Rare Disease Company Coalition

July 29, 2021

The Honorable Patty Murray
Chairwoman
Senate Committee on Health, Education, Labor & Pensions
U.S. Senate
Washington, DC 20510

The Honorable Frank Pallone
Chairman
House Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Richard Burr
Ranking Member
Senate Committee on Health, Education, Labor & Pensions
U.S. Senate
Washington, DC 20510

The Honorable Cathy McMorris Rodgers
Ranking Member
House Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

Re: Support for the Accelerated Approval Program

Dear Chairwoman Murray, Ranking Member Burr, Chairman Pallone, and Ranking Member McMorris Rodgers,

On behalf of the life science companies that comprise the Rare Disease Company Coalition (RDCC), we are writing to express our support for the Food and Drug Administration's (FDA) Accelerated Approval Program and urge members of Congress to preserve and strengthen this critical mechanism to expedite the availability of safe and effective therapies for patients who have serious conditions with an unmet need. We would also like to share our concerns with recent policy recommendations put forth by the Medicaid and CHIP Payment and Access Commission (MACPAC), certain state Medicaid programs, and others that would undermine the intent of the accelerated approval pathway, prevent and discourage investment, research, and development into rare disease treatments, and hinder access to treatments for patients who have serious conditions.

In the United States, a rare disease is defined as a condition that affects fewer than 200,000 people. There may be as many as 7,000 rare diseases with an estimated 25 to 30 million Americans living with a rare disease. 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 life science companies comprising the RDCC are committed to continuing to change these statistics by discovering, developing, and bringing valuable treatments – and even potential cures – for the many patients still

awaiting treatment options. Collectively, we spend over half of our annual budgets on research and development. Coalition members invested over $4.1 billion in R&D in 2020; have brought 25 treatments to market to date, the majority of which are first-to-market therapies; and are presently working on more than 190 rare disease development programs, many of which would be first-to-market therapies if approved.

We are reaching out to you, as members of Congress, to underscore the importance of the Accelerated Approval Program and a continued need to uphold its intent to expedite the availability of innovative treatments for patients with serious and often life-threatening diseases and unmet need.

The Accelerated Approval Program is a well-established and proven regulatory framework.

The Accelerated Approval Program 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 FDA's rigorous standards for safety and effectiveness. In 1992, the FDA established the accelerated approval pathway which was later codified by Congress in 1997.[2] Subsequently, 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 reinforce and enhance the accelerated approval pathway and encourage 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 151 oncology accelerated approvals through January 1, 2021.[4] As Congress articulated through FDASIA, accelerated approval can be a critical pathway for rare diseases as well.

The FDA has established specific requirements for drugs to be considered through the Accelerated Approval Program; moreover, drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. Under 21 CFR part 314, subpart H, a drug is considered for the accelerated approval pathway if it "treats a serious condition AND generally provides a meaningful advantage over available therapies AND demonstrates 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 (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit (i.e., an intermediate clinical endpoint)." Section 505(d)(1) of the FD&C

[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 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] https://www.fda.gov/media/147925/download

Act established the standard for effectiveness, for all drugs, as substantial evidence based on adequate and well-controlled clinical investigations and the safety standard as having sufficient information to determine whether the drug is safe for use under conditions prescribed, recommended, or suggested in the proposed labeling.

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 expedited approval pathways 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."*[5] Only a small fraction of novel drugs and biologics are approved under the accelerated approval pathway (65 of 468 or ~14% of novel new drug approvals from 2011-2020)."[6] Accelerated approval has been and continues to be used in select and appropriate circumstances where evaluating efficacy on clinical endpoints isn't practical, feasible, or ethical in a reasonable timeframe.

Ill-informed policy proposals threaten ability to innovate and may hinder patient access.

Given the success of the accelerated approval pathway as a means of expediting the delivery of new innovative therapies to patients who cannot afford to wait, we are greatly concerned by recent policy recommendations put forth by MACPAC to address "high-cost specialty drugs" in Medicaid that would effectively curtail the accelerated approval pathway and directly impact the accessibility of new treatments for patients, particularly those with rare diseases. Like recent state proposals requesting the authority to implement closed formularies for their Medicaid programs that would exclude coverage of accelerated approval products, MACPAC's recommendations would compound access issues already faced by patients with rare diseases. Medicaid is a federal-state partnership that plays a critical role for access to care for low-income individuals, and vulnerable populations, including patients with rare diseases. Specifically, MACPAC recommends that Congress increase the minimum rebate percentage and the additional inflationary rebate in the Medicaid program for drugs approved via the Accelerated Approval Program tied to the completion of post-marketing confirmatory trials, claiming this approach strikes a balance between reducing Medicaid costs while still maintaining access.[7] We strongly disagree.

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[5] 57 Fed. Reg. at 58944.

[6] 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 Accessed February 23, 2021
FDA. Advancing Health Through Innovation: New Drug Therapy Approvals 2020. January 2021. Available at: https://www.fda.gov/media/144982/download Accessed February 23, 2021.

[7] https://www.macpac.gov/wp-content/uploads/2021/06/June-2021-Report-to-Congress-on-Medicaid-and-CHIP.pdf

We believe MACPAC's policy recommendations are not in the interests of patients. Their approach simply does not align with the intent of the Accelerated Approval Program to expedite access to rare disease treatments for patients with serious conditions, especially for diseases that have limited or no treatment options. While these policies would apply specifically to the Medicaid program, a significant proportion of rare disease patients are children who are on Medicaid. We are concerned about the impact to these patients and also the broader impact on the entire rare disease community, regardless of payor, believing this policy change would effectively disincentivize and curtail research and development for the treatment of certain rare diseases. Our specific concerns regarding MACPAC's proposals to assess a higher rebate on accelerated approval drugs are as follows:

- Diminishes patient perspective and may ignore the long-term detrimental impact to rare disease patients. Targeting a distinct, and higher rebate for accelerated approval therapies, as MACPAC's proposal does, 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. It is a striking omission that the MACPAC proposal did not include an analysis of the impact on patient access to treatments nor consider the voice of impacted communities.

- Undermines the purpose of the accelerated approval pathway. 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.[8] As noted above, accelerated approval therapies meet the full statutory standards for safety and effectiveness.

- Disincentivizes the development of rare disease treatments. Mandating a higher rebate would counter the economic incentives to pursue accelerated approval drugs, disincentivizing drug developers from pursuing development of therapies in otherwise intractable disease areas. Ultimately, these proposals would punish patients who are forced to suffer as their disease progresses while continuing to wait for a treatment. A large portion of rare disease patients are children, and the Medicaid program plays an important role in their care. Assessing a higher rebate on accelerated approval drugs for rare diseases would impact available resources to execute trials, including post-approval confirmatory trials, and the ability of companies to continue innovating. It is important to note that smaller biotech companies are leading innovators

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

in rare disease development and the prospect of higher rebate for companies not yet profitable could be an extremely limiting barrier.

The RDCC supports policies that will, in reality, strengthen the Accelerated Approval Program and preserve its intent to give patients who have debilitating diseases a chance to be treated with cutting-edge science. We urge members of Congress interested in further strengthening the accelerated approval pathway to recognize the harmful consequences of undercutting reimbursement, coverage and patient access to accelerated approved therapies and instead focus on meaningful opportunities to optimize FDA's governance and implementation of this pathway in a way that accounts for evolving science and data generation in the post-market setting and continues to keep patients front and center. Any future policy reforms to the Accelerated Approval Program should build upon FDA's recent steps to reinforce its oversight of accelerated approval products, leverage and enhance its existing authorities, and protect the integrity of this critical pathway.

Thank you for your consideration. We firmly believe that the Accelerated Approval Program can be credited for advancing science and saving lives and would be available to meet with you in person or virtually at your convenience to discuss this further. In the meantime, should you have any questions, please do not hesitate to contact Taylor Mason, RDCC Executive Director at info@rarecoalition.com.

Sincerely,
Rare Disease Company Coalition

CC: The Honorable Ron Wyden
The Honorable Mike Crapo
The Honorable Robert Casey
The Honorable Bill Cassidy
The Honorable Bernie Sanders
The Honorable Susan Collins
The Honorable Anna Eshoo
The Honorable Brett Guthrie