Rare Disease Company Coalition

March 21, 2023

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The Honorable Mike Crapo
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The Rare Disease Company Coalition (RDCC) is writing to express our strong concerns about recent policy proposals that undermine the intent of the accelerated approval pathway. We ask that Congress act to preserve accelerated approval as a critical lifeline for rare disease patients by contacting Health and Human Services (HHS) and urging them not to move forward with the *Accelerating Clinical Evidence Model*, and by rejecting the Medicaid and CHIP Payment and Access Commission (MACPAC) recommendation regarding state adoption of Medicare's national coverage determination (NCD) for certain medicines approved under accelerated approval.[1]

The RDCC is a coalition of 21 life science companies committed to discovering, developing, and delivering life-changing therapies for rare disease patients around the globe. Collectively, RDCC members invested over $15 billion in R&D in 2021 and are working to advance more than 200 rare disease treatments, many of which would be the first ever FDA-approved therapies for patients with a given rare disorder. While rare disease is generally defined in the United States as a condition that affects fewer than 200,000 people, there are over 10,000 identified rare diseases that impact roughly 30 million Americans,

[1] Secretary Xavier Becerra. A Report in Response to the Executive Order on Lowering Prescription Drug Costs for Americans. CMS. U.S. Department of Health and Human Services. February 14, 2023. https://innovation.cms.gov/data-and-reports/2023/eo-rx-drug-cost-response-report

representing a high unmet need.[2,3] Today, at least 95% of rare diseases lack an FDA-approved treatment. These diseases are devastating and often life-threatening: 50 percent impact children, with many rare diseases resulting in premature deaths of infants and young children.[4]

***Congress Should Uphold Intent of Accelerated Approval as a Pathway to Address High Unmet Medical Need Prevalent in Rare Diseases***

In 1992, the FDA established the accelerated approval pathway which was codified by Congress in 1997. Subsequently, in 2012, Congress passed the *Food and Drug Administration Safety Innovations Act* (FDASIA)[5] amending the *Federal Food, Drug, and Cosmetic Act* (FD&C Act)[6] to reinforce and enhance the accelerated approval pathway and encourage broader applicability for rare disease. Both Congress and the FDA have affirmed that medical products granted approval on the accelerated approval pathway meet FDA's stringent standards for safety and effectiveness. Notably, the FDA has maintained that therapies approved using expedited approval programs must meet clinically meaningful endpoints, and that the benefits of the treatment must outweigh its risks, 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."*[7,8,9]

The accelerated approval pathway has been credited with significant advances in the treatment of serious, life-threatening diseases where patients have limited or no treatment options. Historically, this pathway has benefitted countless patients who have received safe and effective treatments months and sometimes years earlier than if accelerated approval did not exist. For example, the pathway has been particularly impactful in oncology with 160 oncology accelerated approvals through January 1, 2023.[10,11] As Congress articulated through *FDASIA*, accelerated approval can be a critical pathway for rare diseases.[12,13,14,15] Congress, the FDA, and the scientific community have all recognized the important role of reasonably likely 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. Notwithstanding this fact, the accelerated approval pathway has

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[2] Food and Drug Administration. Delivering Promising New Medicines Without Sacrificing Safety and Efficacy. FDA. https://www.fda.gov/news-events/fda-voices/delivering-promising-new-medicines-without-sacrificing-safety-and-efficacy Accessed March 14, 2023

[3] National Center for Advancing Translational Sciences. Delivering Hope for Rare Diseases. National Center for Advancing Translational Sciences. https://ncats.nih.gov/files/NCATS_RareDiseasesFactSheet.pdf Accessed March 8, 2023.

[4] National Organization for Rare Disorders. Barriers to Rare Disease Diagnosis: Care and Treatment in the US. NORD. November 19, 2020. https://rarediseases.org/wp-content/uploads/2022/10/NRD-2088-Barriers-30-Yr-Survey-Report_FNL-2.pdf.

[5] S.3187 - 112th Congress (2011-2012): Food and Drug Administration Safety and Innovation Act, S.3187, 112th Cong. (2012), https://www.congress.gov/bill/112th-congress/senate-bill/3187.

[6] Federal Food, Drug, and Cosmetic Act. Congressional Record Index (2023), https://www.congress.gov/congressional-record/congressional-record-index/115th-congress/2nd-session/federal-food-drug-and-cosmetic-act/316463.

[7] Federal Register Vol. 57, No.73, April 15, 1992

[8] FDA. Delivering Promising New Medicines Without Sacrificing Safety and Efficacy. FDA Voices: Perspectives From FDA Leadership and Experts. August 2019. FDA. Advancing Health Through Innovation: New Drug Therapy Approvals 2019. January 2020. Available at: https://www.fda.gov/media/134493/download.

[9] FDA. Advancing Health Through Innovation: New Drug Therapy Approvals 2020. January 2021. Available at: https://www.fda.gov/media/144982/download.

[10] FDA. Verified Clinical Benefit | Cancer Accelerated Approvals. FDA. February 13, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/verified-clinical-benefit-cancer-accelerated-approvals.

[11] FDA. Ongoing | Cancer Accelerated Approvals. FDA. February 14, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/ongoing-cancer-accelerated-approvals

[12] FDA. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. FDA. May 2014. https://www.fda.gov/media/86377/download

[13] Food and Drug Administration Modernization Act of 1997. U.S.C. 301 (1997). https://www.govinfo.gov/content/pkg/PLAW-105publ115/pdf/PLAW-105publ115.pdf

[14] Food and Drug Administration Safety and Innovation Act. U.S.C. 301 (2012). https://www.govinfo.gov/content/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf

[15] FDA. Accelerated Approval for Oncology Drug Products: Regulatory Overview. FDA. April 28, 2021. https://www.fda.gov/media/147925/download

only been used in the approval of approximately 25 rare disease therapies that are not in the oncology or infectious disease spaces.[16,17]

Rare disease drug development poses unique challenges due to the small number of patients available to participate in clinical trials, variability in disease presentation among patients, and varied progression of some diseases. The accelerated approval pathway is a critical tool, well-suited to recognize these unique circumstances. Instead of erecting additional barriers to utilizing the accelerated approval pathway for rare diseases, access to this pathway should be preserved and encouraged. As Peter Marks, Director of Center for Biologics Evaluation and Research, noted during the FDA's remarks celebrating Rare Disease Day last month, the FDA wants to expand the use of the accelerated approval pathway in certain circumstances for rare diseases. The policy proposals currently being brought forward are antithetical to this goal.[18]

***Congress Should Uphold the Role of FDA as Gold Standard in Safety and Efficacy***

By law (21 U.S.C. § 356(e)(2)), the FDA must find "substantial evidence of effectiveness" to approve any drug, including therapies approved via accelerated approval.[19] Proposals that subject accelerated approval medicines to additional scrutiny based on the approval pathway that FDA determined was appropriate erodes the purpose of the pathway. Recent proposals by state Medicaid programs, the Centers for Medicare & Medicaid Services (CMS) and Congressional advisory bodies—such as MACPAC and the Medicare Payment Advisory Commission (MedPAC)—seek to undermine Congress' intent in establishing this pathway, as well as FDA's approval. These policies imply that the state, CMS, or Congressional advisory bodies are better suited to review drugs than the scientists and clinical experts at the FDA. Establishing this type of framework undermines the important, independent authority of the FDA as the sole arbiter of safety and efficacy.

***Congress Should Reject CMMI Demonstration to Protect Patient Access to Life-Saving Accelerated Approval Treatments***

As proposed, CMMI's mandatory payment model, *Accelerating Clinical Evidence Model,* places a lower value on Medicare Part B prescription drugs approved through the accelerated approval pathway.[20] By lowering reimbursement, CMMI will discourage investment in clinical trials in some of our hardest-to-treat, most complicated diseases, further undermining the fundamental intent of accelerated approval. It is important to note that small biotech companies largely lead innovation in rare disease drug development, and the prospect of limiting reimbursement for accelerated approval therapies in certain settings could be an extremely limiting barrier to continued investment for those companies and the broader industry. With so much unmet need for the rare disease community, and scientific challenges, rare disease drug developers need more research incentives, not fewer.

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[16] FDA. Verified Clinical Benefit | Non-malignant Hematological, Neurological, and Other Disorder Indications Accelerated Approvals. FDA. https://www.fda.gov/drugs/accelerated-approval-program/verified-clinical-benefit-non-malignant-hematological-neurological-and-other-disorder-indications. Accessed March 6, 2023.

[17] FDA. Ongoing| Non-malignant Hematological, Neurological, and Other Disorder Indications Accelerated Approvals. FDA. https://www.fda.gov/drugs/accelerated-approval-program/ongoing-non-malignant-hematology-neurological-disorders-and-other-indications-accelerated-approvals Accessed March 6, 2023.

[18] Karins, J., Wang, B. Marks: Accelerated Approval Can Spur Gene Therapies For Rare Diseases. Inside Health Policy. March 6, 2023. https://insidehealthpolicy.com/daily-news/marks-accelerated-approval-can-spur-gene-therapies-rare-diseases.

[19] Federal Food, Drug, and Cosmetic Act. Congressional Record Index (2023), https://www.congress.gov/congressional-record/congressional-record-index/115th-congress/2nd-session/federal-food-drug-and-cosmetic-act/316463.

[20] Secretary Xavier Becerra. A Report in Response to the Executive Order on Lowering Prescription Drug Costs for Americans. CMS. U.S. Department of Health and Human Services. February 14, 2023. https://innovation.cms.gov/data-and-reports/2023/eo-rx-drug-cost-response-report

A recent study by Vital Transformation found that "Substantial changes to the accelerated approval pathway will likely render the potential development of therapies for most untreated orphan conditions economically untenable."[21] Specifically, the study cites that possible changes to the accelerated approval at the federal level put therapies at risk of withdrawal which would have addressed the needs of up to 3.6 million patients. Two of the Centers for Medicare & Medicaid Innovation's (CMMI) strategic objectives are to advance health equity and support innovation.[22] Not only will this outcome run counter to CMMI's objective to support underserved populations, but it will also stifle much-needed medical innovation for rare disease patients.

Furthermore, the CMMI model fails to account for the life-changing benefits of the accelerated approval pathway, which, in many cases, the only FDA-approved treatment available to rare disease patients. Accelerated approval can provide treatments to patient years earlier, giving extra time and improved quality of life to patients and their families. Congress should protect rare disease patient access to life-saving treatments by rejecting the *Accelerating Clinical Evidence Model*.[23]

***Congress Should Allow FDA Time to Implement Recent Accelerated Approval Changes Before Considering Further Proposals***

Many critics and proponents of misguided accelerated approval policy proposals claim that manufacturers take too long to complete confirmatory trials. However, it is important to note that timelines for conducting post-approval confirmatory trials are driven by disease-specific considerations. It is reasonable to expect verification of clinical benefit to take many years, particularly for slowly progressing, heterogeneous rare diseases, and factors such as challenging in study recruitment due to a limited patient population. Despite these obstacles, research shows that half of all accelerated approval drugs convert to traditional approval in approximately 3.2 years.[24]

The FY2023 *Food and Drug Omnibus Reform Act* (*FDORA*), passed in December 2022, addresses the concerns about post-market studies by empowering the FDA to ensure timely conduct of confirmatory trials and implements streamlined withdrawal procedures.[25] *FDORA* has given FDA the legal clarity needed to withdraw an accelerated approval drug if the sponsor fails to conduct post-market studies appropriately, or if the studies fail to verify the safety and efficacy benefits. Collectively, these changes represent significant steps toward equipping the FDA with the tools necessary to ensure post-market studies are completed in a timely manner as appropriate. As such, reimbursement policy proposals designed to "incentivize" completion of confirmatory trials are premature. We ask that Congress provide FDA with adequate time to implement new measures that add more rigor to the accelerated approval process before moving forward with additional new policies. Doing so will give confidence to all stakeholders and recognize the importance of maintaining incentives for innovation.

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[21] Vital Transformation. Calculating the Value and Impact of Accelerated Approvals: Preliminary Findings. Vital Transformation. https://vitaltransformation.com/2022/06/calculating-the-value-and-impact-of-accelerated-approvals/ Accessed March 8, 2023.
[22] CMMI. Strategic Direction. CMS. https://innovation.cms.gov/strategic-direction. Accessed March 14, 2023.
[23] Secretary Xavier Becerra. A Report in Response to the Executive Order on Lowering Prescription Drug Costs for Americans. CMS. U.S. Department of Health and Human Services. February 14, 2023. https://innovation.cms.gov/data-and-reports/2023/eo-rx-drug-cost-response-report
[24] Vital Transformation. Calculating the Value and Impact of Accelerated Approvals: Preliminary Findings. Vital Transformation. https://vitaltransformation.com/2022/06/calculating-the-value-and-impact-of-accelerated-approvals/ Accessed March 8, 2023.
[25] Text - H.R.2617 - 117th Congress (2021-2022): Consolidated Appropriations Act, 2023, H.R.2617, 117th Cong. (2022), https://www.congress.gov/bill/117th-congress/house-bill/2617/text.

***Congress Should Reject Medicaid Proposals That Seek to Jeopardize Rare Disease Therapies Approved Using Accelerated Approval***

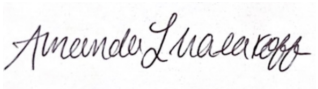
In addition to the CMMI demonstration, we are concerned about the recent rise in state Medicaid 1115 waiver requests aimed at restricting coverage of accelerated approval drugs, and MACPAC's recommendations to Congress to apply a differential mandatory Medicaid rebate to accelerated approval drugs and adopt Medicare's NCDs. As Medicaid plays a critical role in supporting the rare disease community, particularly children with rare genetic conditions, these proposals would have a devastating impact on patients benefiting from this innovation and create a greater health equity divide, all while resulting in limited budget savings. Research shows that targeting accelerated approval drugs will not save state Medicaid programs money, as the therapies represent less than one percent of program spending.[26] The recent Vital Transformation study found that state proposals to limit Medicaid coverage for rare disease treatments, like the ones proposed in Massachusetts, Tennessee and Oregon, would result in up to 400,000 patients losing access to life-saving treatments.[27] These proposals only serve to limit patient access to critical life-altering drugs or treatments for individuals with rare diseases, and are the wrong solution for patients.

***Conclusion***

Any future policy reforms to accelerated approval should protect patient access, build upon Congress' recent steps to boost FDA oversight of accelerated approval products, leverage and enhance its existing authorities, and protect the integrity of this critical pathway. As such, we urge Congress to protect rare disease patients by rejecting any policy proposals that would create harmful consequences for patients, particularly in light of recent bipartisan reforms to the accelerated approval pathway passed under *FDORA*. We ask that leaders in Congress instruct CMMI not to implement the *Accelerating Clinical Evidence Model* proposal and reject MACPAC's harmful and misguided policy recommendations.

Should you have any questions, please contact me at amanda@rarecoalition.com.

Best,



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[26] Kenneth E. Thorpe. Quantifying Impact of Accelerated Approval Drugs on Medicaid Spending. Partnership to Fight Chronic Disease. May 2022. https://www.fightchronicdisease.org/sites/default/files/FINAL%20Quantifying%20Impact%20of%20Accelerated%20Approval%20Drugs%20on%20Medicaid%20Spending%20060222.pdf

[27] Vital Transformation. Calculating the Value and Impact of Accelerated Approvals: Preliminary Findings. Vital Transformation. https://vitaltransformation.com/2022/06/calculating-the-value-and-impact-of-accelerated-approvals/ Accessed March 8, 2023.