February 18, 2025

Lisa Harris, M.D.
Senior Vice President and Chief Medical Officer
Excellus Blue Cross Blue Shield
165 Court Street
Rochester, NY 14647

Dear Dr. Harris,

On behalf of the National Organization for Rare Disorders (NORD), I am writing to express our deep concern regarding the recent decision by Excellus Blue Cross Blue Shield to eliminate coverage for a number of therapies approved through the U.S. Food and Drug Administration (FDA) accelerated approval pathway for a period of 18 months following FDA approval and urge its swift reversal.

With a more than 40-year history, NORD is the leading and longest-standing patient advocacy group for the more than 30 million Americans living with a rare disease. An independent 501(c)(3) nonprofit, NORD is dedicated to individuals with rare diseases and the organizations that serve them. NORD, along with its more than 355 patient organization members, is committed to improving the health and well-being of people with rare diseases by driving advances in care, research, and policy. NORD believes that all individuals with a rare disease should have access to high quality, affordable health care that is best suited to meet their medical needs.

NORD urges Excellus Blue Cross Blue Shield to immediately reconsider its decision to deny coverage for therapies approved via the FDA accelerated approval pathway. Accelerated approval is an essential regulatory mechanism for ensuring that patients with serious and life-threatening conditions, particularly those with rare diseases, can access effective and potentially lifesaving therapies as quickly as possible. Given the nature of rare diseases— which are often characterized by small, heterogenous patient populations with limited knowledge of natural history available — this pathway allows for timely patient access to critical therapies that may otherwise face insurmountable hurdles with more traditional clinical trial approaches. By denying coverage of these FDA-approved therapies, Excellus Blue Cross Blue Shield is hampering access to potentially lifesaving medications for rare disease patients who often have no alternative treatment options available.

The accelerated approval pathway, established by the FDA in the 1990s, was designed to expedite the development process for drugs intended to treat serious and life-threatening

conditions, including rare diseases, where significant unmet treatment need exists.[1] Under Federal law, accelerated approval is neither conditional nor partial approval: it is, as FDA attests, a full and complete approval of a new drug as safe and effective, which renders the treatment by definition non-experimental for its intended use. The program allows for early regulatory review and approval of medical products based on the use of surrogate endpoints that are either known or reasonably likely to predict clinical benefit. Products receiving accelerated approval are subject to post-marketing requirements that ensure the safety and efficacy profile is confirmed through additional study.

In 2012, Congress codified into law the accelerated approval pathway as part of the Food and Drug Administration Safety and Innovation Act (FDASIA).[2] In codifying the pathway, Congress acknowledged the vital role the accelerated approval pathway served for patients with rare diseases and expressed their hope that it would bring life-saving drugs to the market expeditiously.[3] Congress also affirmed FDA's conclusion that accelerated approval did not create a different standard for drug approval, stating that accelerated approval "may result in fewer, smaller, or shorter clinical trials... without compromising or altering the high standards of the FDA for the approval of drugs."[4]

The FDA maintains a strong track record of ensuring that therapies initially receiving accelerated approval meet the same regulatory standards for demonstrating substantial evidence of effectiveness as those receiving traditional approval. The vast majority of products receiving accelerated approval go on to successfully demonstrate safety and efficacy through completion of FDA-required post-marketing activities. More than three out of four drugs that received accelerated approval from 1992 to 2016 successfully converted to traditional approval, and only about 10 percent of the 278 accelerated approval drugs approved from 1992 to 2023 were past their original confirmatory trial completion date.[5] Among these 'late' products, more than half were less than a year past their confirmatory trial date, and only four drugs were five or more years late.[6]

The success of the accelerated approval pathway is evidenced not only by high conversion rates to traditional approval, but also by the tangible benefits it has delivered to many rare disease

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[1] NORD, Temkin, E. & Trihn, J. FDA's Accelerated Approval Pathway: A Rare Disease Perspective. https://rarediseases.org/wp-content/uploads/2022/10/NRD-2182-Policy-Report_Accelerated-Approval_FNL.pdf

[2] Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112–144, §§ 803, 901(b), 902(a), 126 Stat. 993, 1079, 1083–87 (2012)

[3] See H.R. Rep. 112-495, *35–36 (2012).

[4] See 158 Cong. Rec. H3825-01, H3848 (2012).

[5] Health and Human Services (2022, September 29). *Delays in Confirmatory Trials for Drug Applications Granted FDA's Accelerated Approval Raise Concerns*. Office of Inspector General. Retrieved May 15, 2023, from https://oig.hhs.gov/oei/reports/OEI-01-21-00401.asp

[6] Health and Human Services (2022, September 29). *Delays in Confirmatory Trials for Drug Applications Granted FDA's Accelerated Approval Raise Concerns*. Office of Inspector General. Retrieved May 15, 2023, from https://oig.hhs.gov/oei/reports/OEI-01-21-00401.asp

patients who might not otherwise have access to vital treatments. Of the 252 novel orphan products – those intended to treat rare disease patient populations – approved from 2008 to 2021, over a quarter were approved through the accelerated approval pathway.[7] Notably, orphan drugs accounted for 85 percent of all novel drugs receiving accelerated approval during this time.[8] As these data show, the accelerated approval pathway has had tremendous benefits for patients in the rare disease community.

Provisions of the FDA Omnibus Reform Act (FDORA), passed as part of the Consolidated Appropriations Act of 2023 (P.L. 117-328), are empowering FDA to further strengthen the accelerated approval pathway. FDORA enhances the post-approval process by giving the agency greater authority to require sponsors to submit more robust data from confirmatory trials and take steps to ensure such trials are completed in a timely manner.[9] Additionally, FDORA increases transparency by mandating that more detailed information about accelerated approvals be made available to the public.[10] This law further establishes an expedited withdrawal process for taking action if confirmatory trials are not completed on time, ensuring that drugs approved via this pathway ultimately deliver the benefits promised to patients.[11] These combined efforts from the FDA and FDORA work to uphold and enhance the integrity of the accelerated approval pathway while ensuring that much needed treatments can continue to reach patients in an expeditious manner.

In conclusion, the accelerated approval pathway is a critical tool that upholds the FDA's rigorous standards while ensuring that safe and effective treatments are available to rare disease patients in a timely manner. However, insurers like Excellus Blue Cross Blue Shield have a critical role in ensuring patients can actually access these safe and effective therapies, and coverage decisions to delay access to potentially lifesaving treatment based on FDA approval pathway are deeply concerning. NORD is committed to working with payers to ensure that patients with rare diseases have access to the care and therapies they need. NORD would welcome the opportunity to discuss this matter further and collaborate on solutions that will best support the rare disease community Excellus Blue Cross Blue Shield serves.

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[7] Monge AN, Sigelman DW, Temple RJ, Chahal HS. Use of US Food and Drug Administration Expedited Drug Development and Review Programs by Orphan and Nonorphan Novel Drugs Approved From 2008 to 2021. JAMA Netw Open. 2022;5(11):e2239336. doi:10.1001/jamanetworkopen.2022.39336

[8] Monge AN, Sigelman DW, Temple RJ, Chahal HS. Use of US Food and Drug Administration Expedited Drug Development and Review Programs by Orphan and Nonorphan Novel Drugs Approved From 2008 to 2021. JAMA Netw Open. 2022;5(11):e2239336. doi:10.1001/jamanetworkopen.2022.39336

[9] See: https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-omnibus-reform-act-fdora-2022

[10] See: https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-omnibus-reform-act-fdora-2022

[11] Lupkin, S. (2023, March 3). *FDA has new leverage over companies looking for a quicker drug approval*. Retrieved May 15, 2023, from https://www.npr.org/sections/health-shots/2023/03/03/1160702899/fda-enforcement-drug-approval-manufacturer-promises#:~:text=Changes%20to%20the%20accelerated%20approval,accelerated%20approval%20to%20the%20drug

Thank you for your attention to this important issue. I look forward to your response and hope to establish an effective partnership to ensure access to effective therapies for all patients, particularly those with rare diseases.

Sincerely,

Edward Neilan, M.D., Ph.D.
Chief Medical and Scientific Officer
National Organization for Rare Disorders