July 25, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Re: Medicaid Program; Misclassification of Drugs, Program Administration and Program Integrity Updates Under the Medicaid Drug Rebate Program [CMS–2434–P]

Dear Administrator Brooks-LaSure,

On behalf of the more than 25 million Americans living with one or more of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Centers for Medicare and Medicaid Services (CMS) for the opportunity to comment on the "Medicaid Program; Misclassification of Drugs, Program Administration and Program Integrity Updates Under the Medicaid Drug Rebate Program" 2023 proposed rule.

NORD is a unique federation of non-profits and health organizations dedicated to improving the health and well-being of people living with rare diseases. NORD was founded 40 years ago, after the passage of the Orphan Drug Act (ODA) to formalize the coalition of patient advocacy groups that were instrumental in passing that landmark law. Our mission has always been and continues to be to improve the health and well-being of people with rare diseases by driving advances in care, research and policy.

The Medicaid Drug Rebate Program is a critical component to ensuring Medicaid beneficiaries have access to necessary, often life-saving therapies. NORD appreciates CMS' efforts to clarify key program definitions and improve the integrity, effectiveness, and administration of the program, given its importance to many in the rare disease community. Our comments focus on four specific issues that we believe will have the greatest impact on the rare disease community.

1. **NORD urges CMS to ensure any drug price verification surveys do not inadvertently disincentivize rare disease drug development or FDA's accelerated approval pathway.**

Changing mechanisms through which some covered outpatient drugs are distributed, evolving pricing structures for these drugs, and the increase in novel, high-cost Medicaid drugs, including many newly approved cell and gene therapies, have created a changed drug price ecosystem that could potentially benefit from additional data collection.

1779 MASSACHUSETTS AVENUE NW, SUITE 500
WASHINGTON, DC 20036
T 202-588-5700 ▪ F 202-588-5701

55 KENOSIA AVENUE
DANBURY, CT 06810
T 203-744-0100 ▪ F 203-263-9938

1900 CROWN COLONY DRIVE, SUITE 310
QUINCY, MA 02169
T 617-249-7300 ▪ F 617-249-7301

rarediseases.org ▪ orphan@rarediseases.org

NORD supports CMS' plan to exclude covered outpatient drugs that are already subject to other CMS drug price negotiation programs from the survey. However, we urge CMS to further clarify how it intends to interpret whether a drug is subject to these negotiation programs and pilots or initiatives. For instance, further clarifications regarding how and when voluntary participation in potential CMMI pricing models may exempt drugs from the drug price verification survey could incentivize participation in these pilot programs. Similarly, the Inflation Reduction Act (IRA) of 2022 created a Medicare Drug Price Negotiation Program that excludes certain orphan drugs from drug price negotiation. Reassurance that these excluded drugs will also be exempt from the drug price verification survey would create regulatory certainty vital to maintaining investments in rare disease drug development programs.

The details of how the drug price verification survey will be implemented are key to the survey's resulting benefits – or harms. Given the complexity of establishing a robust and meaningful drug price verification survey and the potential for considerable unintended consequences, incorrect or incomplete data, and perverse incentives, we urge CMS to go through a formal comment process for the selection of drugs subject to the survey. This will provide extensive opportunities for patients and stakeholders to weigh in on vital issues including the criteria used to select drugs for inclusion in the survey, the data elements to collect for a robust and meaningful survey, and key scientific and methodological details for the survey design and analysis. For instance, while we understand CMS's rationale to only consider states that cover outpatient drugs entirely through fee-for-service (FFS) arrangements in the survey, we are concerned about the inherent biases introduced by basing these key calculations only on 10 of the 50 states. The 10 states that currently rely entirely on FFS arrangements for covered outpatient drugs are likely substantially different from the remaining states in a variety of ways, limiting the generalizability of the data, in particular for rare diseases that are already more difficult to calculate given the smaller population sizes.

To achieve the survey's stated goals, we recommend CMS follow a notice and comment process starting with stakeholder listening sessions and workshops, followed by a draft program implementation guidance, followed by ample additional opportunities for community input. Throughout the process, we recommend CMS work closely with FDA to ensure alignment and a seamless 'baton hand-off' so that all stakeholders can make the best use of any collected data.

We urge CMS not to select drugs for the survey simply because they have gone through FDA's accelerated approval pathway. The accelerated approval pathway has been, and continues to be, vital to rare disease patients.[1] For example, among 252 FDA-approved novel orphan drugs and indications approved from 2008 to 2021, about a quarter were approved through the accelerated approval pathway.[2] In fact, orphan drugs accounted for 85% of all novel drugs approved through

[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] 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

the accelerated approval pathway during this time period.[3] Drugs receiving accelerated approval are available to patients years earlier – according to at least one 2011 study of oncology drugs at a median 3.9 years faster than oncology drugs that receive traditional approval.[4] Nearly all accelerated approval drugs are ultimately able to confirm clinical benefit and are eventually converted to traditional approvals. For instance, more than three out of four drugs that received accelerated approval from 1992 to 2016 have already been successfully converted to traditional approvals.[5] In fact, only about 10 percent of the 278 accelerated approval drugs approved from 1992 to now are currently past their original confirmatory trial completion date.[6] Among these 'late' drugs, more than half are less than a year past their confirmatory trial date.[7] As these data show, accelerated approval has had tremendous positive impacts on rare disease patients.

Although most confirmatory trials are completed expeditiously, NORD recognizes the challenge a lagging confirmatory trial creates for patients, providers and payors. Provisions in the Food and Drug Omnibus Reform Act of 2022 (FDORA) direct FDA to implement changes to ensure more drugs meet their target date for confirmatory trial completion and NORD supports the use of FDA's new authorities to hold sponsors of accelerated approval drugs accountable for the expeditious completion of all post-market requirements. Provisions in the Food and Drug Omnibus Reform Act of 2022 (FDORA) direct FDA to implement changes to ensure more drugs meet their target date for confirmatory trial completion. Moving forward, FDA will have greater authority to require drug companies to begin enrollment in their confirmatory studies before being granted accelerated approval.[8] Similarly, thanks to FDORA, it will be easier for FDA to withdraw drugs that fail to demonstrate clinical benefit, and a new FDA council will help improve transparency and alignment across the FDA's centers and review divisions.[9]

NORD agrees that under certain, narrowly defined circumstances, additional data collection may complement FDA's new authorities and provide valuable additional insights. We further recognize that data collection efforts may be less disruptive and more effective than other policy proposals that outright seek to limit patient access to accelerated approval products or increase required rebates for products that utilize the accelerated approval pathway. However, it is questionable to what extent the drug price verification survey, as it has been outlined to date, would be able to collect data of sufficient granularity, reach, and representativeness to meaningfully achieve these stated objectives, and to what extent such data collection efforts in

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[3] Ibid
[4] https://www.fda.gov/drugs/resources-information-approved-drugs/ongoing-cancer-accelerated-approvals
[5] Johnson, J., Ning, Y., Farrell, A. , Justice, R., Keegan, P., Pazdur, R.,, Accelerated Approval of Oncology Products: The Food and Drug Administration Experience, *JNCI: Journal of the National Cancer Institute*, Volume 103, Issue 8, 20 April 2011, Pages 636–644, https://doi.org/10.1093/jnci/djr062
[6] Stengel, K., Zalewski, Z., West, M., Gustafson, K., & Nell, A. (2022, January 4). *Understanding the History and Use of the Accelerated Approval Pathway*. Retrieved May 11, 2023, from https://avalere.com/insights/understanding-the-history-and-use-of-the-accelerated-approval-pathway#:~:text=In%20a%20review%20of%20accelerated,9.5%20years%20without%20confirmatory%20evidence
[7] 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
[8] 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.
[9] Ibid

general would meaningfully benefit state Medicaid offices and the rare disease patients who rely on the drugs approved through accelerated approval. As stated above, most drugs approved through accelerated approval are orphan drugs, which makes meaningful data collection particularly challenging given the small, geographically dispersed patient populations, heterogenous disease manifestations, and lack of data on disease progression. Given the potentially detrimental impacts on patient access and the broader use of accelerated approval, we urge CMS to proceed with utmost caution.

2. **NORD is concerned about the logistical challenges of requiring a diagnosis on prescriptions given rare diseases often lack disease-specific coding.**

NORD appreciates CMS' efforts to reduce out-of-pocket costs for patients such as pregnant women or individuals infected with COVID-19 that qualify for exemptions from out-of-pocket costs and copayments. However, the logistical challenges associated with expanding diagnosis requirements across the Medicaid system, and the potential for errors, are immense. This is particularly true for rare diseases.

Many rare diseases do not have an appropriate disease-specific diagnostic, or ICD-10, code that allows the condition to be appropriately captured with relevant specificity. Of the over 7,000 known rare diseases, only around 500 have an ICD-10 code.[10] As a result, diagnostic coding has remained inconsistent for many rare diseases. Based on the experience with the transition from ICD-9 to ICD-10 coding, the implementation of CMS' proposal will likely lead to impacts on productivity and staffing, coding accuracy, and possibly patient care. All of these impacts will likely disproportionately impact rare disease patients and providers. Specifically, NORD is concerned about the feasibility of effectively capturing diagnoses for all relevant conditions in a meaningful and reproducible way. Moreover, NORD recognizes CMS' intent to conform closely to the statute requiring all covered outpatient drugs to have a medically accepted indication. Yet, as many as 95% of rare diseases do not have an FDA approved treatment.[11] Relying on clinical guidelines, rather than FDA-approved indications, to verify compliance with the statute is logistically considerably more challenging to implement, and NORD is concerned errors and glitches will disproportionately affect rare disease patients and providers who predominantly rely on clinical guidelines, rather than FDA approved indications.

Ultimately, we are concerned that the new process would place an unnecessary burden on providers, pharmacies, and state Medicaid offices, who would struggle to handle the process uniformly, reducing the utility of data collection nationwide while leading to a substantial increase in wrongful coverage denials, in particular for rare disease patients. Many rare disease patients already face a number of diagnostic challenges and utilization management measures

[10] Rare Diseases Europe (2015) Does Your Rare Disease Have a Code? https://www.eurordis.org/does-your-rare-disease-have-a-code/#:~:text=Nearly%20500%20rare%20diseases%20have,available%20in%20over%2050%20countries..

[11] Health Affairs. (2017). For Rare Disease Patients, A Pathway To Hundreds of New Therapies. https://www.healthaffairs.org/content/forefront/rare-disease-patients-pathway-hundreds-new-therapies#:~:text=Many%20rare%20disease%20patients%20use,a%20single%20FDA%2Dapproved%20treatment.

that unduly delay access to appropriate treatment. Requiring a diagnosis on a prescription would only add to the challenges that many rare disease patients already face.

3. NORD urges CMS to ensure patients will directly benefit from lower prices as a result of accumulate price concessions and discounts ("stacking")

Given the complexity in the healthcare ecosystem and the variety of discounts, rebates, and other concession arrangements commonly provide to best price eligible entities, CMS' proposal to accumulate price concessions and discounts ("stacking") when determining the best price of a covered outpatient drug will prove difficult to implement.

NORD urges CMS to provide the additional education, technical and policy support, and commensurate oversight needed to ensure a smooth and robust implementation of the stacking provision. Changing the current practice of calculating rebates by identifying the largest cumulative rebates available to a single purchaser to tracking all available rebates across all steps of the supply chain will be a big adjustment, both for manufacturers and CMS. In fact, OMB noted in the regulatory impact statement that they were unable to determine cost estimates for the implementation of the stacking provision. As the necessary systems and processes are established and analysts navigate a myriad of practical questions to content with the heterogeneity of concessions and data limitation in a fragmented healthcare ecosystem, the best price calculation will initially be time intensive and potentially error prone. Best price calculations may be particularly challenging for orphan drugs given the increased complexity of the care environment for rare disease patients, and the smaller number of patients receiving the drug. CMS' best price calculations have a considerable impact on drug pricing even well beyond the Medicaid program, and maintaining the high level of reliability and trust in the calculated prices will be vitally important for rare disease patients and the larger healthcare ecosystem.

In addition, NORD urges CMS to ensure patients directly benefit from any additional savings through lower premiums and out-of-pocket costs. Out-of-pocket costs in particular pose high and sometimes prohibitive burdens on rare disease patients, and patient cost-sharing is on the rise across many health insurance segments.[12,13] While the majority of Medicaid beneficiaries have relatively low cost-sharing payments on most covered outpatient drugs, rare disease patients often experience a considerable economic burden to afford the care they need, including numerous covered (as well as not covered) outpatient drugs, routine and specialist provider visits, and ancillary costs such as travel, with many disease patients routinely traveling a far distance to receive the specialized care they need.[14] Moreover, beneficiaries with incomes higher than 150% of the federal poverty line covered by Medicaid can be subject to co-insurance up to

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[12] RWJF (2021) Marketplace Pulse: Cost-Sharing in the Marketplace, 2021. https://www.rwjf.org/en/insights/our-research/2021/06/marketplace-pulse-cost-sharing-in-the-marketplace-2021.html

[13] NORD (2023) Prescription Drug Out-of-Pocket Costs. https://rarediseases.org/policy-issues/out-of-pocket/

[14] NORD (2020). Barriers to Rare Disease Diagnosis, Care and Treatment in the US; National Organization for Rare Disorders. https://rarediseases.org/wp-content/uploads/2020/11/NRD-2088-Barriers-30-Yr-Survey-Report_FNL-2.pdf

20% on non-preferred drugs.[15] Data demonstrates that any cost-sharing decreases utilization of necessary care, as well as increases financial burden for families.[16] While caps limit total out of pocket costs for Medicaid beneficiaries, any reduction in total spend on medical costs is important, particularly for rare disease beneficiaries who may incur supplemental out-of-pocket costs not covered by Medicaid.

4. **NORD is supportive of CMS efforts to further clarify key program definitions and require increased drug price transparency in Medicaid Managed Care plans.**

Greater clarity about key terms such as the definition of covered outpatient drug, noninnovator multiple source drug, market dates, and vaccine (for the purpose of MDRP) will help reduce inadvertent errors and help ensure rare disease Medicaid patients continue to have access to affordable outpatient drugs. Similarly, NORD is supportive of provisions to require greater price transparency in Medicaid Managed Care Plan contracts. Greater visibility into prices, rebates and fees will increase the robustness of CMS' calculated drug prices and ultimately benefit rare disease patients.

In summary, NORD supports CMS' efforts to increase the effectiveness and transparency of the Medicaid Drug Rebate Program and appreciates the opportunity to provide comments to ensure the program revisions will benefit all Medicaid beneficiaries, including those impacted by rare diseases. We look forward to working with the Agency to ensure rare disease patients can fully participate in and benefit from the Medicaid program. For questions related to this letter, please contact Karin Hoelzer (khoelzer@rarediseases.org) or Mason Barrett (mbarrett@rarediseases.org).

Karin Hoelzer, DVM, PhD
Director, Policy and Regulatory Affairs
National Organization for Rare Disorders

Mason Barrett
Policy Analyst
National Organization for Rare Disorders

[15] Medicaid.gov. (2023) Cost Sharing Out of Pocket Costs. https://www.medicaid.gov/medicaid/cost-sharing/cost-sharing-out-pocket-costs/index.html
[16] KFF (2021) Understanding the Impact of Medicaid Premiums & Cost-Sharing: Updated Evidence from the Literature and Section 1115 Waivers. https://www.kff.org/medicaid/issue-brief/understanding-the-impact-of-medicaid-premiums-cost-sharing-updated-evidence-from-the-literature-and-section-1115-waivers/