



**VIA ELECTRONIC DELIVERY**  
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March 25, 2021

Medicaid and CHIP Payment and Access Commission (MACPAC)  
1800 M Street NW  
Suite 650 South  
Washington, DC 20036  
Re: Accelerated Approval Higher and Inflationary Rebates

Dear MACPAC Commissioners and Staff:

On behalf of the Rare Access Action Project (RAAP), we appreciate the opportunity to submit the following comments in response to MACPAC's recent recommendations for the 2021 Congressional report that could adversely and disproportionately affect development of orphan drugs and biologics. Specifically, MACPAC recommends that Congress:

- Amend Section 1927(c)(1) of the Social Security Act (SSA) to increase the minimum rebate percentage on drugs that receive approval from the US Food and Drug Administration (FDA) through the accelerated approval pathway under Section 506(c) of the Federal Food, Drug and Cosmetic Act (FD&CA). This increased percentage would apply until the manufacturer has completed the confirmatory trial and been granted traditional FDA approval. Once FDA grants traditional approval, the minimum rebate percentage reverts to the amount listed under Section 1927(c)(B)(i) of the SSA.
- Amend Section 1927(c)(2) of the SSA to increase the inflationary rebate on drugs that receive approval from the FDA through the accelerated approval pathway under Section 506(c) of the FD&CA. This increased inflationary rebate would go into effect if the manufacturer has not yet completed the confirmatory trial and been granted traditional FDA approval after a certain number of years. Once the FDA grants traditional approval, the inflationary rebate reverts to the amount typically calculated under Section 1927(c)(2) of the SSA.

[RAAP](#) is a policy coalition made up of rare disease advocates, emerging life sciences companies, and other rare disease stakeholders. Collectively, we seek innovative solutions to current barriers that hinder patient access to orphan therapies. RAAP continuously explores policy solutions that address structural issues in access and coverage for patients with rare diseases. While we recognize the intricate dynamics of drug pricing and the relationship to patient access, we also understand the importance of thoughtful policy changes that protect development of innovation along with patient access to that innovation, particularly in the case of rare diseases. We appreciate the opportunity to share perspectives from the rare disease patient and families.

#### **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 persons but are not expected to recover the costs of developing and marketing a treatment drug<sup>1</sup>. 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.

[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 will not live to see their 5th birthday<sup>2</sup>.

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 these proposals.

### **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 availability or lack of alternative treatments<sup>3</sup>.*

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<sup>1</sup> 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.

<sup>2</sup> 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>

<sup>3</sup> 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](#),<sup>4</sup>

*... 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**

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, Senior Research Analyst with the Tufts Center for the Study of Drug Development<sup>5</sup>, 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<sup>6</sup>. 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 identification and enrollment.<sup>7,8,9</sup> Coverage, 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.

Broad penalties 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

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<sup>4</sup> 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.

<sup>5</sup>Tufts Center for the Study of Drug Development, *Impact Report Analysis & Insight into Critical Drug Development Issues*. Vol. 15, No. 1, Tufts University, 2013.

<sup>6</sup> 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.

<sup>7</sup>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](https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5d2490ae0072ee0001a1a198/1562677423360/summary_julyaugust_2019.pdf). Accessed March 13, 2021.

<sup>8</sup> Tambuyzer E. Rare diseases, orphan drugs and their regulation: questions and misconceptions. *Nat Rev Drug Discov*. 2010;9(12):921–9.

<sup>9</sup> Sharma A, et al. Orphan drug: Development trends and strategies. *J Pharmacy and Bioallied Sciences*. 2010;2(4):290–9.



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.*<sup>10</sup>

### **Consider Orphan Drug Exclusion**

While RAAP does not support the proposed recommendations given the risks to rare disease drug development and commercialization, should MACPAC move forward with the recommendations for inclusion in the Congressional report, RAAP recommends considering carve out protections for products with orphan designation so that rare diseases and the manufacturers bringing innovations to these rare disease patient populations are not disproportionately penalized given the unique challenges of patient recruitment for confirmatory trials. The FDA is best positioned to determine and address the unique circumstances of each of these case scenarios.

MACPAC responsibilities include ensuring coverage and access to care. Should MACPAC proceed with the recommendations outlined above, RAAP also recommends, given the continued access challenges for rare disease treatments (sometimes as great as 6-12 agonizing months after expedited FDA approval), that state Medicaid programs be reminded of their duty to provide access to these FDA approved products consistent with the FDA label upon FDA approval and rebate agreement signing.

### **Conclusion**

In summary, RAAP raises concern regarding MACPAC's recommendations to increase Medicaid rebates for accelerated approval products. RAAP opposes such policy recommendations given the risks to continued development and commercialization of treatments for rare diseases. Should MACPAC move forward with the recommendations, RAAP recommends an exclusion for products with orphan designation. The FDA is in the best position to carefully weigh the unique circumstances of public welfare, safety, efficacy and additional clinical trials in the case of orphan products. Should MACPAC move forward with the recommendation, such a policy should be considered in the context of immediate access to orphan therapeutic treatments consistent with the intention of the expedited approval pathways due to the unmet medical need.

RAAP continues to work to:

- **Protect Research and Development for Rare Disease**—ensure health policies do not undermine the investment in innovation for rare diseases;

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<sup>10</sup>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.



- **Ensure Rare Disease Representation in Coverage and Access**—require government payment programs to impanel rare specialists and patient/patient advocates to ensure that the rare disease patient perspective is included in decision-making at the federal, state, and local level;
- **Address Rare Disease Patient Cost Share Burden**—implement cost share policies that address the disproportionate effect on patients with rare diseases. For example, capping out of pocket costs for rare patients in the Medicare Part D program or ensuring all patient copays are counted toward out-of-pocket costs by commercial plans;
- **Propose Innovative Solutions to Manage the Cost of Therapies**—propose payment solutions such as reinsurance or value-based pricing to ensure access to rare therapies at FDA approval;
- **Protect and Improve Timely Access to Innovative Treatment**—implement policies that permit timely access to rare therapies at FDA approval across payers, including therapies with [FDA Break Through and Accelerated Approval](#) that meet significant unmet medical needs.

Thank you for this opportunity to comment. With innovative therapies that have the potential to change the course of rare patient lives, it is imperative that we protect beneficiary access to these products that can be life sustaining, affect disease progression, or quality of life for some of our most vulnerable Medicaid beneficiaries. We respectfully request that you consider our concerns, and if we can provide further insights into the implications on the rare disease stakeholder community, we stand ready to be of assistance.

Regards,

A handwritten signature in black ink, appearing to read "Michael Eging", is written over a thin horizontal line.

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