy findings from the ECLIPSE trial were further evaluated in post hoc analyses by baseline body weight and body mass index and prior psoriasis medication history.[10]

[l] COSMOS was a phase 3b, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of TREMFYA in adult patients with active PsA who demonstrated inadequate response to 1-2 TNF inhibitors. The primary endpoint was an ACR20 response at week 24. Patients with missing data or who met treatment failure (TF) criteria through week 24 (defined as discontinuation of study agent and/or study participation for any reason, initiation or increase in the dose of allowed conventional synthetic DMARDs (csDMARDs) or oral corticosteroids for PsA, initiation of protocol-prohibited medications/therapies for PsA or met early escape [EE] criteria) were considered nonresponders. In the EE-correction analysis, 12 patients in the guselkumab group did not meet any other TF criteria (ie, introduction/change in dose of concomitant therapy) through week 24 and their response was included with other patients in the guselkumab group; 8 patients in the placebo group received guselkumab as EE therapy at weeks 16 and 20, met TF criteria, and were considered nonresponders. Through week 44, 88% of patients treated with guselkumab 100 mg completed the study.[13]

[j] In COSMOS, at week 24, the primary endpoint for ACR20 response rates in the TREMFYA group was 44.4% (84/189) vs 9.8% (19/96) of placebo-treated patients (*P*<0.001). Efficacy findings from the COSMOS trial were further evaluated in post hoc analyses by body weight and prior and concomitant medications.[13]

[k] First large-scale, prospective PsO biologic study in patients with skin of color across the entire spectrum of the Fitzpatrick scale (I-VI).[15-17]

[l] Health claims data from the IQVIA PharMetrics® Plus Database were used to compare real-world persistence among patients with psoriasis switching to treatment with US-labeled dosing for TREMFYA (N=935) versus subcutaneous IL-17A inhibitors (SC IL-17Ai, including Taltz® [ixekizumab], Cosentyx® [secukinumab], and Siliq® [brodalumab]; N=1,466). Patient inclusion criteria included adults switching to TREMFYA or SC IL-17Ais during the intake period (07/13/2017-06/30/2023) from another psoriasis-indicated advanced therapy. Index date was the first observed claim for TREMFYA or any SC IL-17ai agent after switching from another systemic advanced therapy. Baseline period included the 12 months before the index date; follow-up period spanned the start of the maintenance phase until the earliest of end of data availability or end of continuous health plan eligibility. Persistence was defined as no gaps in treatment supply >120 days for TREMFYA (twice the 8-week maintenance dosing interval) or >60 days for SC IL-17Ai (ixekizumab and secukinumab: twice the 4-week maintenance dosing interval; brodalumab: twice the typical dispensing interval of 2 doses for 4 weeks). A sensitivity analysis was conducted using a gap of >120 days for all agents; the last day of index agent supply before the gap defined the discontinuation date. Persistence while receiving on-label United States maintenance dosing was assessed from the start of the maintenance phase by weighted Kaplan-Meier (KM) analysis and Cox proportional hazard models. **At 2 years, persistence for the TREMFYA cohort was 1.5x greater than the IL-17Ai cohort** (primary analysis 59.2% versus 35.4%; HR [95% CI] 1.91 [1.61; 2.22]; *P*<0.001). Limitations: Results may not be generalized to the uninsured, pts insured with plans other than commercial or self-insured plans, or those who do not continue treatment up to the maintenance phase. Prescription fills do not guarantee the medication was taken as prescribed. Results may be subject to residual confounding due to unmeasured confounders.[18]

[m] Health claims data from the IQVIA PharMetrics® Plus Database were used to compare real-world persistence

among patients with psoriasis switching to treatment with US-labeled dosing for TREMFYA (N=1,037) versus subcutaneous TNF inhibitors (SC TNFi, including Humira® [adalimumab], Cimzia® [certolizumab pegol], Enbrel® [etanercept], and infliximab; N=345). Patient inclusion criteria included adults switching to TREMFYA or SC TNFis during the intake period (07/13/2017-06/30/2023) from another psoriasis-indicated advanced therapy. Baseline period included the 12 months before the index date; follow-up period spanned the start of the maintenance phase until the earliest of end of data availability or end of continuous health plan eligibility. Persistence was defined as no gaps in treatment supply >120 days for TREMFYA and infliximab (twice the 8-week maintenance dosing interval) or >60 days for adalimumab, certolizumab pegol, and etanercept (twice the typical dispensing interval of 4 weeks). A sensitivity analysis was conducted using a gap >120 days for all agents; the last day of index agent supply before the gap defined the discontinuation date. Persistence while receiving on-label United States maintenance dosing was assessed from the start of the maintenance phase by weighted Kaplan-Meier (KM) analysis and Cox proportional hazard models. **At 2 years, persistence for the TREMFYA cohort was 2.3x greater than the TNFi cohort** (primary analysis 50.9% versus 19.1%; HR [95% CI] 2.79 [2.34; 3.33]; *P*<0.001). Limitations: Results may not be generalized to the uninsured, pts insured with plans other than commercial or self-insured plans, or those who do not continue treatment up to the maintenance phase. Prescription fills do not guarantee the medication was taken as prescribed. Results may be subject to residual confounding due to unmeasured confounders.[19]

[n] Health claims data from the IQVIA PharMetrics® Plus Database were used to compare treatment persistence among both biologic-naïve (bio-naïve) and biologic-experienced (bio-experienced) patients with active psoriatic arthritis who initiated TREMFYA (bio-naïve population N=362, bio-experienced population N=487) versus subcutaneous IL-17A inhibitors (SC IL-17Ai, including Cosentyx® [secukinumab] and Taltz® [ixekizumab]; bio-naïve population N=845, bio-experienced population N=1,756). Patient inclusion criteria included adults with a 1st claim for TREMFYA or SC Il-17Ai during the intake period (07/14/2020- 12/31/2022). Patients were classified as bio-experienced if they had ≥1 claim for a PsA-indicated biologic disease-modifying antirheumatic drug (bDMARD) at any time prior to the index date, and bio-naïve otherwise. On-label persistence up to 24 months post-index included no treatment discontinuation or dose modification relative to US FDA-approved labeling. The proportion of patients for persistence was determined using weighted KM curves, and the TREMFYA versus SC IL-17Ai cohorts were compared using weighted Cox proportional hazard models. Primary analysis was conducted based on 2x the FDA maintenance interval between administration per label after induction. Sensitivity analyses were conducted based on 1x the FDA maintenance interval between administration per label after induction as well as a fixed discontinuation gap of 112 days. **At 2 years, the TREMFYA cohort was ~1.7x more likely to remain persistent in both bio-naïve and bio-experienced cohorts** (bio-naïve: 47.5% vs 40.3%, primary analysis: HR [95% CI] 1.70 [1.32; 2.20]; *P*<0.001; bio-experienced: 43.3% vs 32.0%, primary analysis: HR [95% CI] 1.33 [1.11; 1.59]; *P*=0.002). Limitations: Results may not be generalized to the uninsured, pts insured with plans other than commercial or self-insured plans, or those who do not continue treatment up to the maintenance phase. Prescription fills do not guarantee the medication was taken as prescribed. Results may be subject to residual confounding due to unmeasured confounders. Treatment effectiveness and reasons for discontinuation could not be assessed using claims data.[20]

[o] Health claims data from the IQVIA PharMetrics® Plus Database were used to compare treatment persistence among both bio-naïve and bio-experienced patients with active psoriatic arthritis who initiated TREMFYA® (bio-naïve population N=361, bio-experienced population N=443) versus subcutaneous TNF inhibitors (SC TNFi, including Humira® [adalimumab], Enbrel® [etanercept], Cimzia® [certolizumab pegol], and SIMPONI® [golimumab]; bio-naïve population N=2,171, bio-experienced population N=319). Patient inclusion criteria included adults with a 1st claim for TREMFYA or SC TNFi during the intake period (07/14/2020- 12/31/2022). Patients were classified as bio-experienced if they had ≥1 claim for a PsA-indicated biologic disease-modifying antirheumatic drug (bDMARD) at any time prior to the index date, and bio-naïve otherwise. On-label persistence up to 24 months post-index included no treatment discontinuation or dose modification relative to US FDA-approved labeling. The proportion of patients for persistence was determined using weighted KM curves, and the TREMFYA® versus SC TNFi cohorts were compared using weighted Cox proportional hazard models, further adjusted for csDMARD and tsDMARD use in bio-naive cohort only. Primary analysis was conducted based on 2x the FDA maintenance interval between administration per label after induction. Sensitivity analyses were conducted based on 1x the FDA maintenance

interval between administration per label after induction as well as a fixed discontinuation gap of 112 days. **At 2 years, the TREMFYA cohort was 2x more likely to remain persistent in both bio-naïve and bio-experienced cohorts** (bio-naïve: 48.9% vs 28.4%, primary analysis: HR [95% CI] 2.36 [1.88; 2.98]; *P*<0.001; bio-experienced: 39.5% vs 23.3%, Primary analysis: HR [95% CI] 1.86 [1.46; 2.37]; *P*<0.001)**.** Limitations: Results may not be generalized to the uninsured, pts insured with plans other than commercial or self-insured plans, or those who do not continue treatment up to the maintenance phase. Prescription fills do not guarantee the medication was taken as prescribed. Results may be subject to residual confounding due to unmeasured confounders. Treatment effectiveness and reasons for discontinuation could not be assessed using claims data.[21]

[p] Health claims data from the CorEvitas Psoriasis Registry were used to compare the long-term effectiveness of TREMFYA with Humira® (adalimumab), Taltz® (ixekizumab), Cosentyx® (secukinumab), and STELARA® (ustekinumab) in patients with psoriasis. Patient inclusion criteria included adults with plaque psoriasis who had an Investigator's Global Assessment (IGA) score of ≥2 and at least 30 months of follow-up prior to the data cutoff (June 2024). The primary outcome was achievement of IGA 0/1 (clear or almost clear) at 30 months. Dermatology Life Quality Index (DLQI) 0/1 (no impact on quality of life) at 30 months was assessed as a secondary outcome among patients with DLQI>1 at baseline. Stabilized standardized mortality ratio (SMR) weights were used to balance all baseline characteristics between each GUS group and each comparator. Non-responder imputation was used for all patients who discontinued GUS or the comparator prior to the 30-month visit. TREMFYA **was superior to Humira®, Taltz®, Cosentyx®, and STELARA® in achieving clear or almost clear skin and no impact of psoriasis on quality of life at 30 months.** TREMFYA (N=431) vs Humira® (N=309): IGA 0/1: 50.7% vs 24.0%, Δ 26.7% (95% CI 13.6, 39.7), *P*<0.001; DLQI: 43.4% vs 21.2%, Δ 22.3% (95% CI 8.8, 35.7), *P*<0.001. TREMFYA (N=590) vs Taltz® (N=580): IGA 0/1: 43.4% vs 33.6%, Δ 9.9% (95% CI 2.6, 17.1), *P*=0.005; DLQI: 39.6% vs 30.8%, Δ 8.8% (95% CI 2.4, 15.1), *P*=0.007. TREMFYA (N=549) vs Cosentyx® (N=617): IGA 0/1: 45.8% vs 29.9%, Δ 15.9% (95% CI 6.8, 25.0), *P*<0.001; DLQI: 41.3% vs 23.7%, Δ 17.6% (95% CI 8.7, 26.5), *P*<0.001. TREMFYA (N=467) vs STELARA® (N=224): IGA 0/1: 45.9% vs 36.2%, Δ 9.7% (95% CI 0.6, 18.7), *P*=0.036; DLQI: 39.5% vs 25.8%, Δ 13.8% (95% CI 3.9, 23.7), *P*=0.004. Limitations: The new-user design of the study required distinct TREMFYA and comparator cohorts for each comparison. Patients may have been classified as a TREMFYA initiator in one comparison and as a comparator for another comparison. Inferences should be made within and not across the comparisons. Due to the timing of the study, the registry did not have enough patients using risankizumab or bimekizumab to allow comparisons. Results may be subject to channeling bias and residual confounding if dermatologists preferentially prescribed TREMFYA®, the most recently approved biologic at the time of the analysis.[22]

[q] TREMFYA was assessed in patients with active PsA with persistent TREMFYA® use at the 6-month visit from CorEvitas PsA/SpA Registry data. Eligible patients had a 6-month visit (within a 5- to 9-month window following guselkumab initiation) occurring on or before March 31, 2023. The primary endpoint was mean change (95% CI) in Clinical Disease Activity Index for PsA score (cDAPSA) at 6 months. The major secondary endpoints included Physician Global Assessment (PGA) of PsA and PsO, Patient Pain (Patient-Reported Pain), and percent body surface area (BSA) with PsO. Changes in continuous outcomes from baseline (guselkumab initiation) to 6 months are reported as mean (95% CI). Each measure was evaluated only among patients with data at both timepoints. Paired t-tests determined whether changes were statistically significantly different from 0 (α=0.05). 90 patients persisted on TREMFYA at 6 months on labeled dose (90/114; 78.9%). At baseline, persistent TREMFYA users were on average biologic-experienced, with long-standing PsA and active peripheral joint and skin disease, moderate pain, and moderate disease activity. TREMFYA® significantly improved disease activity at 6 months versus baseline as assessed by cDAPSA (baseline versus 6-month follow-up, 21.6% (N=75) versus 16.1% (N=75), *P*<0.001). TREMFYA significantly improved disease activity at 6 months vs BL in PGA, Patient Pain, and % BSA with PsO (baseline versus 6-month follow-up, PGA: 41.3% [N=82] versus 22.4% [N=82], *P*<0.001; Patient Pain: 58.1% [N=87] versus 48.9% [N=87], *P*<0.001; Percent BSA with PsO, 8.0% [N=79] versus 2.9% [N=79], *P*<0.001). Limitations of the study included: modest sample size, the study may not be generalizable outside of the US, patient selection based on requirement for TREMFYA® persistence at a 6-month follow-up visit may introduce time and selection bias, limited details are available regarding end of treatment exposure (eg, a small subset of patients identified as non-persisters may have still been exposed to TREMFYA at the follow-up visit).[23]

[r] The efficacy and safety of TREMFYA in adult patients with moderately to severely active UC was evaluated in a

randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial program (QUASAR). For the induction study, a total of 701 patients were included in the phase 3 studies primary analysis set, and a total of 568 patients were included in the primary analysis population during the maintenance study, which was a re-randomized withdrawal study where clinical responders to intravenous (IV) TREMFYA induction were re-randomized to two different TREMFYA doses (TREMFYA 200 mg subcutaneous [SC] every 4 weeks [Q4W] and TREMFYA 100 mg SC every 8 weeks [Q8W]) or placebo. Patients from the phase 2b induction dose-finding study who demonstrated clinical response to IV TREMFYA induction were also randomized into the phase 3 maintenance study. Primary endpoints were clinical remission at week 12 in the induction study and at week 44 in the maintenance study. Clinical remission was defined as a Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability. At week 12, a significantly greater proportion of patients in the TREMFYA 200 mg IV Q4W group achieved clinical remission compared to those in the placebo group (TREMFYA 200 mg IV Q4W [23% N=421] vs placebo [8% N=280]; *P*<0.0001). At week 44, a significantly greater proportion of patients treated with TREMFYA achieved clinical remission (for both dosing regimens) compared with the placebo group (TREMFYA 100 mg SC Q8W [45% N=188; *P*<0.0001]; TREMFYA 200 mg SC Q4W [50% N=190; *P*<0.0001]; vs placebo [19% N=190]). Additionally, a significantly greater proportion of patients treated with TREMFYA achieved endoscopic remission at week 44 compared to placebo-treated patients (both dosing regimens; TREMFYA 100 mg SC Q8W [35% N=188; *P*<0.0001]; TREMFYA 200 mg SC Q4W [34% N=190; *P*<0.0001]; vs placebo [15% N=190]). Endoscopic remission (normalization) was defined as a Mayo endoscopic subscore of 0.[3,24-26]

[s] The efficacy and safety of TREMFYA induction administered subcutaneously was evaluated in a phase 3, treat-through clinical study (GRAVITI-subcutaneous induction followed by subcutaneous maintenance) in adult patients with moderately to severely active CD.[3,29] A total of 340 patients were randomized in a 1:1:1 ratio to TREMFYA 400 mg SC at weeks 0, 4, and 8 followed by 200 mg SC Q4W (N=111); TREMFYA 400 mg SC at weeks 0, 4, and 8 followed by 100 mg SC Q8W (N=114); or placebo (N=115). Co-primary endpoints were clinical remission at week 12 (defined as CD Activity Index [CDAI] <150) and endoscopic response at week 12 (defined as >50% improvement from baseline in the Simple Endoscopic Score for Crohn's Disease [SES-CD]). Treatment with TREMFYA was superior to placebo in achieving the clinical remission and endoscopic response at week 12 (co-primary endpoints) as well as clinical remission and endoscopic response at week 48. Clinical remission at week 12: TREMFYA 400 mg SC Q4W (N=225) 56% vs placebo (N=115) 22%; *P*<0.001. Endoscopic response at week 12: TREMFYA 400 mg SC Q4W (N=225) 34% vs placebo (N=115) 15%; *P*<0.001. Clinical remission at week 48: TREMFYA 100 mg SC Q8W (N=114) 59%; TREMFYA 200 mg SC Q4W (N=111) 65%% vs placebo (N=115) 17%; *P*<0.001. Endoscopic response at week 48: TREMFYA 100 mg SC Q8W (N=114) 39%; TREMFYA 200 mg SC Q4W (N=111) 48% vs placebo (N=115) 5%; *P*<0.001.[3]

[t] Additionally, the efficacy and safety of TREMFYA in adult patients with moderately to severely active CD was evaluated in two identical, phase 3 randomized, double-blind, placebo and active-controlled (versus STELARA® [ustekinumab], a Janssen Biotech product), treat through studies (GALAXI 2 and GALAXI 3- intravenous induction followed by subcutaneous maintenance). In both GALAXI 2 and 3, patients were randomized to receive TREMFYA 200 mg IV at weeks 0, 4, and 8 followed by 200 mg SC Q4W, TREMFYA 200 mg IV at weeks 0, 4, and 8 followed by 100 mg SC Q8W, or placebo. A total of 508 and 513 patients were included in the primary analysis sets in GALAXI 2 and GALAXI 3, respectively. Composite co-primary endpoints included (1) clinical response (≥100 point reduction from baseline in CDAI score or CDAI <150) at week 12 + clinical remission at week 48 and (2) clinical response at week 12 + endoscopic response (≥50% improvement from baseline in SES-CD or SES-CD ≤2) at week 48. Significantly more patients receiving TREMYA 100 mg SC Q8W or 200 mg SC Q4W achieved the composite co-primary endpoints compared to those receiving placebo (*P*<0.001) in both GALAXI 2 and GALAXI 3 studies. **Clinical response at week 12 + clinical remission at week 48**: GALAXI 2 (TREMFYA 100 mg SC Q8W [49.0% N=143]; TREMFYA 200 mg SC Q4W [54.8% N=146]; vs. placebo [11.8% N=76] *P*<0.001). GALAXI 3 (TREMFYA 100 mg SC Q8W [46.9% N=143]; TREMFYA 200 mg Q4W [48.0% N=150]; vs. placebo [12.5% N=72 *P*<0.001]). **Clinical response at week 12 + endoscopic response) at week 48**: GALAXI 2 (TREMFYA 100 mg SC Q8W [39.2% N=143]; TREMFYA 200 mg SC Q4W [38.4% N=146]; vs. placebo [5.3% N=76] *P*<0.001). GALAXI 3 (TREMFYA 100 mg SC Q8W [33.6% N=143]; TREMFYA 200 mg Q4W [36.0% N=150]; vs. Placebo [5.6% N=72 *P*<0.001]). In pre-specified pooled analyses (GALAXI 2 and GALAXI 3) at week 48, both TREMFYA maintenance doses (100 mg Q8W and 200 mg Q4W)

demonstrated superiority to STELARA for endoscopic response, endoscopic remission (SES-CD ≤4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component), deep remission (combination of both clinical remission and endoscopic remission), and a composite endpoint of clinical remission + endoscopic response. Additionally, a numerically greater proportion of patients receiving either TREMFYA maintenance doses achieved clinical remission at week 48 vs STELARA. Endoscopic response at week 48: TREMFYA 100 mg SC Q8W (47.9% [N=286]; *P*=0.009); TREMFYA 200 mg Q4W (52.7% [N=296]; *P*<0.001); vs. STELARA (37.1% [N=291]). Endoscopic remission at week 48: TREMFYA 100 mg SC Q8W (33.2% [N=286]; *P*=0.024); TREMFYA 200 mg Q4W (37.2% [N=296]; *P*=0.001); vs. STELARA (24.7% [N=291]).Deep remission at week 48: TREMFYA 100 mg SC Q8W (29.7% [N=286]; *P*=0.040); TREMFYA 200 mg Q4W (33.8% [N=296]; *P*=0.002); vs. STELARA (22.3 % [N=291]).Clinical remission + endoscopic response at week 48: TREMFYA 100 mg SC Q8W (41.6% [N=286]; *P*=0.049); TREMFYA 200 mg Q4W (47.3% [N=296]; *P*<0.001); vs. STELARA (33.7% [N=291]).Clinical remission at week 48: TREMFYA 100 mg SC Q8W (65.4% [N=286]; *P*=0.512); TREMFYA 200 mg Q4W (70.3% [N=296]; *P*=0.058); vs. STELARA (62.9% [N=291]).[27-28]

[u] During the QUASAR UC induction study: 138/280 (49%) of patients in the placebo arm and 208/421 (49%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a treatment-emergent adverse event; 20/280 (7%) of patients in the placebo arm and 12/421 (3%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious adverse event; 43/280 (15%) of patients in the placebo arm and 66/421 (16%) of patients in the TREMFYA 200 mg IV Q4W arm experienced an infection; 1/280 (0.4%) of patients in the placebo arm and 3/421 (1%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious infection. At approximately 1 year (week 44) during the QUASAR UC maintenance study, 131/192 (68%) of patients in the placebo arm, 120/186 (65%) of patients in the TREMFYA 100 mg SC Q8W arm and 133/190 (70%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a treatment-emergent adverse event; 1/192 (1%) of patients in the placebo arm, 5/186 (3%) of patients in the TREMFYA 100 mg SC Q8W arm and 12/190 (6%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious adverse event; 63/192 (33%) of patients in the placebo arm, 59/186 (32%) of patients in the TREMFYA 100 mg SC Q8W arm and 59/190 (31%) of patients in the TREMFYA 200 mg IV Q4W arm experienced an infection; 0/192 (0%) of patients in the placebo arm, 1/186 (1%) of patients in the TREMFYA 100 mg SC Q8W arm and 2/190 (1%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious infection. In a pooled GALAXI 2&3 safety analysis conducted at approximately 1 year (week 48), 82/153 (53.6%; events/100 PY of follow-up: 499.7) of patients in the placebo arm, 225/296 (76.0%; events/100 PY of follow-up: 327.3) of patients in the TREMFYA 100 mg SC Q8W arm, 233/299 (77.9%; events/100 PY of follow-up: 353.5) of patients in the TREMFYA 200 mg IV Q4W arm, and 236/300 (78.7%; events/100 PY of follow-up: 340.5) of patients in the STELARA 90 mg SC Q8W arm experienced a treatment-emergent adverse event; 16/153 (10.5%; events/100 PY of follow-up: 32.8) of patients in the placebo arm, 32/296 (10.8%; events/100 PY of follow-up: 14.9) of patients in the TREMFYA 100 mg SC Q8W arm, 21/299 (7.0%; events/100 PY of follow-up: 9.7) of patients in the TREMFYA 200 mg IV Q4W arm, and 35/300 (11.7%; events/100 PY of follow-up: 18.4) of patients in the STELARA 90 mg SC Q8W arm experienced a serious adverse event; 39/153 (25.5%; events/100 PY of follow-up: 87.5) of patients in the placebo arm, 127/296 (42.9%; events/100 PY of follow-up: 77.9) of patients in the TREMFYA 100 mg SC Q8W arm, 147/299 (49.2%; events/100 PY of follow-up: 88.3) of patients in the TREMFYA 200 mg IV Q4W arm, and 126/300 (42.0%; events/100 PY of follow-up: 77.7) of patients in the STELARA 90 mg SC Q8W arm experienced an infection; 2/153 (1.3%) of patients in the placebo arm, 1/296 (0.3%) of patients in the TREMFYA 100 mg SC Q8W arm, 3/299 (1.0%) of patients in the TREMFYA 200 mg IV Q4W arm, and 12/300 (4.0%) of patients in the STELARA 90 mg SC Q8W arm experienced a serious infection. Serious infections included liver abscess/bacterial infection and postop wound infection/vascular device infection (placebo group), anal abscess (TREMFYA 100 mg SC q8w group), and acute sinusitis, abscess intestinal, and intestinal fistula infection (TREMFYA 200 mg SC q4w group). In a pooled GRAVITI safety analysis conducted at approximately 1 year (week 48), 77/117 (65.8%; events/100 PY of follow-up: 413.0) of patients in the placebo arm, 95/115 (82.6%; events/100 PY of follow-up: 307.2) of patients in the TREMFYA 100 mg SC Q8W arm, and 92/115 (80.0%; events/100 PY of follow-up: 327.2) of patients in the TREMFYA 200 mg IV Q4W arm experienced a treatment-emergent adverse event; 16/117 (13.7%; events/100 PY of follow-up: 37.1) of patients in the placebo arm, 15/115 (13.0%; events/100 PY of follow-up: 15.5) of patients in the TREMFYA 100 mg SC Q8W arm, and 9/115 (7.8%; events/100 PY of follow-up: 13.2) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious adverse event; 36/117 (30.8%; events/100 PY of follow-up: 81.7) of patients in the placebo arm, 56/115 (48.7; events/100 PY of follow-up: 91.8) of patients in the TREMFYA 100 mg SC Q8W arm, and 47/115

(40.9%; events/100 PY of follow-up: 70.0) of patients in the TREMFYA 200 mg IV Q4W arm experienced an infection; 0/117 (0%) of patients in the placebo arm, 2/115 (1.7%) of patients in the TREMFYA 100 mg SC Q8W arm, and 1/115 (0.9%) of patients in the TREMFYA 200 mg IV Q4W arm experienced a serious infection. Serious infections included bronchitis and appendicitis (TREMFYA 100 mg q8w group) and gastroenteritis (TREMFYA 200 mg q4w group). An additional serious infection of anal abscess was reported in the placebo to TREMFYA rescue group.[24,27,29, 67]

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PERJETA DATA DOSSIER - ATTACHMENT TO OR PDAB RFI RESPONSE - APRIL 30, 2025

Genentech appreciates the opportunity to share additional information relevant to the Board's affordability review process and encourages the Board to fully review this submission in conjunction with Genentech's response to the manufacturer request for information (RFI) form. The manufacturer RFI form focuses heavily on price concession and financial assistance provided by manufacturers ignoring key access metrics specified in OAR 925-200-020 that are essential to assessing a drug's affordability to Oregonians. Further, many of these important access metrics are not adequately incorporated across all stakeholder RFI forms or the carrier data call. In addition to better alignment with the Board's statutory obligations, inclusion of these metrics in any affordability reviews, with input from varied stakeholders, would allow the Board to consider a more holistic, and accurate, view of a drug's value**.** For these reasons, Genentech is submitting additional information on the value and affordability of Perjeta as a supplemental response to Question 25 on the Board's manufacturer RFI form.[1]

As demonstrated by the data included in our RFI response and this additional information submitted on April 30, 2025, Perjeta should be removed from the Board's 2025 subset list of drugs for review based on, among other things: Perjeta's NCCN Category 1 Preferred recommendation for adjuvant and first-line metastatic treatment; the expiration of primary patents in the US in 2025; and Perjeta's significant clinical benefit and overall affordability. Further, it is important to consider that treatment of HER2-positive breast cancer, and many other cancers, consists of multi-therapy regimens to provide patients with the best possible clinical outcome. **Given the complexities of combination treatment regimens and the limitations of the Board to fully collect and interpret patient-specific data, any affordability review of these medicines would be incomplete.**

First approved in June 2012, Perjeta is a targeted cancer treatment and is FDA-approved for use in combination with trastuzumab and docetaxel in people who have HER2-positive breast cancer that has spread to different parts of the body (metastatic) and who have not received anti-HER2 therapy or chemotherapy for metastatic breast cancer. Perjeta is also indicated for the neoadjuvant treatment of adults with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer and for adjuvant treatment of adults with HER2-positive early breast cancer at high risk of recurrence.

[1] In addition to sharing these drug-specific data, Genentech would also like to remind the Board of our substantial comment record to provide feedback and recommendations on the Board's processes including its approach to drug selection and affordability reviews which encompasses six comment letters submitted between October 2023 and February 2025. Genentech incorporates these letters into its April 30, 2025 submissions to the Board.

Clinical trial data demonstrated that the Perjeta regimen added six (6) months median progression-free survival and reduced the risk of death by 32% compared to a standard of care at the time for metastatic breast cancer patients.[2] In addition, Perjeta is part of a complete, FDA-approved treatment regimen that is given with trastuzumab and chemotherapy for HER2-positive early breast cancer (eBC). Adjuvant treatment is given with curative intent to kill any cancer cells left behind after surgery, with the important goal of keeping patients cancer-free for as long as possible. Clinical data has shown that the Perjeta adjuvant treatment regimen in 2,400 people lowered the risk of the cancer coming back by 18% when compared with the control arm, and most patients were still cancer-free eight (8) years after starting the trial in both arms of the study. Further, adjuvant treatment with the Perjeta regimen is limited to a maximum of 18 cycles (or 1 year), inclusive of any treatment with this regimen before surgery (neoadjuvant). In fact, Perjeta creates more certainty for payer budget impact, with a maximum duration of treatment per the drug label for patients in either adjuvant or neoadjuvant regimens.[3]

To date, more than 260,000 breast cancer patients in the United States have been treated with Perjeta.[4] Approximately **461 Oregonians are diagnosed with HER2-positive breast cancer annually, according to the National Cancer Institute SEER database.[5]**

Importantly, Perjeta's indication in the adjuvant setting carries an National Comprehensive Cancer Network (NCCN) Category 1 Preferred recommendation, highlighting its clinical value to patients. NCCN guidelines are considered the "gold standard" in clinical practice guidelines and reflect standards-of-care across oncology. Products with Category 1 status meet the highest levels of evidence and have uniform consensus that the treatment is appropriate for the indicated patients. Perjeta also carries Category 1 NCCN recommendations for the adjuvant setting as well as the metastatic setting for patients with HER2-positive disease.

Simply evaluating list price and net price dynamics is insufficient for determining Perjeta's value and affordability to patients, payers and health care systems. Its clinical benefits - particularly those demonstrated by the APHINITY trial - extend well beyond its relatively short duration of therapy. Several of Pejeta's clinical benefits - across the adjuvant, neoadjuvant, and metastatic setting - are highlighted below.

Perjeta demonstrates long-term efficacy - 8.4 years - in the adjuvant setting for patients with eBC at high risk of recurrence.[6]

- The APHINITY trial has had a significant impact on clinical practice. With **8.4 years of median follow-up**, it has presented compelling evidence that Perjeta's benefit in HER2-positive eBC endures, with the greatest advantages seen in the node-positive cohort - including a 28% reduction in risk of recurrence at 8 years - irrespective of hormone receptor (HR) status.
- Results from the updated trial prompted NCCN to elevate the combination of Perjeta and

[2]Genentech. Outcomes In Metastatic Breast Cancer. https://www.perjeta-hcp.com/metastatic/efficacy.html. Accessed April 2025.
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[5] NIH SEER. Female Breast Cancer Subtypes. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed April 2025
[6] Loibl S, Jassem J, Sonnenblick A, et al. VP6-2022: Adjuvant pertuzumab and trastuzumab in patients with early HER-2 positive breast cancer in APHINITY: 8.4 years' follow-up. *Annals of Oncology.* 2022;33(9):986-987.10.1016/j.annonc.2022.06.009

trastuzumab to Category 1 status for this population, playing a pivotal role in shaping treatment strategies for high-risk eBC patients.

Perjeta is NCCN-guideline recommended for metastatic breast cancer patients with central nervous system (CNS) metastases, a population with high unmet need.[7]

- A clinical study called CLEOPATRA studied efficacy and safety in 808 patients who were given PERJETA with trastuzumab and docetaxel or trastuzumab and docetaxel alone.
- Adding PERJETA to trastuzumab and docetaxel increased the time people lived without their cancer growing or spreading by an average of 50%, compared with people who took trastuzumab and docetaxel alone.
- People taking PERJETA, along with trastuzumab and docetaxel, experienced an average of 6.1 more months of progression-free survival, which is time without their cancer progressing, compared with people taking only trastuzumab and docetaxel (18.5 months compared with 12.4 months).
- On average, people who were given PERJETA, trastuzumab, and docetaxel lived 15.7 months longer than people given only trastuzumab and docetaxel (56.5 months compared to 40.8 months).
- Furthermore, based on the evidence from the Phase II PATRICIA trial, and a non-pre-specified exploratory analysis of the pivotal Phase 3 CLEOPATRA, Perjeta, in combination with trastuzumab, is NCCN-guideline recommended as a viable option for treating brain metastases in previously untreated HER2-positive metastatic breast cancer (mBC).

Perjeta shows efficacy when used both pre- and post-surgery in eBC.[8]

- This analysis suggests that Perjeta, in combination with trastuzumab, **provides significant clinical benefit, when included in both neoadjuvant and adjuvant setting** among patients with HER2-positive eBC who have a pathological complete response after neoadjuvant HER2-targeted therapy plus chemotherapy. The results reinforce the clinical benefits of Perjeta in eBC.

The following criteria under OAR 925-200-020 demonstrate the affordability of Perjeta. Genentech urges the Board to ensure all of these elements are adequately incorporated in any future Board evaluation and discussion.

"*The total cost of the disease and the drug price offset*"

- Perjeta confers significant non-clinical benefits to society that remain uncaptured by the PDAB process. For example, in 2023, a model was published that exemplifies the potential long-term benefits of Perjeta. By translating individual outcomes to projected population benefits, the model estimates that Perjeta's use in both neoadjuvant and adjuvant settings will prevent over 20,000 recurrences in HER2-positive early breast cancer patients between 2013 and 2031. This prevention translates to over $8.5 billion in total healthcare cost savings during the same period, highlighting the significant positive

[7] Lin NU, Pegram M, Sahebjam S, et al. Pertuzumab Plus High-Dose Trastuzumab in Patients With Progressive Brain Metastases and HER2-Positive Metastatic Breast Cancer: Primary Analysis of a Phase II Study. *J Clin Oncol.* 2021;39(24):2667-2675.10.1200/JCO.20.02822
[8] Swain SM, Macharia H, Cortes J, et al. Event-Free Survival in Patients with Early HER2-Positive Breast Cancer with a Pathological Complete Response after HER2-Targeted Therapy: A Pooled Analysis. *Cancers (Basel).* 2022;14(20).10.3390/cancers14205051

impact Perjeta can have on patients and the US health care system.[9][10] When scaled to the population of Oregon using census data, this translates to approximately $106 million in savings over this time period.[11,12]

"*Patient copayment or other cost sharing data, across different health benefit plan designs, including copayment and coinsurance impacts from patient assistance programs and copay coupons; deductible; patient out-of-pocket costs; and any other cost sharing data*."

- Insurance type, benefit design, and site of care are a few of these factors outside of Wholesale Acquisition Cost (WAC) (or "list") price that can impact a patient's final out of pocket costs, as well as cost to the system. As a medicine traverses the delivery supply chain, it can be subject to a variety of factors across several intermediary stakeholders which impact costs, ranging from negotiated rebates and discounts to significant markup at the point of care.

"*Patient treatment preferences*" and patient and caregiver "*perspective on benefits and disadvantages of using the prescription drug*."

- The APHINITY trial has produced one of the largest datasets of health-related quality of life (HRQoL) reported to date in patients with HER2-positive eBC. Analyses of these data indicate that patients' ability to conduct daily activities, as assessed by role function, was maintained throughout treatment.[13]
- In the APHINITY trial, the addition of Perjeta to adjuvant trastuzumab and chemotherapy improved clinical outcomes in patients with HER2-positive eBC and did not adversely affect patients' ability to conduct activities of daily living versus trastuzumab and chemotherapy alone.[14]

"*Changes in the prescription drug's net cost over time*."

- Since the enactment of Oregon price transparency reporting laws, Perjeta pricing has never triggered price increase advance notice nor reporting requirements.

Regarding our response to Question 6 on the manufacturer RFI form, we wanted to provide a more detailed response than online formatting of the RFI would allow. **Question 6: "If the prescription drug was approved through an expedited pathway, please select all that apply."**

- In 2012, Perjeta was first granted full FDA approval for its metastatic breast cancer indication, based on the results from the CLEOPATRA trial.

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[9] Sussell JA, Press DJ, Hansen SA, Kim E, Du Toit Y, Fung A. Impact of Pertuzumab and Ado-Trastuzumab Emtansine on Cumulative Avoidance of Recurrence Among Women Treated for Locally Advanced, Inflammatory, or Early-Stage Nonmetastatic HER2-Positive Breast Cancer in the United States. *Adv Ther.* 2023;40(9):3857-3874.10.1007/s12325-023-02554-6

[10] Sussell JA, Sheinson D, Wu N, Shah-Manek B, Seetasith A. HER2-Positive Metastatic Breast Cancer: A Retrospective Cohort Study of Healthcare Costs in the Targeted-Therapy Age. *Adv Ther.* 2020;37(4):1632-1645.10.1007/s12325-020-01283-4

[11] US Census Bureau Quick Facts. https://www.census.gov/quickfacts/fact/table/US/PST045224. Accessed April 2025

[12] US Census Bureau Quick Facts. https://www.census.gov/quickfacts/fact/table/US,OR/PST045224. Accessed April 2025.

[13] British Journal of Cancer (2021) 125:38–47; https://doi.org/10.1038/s41416-021-01323-y

[14] British Journal of Cancer (2021) 125:38–47; https://doi.org/10.1038/s41416-021-01323-y

- Perjeta was subsequently approved via the accelerated approval pathway in 2013 for its neoadjuvant indication, based on results from the NeoSphere trial. This approval was converted to a full approval in 2017.
- Perjeta was also approved via the traditional review pathway for its adjuvant breast cancer indication in 2017, based on results from the APHINITY trial.

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OCREVUS DATA SUBMISSION DOSSIER - ATTACHMENT TO OR PDAB RFI RESPONSE - APRIL 30, 2025

Genentech appreciates the opportunity to share additional information relevant to the Board's affordability review process and encourages the Board to fully review this submission in conjunction with Genentech's response to the manufacturer request for information (RFI) form. The manufacturer RFI form focuses heavily on price concession and financial assistance provided by manufacturers ignoring key access metrics specified in OAR 925-200-020 that are essential to assessing a drug's affordability to Oregonians. Further, many of these important access metrics are not adequately incorporated across all stakeholder RFI forms or the carrier data call. In addition to better alignment with the Board's statutory obligations, inclusion of these metrics in the eventual affordability reviews, with input from varied stakeholders, would allow the Board to consider a more holistic, and accurate, view of a drug's value. For these reasons, Genentech is submitting additional information on the value and affordability of Ocrevus as a supplemental response to Question 25 on the Board's manufacturer RFI form.[1]

Ocrevus, first approved in 2017, is the first and only approved disease-modifying therapy (DMT) for both the relapsing-remitting (RMS) and primary progressive (PPMS) forms of multiple sclerosis (MS), the latter of which is one of the most debilitating forms of multiple MS. **As demonstrated by the data included in our RFI response, this additional information submitted on April 30, 2025, plus prior comment letters as noted, Ocrevus is accessible and affordable for Oregonians, health systems and payers and therefore should be removed from the Board's 2025 subset list of drugs for review.**

However, should the Board proceed with an affordability review, the Board is directed by OAR 925-200-020 to consider the following criteria for affordability reviews. The criteria under OAR 925-200-020 listed below demonstrate the affordability of Ocrevus. Genentech urges the Board to ensure all of these elements are adequately incorporated in any future Board evaluation and discussion.

1. ***"The relative financial impacts to health, medical or social services costs as can be quantified and compared to the costs of existing therapeutic alternatives."***

   Based on the Board's carrier data for proposed 2024 affordability reviews, Ocrevus is the most affordable option within its therapeutic class.

[1] This complete response supplements drug-specific data provided to the Board on Ocrevus in four prior comment letters in October 2023, November 2023, February 2024 and June 2024. In addition to sharing these drug-specific data, Genentech would also like to remind the Board of our substantial comment record to provide feedback and recommendations on the Board's processes including its approach to drug selection and affordability reviews which encompasses six comment letters submitted between October 2023 and February 2025. Genentech incorporates these letters into its April 30, 2025 submissions to the Board.

- Ocrevus is priced lower than 15 other DMTs that represent treatment options for MS patients.[2]
- In the materials from the June 2024 Board meeting, Ocrevus was determined to have the lowest average health care spend per enrollee per year relative to Board-determined therapeutic alternatives per the Board's data analysis of Oregon all-payer claims data from 2022 (see table from the materials for June 2024 Board meeting below). While Ocrevus does have higher total annual health plan spend than therapeutic alternatives, it is more affordable to the health care system on a per patient basis. These data demonstrate the health care system in Oregon has recognized Ocrevus as among the most affordable options in its therapeutic class and data shows higher utilization as a result.
    - Importantly, out-of-pocket (OOP) costs captured in this table do not consider co-pay assistance programs intended to assist patients in the cost sharing imposed by their health insurance. Genentech provided Oregon-specific Ocrevus co-pay assistance estimates and additional information in our response to Question 17 on the RFI form.

Table 3 Average healthcare and average patient OoP costs for Ocrevus vs therapeutic alternatives

Drug	Average gross healthcare spend per enrollee per year[18]	Average patient out-of-pocket cost per year[19]
Subject drug Ocrevus	$45,133	$2,381
Kesimpta	$63,514	$1,625
Tysabri	$67,594	$2,795
Average	**$58,747**	**$2,267**

Ocrevus treatment is associated with improved work productivity versus other MS DMTs.

- As MS onset occurs during an individual's most productive years, a reduction in the ability to do routine activities, including being employed, results in a substantial economic burden.[3,4] In lieu of head-to-head direct comparisons across DMTs, a network meta-analysis was conducted to compare completed clinical trials and predict the impact of DMTs on work productivity. **The model predicted that over 10 years, productivity losses were lowest for Ocrevus compared with other DMTs.**[5]
- In addition, the estimated percent employment among patients treated with Ocrevus was highest compared to other DMTs (53.3% versus 41.7%) in year 10.

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[2] Genentech (2025 April). *Ocrevus® (ocrelizumab) Multiple Sclerosis (MS) WAC Flash Card.*
[3] Nicholas JA, Electricwala B, Lee LK, Johnson KM. Burden of relapsing-remitting multiple sclerosis on workers in the US: a cross-sectional analysis of survey data. BMC Neurol. 2019;19(1):258.
[4] Chen, Jing, et al. "Effects of multiple sclerosis disease-modifying therapies on employment measures using patient-reported data." *Journal of Neurology, Neurosurgery & Psychiatry* 89.11 (2018): 1200-1207.
[5] Geiger C, et al.Productivity Loss Among Persons With Multiple Sclerosis Treated With Ocrelizumab vs Other Disease-Modifying Therapies. Presented at the ISPOR Meeting. Atlanta, GA. May 5 - May 8 2024.

- **The economic benefit for patients treated with Ocrevus resulted from an improved ability to work due to delayed progression leading to productivity gains of up to $25 million over 10 years relative to other MS treatments.**

2. ***"The total cost of the disease and the drug price offset."***

Oregon-specific disease modeling predicts that improved access to first-line use of Ocrevus would lead to reduced long-term disability and increased productivity in patients with MS, corresponding to a potential savings of over $14 million to the state of Oregon over a 10-year period.

- The need for walking aids and wheelchairs highlights the critical stages of disease progression that are associated with not only a decreased quality of life, but also reduced work productivity, and increased health care resource use and costs.[6,7,8,9] This model predicted that over 10 years, improved access to first-line treatment with Ocrevus would result in a lower likelihood of reaching significant disability and the need for walking aids and wheelchairs, compared to non-preferred access to Ocrevus for patients with MS in Oregon.[10] These improved disability outcomes translate to a potential savings of over $14 million to the state of Oregon due to reduced disability and increased productivity in those with MS.

Patients treated with Ocrevus are highly adherent and persistent with therapy, corresponding to an average savings of $16,000 over 24 months in non-drug medical cost offsets per patient, compared to those patients with MS who are non-adherent.

- Real-world research has shown that people with MS who were adherent and persistent with their DMT had substantially lower medical costs compared with those who were not.[11] Specifically, those who were persistent with medication for 24 months showed a reduction in mean total non-drug medical costs of approximately $19,000 compared with non-persistent patients. A similar pattern was observed for adherent versus non-adherent patients (reduction in costs at 24 months was about $16,000).
- Relatedly, when assessing Ocrevus compared with other MS DMTs (based on route of administration), one study found patients treated with Ocrevus had higher adherence than other therapeutic alternatives that were FDA-approved in

[6] Kwiatkowski A, et al. Social participation in patients with multiple sclerosis: correlations between disability and economic burden. BMC Neurology. 2014;14:1-8.
[7] Rezapour A, et al. The impact of disease characteristics on multiple sclerosis patients' quality of life. Epidemiology and Health. 2017:39.
[8] Geiger C, et al. Declines in Work Productivity in Persons With Multiple Sclerosis by PDDS Score. Presented at the American Academy of Neurology Annual Meeting. Boston, MA. 22-27 April, 2023. Poster #13-3.005.
[9] Simoens S. Societal economic burden of multiple sclerosis and cost-effectiveness of disease-modifying therapies. Frontiers in Neurology. 2022;13:1015256.
[10] Pineda E, et. al. National and State Population-Level Estimated Economic Impact of Ocrelizumab on Cumulative Disabilities Avoided and Work Productivity Under Different Access Scenarios in the United States. To be presented at ISPOR Annual Meeting. Montreal, QC. May 2025.
[11] Pardo G et al. The Association Between Persistence and Adherence to Disease-Modifying Therapies and Healthcare Resource Utilization and Costs in Patients With Multiple Sclerosis. J Health Econ Outcomes Res. 2022 Apr 26;9(1):111-116.

or before 2019. Specifically, 80% of Ocrevus patients were adherent compared to 55%, 35%, and 54% for oral, injectable, and other intravenous (IV) treatments, respectively, over two years.[12] Similarly, at 24 months, 75% of patients initiating Ocrevus were persistent with therapy compared with 54%, 33%, and 55% on oral, injectable, and other IV treatments, respectively. In comparing Ocrevus to other therapies and in assessing its overall costs, the Board must consider the cost offsets enabled by Ocrevus's method of administration and its six-month dosing regimen, which results in improvements in adherence and persistence and significant associated cost savings.

Patients using Ocrevus as a first-line treatment had better clinical outcomes and lower health care resource use, including a lower probability of hospitalization, corresponding to payor savings of approximately $11,500 per year compared to those who were treated second-line or later.

- A recent retrospective claims study demonstrated that patients who initiated Ocrevus as a first-line treatment had better clinical outcomes and lower events often associated with relapse[13] than those who initiated it as a second-line or later treatment option.[14]
- Patients on first-line Ocrevus also had lower health care resource use, including a lower probability of hospitalization, and longer time to events often associated with relapse compared to those who used Ocrevus as second line treatment or later. Notably, these findings of first-line Ocrevus use correspond to an annual payor savings of approximately $11,500 per patient, compared to those who were treated second-line or later.

3. **"*Patient copayment or other cost sharing data, across different health benefit plan designs, including copayment and coinsurance impacts from patient assistance programs and copay coupons; deductible; patient out-of-pocket costs; and any other cost sharing data*."**

Ocrevus' cost to patients can vary due to a myriad of factors. Insurance type, benefit design, and site of care are a few of these factors outside of Wholesale Acquisition Cost (WAC) (or "list") price that can impact a patient's final out-of-pocket (OOP) costs, as well as cost to the system. As a medicine traverses the delivery supply chain, it can be subject to a variety of factors across several intermediary stakeholders which impact costs, ranging from negotiated rebates and discounts to significant markup at the point of care.[15]

[12] Pardo G et al. Adherence to and Persistence with Disease-Modifying Therapies for Multiple Sclerosis Over 24 Months: A Retrospective Claims Analysis. Neurol Ther. 2022 Mar;11(1):337-351. Note, this study was conducted using claims data from April 2016 through December 2019.
[13] Events often associated with relapse were defined as any inpatient stay with primary diagnosis of MS; or an outpatient visit with an MS diagnosis with evidence of high-dose steroids, IV corticosteroids, adrenocorticotropic hormone, or plasma exchange within 30 days of the outpatient visit. All patient characteristics, use of DMTs, and outcomes were identified using claims data.
[14] Geiger CK et al. Real-World Clinical and Economic Outcomes Among Persons With Multiple Sclerosis Initiating First- Versus Second- or Later-Line Treatment With Ocrelizumab. Neurol Ther. 2023 Oct;12(5):1709-1728.
[15] https://www.gene.com/stories/the-science-of-pricing. Accessed 22 April 2025.

- While average patient copayment/cost sharing is requested in the carrier data call, it is not specifically assessed by health plan type or plan benefit designs. It is critical to assess the health plan type and benefit design impact on OOP costs as evident in the June 2024 Board materials from the previous Ocrevus carrier data call where OOP varied greatly by type of commercial health plan while the average drug cost to the plans remained similar across plan types. The table from that board meeting is reproduced below.

Table 5 2022 data call reported costs to Oregon payers and enrollees

Market	Total enrollees	Total claims	Total of paid claims	Total payer cost	Average paid claim	Average paid per enrollee	Total annual out-of-pocket cost for enrollees	Out-of-pocket cost per enrollee
Individual	58	174	112	$3,728,561	$33,291	$64,286	$352,289	$6,074
Small Group	57	143	111	$3,630,011	$32,703	$63,684	$306,568	$5,378
Large Group	75	190	166	$5,104,892	$30,752	$68,065	$262,607	$3,501
OEBB	44	246	91	$2,426,422	$26,664	$55,146	$93,586	$2,127
PEBB	54	170	106	$3,705,192	$34,955	$68,615	$40,386	$748
TOTAL	**288**	**923**	**586**	**$18,595,078**			**$1,055,436**	

- From the table, Public Employees' Benefit Board (PEBB) that has the highest annual spend noted for the plan, has the lowest OOP cost per enrollee of all data collected. Further, the percentage of the average cost plans paid for Ocrevus per enrollee that was passed along as OOP costs to patients varied from 9.4% to 1% across commercial plan types. This highlights that other factors outside of drug price (list or net) are driving patient OOP spending.
- Another such factor that can drive variations in drug cost is site of care (i.e., where a patient receives their medication).
    - For example, the setting in which the patient receives their infusion of Ocrevus may create significant variation in their OOP cost and overall cost to the health care system. Research published by a health insurer shows a 93% variation in the cost of MS treatments, depending on where the patient received their care.[16]
- Finally, Genentech provided Oregon-specific Ocrevus co-pay assistance estimates and additional information in our response to Question 17 on the RFI form.

4. "*Patient treatment preferences*" and patient and caregiver "*perspective on benefits and disadvantages of using the prescription drug*."

[16] https://www.unitedhealthgroup.com/content/dam/UHG/PDF/2019/UHG-Administered-Specialty-Drugs.pdf. Accessed on 22 April 2025.

In a study of patient preferences of those taking Ocrevus, 82% of patients preferred Ocrevus to the other DMTs taken prior to starting Ocrevus when surveyed after 48 weeks of treatment.[17]

- In this same study, 98% of patients were either satisfied or very satisfied with Ocrevus as a treatment for their MS symptoms.

5. **Input on "*the availability of therapeutic alternatives on the formulary.*"**
Because the Board did not request the formulary status of therapeutic alternatives via the carrier data call or the PBM RFI, estimates of national commercial and government payer coverage of therapeutic alternatives using Managed Markets Insight & Technology (MMIT) data are below.[18]

In its June 2024 meeting materials, the Board included a draft affordability report for the potential review of Ocrevus which included the following drugs identified by the Board as therapeutic alternatives: ublituximab, ofatumumab, alemtuzumab, and natalizumab.

Status	Ocrelizumab	Ublituximab	Ofatumumab	Alemtuzumab	Natalizumab
Covered	11.28%	15.58%	16.08%	15.04%	13.37%
Covered (PA/ST)	84.83%	70.85%	69.60%	72.55%	79.65%
Not Covered	3.03%	11.98%	10.52%	11.47%	6.01%
Unknown	0.86%	1.60%	3.80%	0.95%	0.96%

- Per the table above, Ocrevus has the lowest "not covered" proportion among its therapeutic alternatives, highlighting that payers recognize the value of Ocrevus to their health plans and enrollees.

6. **"*Changes in the prescription drug's net cost over time.*"**
    - Genentech has a long-standing pricing philosophy that is designed to strike a balance between ensuring patients have rapid, broad and sustainable access to our medicines, while at the same time preserving our ability to invest in future scientific innovations that drive the important medical breakthroughs that patients depend on us for. Since its launch in 2017, the WAC price of Ocrevus remained at $65,000 and was not increased until 2021.
    - Genentech provided information on price concessions over time in our response on the RFI to Question 13.
    - Ocrevus is priced lower than 15 other DMTs that represent treatment options for MS patients,[19] and has been consistently priced approximately 27% less than the average annual WAC for MS medications.

[17] SD Newsome et. al. Presented at the ACTRIMS Forum 2025; February 27–March 1, 2025; West Palm Beach, FL, USA, and virtual.
[18] MMIT Coverage Data and DRG Payer Lives. Data as of April 2025.
[19] Genentech (2025 April). *Ocrevus® (ocrelizumab) Multiple Sclerosis (MS) WAC Flash Card.*

- In its nearly eight years on the market, Ocrevus pricing has not triggered price increase advance notice nor reporting requirements under Oregon's price transparency reporting laws.

Beyond the additional criteria the Board must consider per OAR 925-200-020, Genentech has chosen to provide additional clinical information that we believe the Board should review and include in any affordability review to holistically consider the full value of Ocrevus.

1. **Ocrevus has established long-term benefits in slowing disease progression.**
    - The recent publication of 10-year milestone data from the Ocrevus open-label extensions of the Phase III RMS and PPMS studies demonstrated benefits in slowing long-term disability progression.[20] In a 10 year study of Ocrevus, 77% of patients with RMS were free from disability progression, and 92% were still walking unassisted.
    - In patients with PPMS, 36% were free from disability progression, and 80% of those patients treated with Ocrevus over 10 years could still walk unassisted. Importantly, the 10-year pooled safety data across a number of studies from over 6,000 patients continues to reinforce the consistent long-term safety profile of Ocrevus.[21]

2. **Ocrevus is a critical option for Oregonians with MS who are family planning based on recent real-world evidence.**
    - Although historically women with MS have been discouraged from pregnancy, a recent review works to educate the MS community on evidence-based considerations before, during, and after pregnancy.[22]
    - An analysis from the Roche safety database found that maternal exposure to Ocrevus (ie., *in utero* exposure to Ocrevus) was not associated with increases in the risk of adverse pregnancy or infant outcomes compared with the general population.[23]
    - Recent evidence shows that among women with MS with a live birth, Ocrevus (25%) was the most commonly prescribed DMT in the preconception and postpartum period versus other DMTs in its therapeutic class (5%). This evidence suggests growing confidence in the MS community in Ocrevus, with limited administration during pregnancy due to its extended dosing schedule (every 6 months), as a suitable DMT strategy for those who are family planning.[24]

[20] Weber M, et al. The Patient Impact of 10 Years of Ocrelizumab Treatment in Multiple Sclerosis: Long-Term Data from the Phase III OPERA and ORATORIO Studies.Presented at the 9th Joint ECTRIMS-ACTRIMS Meeting. Milan, Italy. 11–13 October 2023.
[21] Hauser et al. Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Progressive Multiple Sclerosis Presented at the 9th Joint ECTRIMS-ACTRIMS Meeting. Milan, Italy. 11–13 October 2023.
[22] Graham EL, et al. "Practical Considerations for Managing Pregnancy in Patients With Multiple Sclerosis: Dispelling the Myths." Neurol Clin Pract. 2024;14(2):e200253.
[23] Hellwig, Kerstin, et al. "Pregnancy and Infant Outcomes in Women Receiving Ocrelizumab for the Treatment of Multiple Sclerosis: Analysis of the Largest Available Outcomes Database." Multiple Sclerosis and Related Disorders 80 (2023): 105306.
[24] Houtchens MK, et. al. Real-world patterns of ocrelizumab and other disease-modifying therapy utilization before, during and after pregnancy in women with multiple sclerosis: a retrospective claims-based cohort study." To be presented at ECTRIMS September 2025.

National
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Society

April 30, 2025

Oregon Division of Financial Regulation
Oregon Prescription Drug Affordability Board
350 Winter St. SE
Salem, OR 97309

RE: Request for information: patients, caregivers, or advocacy groups

Members of the Oregon Prescription Drug Affordability Board:

Thank you for the opportunity to continue to submit comments on the Oregon Prescription Drug Affordability Board. The National Multiple Sclerosis Society (Society) is pleased that the State of Oregon and the Prescription Drug Affordability Board (Board) continues robust public outreach and comment solicitation throughout each step in this process. The Society will continue to be involved as we believe Boards such as these provide important information and transparency regarding the high cost of prescription medications. The Board and the Society share a common goal in ensuring affordable access to medications for all Oregon residents.

Background
Multiple sclerosis (MS) is an unpredictable disease of the central nervous system. Currently there is no cure. Symptoms vary from person to person and may include disabling fatigue, mobility challenges, cognitive changes, and vision issues. An estimated 1 million people live with MS in the United States. While there is not yet a cure, we do know that early diagnosis and treatment are critical to minimizing disability. Significant progress is being made to achieve a world free of MS.

Affordability Review RFI Forms, Continued Comments: Patients, Caregivers, Advocacy Groups
In our March 2025 letter, the Society recommended that separate forms be created for patients/caregivers and the patient advocacy community due to the differing levels of expertise, knowledge, and experience related to the data being collected and the questions the board is seeking to answer. As the Board elected to maintain the single RFI, the Society was not able to complete the form. This is in large part due to (1) question formatting that requires individualized information such as dosage, length of time on the medication, insurance type, and out-of-pocket cost and (2) several required entry fields on specific patient data that we neither can nor would share. This letter aims to provide the patient advocacy group information and perspective the Board is endeavoring to collect related to the disease-modifying therapy Ocrevus®.

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MS Disease-Modifying Therapies and Ocrevus®

Today there are more than 20 disease-modifying therapies (DMTs), both name brand and generic, approved by the FDA for treatment of MS. Ocrevus® was approved by the FDA in 2017, is considered to be in the category of high efficacy treatments, and was the first medication approved with the specific anti-CD20 mechanism of action. Anti-CD20 action is beneficial for people living with MS because it specifically reduces nerve damage which can lead to irreversible disability progression.

Of the more than 20 FDA approved DMTs for relapsing forms of MS, it's important to note that Ocrevus® is the only FDA approved DMT treatment for primary progressive MS (PPMS). Approximately ten to fifteen percent of people with MS have PPMS; these individuals can expect to experience gradually worsening neurologic symptoms and an accumulation of disability without relapses.

Ocrevus® is an infused DMT with 2 doses per year, with the first dose being split into two 300mg infusions 2 weeks apart. Further doses are administered as one 600mg infusion every 6 months with each infusion session lasting 2-4 hours.

Our most recent pricing data shows the FY25 wholesale acquisition price (WAC) for Ocrevus® to be $82,564 (fig. 1). From our experience working with people living with MS, most patients do not differentiate between the cost of the DMT and the total cost of the infusion including provider fees, ancillary infusion costs, facility fees, etc. These additional costs are what patients see on their explanation of benefits and can put the total billed into the $100-120,000 range. In analyzing the reported out-of-pocket costs, we would urge the Board to ensure that all cost reporting is accurate and clear on what out-of-pocket costs are related to the price of the drug and what costs are associated with administrative/infusion costs.

Costs of Living with MS

People with MS have a variety of healthcare needs including but not limited to addressing neurological symptoms; emotional and psychological issues; rehabilitation therapies to improve and maintain function and independence; and long-term care. These needs vary dramatically from person to person and can change year on year as the disease progresses. Prescription medications are central to most treatment regimes.

Due to the range of health care and associated needs, the average total cost of living with MS is calculated at $88,487 per year[1]. MS may impact one's ability to work and can generate steep out-of-pocket costs related to medical care, rehabilitation, home & auto modifications, and more. For individuals with MS, medical costs are an average of $65,612 more than for

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9109149/

National
Multiple Sclerosis
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individuals who do not live with the disease. Disease-modifying therapies are the single largest component of these medical costs. As of April 2025, the median annual brand price of MS DMTs is more than $112,000. Seven out of the nine DMTs that have been on the market for at least 12 years are priced over $100,000 annually and continue to see regular price increases (fig. 1).

Application Based, Time-Limited Patient Assistance Programs

Survey results have shown that over 70% of people with MS have relied on copay assistance to maintain access to their DMTs and 40% of individuals living with MS alter their treatment plans due to cost. It is reasonable to question the role of copay assistance programs and the potential role they inadvertently play in raising costs. However, until real solutions to the challenges of unaffordable MS DMTs and other prescription medications are found, application based, manufacturer patient assistance programs will continue to play a necessary and vital role in keeping these products accessible. Loss of this vital assistance would be devastating.

Additional Commentary

Along with mechanism of action, there are several other factors which influence the shared decision-making of a patient and doctor's choice of a DMT. Some of the top factors in shared decision-making conversations include efficacy, tolerance of side effects, dosage frequency and route of administration - all of which can affect adherence to treatment. Ocrevus® is administered by infusion every six months; this dosing schedule is often appealing to people with MS as they may have increased quality of life due to the dosing infrequency. For some individuals, infusions may prove challenging if access to infusion sites is limited.

The Society best estimates based on claims data is that from 2023-2024 almost 1,100 Oregonians living with MS utilized the DMT Ocrevus®. This is out of an estimated MS population of just over 11,000, showing Ocrevus® DMT usage representing approximately 10% of Oregonians living with MS[2].

The National Multiple Sclerosis Society thanks the Board again for the opportunity to provide comments throughout the drug review process. Should you have any questions, please contact Seth Greiner, Senior Manager of Advocacy, at seth.greiner@nmss.org.

Sincerely,

Seth Greiner
Senior Manager, Advocacy
National Multiple Sclerosis Society

[2] Komodo Health. (2025, April 29). *Oregon Ocrevus Multiple Sclerosis Utilization 2023-2024* [Data set]. Komodo Prism.

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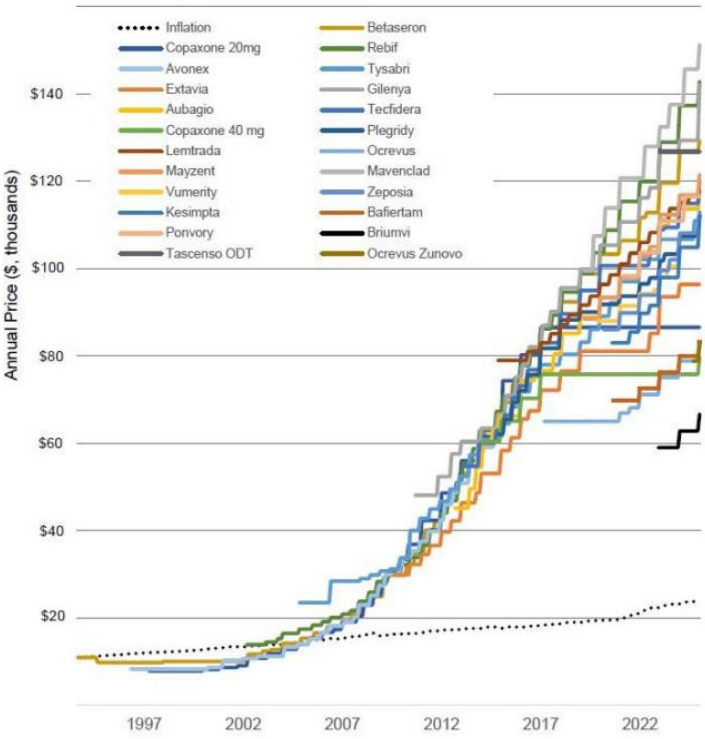
Figure 1

Trends in annual price for branded disease-modifying therapies for multiple sclerosis; 1993 to 2025



Drug (manufacturer; market entry)	1 Year Change*	Annual Price 2025
Interferons		
Betaseron (Bayer, July 1993)	2.0%	$129,322
Avonex (Biogen, May 1996)	4.5%	$112,291
Rebif (EMD Serono, Mar 2002)	4.0%	$142,848
Extavia (Novartis, Aug 2009)	0.0%	$96,373
Plegridy (Biogen, Aug 2014)	4.5%	$112,291
Glatiramer Acetate		
Copaxone 20mg (Teva, Dec 1996)	0.0%	$86,554
Copaxone 40 mg (Teva, Jan 2014)	5.0%	$79,607
S1P Receptor Modulators		
Gilenya (Novartis, Sept 2010)	9.9%	$142,155
Mayzent (Novartis, Mar 2019)	4.0%	$121,514
Zeposia (BMS, March 2020)	4.5%	$113,027
Ponvory (Janssen, March 2021)	5.0%	$116,462
Tascenso ODT (Cycle, Jan 2023)	0.0%	$126,813
Fumarates		
Tecfidera (Biogen, Mar 2013)	4.5%	$120,083
Vumerity (Biogen, Nov 2019)	4.9%	$110,186
Bafiertam (Banner, Sept 2020)	4.0%	$83,193
Other Oral DMTs		
Aubagio (Sanofi, Sept 2012)	2.0%	$115,981
Mavenclad (EMD Serono, Mar 2019)	10.0%	$151,291
Monoclonal Antibodies		
Tysabri (Biogen, Nov 2004)	4.0%	$110,990
Lemtrada (Sanofi, Nov 2014)	2.3%	$117,799
Ocrevus (Genentech, Mar 2017)	4.7%	$82,564
Kesimpta (Novartis, Aug 2020)	7.0%	$112,165
Briumvi (TG Therapeutics, Jan 2023)	6.1%	$66,660
Ocrevus Zunovo (Genentech, Sept 2024)	NA	$82,564

Notes: Annual price estimated from wholesale acquisition costs (First Databank)
Dashed line is projected annual price of Betaseron assuming only inflationary increases in price (CPI)
Lemtrada is based on four 12 mg vials (Package insert dosing: 12 mg/day (5 vials) for five consecutive days in first year; 12 mg/day (3 vials) for three days in year 2
Briumvi is based on maintenance dose of 450 mg (3 vials) twice a year;
*2024 to 2025 (January);

MS Society disclosure: *The MS Society receives up-to-date drug price information twice a year through a contract with health economist/researcher Dr. Daniel Hartung, OHSU.*

April 30, 2025

VIA ELECTRONIC FILING

Oregon Prescription Drug Affordability Board
350 Winter Street NE
Salem, OR 97309-0405
pdab@dcbs.oregon.gov

Dear Members of the Oregon Prescription Drug Affordability Board,

GSK appreciates the opportunity to provide information on Trelegy Ellipta ("Trelegy") as part of the state's affordability review process. GSK has completed the voluntary online survey and included information regarding Trelegy that is in the public domain not proprietary or confidential in nature. GSK did not respond to the data elements requested by Oregon that are confidential, commercially sensitive or otherwise proprietary.

GSK is a science-led global healthcare company with a special purpose to unite science, technology, and talent to get ahead of disease together. We focus on science of the immune system, human genetics, and advanced technologies to impact health at scale. We prevent and treat disease with vaccines, as well as specialty and general medicines.

GSK remains committed to ensuring that innovation and affordability can coexist. We extend this spirit of innovation to the way we responsibly do business. When establishing our prices in the US, we strive for a fair and appropriate balance that rewards innovation while affording access for appropriate patients. Our goal is to work in the best interests of patients and for the good of our company; we systematically apply a value-based framework that looks at the benefits of our medicines compared to alternatives, and we focus on improving health outcomes for patients. We conduct extensive research both internally and externally to ensure we understand the patient, payer, and physician perspectives on a potential drug's value to the system and its appropriate price.

As outlined below, GSK believes Trelegy is appropriately priced for the value it brings to patients and the State of Oregon, and it should not be considered for a full affordability review.

Trelegy Provides Significant Clinical Value

Trelegy is a fixed-dose single inhaler combination of fluticasone furoate (FF), an inhaled corticosteroid (ICS); umeclidinium (UMEC), a long-acting muscarinic antagonist (LAMA); and vilanterol (VI), a long-acting β2-agonist (LABA). It is the only single inhaler ICS/LABA/LAMA (or "triple therapy") administered via one inhalation once daily. Trelegy is delivered in a dry powder inhaler (DPI) device called Ellipta and is indicated for maintenance treatment of chronic obstructive pulmonary disease (COPD) and asthma in patients aged 18 years and older. As noted below, Trelegy is guideline-recommended and multiple studies show that it improves outcomes and reduces health care spending compared to other available triple therapies.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report is a set of COPD clinical guidelines revised annually and accepted by clinicians and experts internationally for the management of

COPD.[1] These guidelines recommend ICS/LABA/LAMA triple therapies as a preferred option for patients at high risk of future exacerbations and for those patients who are uncontrolled on dual therapies (e.g., ICS/LABAs).

The only other single inhaler triple therapy available in the US is Breztri, which is administered via two inhalations, twice daily (i.e., four total daily inhalations). Breztri is indicated for COPD but not for asthma. In studies comparing Trelegy to Breztri, Trelegy has been associated with significantly improved adherence, reduced exacerbation rates, improved lung function, and reduced mortality in patients with COPD with a similar safety profile.[2,3,4,5]

Patients may also receive triple therapy via multiple inhalers (e.g., an ICS/LABA in one inhaler, plus a LAMA in a second inhaler), although GOLD guidelines note that "single inhaler therapy may be more convenient and effective than multiple inhalers."[1] Across studies comparing Trelegy to multi-inhaler triple therapies (MITT) in COPD, Trelegy has been associated with improved lung function, reduced exacerbation rates, and better adherence while maintaining a similar safety profile.[2,6,7]

In asthma, leading clinical guidelines from the Global Initiative for Asthma (GINA) recommend triple therapies like Trelegy for use in patients that remain symptomatic on dual therapy ICS/LABAs.[8] Trelegy is the only approved single inhaler triple therapy for asthma, and GINA guidelines recommend single inhalers over multiple inhalers, stating "where more than one medication is needed, a single (combination) inhaler is preferable to multiple inhalers."

Trelegy is associated with improved adherence, reduced exacerbation rates, and improved asthma control compared with other treatments, including MITTs and ICS/LABAs.[9,10] Additionally, use of Trelegy in asthma is associated with lower health care spending. Asthma patients progressing to Trelegy from ICS/LABA saw a 26 percent reduction in asthma-related medical costs due to lower rates of outpatient, emergency department, and urgent care visits.[11]

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[1]Global Initiative for Chronic Obstructive Lung Disease (GOLD). "Global Strategy for Prevention, Diagnosis, and Management of COPD (2025 Report)". Available from: https://goldcopd.org/2025-gold-report/.
[2] Ismaila, A.S., et al. "Fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) triple therapy compared with other therapies for the treatment of COPD: a network meta-analysis." Advances in Therapy, 2022. 39(9): p. 3957-3978.
[3] Mannino, D., Weng, S., Germain, G., Boudreau, J., Tardif-Samson, A., Forero-Schwanhaeuser, S., Laliberté, F., Gravelle, P., Compton, C.H., Noorduyn, S.G. and Paczkowski, R. "Comparative Effectiveness of Fluticasone Furoate/Umeclidinium/Vilanterol and Budesonide/Glycopyrrolate/Formoterol Fumarate among US Patients with Chronic Obstructive Pulmonary Disease." Advances in Therapy, 2024. 42(2): p. 1131-1146.
[4] Feldman, W.B., et al. "Comparative effectiveness and safety of single inhaler triple therapies for chronic obstructive pulmonary disease: new user cohort study." bmj, 2024. 387.
[5] Young, C., Lee, L.Y., DiRocco, K.K., Germain, G., Klimek, J., Laliberté, F., Lejeune, D., Noorduyn, S.G. and Paczkowski, R. "Adherence and Persistence with Single-Inhaler Triple Therapy Among Patients with COPD Using Commercial and Medicare Advantage US Health Plan Claims Data." Advances in Therapy, 2024.
[6] Ferguson, G.T., et al. "Once-daily single-inhaler versus twice-daily multiple-inhaler triple therapy in patients with COPD: lung function and health status results from two replicate randomized controlled trials." Respiratory Research, 2020. 21(1): p. 1-15.
[7] Mannino, D., et al. "Adherence and persistence to once-daily single-inhaler versus multiple-inhaler triple therapy among patients with chronic obstructive pulmonary disease in the USA: a real-world study." Respiratory Medicine, 2022. 197: p. 106807.
[8] Global Initiative for Asthma (GINA). "Global Strategy for Asthma Management and Prevention (2024 Report)". Available from: https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24_05_22_WMS.pdf.
[9] Bogart, M., et al. "Real-World Study of Single-Inhaler Triple Therapy with Fluticasone Furoate/Umeclidinium/Vilanterol on Asthma Control in the US." Journal of Asthma and Allergy, 2023: p. 1309-1322.
[10] Lee, L.A., et al. "Efficacy and safety of once-daily single-inhaler triple therapy (FF/UMEC/VI) versus FF/VI in patients with inadequately controlled asthma (CAPTAIN): a double-blind, randomised, phase 3A trial." The Lancet Respiratory Medicine, 2021. 9(1): p. 69-84.
[11] Baptist, A.P., Germain, G., Klimek, J., Laliberté, F., Schell, R.C., Forero-Schwanhaeuser, S., Moore, A., Noorduyn, S.G. and Paczkowski, R. "Medicare Advantage Population in the United States: Outcomes of Patients with Asthma Treated with ICS/LABA Before and After Initiation with Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI)." Advances in Therapy, 2024. 42(2): p. 1061-1074.

Trelegy Provides Significant Economic Value

In addition to these clinical outcomes, Trelegy is associated with lower overall health care spending compared to MITT. Total COPD-related costs, which include pharmacy costs (including inhalers), inpatient, outpatient, emergency department (ED), office visit, and other medical costs, were about 19 percent lower in Medicare patients using Trelegy compared to those using MITT.[12]

Trelegy is Affordable to the State of Oregon and to Patients

Based on review of Oregon's data, GSK believes that Trelegy does not represent an affordability challenge to the state. The Oregon PDAB's Preliminary Aggregated Carrier Data, which utilizes claims from 2023, shows that Oregon's 2023 total annual net spend of Trelegy was $627,285.81, which ranks 125th out of the 158 drugs reported in this list. Oregon's Carrier Data also shows Trelegy's total 2023 annual net spend per Oregon enrollee was $2,133.63, which ranks 90 out of 158.

Trelegy was selected by the Centers for Medicare and Medicaid Services (CMS) this year for IPAY 2027 Medicare Negotiations. CMS selects drugs based on how much Medicare spends on them overall and, in Trelegy's case, this appears to be driven mostly by Medicare enrollee utilization (1.25 million people) given its market leader status rather than its price per unit. Importantly, CMS' selection criteria did not account for discounts already in the market in their selection process. In contrast, Oregon's drug pricing dashboard looks at net spending (after discounts), and it indicates Trelegy does not pose a high affordability concern relative to other widely used drugs in the state.

GSK is committed to increasing patient access to Trelegy. In addition to the significant rebates and discounts we provide for our products, GSK has multiple patient support programs for eligible patients that can reduce their out-of-pocket (OOP) spend to or below $35 per month.

- GSK offers a coupon for Trelegy where eligible commercially insured and cash paying patients may pay as little as $0.
- GSK offers a coupon for our entire portfolio of inhalers, including Trelegy, which caps patient OOP costs at $35-per-month for eligible commercially insured and cash paying patients.[13]
- Patients who are unable to afford the cost of their GSK medicines may be eligible to receive certain medicines, including Trelegy, at no cost through the GSK Access Programs Foundation, an independent, 501(c) (3) charitable foundation.

Potential for Access Challenges

While the OR PDAB currently does not have UPL authority, GSK is concerned over access issues that may be created if UPLs are set for drugs in the future. In addition, changes to formularies and patient drug benefits resulting from upper payment limits (UPLs) could create market disincentives, forcing providers to adjust referral, prescribing, and acquisition patterns for UPL-selected drugs. Such disincentives and market disruptions could create provider pressure to choose specific medications over the clinically appropriate product a provider deems best for the patient based on their individual and unique diagnosis. Research demonstrates that payers will likely change their formularies to account for UPLs, with 27% of survey

[12] Bogart, M., et al. "Outcomes Following Initiation of Triple Therapy with Fluticasone Furoate/Umeclidinium/Vilanterol versus Multiple-Inhaler Triple Therapy Among Medicare Advantage with Part D Beneficiaries and Those Commercially Enrolled for Health Care Insurance in the United States." International Journal of Chronic Obstructive Pulmonary Disease, 2024. 19: p. 97-110.

[13] GSK. GSK Announces Cap of $35 Per Month on U.S. Patient Out-of-Pocket Costs for its Entire Portfolio of Asthma and COPD Inhalers. https://us.gsk.com/en-us/media/press-releases/gsk-announces-cap-of-35-per-month-on-us-patient-out-of-pocket-costs-for-its-entire-portfolio-of-asthma-and-copd-inhalers/.

respondents noting that they will place a UPL-affected drug on a “less preferred tier”.[14] UPLs could negatively influence provider treatment choices and patient therapy access as plan formulary changes driven by the UPL, may alter autonomous provider decision making of clinically appropriate treatment pathways and prevent patients from getting access to a high value treatment.

Conclusion

In summary, we believe Trelegy is appropriately priced for the significant value it brings to patients and does not pose an affordability challenge. Trelegy is an affordable, high-value option for severe asthma or COPD before patients escalate to more expensive biologics. As such, Trelegy does not pose an affordability challenge and should not qualify for the OR PDAB affordability review.

Thank you again for your consideration and for the opportunity to engage with the Board. Please feel free to contact Christian Omar Cruz at Christian.O.Cruz@gsk.com with any questions.

Sincerely,

Harmeet Dhillon
VP, Government Affairs, Public Policy, Patient Advocacy
GSK

[14] Partnership to Fight Chronic Disease. Payer Perspectives Confirm UPLs Will Likely Raise Costs and Hinder Patient Access to Medicines. https://www.fightchronicdisease.org/post/new-research-shows-prescription-drug-affordability-boards-will-not-benefit-patients.

Eli Lilly and Company

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April 25, 2025

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

Oregon Department of Consumer and Business Services
ATTN: Oregon Prescription Drug Affordability Board (the "Board")
P.O. Box 14480
Salem, OR 97309

Re: Prescription Drug Affordability Review of Lilly Products

Dear Board,

I write on behalf of Eli Lilly and Company ("Lilly"), the manufacturer of Emgality®, Mounjaro®, Taltz®, Trulicity®, Verzenio®, Basaglar KwikPen®, Basaglar Tempo Pen® and Rezvoglar KwikPen™. According to the subset lists of products selected for affordability reviews published on the public website for the Oregon Prescription Drug Affordability Board, the Board intends to review these drugs listed above to determine whether the selected products "may create affordability challenges for the health care systems or high out-of-pocket costs for patients"[1]. We appreciate the opportunity to provide our perspective and insights on this critical issue and also provide our perspective on the Request for Information: Manufacturers ("Manufacturer's RFI") posted on the Board's website due April 30, 2025.

Lilly is Committed to Patient Affordability.

Throughout our nearly 150-year history, Lilly has worked to address some of the most pressing health challenges facing humanity, including infections, diabetes, depression, cancer and obesity. Today, more than 55 million people are estimated to use Lilly medicines. We know that our commitment to patients and society goes beyond the medicines we make. We are committed to equitable and affordable access to our medicines so that our breakthroughs can transform more people's lives. This includes our approach to pricing in the U.S.

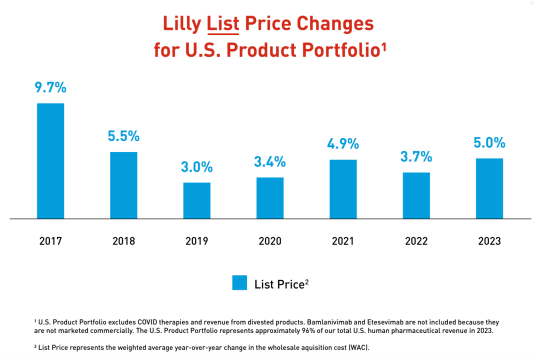
Pricing medicines to achieve the optimal balance between patient access and sustained investment in innovative treatments is complex. At Lilly, we know that pricing our medicines is one of the most important decisions we make as a company. We use a value-based approach to pricing, taking into account customer perspective, company considerations, competitive landscape and other contributing factors like health system changes and policy guidelines. Lilly also makes price adjustments over a product's lifecycle

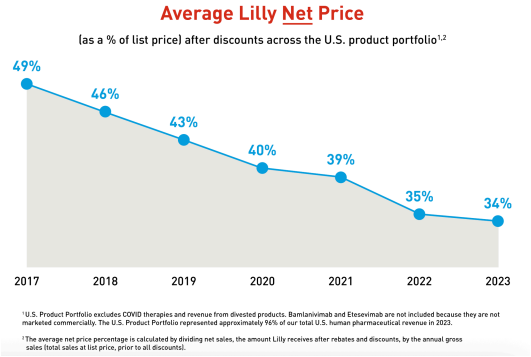
[1] ORS 646A.694.

that are based on the factors above as well as post-approval clinical data. We are committed to educating stakeholders about the value of our medicines and ensuring transparency about our prices. List prices for many of our medicines, as well as average out-of-pocket costs and financial assistance information, are published online[2].

A list price for each of our medicines is set using the considerations noted above. We pay rebates and other discounts and fees to payers, pharmacy benefit managers (PBMs), the U.S. government and other supply chain entities such as wholesalers and distributors. After paying these rebates, discounts and channel costs, the final dollar amount that Lilly ultimately receives is called the net price.

These rebates and discounts have continued to grow over the years for Lilly's U.S. portfolio while net prices for many of our medicines have continued to decrease.





Lilly Patient Support Programs Offer Affordability Solutions.

We're a medicine company turning science into healing to make life better for as many people as possible. We work to improve access to our treatments and increase equity throughout the health care system. We actively advocate for and participate in the process of driving systemic positive changes. We support the realignment of financial incentives for the entire pharmaceutical supply chain so that patients directly benefit from the net pricing we provide. We are also taking important steps within our own control to increase access to Lilly medicines today.

Lilly offers a variety of affordability solutions through patient support programs and copay assistance across the major products in our portfolio. For many of our migraine, immunology, diabetes and obesity medicines, we have copay assistance programs to bring eligible patients' monthly out-of-pocket costs to as little as $25 or lower. For cancer, the Lilly Oncology Support Center assists eligible patients in

[2] https://pricinginfo.lilly.com

identifying affordability options related to their Lilly treatment. The Lilly Diabetes Solution Center is a resource for patients to learn about our different insulin affordability solutions, which are outlined below.

For millions of people with diabetes, insulin is a life-saving medicine. Over the last century, this medicine has improved and extended countless lives around the world. Lilly understands the importance of our role as a leading diabetes company – and that includes supporting affordable access to insulin therapies. While many people in the U.S. have insurance coverage with affordable copays, some have large deductibles they must satisfy before insurance will cover their medicines and others have no insurance at all. And, for many people, insulin is just one of several interventions used to control diabetes, such as blood glucose monitoring devices and other medicines.

Over the past several years, Lilly has introduced multiple insulin affordability solutions, including our Lilly Insulin Value Program. As a result of our efforts, anyone – whether they are uninsured or use commercial insurance – is eligible to buy their monthly prescription of Lilly insulin for $35 or less, regardless of the number of pens or vials they use. To make it even easier for people to access Lilly insulin, we took additional steps in 2023, including:

- Reducing the list price of our most commonly prescribed insulins by 70%.
- Automating the $35 out-of-pocket monthly cap for people with commercial insurance at participating retail pharmacies.
- Cutting the price of our non-branded insulin, Insulin Lispro, which is the same molecule as Humalog, to $25 per vial, making it the lowest list-priced mealtime insulin available.
- Launching a biosimilar basal insulin, Rezvoglar, at a lower list price.

Under the Inflation Reduction Act (IRA), more than 3 million Medicare beneficiaries who take insulin will pay $35 per month or less on their insulin. Lilly was a strong supporter of this provision as it aligns with the affordability solutions we've had in-place years before the IRA became law.

All of these initiatives have made a real impact, helping 100,000 people save $20 million each month. Importantly, despite rising insurance deductibles, Lilly was the first and still only company to cap what people pay at $35 per month for all of our insulins, we cut insulin prices by 70%, and in 2023 the average monthly out-of-pocket cost for Lilly insulin was just $17.16.

The Board's Affordability Review Should Focus on Patient Affordability.

While we share the Board's goal of improving access to medicines and drug affordability for patients, we have concerns regarding the ambiguity of the Board's focus on affordability. It is unclear whether the primary focus of the Board's affordability review is on cost-sharing for patients, specifically

patient out-of-pocket costs, or for the healthcare system as a whole. We believe it is crucial to prioritize patient affordability and the patient out-of-pocket experience to ensure that Oregon patients can access the medications they need without undue financial burden. Clarifying this focus on affordability for patients through the Board's drug affordability process will align efforts for access and affordability of medicines for the intended beneficiaries—patients in Oregon.

The Manufacturer's RFI Requests Speculative and Unavailable Data and Lacks Adequate Protections of Confidential Information.

Lilly highlights that the data collection process employed by the Board requests data that is not available, speculative, and/or highly confidential. Much of the information listed in the Manufacturer's RFI is non-public confidential information and/or information that is not collected, calculated, or allocated by manufacturers on a product or state-level basis. Notably, the Manufacturer's RFI also asks manufacturers to submit pricing and cost information on competitors' therapeutic alternatives, information which manufacturers neither have access to nor can provide.

In addition, we are concerned with the proposed collection of data requested by the Manufacturer's RFI through a Microsoft survey tool – a method that is unprotected and lacks sufficient controls for receiving confidential, proprietary and trade secret information. It is essential to ensure that any confidential data that is collected is protected as required by federal and state law to maintain the integrity of proprietary and trade secret data and information. We urge the Board to consider implementing measures to safeguard any proprietary, confidential, and/or trade secret information that it receives. Ensuring secure data handling practices is crucial for maintaining the integrity and effectiveness of an affordability review process as well as guarding information that is entitled to statutory protections.

We are also concerned with the Board's affordability review process in connection with the lack of notice and submission timing requirements of the Manufacturer's RFI. The Board's request for information to manufacturers was published on the public website for the PDAB on or around March 31, 2025, without direct notification to manufacturers with a response deadline for the Manufacturer's RFI within a month on April 30, 2025. The Manufacturer's RFI timing does not sufficiently allow for complete and meaningful responses (and in some cases for a manufacturer, responses for multiple drugs), and we request that the Board implement a transparent and reasonable process to help the Board determine a drug's therapeutic benefit, cost value, and affordability for patients.

We appreciate that the Board shares our commitment to prescription drug access and patient affordability. We are proud of the impact that our efforts have had on making prescription drugs more

affordable for patients and believe Lilly medicines like those selected by the Board help make the lives of Oregon patients healthier and better.

Sincerely,

Cynthia Ransom
Sr. Director, US Government Pricing & Payer

Novartis Services, Inc.
801 Pennsylvania Avenue NW
Suite 700
Washington, DC 20004

Courtney Piron
US Country President
Head, US Public Affairs
Telephone +1 202-253-1803

May 1, 2025

VIA ELECTRONIC DELIVERY
Oregon Prescription Drug Affordability Review Board
Labor & Industry Building
350 Winter Street NE
Salem, OR 97309-0405

Care of: pdab@dcbs.oregon.gov

Re: Selection of Cosentyx® and Entresto® for Affordability Review

Dear Oregon Prescription Drug Affordability Board ("Board"):

Novartis Services, Inc. submits this letter on behalf of Novartis Pharmaceuticals Corporation and its affiliates referred to collectively herein as "Novartis." We appreciate the opportunity to respond to comment on the Board's selection of Cosentyx® (secukinumab) and Entresto® (sacubitril/valsartan) for affordability review pursuant to *OR. Rev. Stat. § 646A.693 - 646A.697*.[1]

Novartis is an innovative medicines company concentrated on the core therapeutic areas of cardiovascular, immunology, neuroscience, and oncology. At Novartis, we are united by a single purpose to reimagine medicine to improve and extend lives. We believe everyone should have access to the medicines they need. When we determine the prices for our medicines, we consider the value that these medicines provide to patients as well as health care systems and society at large.

Entresto and Cosentyx are both proven medicines backed by robust clinical evidence. Patients in Oregon have broad affordable access to these medicines:

- Eligible patients with commercial health coverage can access Cosentyx and Entresto at a cost as low as zero dollars with the Novartis co-pay support program.
- Eligible patients who are uninsured or underinsured pay nothing for Cosentyx and Entresto via the Novartis Patient Assistance Foundation.
- When adjusted for inflation, the average net prices of Cosentyx and Entresto have declined between January 2018 and December 2023.

[1] By making this submission, Novartis does not waive its rights with regard to any legal challenge to ORS § 646A.694 and OAR 925-200-0020 and the Board's implementing regulations.

- Cosentyx and Entresto provide value to the broader health care system. This is particularly clear for Cosentyx when compared to therapeutic alternatives. It is also clear for Entresto when compared to the former standard of care, enalapril, since Entresto is a first-in-class heart failure therapy without a current therapeutic alternative.[2]

Additionally, for forecasting purposes, Novartis currently assumes Entresto loss of exclusivity in mid-2025.[3]

Cosentyx and Entresto Are Proven Medicines Backed by Robust Evidence.

Cosentyx has been studied clinically for more than 17 years and used to treat more than 1 million patients globally since its approval by the FDA in 2015.[4]

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years of age and older who are candidates for systemic therapy or phototherapy. Cosentyx is also indicated for the treatment of active psoriatic arthritis in patients 2 years of age and older.

Affecting 7.5 million Americans, psoriasis is a chronic autoimmune inflammatory disease characterized by thick and oftentimes extensive skin plaques that cause itching, scaling, and pain. Psoriasis can negatively impact patients' quality of life, both psychosocially and physically.[5]

However, psoriasis is not simply a skin disease. Up to 41% of patients with certain types of psoriasis may also have psoriatic arthritis, which - through destructive inflammation - can lead to irreversible joint damage if not properly treated.[6]

In clinical trials, Cosentyx has been shown to help achieve clear skin in plaque psoriasis and help stop progressive joint damage and improve physical function

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[2] McMurray JJ et al. (2014). Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. NEJM**.** https://www.nejm.org/doi/full/10.1056/nejmoa1409077; Solomon SD et al. (2019). Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. NEJM. https://www.nejm.org/doi/full/10.1056/NEJMoa1908655

[3] Novartis Q4 2024 Results Investor Presentation, Slide 6. https//www.novartis.com/sites/novartis_com/files/q4-2024-investor-presentation.pdf

[4] Data on file. COSENTYX Patient Reach. Novartis Pharmaceuticals Corp; January 2023.

[5] Armstrong A, Mehta M, et al. Psoriasis Prevalence in Adults in the United States. JAMA Dermatol. 2021 Aug; 157(8): 1–7. doi: 10.1001/jamadermatol.2021.2007.
National Psoriasis Foundation. About Psoriasis. https://www.psoriasis.org/about-psoriasis/. Accessed September 27, 2023.

[6] Rech J, Sticherling M, et al. Psoriatic arthritis epidemiology, comorbid disease profiles and risk factors: results from a claims database analysis. Rheumatol Adv Pract. 2020; 4(2): rkaa033. doi: 10.1093/rap/rkaa033.

in patients with psoriatic arthritis. Cosentyx generally starts working in as little as 3 to 4 weeks with positive results observed up through 5 years.[7]

Cosentyx is also approved for active ankylosing spondylitis and active non-radiographic axial spondyloarthritis – two inflammatory arthritis conditions that affect the spine - as well as active enthesitis-related arthritis (ERA). Additionally, in 2023, Cosentyx was approved as the first new biologic treatment in nearly a decade for adults with moderate to severe hidradenitis suppurativa (HS), a painful and often debilitating inflammatory skin condition.

Further, Cosentyx is the only medicine FDA approved to treat 2 types of juvenile idiopathic arthritis (JIA), the most common form of juvenile arthritis: Enthesitis-Related Arthritis (ERA) and Juvenile Psoriatic Arthritis (JPsA). ERA is a type of JIA that affects the tissue where the muscles, ligaments, or tendons meet the bone (entheses). Symptoms may include swelling, joint pain, and stiffness at the hips, knees, and feet. The fingers, elbows, pelvis, chest, and lower back can also be affected. JPsA is a type of JIA that may include symptoms of both arthritis and plaque psoriasis. Arthritis symptoms can show up before skin symptoms and may affect 1 or more joints, often in the wrists, ankles, fingers, or toes. Psoriasis can appear as a scaly rash behind the ears, on the eyelids, elbows, knees, belly button, or scalp. In a clinical trial of kids and teens with ERA or JPsA taking Cosentx, those with ERA had a 53% reduced risk of flares and those with JPsA had an 85% reduced risk of flares.[8]

We have ongoing development programs for Cosentyx in other areas of high unmet need such as giant cell arteritis (GCA) a condition that can cause pain and swelling in blood vessels.

Entresto

Entresto is the first and only angiotensin receptor-neprilysin inhibitor (ARNi) approved for the treatment of heart failure in the United States that helps patients stay alive longer and out of the hospital.[9] Entresto is the #1 heart failure brand prescribed by cardiologists and has helped over 2 million people with heart failure.[10]

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[7] Cosentyx Prescribing Information. East Handover, NJ: Novartis Pharmaceuticals Corp; July 2023. Cosentyx.com. Results with Cosentyx. https://www.cosentyx.com/psoriatic-arthritis/treatment-results. Accessed September 27, 2023.
[8] Cosentyx Webpage. Accessed April 2025. https://www.cosentyx.com/kids-and-teens/juvenile-idiopathic-arthritis
[9] McMurray JJ et al. (2014). Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. NEJM. https://www.nejm.org/doi/full/10.1056/nejmoa1409077
[10] Entresto Webpage. Accessed April 10, 2025. https://www.entresto.com/

Entresto targets two complementary pathways to help the heart's ability to pump blood to the body. [11] It has a Class I recommendation by the American Heart Association / American College of Cardiology / Heart Failure Society of America (AHA/ACC/HFSA) treatment guidelines for people with heart failure with reduced ejection fraction (HFrEF).[12]

Cosentyx and Entresto Are Affordable for Oregonians and the Health Care System

At its core, the question of whether Cosentyx and Entresto are "affordable" for Oregonians has a simple answer: they are affordable because eligible Oregon patients with commercial health coverage can access them at a cost as low as zero dollars with the assistance of the Cosentyx and Entresto Co-pay Card Programs.[13,14] Additionally, pursuant to state and federal regulations, patients who access prescription drugs through Oregon's Medicaid program do not pay anything out-of-pocket for covered drugs.[15]

Furthermore, the health plans that pay a portion of the cost of Cosentyx and Entresto benefit from heavily discounted prices. The complicated interplay of drug pricing and rebates throughout the supply chain and the selective use of pricing data can misleadingly complicate what should be a straight-forward analysis of affordability.

Chief among these complicating factors is a reliance on "list" prices as a proxy for patient costs and affordability. A patient or health plan rarely if ever pays the list price of a drug. In Oregon, as in the rest of the United States, where third-party payers and government health care programs negotiate the price of drugs they buy, Novartis works with third parties to negotiate significant rebates and other price concessions on our medicines. When adjusted for inflation, the average net prices of Cosentyx and Entresto have declined between January 2018 and December 2023. The vast majority of patients, too, receive significant assistance even beyond the net price of Cosentyx and their insurance coverage through the Cosentyx Co-Pay Programs or the charitable assistance of the Novartis Patient

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[11] ENTRESTO NDA Approval Letter, https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/207620orig1s000ltr.pdf

[12] Heidenreich PA, et al. on behalf of the American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council (2013). Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. https://pubmed.ncbi.nlm.nih.gov/23616602/

[13] Novartis.com, Paying for Cosentyx, https://www.cosentyx.com/all/treatment-cost

[14] Entresto.com, Savings and Support. https://www.entresto.com/financial-support

[15] Oregon Health Plan, What to Do If You Are Asked to Pay for a Prescription, https://www.oregon.gov/oha/hsd/ohp/pages/prescriptions.aspx#:~:text=The%20Oregon%20Health%20Plan%20(OHP,they%20give%20them%20to%20you.., Accessed February 25, 2024.

Assistance Foundation (NPAF). These programs further reduce the costs patients pay, in many cases to as little as $0[16].

Cosentyx and Entresto Are Affordable for Oregon Patients.

For patients, the most significant hallmark of "affordability" is the price they pay out-of-pocket. Patients judge the cost of a medicine not by reference to complicated gross or net price formulas, but by how much they must pay out-of-pocket to access their medication.

Novartis negotiates with third-party payers for affordable coverage for patients and provides programs to help address residual affordability challenges once coverage is determined by payers. Over 70% of commercial lives in Oregon have coverage for Entresto on the preferred brand tier or lowest branded copay tier.[17] Further, through our Patient Assistance website[18], we inform patients about programs that may provide savings or resources that can help them access Cosentyx, Entresto, or any other Novartis prescription medication. We do this because Novartis believes that medicines should be available to all who need them.

Novartis has a co-pay assistance program in the US that helps thousands of patients with commercial health coverage access our medicines for as little as zero cost to them. In 2024, 72% of Oregon patients accessing Cosentyx through their commercial coverage used a Cosentyx co-pay card.[19] Manufacturer co-pay card programs play a critical role in helping eligible commercially-insured patients satisfy the cost-sharing requirements dictated by their health insurance coverage. Alarmingly, insurers and pharmacy benefit managers are increasingly subjecting this assistance to accumulator adjustment programs, which prevent co-pay card amounts from counting toward a patient's deductible and out-of-pocket maximum. This can lead to surprise increases in out-of-pocket costs for patients once the pharmacy benefit manager has exhausted the total value of the co-pay card.

Twenty-one states, the District of Columbia, and Puerto Rico have enacted laws banning accumulator adjustment programs in state-regulated commercial plans.[20] We commend Oregon for taking similar action to protect patients in

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[16] IQVIA Claim Data FY 2022, 2023.
[17] Internal Analysis of MMIT Data. February 2025.
[18] Novartis.com. Patient Assistance. https://www.novartis.com/us-en/patients-and-caregivers/patient-assistance. Accessed April 10, 2025.
[19] IQVIA Claim Data FY 2023, SP Dispense Data FY 2023.
[20] All Copays Count Coalition. State Legislation Against Copay Accumulators. Accessed April 10, 2025. https://allcopayscount.org/state-legislation-against-copay-accumulators/

2024.[21] However, payers are still using other tactics, such as copay maximizers[22] and alternative funding programs[23], that disrupt the value of copay cards for patients. Any affordability determination by the Oregon PDAB must consider these health insurer tactics that result in Oregonians paying more out-of-pocket for a necessary medication than they should.

Additionally, our “Covered Until You're Covered Program” is available for eligible patients taking Cosentyx in subcutaneous form who have commercial insurance, a valid prescription for Cosentyx, and a denial of insurance coverage based on a prior authorization request. The program provides Cosentyx for free to eligible patients for up to two years, or until they receive insurance coverage approval, whichever occurs first.[24]

Patients who cannot afford the cost of their Novartis medication, do not have private insurance, and meet income guidelines and other relevant criteria may be eligible to receive the medication at no cost from the Novartis Patient Assistance Foundation (NPAF), an independent, 501(c)(3) non-profit, non-commercial entity. Income and affordability guidelines vary by drug but are generally well above federal poverty levels.[25]

In 2024, NPAF provided approximately $6.0 billion in free medicines to approximately 146,000 patients, covering 42 medicines from our portfolio. Over the last five years, medication has been made available to over 300,000 patients valued at more than $23.0 billion.[26]

We caution the Board against relying on data from third-party sources, including the state’s All Payer All Claims Reporting program, that purports to indicate a patient out-of-pocket cost for Cosentyx and Entresto. That cost may well have been borne by Novartis or the NPAF for the benefit of patients through the mechanisms described above.

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[21] Oregon House Bill 4113. https://olis.oregonlegislature.gov/liz/2024R1/Measures/Overview/HB4113

[22] Copay maximizers allow plans to “maximize” the value extracted from copay assistance programs by adjusting a patient’s cost-sharing to the maximum amount of available assistance and not allowing the funds to count toward the patient’s deductible or out-of-pocket maximum.

[23] Alternative funding programs are strategies used by employer-sponsored health plans to exclude certain medications from coverage, redirecting patients to external assistance programs which can be result in significant burden and delays for patients trying to obtain the medications they need.

[24] The Covered Until You're Covered Program requires the submission of an appeal of a coverage denial within the first 90 days of enrollment in order to remain eligible. A valid prescription consistent with FDA-approved labeling is required. Program is not available to patients whose medications are reimbursed in whole or in part by Medicare, Medicaid, TRICARE, or any other federal or state program. Novartis.com Cosentyx Connect. https://www.cosentyx.com/psoriatic-arthritis/cosentyx-connect-personal-support-program. Accessed March 7, 2024.

[25] Novartis Patient Assistance Foundation. https://pap.novartis.com/ Accessed April 29, 2025.

[26] Novartis Internal Data Analysis. April 10, 2025.

Oregon Payers Benefit from Significant Discounts on Cosentyx and Entresto.

Payers such as commercial insurers routinely negotiate rebates and other price concessions from the Novartis list price. These rebates and price concessions lower the final "net" price of the drug significantly below the initial list price. Payers and employers in turn can pass these rebates and price concessions on to patients by reducing their out-of-pocket costs, or use them in other ways, such as lowering premiums, applying the discount to administrative costs, or other uses.

The continuing gap between list and net prices generated by this practice fuels increasing confusion and misperceptions about the real price paid for drugs by the health care system. While industry critics focus on the rise in wholesale acquisition cost (WAC), also known as the list or gross price, the reality is that price increases are often outpaced by rebates and price concessions to third-party payers and other channel intermediaries (e.g., wholesalers, pharmacies). Oregon, unlike some states, does not require payers and intermediaries to share these rebates and price concessions with patients.

Novartis rebates and price concessions to payers are important not just to understanding why Cosentyx and Entresto are *currently* affordable to patients, but also why Cosentyx's and Entresto's net prices have declined when adjusted for inflation, despite WAC price increases over the same period. It is critical that the Board base its affordability determination on the net price. The Board must take account of these rebates and price concessions, which are a significant component of the affordability of Cosentyx and Entresto.

Notably, between January 2018 and January 2023, inflation, measured by the CPI, was 22.9%. By our estimate this means the Cosentyx and Entresto net prices declined over this timeframe when adjusted for inflation.

Cosentyx and Entresto Provide Value to the Broader Health Care System.

In evaluating a drug's affordability, the Board must take account of its "relative financial effects on health, medical, or social services costs."[27] In this regard, Cosentyx should be recognized as effectively treating multiple indications and Entresto is recognized as the standard of care for treatment of heart failure. [28] Both drugs treat conditions that would otherwise significantly limit patient health and impose major costs on the state.

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[27] OAR 925-200-0020-(1)-(j)

[28] Novartis. The 2024 ACC Expert Consensus Decision Pathway for the treatment of HFrEF recommends ARNi as the only first-line RASi. Accessed April 2025. https://www.entrestohcp.com/sites/entrestohcp_com/files/documents/entresto-acc-ecdp-digital-flashcard.pdf

The major indications for which Cosentyx and Entresto are used[29] are associated with significant economic burden. We strongly urge the Board to consider the value Cosentyx and Entresto provide in reducing the direct and indirect costs of these diseases to the workforce, communities, and overall health care system as described below.

Cosentyx

Psoriasis:

Total direct and indirect costs associated with the disease have been estimated at $11.3 billion annually.[30]

A claims database from 31 self-insured employers (representing 5.1 million employees, their spouses, and dependents) during the period from 1998 to 2005 was used to evaluate both the direct medical and indirect work-loss costs associated with psoriasis.[31] After multivariate adjustment, psoriasis patients demonstrated significantly higher direct and indirect costs compared to other patients.[32] Approximately 40% of the total cost burden was associated with work loss (i.e., indirect costs).[33]

Cosentyx is effective in relieving this burden. A health economic model was developed to demonstrate the cost-effectiveness of Cosentyx for patients with plaque psoriasis. The patient population of interest included adults diagnosed with moderate-to-severe plaque psoriasis who are candidates for systemic or biologic therapy. The model demonstrated that the cost per responder was lower for Cosentyx 150 mg and 300 mg than some leading therapeutic alternatives.[34]

Psoriatic Arthritis (PsA):

The total direct costs of PsA in the US have been estimated at $1.9 billion annually.[35] There are limited data on the indirect costs (e.g., lost productivity and absenteeism) attributable to PsA in the US; however, it was reported that total

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[29] For this analysis, Novartis focuses on Cosentyx's approved indications for treatment of psoriasis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, non-radiographic axial spondyloarthritis, and hidradenitis suppurativa, and Entresto's approved indication for chronic heart failure.
[30] NPF, National Psoriasis Foundation Statistics [Online]. 2015b. Available: http://www.psoriasis.org/research/science-of-psoriasis/statistics [Accessed November 17, 2015].
[31] Fowler, J.F., Duh, M.S., Rovba, L., Buteau, S., et al. 2008. The impact of psoriasis on health care costs and patient work loss. *J Am Acad Dermatol.* 59(5), 772-780.
[32] *Id*.
[33] *Id*.
[34] Academy of Managed Care Pharmacy (AMCP) Formulary Dossier. Cosentyx. July 2023.
[35] Lee, S., Mendelsohn, A. & Sarnes, E. 2010. The burden of psoriatic arthritis: a literature review from a global health systems perspective. P T. 35(12), 680-689.

indirect costs account for approximately 52% to 72% of total costs.[36] The costs increase with deterioration of disease activity and decline in physical function.[37]

A health economic model explored the cost-effectiveness of Cosentyx for patients with psoriatic arthritis (PsA). The patient population of interest included adults diagnosed with PsA who are candidates for biologic therapy or apremilast. Cosentyx 150 mg and 300 mg had a lower cost per responder than some leading therapeutic alternatives.[38]

Ankylosing Spondylitis (AS):

A health economic model explored the cost-effectiveness of Cosentyx for patients. The patient population of interest included adults with active AS treated with a biologic. The cost per responder was lower for Cosentyx 150 mg than another leading therapeutic alternative.[39]

Non-radiographic axial Spondyloarthritis (nr-axSpA):

The economic impact of work limitations related to *nr-axSpA* is substantial and compounded by the typically young age at diagnosis.[40] Patients treated with Cosentyx showed substantial reduction in work-related impairment, measured through mean change in the Work Productivity and Activity Impairment (WPAI) from baseline to Week 52.[41]

Juvenile Idiopathic Arthritis (JIA):

Several studies have found that patients with JIA of all types have higher health care resource utilization and health care costs than patients without JIA.[42,43,44] As one of the most common chronic conditions in children, JIA places a sizable burden on the pediatric healthcare system and can result in a substantial economic burden for patients and their families. JIA includes several disorders in

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[36] *Id*.
[37] *Id*.
[38] Academy of Managed Care Pharmacy (AMCP) Formulary Dossier. Cosentyx. July 2023.
[39] *Id.*
[40] Strand, V. and Singh, J. A. 2017a. Patient Burden of Axial Spondyloarthritis. *Journal Of Clinical Rheumatology : Practical Reports On Rheumatic & Musculoskeletal Diseases*. 23(7): 383-391.
[41] Academy of Managed Care Pharmacy (AMCP) Formulary Dossier. Cosentyx. July 2023.
[42] Krause ML, Zamora-Legoff JA, Crowson CS, Muskardin TW, Mason T, Matteson EL. Population-based study of outcomes of patients with juvenile idiopathic arthritis (JIA) compared to non-JIA subjects. *Semin Arthritis Rheum*. 2017;46(4):439-443.
[43] Kumar N, Ramphul K, Ramphul Y, et al. Children hospitalized for juvenile arthritis in the United States. Reumatologia. 2021;59(4):270-272.
[44] Marshall A, Gupta K, Pazirandeh M, Bonafede M, McMorrow D. Treatment patterns and economic outcomes in patients with juvenile idiopathic arthritis. Clinicoecon Outcomes Res. 2019;11:361-371.

children involving inflammation of the joints. Cosentyx is approved to treat two of those disorders: ERA and JPsA.[45]

Hidradenitis suppurativa (HS)

Patients with HS have higher rates of hospital emergency department use and higher mean emergency department costs than healthy individuals and patients with psoriasis.[46] Even compared with patients with severe psoriasis, rates of inpatient care and emergency department use are higher for patients with HS.[47] In a retrospective cohort study analyzing indirect costs, patients with HS were found to have more days of work loss (184 vs 77), higher annual total indirect costs ($2925 vs $1483) and lower annual income ($54,925 vs $62,357) than healthy controls. [48]

Cosentyx helps adults with moderate to severe HS find relief at 16 weeks, including at least a 50% reduction in the number of inflammatory bumps and abscesses and no increase in the number of abscesses or draining tunnels.[49] Cosentyx can help reduce flares in adults with moderate to severe HS.

Entresto

Chronic Heart Failure

Almost 7 million Americans are currently living with chronic heart failure, a progressive chronic condition that can lead to hospitalization or shortened life expectancy.[50] Heart failure prevalence is on the rise and is expected to increase

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[45] Angeles-Han ST, Ringold S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis. *Arthritis Care Res (Hoboken)*. 2019;71(6):703-716.

[46] Khalsa, A., Liu, G., & Kirby, J.S. 2015. Increased utilization of emergency department and inpatient care by patients with hidradenitis suppurativa. J Am Acad Dermatol. 73(4), 609-614.

[47] *Id*.

[48] Tzellos, T., Yang, H., Mu, F., Calimlim, B., & Signorovitch, J. 2019. Impact of hidradenitis suppurativa on work loss, indirect costs and income. Br J Dermatol. 181(1), 147-154.

[49] Cosentyx 300mg every 4 weeks (after 5 initial weekly doses). In the 2 clinical trials, 41% and 43% of adults taking COSENTYX 300 mg every 4 weeks (after 5 initial weekly doses) achieved at least a 50% reduction in the number of inflammatory bumps and abscesses, with no increase in the number of abscesses and/or draining tunnels at 16 weeks vs 29% and 26% taking placebo.

[50] Centers for Disease Control and Prevention and National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) public use data files. https://www.cdc.gov/nchs/nhanes/

by 46% by 2030.[51,52,53] It is projected that the total costs of heart failure will reach nearly $70 billion by 2030.[54]

According to benchmarks adopted by the AHA/ACC/HFSA, the heart failure guidelines determined that Entresto delivers a high economic value when compared to ACE inhibitors for patients with chronic symptomatic HFrEF. Entresto delivers value for patients, reducing risk of hospitalization, emergency visits, and premature death[55,56,57] and this is backed up by real-world data.[58,59] It was estimated in a model that use of Entresto compared with enalapril in HFrEF patients was associated with averting over 50,000 hospitalizations in the US, saving $92.3 million annually.[60] As a result, Entresto has set a new standard of care for the treatment of chronic heart failure patients per the 2022 AHA/ACC/HFSA guidelines, and its clinical value was reiterated in the 2024 ACC Expert Consensus Decision Pathway guidelines.[61]

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[51] Oktay AA, Rich JD and Shah SJ (2013). The emerging epidemic of heart failure with preserved ejection fraction. Curr Heart Fail Rep. https://pubmed.ncbi.nlm.nih.gov/24078336/

[52] Heidenreich PA, et al. on behalf of the American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council (2013). Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. https://pubmed.ncbi.nlm.nih.gov/23616602/

[53] CMS Office of Minority Health (2020). Heart Failure Disparities In Medicare Fee-For-Service Beneficiaries. https://www.cms.gov/about-cms/agency-information/omh/downloads/data-snapshot-heart-failure.pdf

[54] Heidenreich PA, et al. on behalf of the American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council (2013). Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. https://pubmed.ncbi.nlm.nih.gov/23616602/

[55] McMurray JJ et al. (2014). Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. NEJM. https://www.nejm.org/doi/full/10.1056/nejmoa1409077

[56] Solomon SD et al. (2019). Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. NEJM. https://www.nejm.org/doi/full/10.1056/NEJMoa1908655

[57] Packer M et al. (2015). Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure. Circulation: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.114.013748?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

[58] Albert NM et al. (2019). Lower Hospitalization and Healthcare Costs With Sacubitril/Valsartan Versus Angiotensin-Converting Enzyme Inhibitor or Angiotensin-Receptor Blocker in a Retrospective Analysis of Patients With Heart Failure
JAHA:
https://www.ahajournals.org/doi/full/10.1161/JAHA.118.011089?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org

[59] Tan NY et al. (2020). Comparative Effectiveness of Sacubitril-Valsartan Versus ACE/ARB Therapy in Heart Failure With Reduced Ejection Fraction. JACC**:**
https://www.sciencedirect.com/science/article/pii/S2213177919306766?via%3Dihub

[60] Gaziano TA et al (2020). Cost-effectiveness of Sacubitril-Valsartan in Hospitalized Patients Who Have Heart Failure With Reduced Ejection Fraction. JAMA Cardiol:
https://jamanetwork.com/journals/jamacardiology/fullarticle/2769180

[61] Novartis. The 2024 ACC Expert Consensus Decision Pathway for the treatment of HFrEF recommends ARNi as the only first-line RASi. Accessed April 2025.
https://www.entrestohcp.com/sites/entrestohcp_com/files/documents/entresto-acc-ecdp-digital-flashcard.pdf

The Board Should Address the Methodological and Implementation Issues with its Processes.

When the Board voted to postpone its affordability reviews during its June 26, 2024, meeting, it did so to, "review, assess and possibly improve both the criteria and methods used to assess and select drugs for potential affordability reviews in 2025".[62] Board members acknowledged data errors, a lack of a clear definition for when a drug "may create affordability challenges for health care systems or high out-of-pocket costs for patients in Oregon," and an incomplete picture of the drug pricing environment as key factors in their decision to postpone affordability reviews.

Unfortunately, the Board's second attempt at selecting drugs for affordability reviews has so far been hampered by many of the same issues. In particular, Novartis would like to bring the Board's attention to the following gaps:

The Board Selected Entresto for Review Based on Incorrect Information.

As explained above, for forecasting purposes, Novartis currently assumes Entresto loss of exclusivity in mid-2025.[63] This is important because the availability of generic alternatives was a key factor in the Board's selection of drugs for affordability reviews. The Board should reconsider its selection of Entresto.

The Board Has Not Defined What Constitutes "Affordability Challenges to the Health Care System" or "High Out-of-Pocket Costs for Patients."

The Board is required in its affordability analysis to determine if a drug "may create affordability challenges for health care systems or high out-of-pocket costs for patients in Oregon." When the Board elected to postpone its affordability reviews during its meeting on June 26, 2024, one of the key reasons was the Board's desire to better define what "affordability challenges to the health care system" or "high out-of-pocket costs for patients" mean, but this has still not been done.

The Board still has not defined what it means for a drug to present "affordability challenges to the health care system" or "high out-of-pocket costs for patients" nor has it developed thresholds that would guide the Board in making such a determination. This striking gap leaves Novartis and the public with no

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[62] Oregon Prescription Drug Affordability Board. June 26, 2024 Meeting Minutes. Minutes approved by the Board on July 24, 2024. https://dfr.oregon.gov/pdab/Documents/20240626-PDAB-approved-minutes.pdf
[63] Novartis Q4 2024 Results Investor Presentation, slide 4. https//www.novartis.com/sites/novartis_com/files/q4-2024-investor-presentation.pdf

understanding of what principles the Board is applying to reach its ultimate conclusions, and no means of verifying that the Board's analysis has been conducted correctly.

While the Board has released additional documentation about the affordability review process and factors that it will consider during the affordability reviews, the relative importance of these factors in determining whether a drug may present "affordability challenges to the health care system" or "high out-of-pocket costs for patients" is unclear. This negatively impacts the ability of Novartis and the public to provide meaningful input.

Ultimately, the Board appears to be making an *ad hoc* determination of whether a drug may create affordability challenges for health care systems or high out-of-pocket costs for patients in Oregon without clearly articulating what those thresholds would look like.

The Board has not instituted protections for commercially sensitive data, limiting its ability to understand the drug pricing environment.

Despite repeated requests by stakeholders, the Board's efforts to gather information for affordability reviews continue to be hamstrung by the lack of a mechanism for manufacturers to submit commercially sensitive information. The Board has not developed a process or provided guidance in its Public Comment Policy on how manufacturers can confidentially submit such data. This refusal by the Board makes it impossible for manufacturers to provide data on net pricing of their products. Several Board members acknowledged net pricing data to be a crucial, but missing, component of affordability reviews during the June 26, 2024, meeting when the Board elected to postpone its affordability reviews. Additionally, there is not an opportunity for the Board to discuss commercially sensitive data or meet with manufacturers in executive session, which could have been another opportunity for manufacturers to provide important data for affordability reviews.

Conclusion

For the reasons detailed above, Cosentyx and Entresto are affordable to patients and the health care system. We welcome the opportunity to answer any questions you may have about the information provided above. Please contact me at courtney.piron@novartis.com.

Sincerely,

Courtney Piron
US Country President
Head, US Public Affairs

CYSTIC FIBROSIS FOUNDATION®

April 30, 2025

Oregon Prescription Drug Affordability Board
Department of Consumer and Business Services
350 Winter St. NE
Salem, Oregon 97309-0405

Dear Members of the Oregon Prescription Drug Affordability Board:

On behalf of people living with cystic fibrosis in Oregon, the Cystic Fibrosis Foundation thanks you for the opportunity to provide written testimony for the affordability review of CREON®. Pancreatic insufficiency remains a significant and lifelong complication of cystic fibrosis, and pancreatic enzyme replacement therapy (PERT) is a cornerstone of CF care. CREON®, a commonly prescribed PERT for people with CF, plays a critical role in supporting nutritional status for people living with this disease. We understand the importance of addressing financial barriers to care and commend efforts to increase transparency around drug pricing, improve affordability, and address sustainability of the healthcare system. Throughout this review, we urge the Board to keep the patient voice at the center of the discussion. We provide the following comments on CREON®'s use among people with CF and the Board's affordability review goals and process.

About Cystic Fibrosis & the Cystic Fibrosis Foundation
Cystic fibrosis is a progressive, genetic disease that affects the lungs, pancreas, and other organs. There are close to 40,000 children and adults living with cystic fibrosis in the United States, including nearly 470 people in Oregon, and CF can affect people of every racial and ethnic group. CF causes the body to produce thick, sticky mucus that clogs the lungs and digestive system, which can lead to lung damage, life-threatening infections, malnutrition, and other complications. Cystic fibrosis is both serious and progressive; lung damage caused by infection is often irreversible and can have a lasting impact on length and quality of life, resulting in extended hospitalizations, transplant, or premature death. The gastrointestinal effects, including pancreatic insufficiency, can lead to malnutrition and intestinal blockage. As a complex, multi-system condition, CF requires targeted, specialized treatment and medications. There is no cure.

As the world's leader in the search for a cure for CF and an organization dedicated to ensuring access to high-quality, specialized CF care, the Cystic Fibrosis Foundation supports the development of CF clinical practice guidelines and accredits more than 130 care centers nationally—including two in Oregon. The Foundation also gathers data on the health of people with CF who receive care at CF Foundation accredited care centers through our patient registry. This data helps inform the development of CF care guidelines, supports care teams in providing care to people with CF, and drives quality improvement initiatives at care centers. Researchers also use the patient registry to study CF treatments and outcomes and to design CF clinical trials.

Pancreatic Enzyme Replacement Therapy in CF Care
PERT is a life-sustaining treatment for individuals living with CF. As a multi-system disease, cystic fibrosis causes the ducts in the pancreas to become clogged with thick, sticky mucus that blocks natural digestive enzymes from reaching food in the small intestine. As a result, the vast majority of people with

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CF have exocrine pancreatic insufficiency (EPI), and 86% of people with CF living in Oregon are prescribed a PERT.[1] These therapies play a critical role in managing nutritional status, which is closely tied to pulmonary health, growth, and long-term survival. Pancreatic insufficiency is associated with a faster rate of pulmonary decline, and people with CF who have a higher weight-for-age percentile at a young age have fewer complications from CF and better survival through age 18.[2,3] If pancreatic insufficiency is left untreated, people with CF face severe consequences including malnutrition, weight loss, poor growth, gastrointestinal distress, and a significant decline in overall health.[4,5]

PERTs, including CREON®, contain pancrelipase—a combination of amylase, lipase, and protease—that replaces the enzymes normally produced by the pancreas . These therapies help individuals with EPI digest food properly and absorb nutrients by providing the enzymes needed to break down fats, proteins, and carbohydrates. These enzymes are released in the small intestine, where they work to digest food more effectively. PERTs must be taken with every meal and snack throughout the day to enable proper digestion and nutrient absorption. CREON® is the most commonly prescribed PERT for people with CF, taken by more than two-thirds of people with CF living in Oregon who are on PERT.[6] Research has shown that CREON® improves fat and protein absorption, reduces steatorrhea, improves stool frequency and consistency, and enhances body weight in individuals with EPI.[7,8]

Alternatives to CREON®

Although there are other FDA-approved PERTs such as Zenpep®, Viokace®, Pancreaze®, and Pertzye®, CREON® is not necessarily interchangeable with these alternatives. While the active ingredient is the same across PERTs, patients experience clinically significant differences in how they respond to individual products. Variations in formulation—including enzyme content, particle size, delivery, and enteric coating—can lead to differences in how well patients absorb nutrients. The degree of acidification of the GI tract in each CF patient also varies, causing some patients to have a better clinical response to one product over another. For some patients, CREON® may be the only product that consistently manages their symptoms and supports nutritional stability.

Given the impacts of CF on the pancreas, people with CF require a higher dosage of enzymes than other disease states that utilize PERT. This dosage is carefully determined to reduce overall pill burden for people with CF. PERTs currently tracked in the CF Foundation Patient Registry have a wide range of strengths available, ranging from two to seven different dosage options (Appendix 1). CREON® specifically has five different dosages listed in the registry. The significant number of strengths available indicates the specificity required by care teams when determining the appropriate PERT and dosing strategy for any given individual with CF; dosing depends on body weight, fat content in meals, and pancreatic lipase output. The process of identifying the right PERT and dose can take time, with care teams factoring in all the above while also seeking to minimize the number of pills a person takes. The

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[1] Cystic Fibrosis Foundation Patient Registry 2023 Annual Data Report. Available at: https://www.cff.org/medical-professionals/patient-registry

[2] Yen, E. H., Quinton, H., & Borowitz, D. (2013). Better nutritional status in early childhood is associated with improved clinical outcomes and survival in patients with cystic fibrosis. *The Journal of pediatrics*, *162*(3), 530-535.

[3] Corey, M., Edwards, L., Levison, H., & Knowles, M. (1997). Longitudinal analysis of pulmonary function decline in patients with cystic fibrosis. *The Journal of pediatrics*, *131*(6), 809-814.

[4] Baker, S. S., Borowitz, D., & Baker, R. D. (2005). Pancreatic exocrine function in patients with cystic fibrosis. *Current gastroenterology reports*, *7*(3), 227-233.

[5] Borowitz, D., Baker, R. D., & Stallings, V. (2002). Consensus report on nutrition for pediatric patients with cystic fibrosis. *Journal of pediatric gastroenterology and nutrition*, *35*(3), 246-259.

[6] Cystic Fibrosis Foundation Patient Registry 2023 Annual Data Report. Available at: https://www.cff.org/medical-professionals/patient-registry

[7] Safdi, M., Bekal, P. K., Martin, S., Saeed, Z. A., Burton, F., & Toskes, P. P. (2006). The effects of oral pancreatic enzymes (Creon 10 capsule) on steatorrhea: a multicenter, placebo-controlled, parallel group trial in subjects with chronic pancreatitis. Pancreas, 33(2), 156-162.

[8] Trapnell, B. C., Maguiness, K., Graff, G. R., Boyd, D., Beckmann, K., & Caras, S. (2009). Efficacy and safety of Creon® 24,000 in subjects with exocrine pancreatic insufficiency due to cystic fibrosis. *Journal of cystic fibrosis*, *8*(6), 370-377.

vast majority of people with CF stay on the same PERT once they have found a treatment they are stable on; less than 2% of people with CF switched enzyme types from one year to another over the past several years (Appendix 2). Once a patient's enzyme regimen is established and effective, changes to that therapy should only be made when medically necessary as any changes made could have adverse clinical consequences.

Access Challenges

Despite the well-documented benefits of PERTs like CREON®, individuals with CF can encounter barriers accessing these life-sustaining medications. Insurance plans often impose formulary exclusions, prior authorization protocols, or step therapy policies that require patients to try and fail alternative treatments before approving the prescribed PERT. For people with CF who take upwards of 20 therapies throughout the day,[9] coverage restrictions or out-of-pocket costs can pose additional hurdles. These administrative hurdles can lead to delays in treatment initiation or disruptions in ongoing therapy, adversely affecting nutritional status and overall health. Consistent access to whichever PERT is most effective for that patient is essential to preventing these complications.

Concerns with the PDAB's Processes

Goals of the PDAB

We caution that the Oregon PDAB may be working towards two separate aims that require separate consideration and policy solutions: evaluating affordability for consumers and evaluating affordability to the state's healthcare system. Any ambiguity about whether the PDAB is reviewing affordability for health care systems or for consumers can create confusion about how the Board should review drugs and recommend appropriate policy remedies to the legislature.

Due to the complexity of the U.S. health care system, there are many factors and entities involved in determining what patients pay for their drugs. For instance, while people with CF rely on expensive specialty drugs, their out-of-pocket costs for these medications are often more affordable because of manufacturer or non-profit copay assistance programs. Navigating intricacies of health plans and assistance programs can be burdensome and time consuming, but often means that people may be able to afford the cost-sharing for their most expensive therapies. Far too many people with CF still struggle to afford all of their care—which includes an extensive treatment and care regimen—but their affordability challenges are not always driven by the cost of one specialty drug. We recognize that copay assistance programs can mask bigger cost and affordability issues; however, we share this information to highlight that affordability challenges for the system do not always align with affordability challenges for consumers. We ask that the PDAB keep these nuances in mind as the Board moves forward with conducting affordability reviews.

Statutory Requirement to Identify a Fixed Number of Unaffordable Drugs

We support the PDAB's request for a statutory amendment to allow for the identification of *up to* nine drugs and one insulin product each year through SB 289. We are concerned that the current statutory requirement that the PDAB identify nine drugs and one insulin product each year that may create affordability challenges creates bias in the affordability review process by requiring the Board to find a specific number of unaffordable drugs. We understand requiring the Board to evaluate a certain number of drugs every year, but pre-determining the outcome of these reviews undermines the credibility and objectivity of the process. This legislation will give the Board the authority to make the best decision

[9] Sawicki, G. S., Sellers, D. E., & Robinson, W. M. (2009). High treatment burden in adults with cystic fibrosis: challenges to disease self-management. Journal of cystic fibrosis, 8(2), 91-96.

based on the data shared during the affordability review and better reflect the true affordability challenges faced by patients and the healthcare system.

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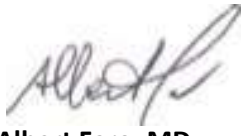
Thank you again for the opportunity to provide comments on the PDAB's review of CREON®. The Cystic Fibrosis Foundation believes the price of drugs must not pose a barrier to access but solutions to improve affordability must also safeguard patient access. We urge the Board to ensure that any recommendations related to CREON® do not limit access to this therapy, particularly for those who have found CREON® to be the most effective treatment option.

We are committed to making sure the Oregon PDAB understands the critical role that PERTs like CREON® play in improving the health and quality of life of many individuals with CF. If you have any questions or need additional information, please contact Amanda Attiya, State Policy Specialist, at aattiya@cff.org.

Sincerely,



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Appendix 1

2023 Cystic Fibrosis Foundation Patient Registry Questionnaire

GI/Nutrition/Endrocrine Medications

This Patient is on enzyme medications: ○ Yes ○ No

For all enzymes, "capsules per largest meal" options are:
○ .5 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9
○ 10 ○ 10+
"Total capsules per day" is a numeric free text field.

Enzymes

Creon

Creon 1203: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Creon 1206: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Creon 1212: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Creon 1224: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Creon 1236: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze

Pancreaze MT4: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze MT10: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze MT16: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze MT20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze MT37: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Ultresa

Ultresa 14: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Ultresa 20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Ultresa 23: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Pertzye (Pancrecarb)

Pertzye 4000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Pertzye 8000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Pertzye 16000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Pertzye 24000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep

Zenpep 3: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 5: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 10: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 15: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 20: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 25: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep 40: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Viokace

Viokace 10: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Viokace 20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day: ____

Key:

FORM NAME

○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

*repeated entries can be recorded
[ ] indicates values calculated by the registry

Appendix 2

	Oregon-Specific Data				**United States**			
Year	Number of people with CF with medication data in the CFF Patient Registry	Number (%) of people with CF on any PERT	Number (%*) of people with CF on Creon	Change in Creon use year-over-year (% not prescribed Creon compared to the previous year)	Number of people with CF with medication data in the CFF Patient Registry	Number (%) of people with CF on any PERT	Number (%*) of people with CF on Creon	Change in Creon use year-over-year (% not prescribed Creon compared to the previous year)
2013	391	351 (89.8%)	197 (56.1%)	--	27211	23831 (87.6%)	16361 (68.7%)	--
2014	394	354 (89.8%)	202 (57.1%)	8 (2.3%)	27843	24349 (87.5%)	16497 (67.8%)	547 (2.2%)
2015	407	359 (88.2%)	208 (57.9%)	6 (1.7%)	28341	24687 (87.1%)	16375 (66.3%)	598 (2.4%)
2016	433	377 (87.1%)	221 (58.6%)	5 (1.3%)	28920	25083 (86.7%)	16543 (66.0%)	562 (2.2%)
2017	433	380 (87.8%)	229 (60.3%)	5 (1.3%)	29548	25439 (86.1%)	16610 (65.3%)	493 (1.9%)
2018	461	404 (87.6%)	251 (62.1%)	6 (1.5%)	30326	25907 (85.4%)	16791 (64.8%)	490 (1.9%)
2019	474	420 (88.6%)	259 (61.7%)	<5	30807	26168 (84.9%)	16872 (64.5%)	464 (1.8%)
2020	443	394 (88.9%)	239 (60.7%)	6 (1.5%)	30770	25995 (84.5%)	16729 (64.4%)	412 (1.6%)
2021	444	391 (88.1%)	246 (62.9%)	<5	31439	26338 (83.8%)	16921 (64.2%)	403 (1.5%)
2022	452	399 (88.3%)	272 (68.2%)	0 (0.0%)	32026	26525 (82.8%)	17019 (64.2%)	415 (1.6%)
2023	463	399 (86.2%)	277 (69.4%)	5 (1.3%)	32599	26697 (81.9%)	17206 (64.4%)	350 (1.3%)

*Denominator only includes people with CF on PERT