Rare Disease Company Coalition

BY ELECTRONIC DELIVERY

January 7, 2022

Mr. Patrick Allen
Director
Oregon Health Authority
Health Policy and Analytics Medicaid Waiver Renewal Team
Attn: Michelle Hatfield
500 Summer St. NE, 5th Floor, E65
Salem, OR 97301

RE: Application for Renewal and Amendment Oregon Health Plan, Section 1115 Demonstration Waiver

Dear Director Allen:

The Rare Disease Company Coalition (RDCC) appreciates the opportunity to provide comments on the state of Oregon's application for a section 1115 Demonstration Waiver. We appreciate the state's intention to be responsive to the community feedback and request the state consider our serious concerns with the potential impact of the demonstration waiver on the discovery and development of new medicines, particularly on treatments and cures for patients with rare diseases who currently have limited or no treatment options.

In the United States, a rare disease is defined as a condition that affects fewer than 200,000 people. There are 7,000 identified rare diseases that impact an estimated 25 to 30 million Americans. These diseases are devastating and often life-threatening: 80 percent of rare diseases are genetic in origin, 50 percent impact children, and 30 percent of those children will not live to see their 5th birthday. While only 7 percent of rare diseases have an FDA-approved treatment, the 20 life science companies comprising the RDCC are committed to continuing to change these statistics by discovering, developing, and delivering rare disease treatments for patients. Our goal is to inform policymakers of the unique challenges—and promises—we face in taking these rare disease drugs from research through development, approval, manufacturing, to delivery to patients. Collectively, Coalition members invested over $4.5 billion in R&D in 2020; have brought 36 treatments to market to date, the majority of which are first-to-market therapies; and are presently working on more than 225 rare disease development programs, many of which would be first-to-market therapies if approved. We are focused on working to meet the needs of rare disease patients with currently limited or no treatment options.

The RDCC has significant concerns with the Oregon Health Authority's (OHA) request to establish a closed formulary for the state's Medicaid program that could limit coverage to one drug for each therapeutic class and would exclude drugs approved via the Accelerated Approval pathway. We believe a closed formulary is not in the best interest of patient health, particularly for patients with rare disease, and that this proposal would curtail innovation in the discovery and

development of new treatments. We believe this could potentially deny Medicaid patients access to important medical advances.

Our specific concerns are as follows:

Oregon's 1115 Demonstration Waiver would impact innovation for rare disease treatments and cures

Rare diseases present specific challenges - such as small population sizes, or slow, irreversible, and variable disease progression - that make it difficult to study in some cases using clinical measures as endpoints. The Accelerated Approval pathway is a critical tool, well-suited to recognize these unique circumstances. If these drugs are not covered by state Medicaid programs thereby limiting patient access, manufacturers have little incentive to pursue research and development in rare diseases, as an already small (rare) population becomes smaller.

Oregon's approach simply does not align with the intent of the Accelerated Approval pathway to expedite access to rare disease treatments for patients with serious conditions, especially for diseases that have limited or no treatment options. We are concerned about the impact to these patients and the broader impact on the entire rare disease community, regardless of payor, because we believe the OHA 1115 Demonstration Waiver would effectively disincentivize and curtail research and development for the treatment of certain rare diseases. Ultimately, this approach would punish patients who are forced to suffer as their disease progresses while continuing to wait for a treatment. For example, the Accelerated Approval pathway can be credited for changing the trajectory of scientific advancement for HIV/AIDS and for oncology. We also note that a significant proportion of rare disease patients are children who are on Medicaid and while the Oregon waiver would maintain an open formulary for children, we note that these children would potentially lose access to these drugs when they reach adulthood.

Oregon's 1115 Demonstration Waiver would undermine the intent of the Accelerated Approval pathway and FDA's role as the sole arbiter of determining safety and efficacy

We believe that subjecting medicines that are approved via the FDA Accelerated Approval pathway to additional scrutiny based on their pathway for approval undermines the purpose of the Accelerated Approval pathway and disregards its benefits to patients with unmet medical needs, including those with rare diseases. Targeting Accelerated Approval therapies could deprive patients who suffer from certain conditions the important, safe, and effective therapies they need. In many cases, these therapies are the only effective course of treatment for their disease.

By law (21 U.S.C. § 356(e)(2)), the FDA must find "substantial evidence of effectiveness" to approve any drug, including drugs approved via the Accelerated Approval pathway. The Accelerated Approval pathway is a targeted and robust, science-based pathway established by Congress and the FDA to speed the availability of new therapies to patients with serious conditions,[1] especially when there are no available alternatives, while preserving the FDA's

[1] Serious condition is defined as: "…a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible if it is

rigorous standards for safety and effectiveness. In 1992, the FDA established a new expedited pathway to speed approval of medicines that treat serious conditions and address an unmet need, later codified by Congress in 1997.[2] In 2012, Congress passed the Food and Drug Administration Safety Innovations Act (FDASIA) that amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to allow the FDA to reinforce and enhance the Accelerated Approval pathway in FDASIA and encouraging broader applicability for rare disease.[3] The Accelerated Approval pathway has been credited with significant advances in the treatment of life-threatening diseases where patients have limited or no treatment options. Historically, this pathway has been used primarily for oncology drugs with 174 oncology accelerated approvals through June 30, 2021.[4] In fact, from 2010-2020, 85 percent of the agency's accelerated approvals have been for oncology indications.[5] We believe this can be a critical pathway for rare diseases as well.

The FDA's Accelerated Approval pathway is a well-established, proven, regulated path forward for certain drugs that rely on the use of surrogate or intermediate clinical endpoints to determine the effectiveness of a therapy. Surrogate endpoints are imperative to getting rare disease treatments to patients as there is limited disease knowledge and small populations so determining a clinical endpoint is rarely feasible. Congress, the FDA, and the scientific community have all recognized the important role of surrogate endpoints as relevant and reliable biomarkers to assess effectiveness in certain circumstances, particularly for slowly progressing, debilitating diseases where verification of clinical benefit may take many years.[6]

Both Congress and the FDA have been clear in affirming that accelerated approval does not diminish or compromise FDA's stringent approval standards. Notably, the FDA has maintained that prescription drugs and biologics approved under the Accelerated Approval pathway must meet clinically meaningful endpoints and that the benefits of the treatment must outweigh the risks of treatment, finding that *"Approval…requires … that the effect shown be, in the judgment of the agency, clinically meaningful, and of such importance as to outweigh the risks of treatment. This judgment does not represent either a "lower standard" or one inconsistent with section 505(d) of the act, but rather an assessment about whether different types of data show that the same statutory standard has been met."*[7]

The FDA has noted that the Accelerated Approval pathway "ensure[s] that therapies for serious

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persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one." 21 CFR 312.300(b)(1); https://www.fda.gov/media/86377/download

[2] https://www.govinfo.gov/content/pkg/PLAW-105publ115/pdf/PLAW-105publ115.pdf

[3] https://www.govinfo.gov/content/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf

[4] CDER Drug and Biologic Accelerated Approvals Based on a Surrogate Endpoint (As of June 30, 2021). Accessed December 22, 2021. https://www.fda.gov/media/151146/download

[5] See Friends of Cancer Res., Optimizing the Use of Accelerated Approval 3(2020) ("FOCR Report"), https://friendsofcancerresearch.org/sites/default/files/2020-11/Optimizing_the_Use_of_Accelerated_Approval-2020.pdf (stating that 84% of accelerated approval drugs from 2010 to 2019 were for oncology indications); CDER Drug and Biologic Accelerated Approvals, supra note 72 (stating that FDA has granted 253 accelerated approvals as of December 31, 2020, of which 9 were approved after June 30, 2020 and 7 were for oncology drugs); see also Julia A. Beaver & Richard Pazdur, "Dangling" Accelerated Approvals in Oncology, 384 New Eng. J. of Med. e68(1), 1 (May 2021) ("[A]pproximately 85% of accelerated approvals in the past 10 years have been granted in oncology.").

[6] https://www.fda.gov/news-events/fda-voices/delivering-promising-new-medicines-without-sacrificing-safety-and-efficacy

[7] 57 Fed. Reg. at 58944.

conditions are approved and available to patients as soon as it can be concluded that the therapies' benefits justify their risks."[8] The Agency has also emphasized that the accelerated approval procedures "are intended to provide expedited marketing of drugs for patients suffering from such [serious or life-threatening] illnesses when the drugs provide meaningful therapeutic advantage over existing treatment"[9] and that "it is in the public interest to make promising new treatments available at the earliest possible point in time for use in life-threatening and serious illnesses."[10]

Oregon's interest in making determinations that would deny coverage for drugs "with limited or inadequate evidence of clinical efficacy" based on the state's own review process is particularly troublesome. We believe it is inappropriate for OHA to substitute its own judgement for determinations related to clinical efficacy of drugs that have been reviewed and approved by the FDA. The FDA remains the gold standard for drug safety and efficacy. Moreover, Oregon's efforts to supplant FDA authority go beyond just excluding Accelerated Approved drugs. Oregon's request would seek to exclude drugs with "no incremental clinical benefit within its therapeutic class, compared to existing alternatives." FDA's drug approval framework does not require evidence of an "incremental benefit" over existing therapies for a demonstration of safety and efficacy. Overall, such an approach implies that Oregon is better suited to review drugs than the scientists and disease experts at the FDA. Establishing such a framework undermines the important, independent authority of the FDA as the sole arbiter of safety and efficacy.

Closed formularies are not in the best interests of rare disease patients with limited to no treatment options

We have great concerns that Oregon's proposal to cover as few as one drug per therapeutic class would seriously jeopardize the health of patients and would hinder access to quality of care for the most vulnerable patients, especially those with rare, life-threatening diseases. For many therapeutic classes, such restrictions could leave impacted Medicaid beneficiaries without access to the physician-prescribed medicine deemed most appropriate. Given the heterogeneity within patient populations and the advancement of precision medicine, providing access to a wide variety of drug options is foundational to appropriate patient care. One formulary agent may not produce the intended therapeutic outcome or have the same side effects across patient types which could be detrimental to Medicaid patients in Oregon, particularly those with rare diseases. The Oregon approach would also provide fewer protections for Medicaid beneficiaries. For example, it does not provide any access protections or require its closed formulary to adhere to the Essential Health Benefits benchmark standards. We also note this approach would not align with the interests of CMS in consistency across programs – specifically Medicaid and Medicare – given the Medicare Part D coverage requirement of at least 2 drugs per drug category/class.

Oregon's 1115 Demonstration waiver is not consistent with foundational Medicaid policies.

[8] FDA. Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014

[9] 57 Fed. Reg. 58942.

[10] 57 Fed. Reg. at 58944

The Medicaid Drug Rebate program represents a carefully balanced compromise made by Congress under the Omnibus Reconciliation Act of 1990 to ensure the federal government has access to the lowest available price for covered outpatient prescription medicines – via a statutorily mandated rebate – while also ensuring that manufacturers' products would be accessible to Medicaid recipients if medically necessary and subject to statutorily defined access restrictions. The Oregon demonstration waiver would disrupt this long-term, successful Medicaid policy that has facilitated access to medicines for beneficiaries with a fiscally prudent approach.

We note that severely limiting beneficiary access to physician-prescribed medicines in the Medicaid program has already been rejected by the Centers for Medicare and Medicaid Services (CMS). In 2017, the Commonwealth of Massachusetts proposed a closed formulary with at least one drug per class, with the intent to exclude drugs approved through the FDA's Accelerated Approval process. These policies were firmly rejected by CMS, indicating that a state cannot simply opt out of the Medicaid Rebate Program, and not provide access to "covered outpatient drugs" for which a manufacturer has a signed National Rebate Agreement.[11] Of note, the same day that CMS responded to the Massachusetts waiver amendment, the agency issued "State Release No. 185," which underscored the fact that drugs approved through the FDA's expedited approval processes "must be covered by state Medicaid programs, if the drug meets the definition of "covered outpatient drug" as found in Section 1927 of the Social Security Act"[12] and the Manufacturer has a signed Medicaid National Rebate agreement. We believe these policies demonstrate continued support by CMS for patient access to medicines facilitated by the Medicaid Drug Rebate Program.

<u>This approach would not promote the elimination of health disparities nor the achievement of health equity</u>

OHA's approach to establish a closed formulary for adults and to not cover drugs approved via the Accelerated Approval pathway is in direct conflict with the state's purported goal of the 1115 Demonstration waiver: "to eliminate inequitable access with strategies to extend and stabilize coverage to every eligible child and adult in Oregon." The Health Equity Committee, a subcommittee of the Oregon Health Policy Board (OHPB) was tasked with coordinating and developing policy that proactively promotes the elimination of health disparities and the achievement of health equity for all people in Oregon and the state has a goal of "eradicating health inequities by 2030." This is an admirable goal for the state, as 27% of the state's population is considered low-income, below 200% of the Federal Poverty Level. However, rather than making progress toward Oregon's goal of eradicating health disparities, Oregon's proposed closed formulary would likely create additional health disparities for rare disease patients, especially those who are also part of racial and/or ethnic minority group. Without the ability to have coverage of a medicine that may not be included in Oregon's closed formulary, these issues will be exacerbated and could result in poor health outcomes and increased costs of care, rather than achieving the state's goals of eliminating health disparities and the achievement of health equity for all people in Oregon. Individuals with rare diseases tend to report common concerns that result from being underserved, such as a long road to diagnosis, limited treatment

[11] CMS letter to Asst. Secretary Tsai, MassHealth, June 27, 2018.

[12] CMS State Release No. 185, June 27, 2018.

options, and a need for research to better understand their medical condition.[13] Rare diseases are disproportionately prevalent among some racial and ethnic minority groups. These patients may also face greater disease burden, earlier age of disease onset, and/or complex sets of comorbidities that limit the safety and effectiveness of older treatment options. We believe the Oregon approach sends a message to patients with high unmet needs that their lives are not worth the investment; we strongly oppose that sentiment.

Oregon's 1115 Demonstration Waiver would have a limited budgetary impact

Historical claims analysis suggests that a closed formulary would not be likely to yield significant savings to OHA. From 2007 to 2018, Accelerated Approval drugs account for less than 1% of overall Medicaid spending while often representing the only treatment options available for beneficiaries.[14] The same analysis continues to conclude that "[l]imiting Medicaid coverage for accelerated approval drugs would have a devastating impact on patients benefiting from these treatments while having a de minimis impact on spending."[15]

Thank you for the opportunity to submit comments on the OHA's section 1115 Demonstration Waiver Renewal and Amendment application. The RDCC is greatly concerned about the impact of the proposed closed formulary provisions on the rare disease community and we respectfully request your reconsideration of this proposal.

Should you have any questions, please feel free to contact Patroski Lawson, Interim Executive Director of the RDCC at patroski@kpmgroupdc.com

Sincerely,
Patroski Lawson

[13] Barriers To Rare Disease Diagnosis, Care and Treatment In The US: A 30-Year Comparative Analysis, NORD 2020, https://rarediseases.org/wp-content/uploads/2020/11/NRD-2088-Barriers-30-Yr-Survey-Report_FNL-2.pdf

[14] Am J Manag Care. 2021;27(6):e178e180. https://doi.org/10.37765/ajmc.2021.88596

[15] Am J Manag Care. 2021;27(6):e178e180. https://doi.org/10.37765/ajmc.2021.88596