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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

Dear Director Allen:

The Rare Access Action Project, (RAAP) appreciates the opportunity to comment on the Oregon Health Authority's (OHA) proposed renewal and amendment of its Section 1115 waiver for the July 1, 2022- June 30, 2027, demonstration period. RAAP agrees with OHA's focus to maximize continuous and equitable access to coverage and supports OHA's goal to eliminate inequitable access with strategies to extend and stabilize coverage to every eligible child and adult in Oregon.

RAAP, however, is concerned that OHA's proposals seeking the authority to implement a closed formulary and limit coverage of drugs approved under the FDA's accelerated approval pathway will have the opposite result. On its face, RAAP understands why Oregon seeks these new authorities, however, these policies are penny wise pound foolish because, if implemented, these policies will have the opposite impact of the state's intent. That is, these policies will reduce access to life saving therapies magnifying the health equity divide amongst Medicaid patients and between other Oregon residents.

The Health Equity Committee, a subcommittee of OHPB seeks to promote elimination of health disparities for all people in Oregon, "eradicating health inequities by 2030." Rather than making progress toward this goal, 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 and face substantial burdens that can cause economic hardship, difficulty accessing care, and poorer health outcomes for themselves and caregivers.

Using accelerated approval as a proxy for high drug costs to Oregon's Medicaid program is misguided. Accelerated approval concerns require accelerated approval solutions that account for the importance of this pathway to rare disease patients. They cannot be solved with solutions designed to resolve drug pricing challenges that would, ultimately, disincentivize research and development and slow the availability of novel drugs to patients with rare diseases.[1]

RAAP is a registered 501(c)(4) non-profit organization that is a coalition of life sciences and patient stakeholders that explore creative policy solutions to address structural issues in access and coverage. Our priority is to help ensure rare disease patients have access to the care and treatments they need and submits the following comments consistent with that objective.

Background: Rare Diseases and Orphan Products

The Orphan Drug Designation Program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the US, or that affect more than 200,000[2] persons but are not expected to recover the costs of developing and marketing a treatment drug. Rare diseases include more familiar conditions, such as cystic fibrosis, Lou Gehrig's disease, and Tourette's syndrome, as well as less familiar conditions, such as Duncan's Syndrome, Madelung's disease, and acromegaly/gigantism. These conditions are complex and often not well understood, which causes great challenges to the diagnosis and treatment as well as research efforts.

Rare disease treatments range from curing the disease, modifying how the disease functions, or treating the symptoms. Truly curative treatments are rare. Disease-modifying therapies target the underlying pathology of a disease to prevent it from worsening. Symptomatic treatments seek to temper symptoms or to maintain physical, emotional, and mental functioning.

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[1] **FDA's Accelerated Approval Pathway: A Rare Disease Perspective, National Organization for Rare Disorders (NORD®), June 11, 2021.**

[2] Department of Health and Human Services, Food and Drug Administration (FDA). Office of Orphan Drug Development. https://www.fda.gov/about-fda/office-clinical-policy-and-programs/office-orphan-products-development. Accessed March 13, 2021.

Only 5% of rare diseases have a treatment approved by the Food and Drug Administration (FDA) and for one-third of individuals with a rare disease, it can take between one and five years to receive a proper diagnosis. Patients with rare diseases often seek treatment in clinics where the condition has never been seen before and have symptoms that are absent, masked, misunderstood, or confused, which often leads to delayed diagnosis further complicating the patient's and family's arduous journey. Half of all patients diagnosed with a rare disease are children, and as many as 3 in 10 children with a rare disease[2] will not live to see their 5th birthday[3].

Many of these patients rely on the CHIP and Medicaid federal safety net programs for healthcare services such that changes to these programs must be carefully analyzed and appreciated so as to not cause more harm than good, which RAAP fears is the case with this waiver request.

Recent Advancements in Rare Disease Treatments

The Orphan Drug Act and the Food and Drug Administration Safety Innovations Act (FDASIA) are clear examples of Congress' recognition of the significant disease burden that rare disease patients face. Each of the Act's provisions create greater incentives towards therapeutic development for these diseases. Specifically, the FDA Guidance Document and the accelerated approval provisions of FDASIA in section 506(c) of the FD&C Act allow the FDA discretion to grant accelerated approval to:

. . . a product for a serious or life-threatening disease or condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the[3] availability or lack of alternative treatments[4].

[3] Slade, A., Isa, F., Kyte, D., Pankhurst, T., Kerecuk, L., Ferguson, J., Lipkin, G., & Calvert, M. (2018). Patient reported outcome measures in rare diseases: a narrative review. *Orphanet journal of rare diseases*, *13*(1), 61. https://doi.org/10.1186/s13023-018-0810-x

[4] Department of Health and Human Services, Food and Drug Administration (FDA). Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

According to the FDA Guidance,[5]

. . . a surrogate endpoint used for accelerated approval is a marker - a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Likewise, an intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality (IMM).

The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug's effect on a surrogate or intermediate clinical endpoint must be "adequate and well controlled" as required by the FD&C Act.

Challenges in Rare Disease Clinical Trials: FDA in Best Position to Balance

Clinical trials for rare disease drugs overall engage more investigative sites to recruit fewer patients and typically have longer trial durations, reflecting the difficulties of patient supplants the judgment of the individual patient/family and their treating physician with that of State Medicaid agencies. The FDA is best positioned to balance the challenges of rare disease clinical trials and the unmet medical need in particular as it relates to rare disease situations.

According to Samiya Luthfia Khaleel, SeniorResearch Analyst with the Tufts Center for the Study of Drug Development[6], patient recruitment and retention is one of the many challenges in rare disease research complicated by the paucity, often scattered nature of the disease patient population and because 50 percent of rare diseases affect the pediatric population identification and enrollment.[7][8][9][10]Coverage,

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[5] Department of Health and Human Services, Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf. Accessed March 13, 2021.

[6] Tufts Center for the Study of Drug Development, *Impact Report Analysis & Insight into Critical Drug Development Issues.* Vol. 15, No. 1, Tufts University, 2013.

[7] Khaleel, Samiya Luthfia. Rare Disease Patient Recruitment and Retention. https://www.clinicalleader.com/doc/rare-disease-patient-recruitment-and-retention-0001. Accessed March 13, 2013.

[8] Tufts Center for the Study of Drug Development, Impact Report Analysis & Insight into Critical Drug Development Issues. https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5d2490ae0072ee0001a1a198/1562677423360/summary_julyaugust_2019.pdf. Accessed March 13, 2021.

[9] Tambuyzer E. Rare diseases, orphan drugs and their regulation: questions and misconceptions. Nat Rev Drug Discov. 2010;9(12):921–9.

[10] Sharma A, et al. Orphan drug: Development trends and strategies. J Pharmacy and Bioallied Sciences. 2010;2(4):290–9.

access and rebate policy should not be based on completion of the FDA confirmatory trial in the case of orphan designated, accelerated approval products. Such a policy is contrary to the established FDA regulatory approval process in the case of orphan designated accelerated approval products that are specifically designed for the FDA to weigh the public interests of safety and efficacy with the unmet medical needs in particular scenarios. Such a proposed policy supplants the judgment of the individual patient/family and their treating physician with that of State Medicaid agencies.

Access restrictions on FDA approved accelerated approval products without understanding the drug development circumstances can undermine the intention of the orphan drug development policies established by Congress and implemented by the FDA that have allowed for the advancements and innovation in so many rare diseases over the years. The FDA, as indicated in the FDA Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologic, is in the best position to balance public welfare needs to further demonstrate safety and efficacy, the unmet medical need in the context of the particular rare disease, and the challenges and unique complexities of confirmatory studies for rare diseases,

> *FDA recognizes that certain aspects of drug development that are feasible for common diseases may not be feasible for rare diseases and that development challenges are often greater with increasing rarity of the disease. FDA will continue to apply flexibility in these situations to address particular challenges posed by each disease.*[11]

RAAP Believes that OHA's Proposals Violate Existing Law

Oregon seeks the ability to more closely manage pharmacy costs in its Medicaid program, through a two-part strategy. First, the state wishes to adopt a commercial style closed formulary approach, which ostensibly means that the state could only cover a single drug per therapeutic class. Second, Oregon seeks new flexibility under this waiver to exclude drugs approved under FDA's accelerated approval pathway that the state deems to have limited or inadequate clinical efficacy under its closed formulary approach. RAAP believes that both proposals violate current law, specifically the Medicaid Drug Rebate Program.[12]

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[11] Department of Health and Human Services, Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf. Accessed March 13, 2021.

[12] Social Security Act (SSA) §1927.

Specifically, on June 27, 2018, the Centers for Medicare & Medicaid Services issued State Release No. 185 (Release) reminding states of their legal obligations to cover all drugs that meet the statutory definition of covered outpatient drugs, including those drugs approved under the FDA's accelerated approval pathway. [13] Specifically, the Release states "that a drug approved by the Food and Drug Administration (FDA) under its "accelerated approval" pathway, which is the approval program authorized under section 506(c) of the Federal Food, Drug, and Cosmetic Act (FFDCA),[14] 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 (the Act)."[15] Therefore, Oregon's two part strategy to manage formulary costs via a closed formulary and limited coverage of accelerated approval drugs violates the parameters of the Medicaid Drug Rebate Program.

Finally, CMS denied the Massachusetts' closed formulary proposal because the state would have also preserved statutory rebates. While CMS noted it would consider proposals to institute a closed formulary in Medicaid, they mentioned it would only consider such a proposal if the state agrees to forgo the federal mandatory rebates available through the federal Medicaid rebate program. Oregon has not included this in their proposed waiver application, and therefore is more likely to also be rejected by CMS in its current form.

SSA § 1115 Waivers Do Not Override the State's Obligations Under the Medicaid Drug Rebate Agreement

Section 1115 of the Social Security Act (SSA) gives the Secretary of Health and Human Services authority to approve experimental, pilot, or demonstration projects that are found by the Secretary to be likely to assist in promoting the objectives of the Medicaid program. The purpose of these demonstrations, which give states additional flexibility to design and improve their programs, is to demonstrate and evaluate state-specific policy approaches to better serve Medicaid populations.[16] The statute provides that waivers must set forth an "experimental, pilot, or demonstration project," that, in the judgment of the Secretary, is "likely to assist in

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

[14] https://www.fda.gov/ForPatients/Approvals/Fast/ucm405447.htm

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

[16] https://www.medicaid.gov/medicaid/section-1115-demonstrations/about-section-1115-demonstrations/index.html

promoting the objectives of title XIX [i.e., the Medicaid program]."[17] RAAP believes that 1115 waivers, in order to better serve Medicaid patients, should demonstrate improved access and/or better outcomes and fails to see how Oregon's two part strategy achieves either of these objectives.

Specifically, the State has not specified a research proposition that it seeks to test. It proposes only to cut costs by restricting coverage of covered outpatient drugs that it would otherwise be required to cover under SSA § 1927. As stated above, SSA § 1115 demonstration projects must test innovative approaches aimed at furthering the objectives of the Medicaid program, for example, by enhancing quality of care or promoting efficient administration. A demonstration project may not operate as a mere benefit cut with no actual experimental value.

Additionally, a waiver of compliance with SSA § 1927 fails to promote the objectives of title XIX, which was enacted by Congress to provide medical care to the needy and medically needy.[18] By denying access to otherwise-covered and potentially life-saving therapies, the State would do precisely the opposite. Congress enacted SSA § 1927 in order to guarantee that "[s]tates that elect to offer prescription drugs … cover all the products of any manufacturer that agrees to provide price rebates."[19] If CMS were to approve a waiver of compliance that enables a state to avoid its drug coverage obligations under SSA § 1927, the agency would undermine the primary objective of SSA § 1927, as stated by Congress itself. On top of this, the State would fail to ensure that "Medicaid beneficiaries have access to the same range of drugs that the private patients or their physicians enjoy," as intended by Congress.[20] CMS has confirmed this with numerous communications to other states and in State Releases.

OHA's Two-Part Strategy to Manage Drug Spend Hinders Access to Innovative Therapies Jeopardizing the Quality of Care For Medicaid Patients

RAAP has concerns that a waiver of compliance with SSA § 1927's coverage requirements will restrict access to medically necessary drugs. Below we highlight

[17] SSA § 1115(a).

[18] Staff of H. Comm. on Ways and Means, 89th Cong., Summary of Major Provisions of H. R. 6675, The "Social Security Amendments of 1965" 1 (Comm. Print 1965).

[19] Id.

[20] H. Rep. No. 101-881, at 96-97 (1990).

only a few examples in which excluding accelerated approval medications is detrimental to rare patients.

Since the introduction of the AAP, more than 250 drugs have received accelerated approval, with roughly 42 percent representing drugs that treat rare diseases or conditions and 65 percent for oncology treatments. Over 25 million Americans suffer from rare diseases, which are particularly likely to be serious and life-threatening diseases with unmet medical needs. Of the 7,000 rare diseases that have been identified, more than 90% of them have no FDA-approved treatment.

As you know, with smaller, ultra-rare populations, traditional clinical trials would delay or halt progress for years while waiting for enrollment. Such a policy could have a disproportionate impact on the future rare patient access to these therapies. Many facets of rare diseases make them particularly difficult to study in clinical trials targeting direct clinical benefit.[21] "[D]eveloping drugs for rare disease can be challenging due to specific rare disease characteristics such as small heterogeneous patient populations, long time-frames for disease progression, a poor understanding of disease natural history, and a lack of prior clinical studies."[22] This makes accelerated approval a particularly important tool for the development of treatments for rare diseases.

For example, Sanfilippo syndrome could provide you with an important analogue to understand the importance of accelerated approval on development of pediatric rare diseases. This syndrome is akin to Alzheimer's disease in children. Children with Sanfilippo syndrome are born with a genetic abnormality so their bodies cannot break down heparan sulfate, a natural cellular product that needs to be recycled. Accumulation of excess heparan sulfate is toxic to both the body and the brain. Almost all children born with this syndrome die before adulthood. Currently, there are no approved therapies for Sanfilippo syndrome, nor are there any approved surrogate biomarkers. If use of the heparan sulfate level in cerebrospinal fluid were to be recognized as a biomarker that reflects underlying disease activity, a number of therapeutic programs that currently are at risk for never being approved could be advanced.[23] However, once a treatment is developed, and

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[21] Emil D. Kakkis et al., *Recommendations for the Development of Rare Disease Drugs Using the Accelerated Approval Pathway and for Qualifying Biomarkers as Primary Endpoints,* 10:16 Orphanet J. of Rare Diseases 1, 1 (2015), available at https://ojrd.biomedcentral.com/track/pdf/10.1186/s13023-014-0195-4.pdf.

[22] U.S. Food & Drug Admin., CDER Drug and Biologic Accelerated Approvals Based on a Surrogate Endpoint (Jan. 14, 2021), https://www.fda.gov/media/88907/download

[23] Emil D. Kakkis, Aduhelm's accelerated approval offers a promising roadmap for rare neurological diseases (July, 2021). https://www.statnews.com/2021/07/07/accelerated-approval-aduhelm-promising-roadmap-rare-diseases/

approved through the accelerated pathway, the Oregon Medicaid program under this waiver request could deny access to patients.

Pediatric neuromuscular therapies, lysosomal disorder medicines, gene therapies, and many other rare pediatric and adult medications–all these important advances could be denied to patients under this waiver, even though they are FDA approved, and must meet rigorous standards for that label and approval none-the-less.

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Thank you for the opportunity to submit comments on the Oregon Health Plan's Section 1115 Demonstration Waiver Renewal and Amendment application. We strongly urge the state to work with the rare patient community to ensure new policies do not severely jeopardize patient access to care, given our belief that Oregon Health Plan can achieve its objectives without any waiver of §1927.

Sincerely,

Michael Eging
Executive Director
Rare Access Action Project