May 22, 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

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Dear Administrator Brooks-LaSure and Dr. Seshamani,

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 their extensive engagement with the rare disease community around implementation of the Inflation Reduction Act (IRA). NORD appreciates this opportunity to provide comments on the Information Collection Request (ICR) Form for Negotiation Data Elements under Section 11001 and 11002 of the IRA (CMS-10847), hereafter referred to as the "ICR."

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 IRA will impact rare disease patients' access to therapies in complex ways. For many Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder patient access to needed therapies**.** Key provisions in the IRA, including the $2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, as well as expanded eligibility for financial assistance for low-income beneficiaries, once fully implemented, will ensure that more rare disease patients on Medicare will be able to afford the life-altering therapies they need.

On the other hand, before the Orphan Drug Act was signed into law in 1983, fewer than 40 FDA-approved therapies were available to treat rare diseases.[1] Thanks to the incentives created by the ODA, rare disease therapies now consistently account for more than half of FDA approvals for new molecular entities.[2] Still, more than 90% of the more than 7,000 known rare diseases do not have an FDA approved treatment, making continued investment in rare disease research and innovation especially important to

[1] Orphan Drugs In The United States: An Examination of Patents and Orphan Drug Exclusivity (2021): available at https://rarediseases.org/wp-content/uploads/2022/10/NORD-Avalere-Report-2021_FNL-1.pdf; accessed 4/2023
[2] New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products; available at: https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products; accessed 4/2023

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the rare disease community.[3] The limited exemption for orphan products approved to treat a single rare disease will help encourage this continued innovation, as will the exemption for products with less than $200 million in annual Medicare spending. However, the small patient populations and medical complexity associated with rare diseases create unique challenges to rare disease drug development, and these same complicating factors may also make it more difficult to determine a fair negotiated price for products that treat rare diseases compared to other therapies.

At the same time, therapies that treat rare diseases are often placed on the non-preferred or specialty tiers of Medicare Part D plan formularies and/or are subject to step therapy and other utilization management strategies, resulting in significant out of pocket costs and access delays - and making some therapeutic options virtually inaccessible to many rare disease patients. These policies *de facto* limit which treatment options are feasible alternatives for many rare disease patients. Given these complex factors and their immense impact on patients' lives, NORD appreciates CMS' efforts to capture and incorporate the patient voice in the negotiation process.

To appropriately capture the patient's voice, patient input must be decoupled from this ICR; CMS must be more proactive in engaging the patient community in the data collection. NORD urges CMS to address three specific areas of concern to ensure the rare disease community fully benefits:

1. Decouple and simplify the collection of patient experience data from this ICR.
2. Proactively collect patient experience data through externally–led patient-listening sessions.
3. Engage FDA's and CMS' patient engagement experts as well other relevant government, academic, and private sector experts at every step of the data collection process.

Specifically, CMS should take the following steps to support rare disease patients and families in providing input into the drug negotiation process:

1. Decouple and simplify the collection of patient experience data from this ICR.

The primary purpose of this specific ICR is to facilitate the mandatory collection of manufacturer data, guided by statutory data elements, rigid processes, and tight timelines. The collection of patient experience data is both qualitatively and quantitatively very different from this primary purpose as collecting patient experience data is neither subject to statutory data elements nor does it have to follow the very tight timelines for manufacturer-provided data that would be virtually impossible for most patients to navigate. The type of data elements collected are also different, as evident from the ICR – with the manufacturer data mostly quantitative and clearly defined, capturing highly concrete issues such as a drug's annual sales volume, unit price of production, or patents and exclusivities.

In contrast, the patient-reported data is by design significantly more qualitative and much less precisely defined, capturing issues such as the extent to which a drug provides a meaningful advantage over an alternative therapy, or the extent to which an unmet medical need is not adequately addressed by

[3] Larkindale J, Betourne A, Borens A, Boulanger V, Theurer Crider V, Gavin P, Burton J, Liwski R, Romero K, Walls R, Barrett JS. Innovations in Therapy Development for Rare Diseases Through the Rare Disease Cures Accelerator-Data and Analytics Platform. Ther Innov Regul Sci. 2022 Sep;56(5):768-776. doi: 10.1007/s43441-022-00408-x.

available therapies. In fact, even the key audience for the patient reported data elements is significantly different from the manufacturers, and is likely to include patients and families, health care providers, academic researchers, and other relevant stakeholders. Additionally, the number of individual potential respondents is exponentially higher than for the manufacturer data. As a result, the ICR is unlikely to be an effective tool for capturing patient-reported data.

NORD is concerned CMS' plans to largely rely on this ICR for voluntary data submissions by the public will be unsuccessful. As proposed, the data collection will occur on very short timelines, without meaningful data standardization, using complicated forms written at too advanced reading levels and depending on hard-to-navigate processes that are neither intuitive nor patient-friendly. NORD is specifically concerned that patients will either not become aware of the data collection effort in time, or struggle to navigate the complex submission process. The extent to which individual data submissions will be confidential and protected from disclosure will be confusing to patients, and we worry the burden for patients not familiar with a process that was developed for manufacturers may be significantly higher than estimated, in particular for patients who may navigate additional challenges such as language barriers, visual impairments, or lack of (broadband) internet access. In addition, the required attestations are worded in a way that will likely discourage many patients from submitting data, and to the extent patients will feel compelled to submit data containing Personal Identifiable Information (PII) and Personal Health Information (PHI), the data collection raises privacy concerns.

Moreover, NORD foresees challenges in aggregating and analyzing individual patient and provider experience data submitted through this process; the data will be collected without a sampling frame and likely not representative while the collection method essentially makes it impossible to determine or account for such inherent biases in the data. In addition, the lack of standardized questions and scientific rigor will likely render this data largely anecdotal as opposed to data collected following appropriate qualitative and/or quantitative research methodologies to collect this information in a scientifically rigorous and reproducible manner as is currently done with data collected through the FDA's patient-focused drug development meetings or patient surveys. FDA's Guidance "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input" [4] for instance, provides detailed and tangible guidance on operationalizing and standardizing data collection and data management in a way that works for the rare disease patient community.

For the reasons outlined above, NORD urges CMS to:

a. **Decouple the collection of patient-reported data from the ICR.** As outlined above, the collection of patient data has virtually nothing in common with the mandatory submission of manufacturer data. Decouple the collection of this important patient data from a process that was never meant to collect this type of data - or to engage this number and diversity of respondents.

b. **b. Simplify and streamline the data submission process for patients, caregivers, and providers so that it is workable and does not provide undue barriers to providing the requested information**.

[4] FDA GFI: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; available at https://www.fda.gov/media/139088/download; accessed 4/2023

Decoupling the process from manufacturer provided data will allow CMS to create a data collection process that is designed to be patient-centered, with input and guidance from patients at every step of the process. This should include pre-testing the forms, attestations, and instructions with representatives of the relevant community to ensure they are clearly understood and easy to navigate, including by individuals with visual and other impairments. Because this data submission is voluntary and not subject to the statutory data submission timeline for mandatory manufacturer-provided data, CMS should work with the patient community to establish feasible timelines that will be workable for the community. Other concerns, such as ensuring the respondents are in fact patients, caregivers, or families afflicted by the disease and report their own experiences and perspectives, will require careful consideration, in close collaboration and with guidance from the patient community. FDA listening sessions, patient-focused drug development meetings, and other FDA-led initiatives routinely navigate these challenges and collect meaningful patient experience data in ways that work for rare disease patients and families and can serve as a valuable guide and resource for CMS, including all applicable attestations and data protections.

c. **Clarify now what information the agency is seeking from patients and in what format to allow data standardization and aggregation.** The short time period outlined for the negotiation process makes it imperative to provide detailed instructions as early as possible, before the negotiation period begins, to facilitate and streamline the collection and submission of meaningful data from a patient perspective. Clarifying the key data elements in sufficient granularity ahead of time will also empower patient advocacy groups and other important stakeholders to proactively collect and collate relevant information in a way that is scientifically rigorous and representative of the relevant patient community.

2. Proactively collect patient experience data through externally-led patient-listening sessions.
NORD thanks CMS for recognizing the unique and nuanced value drugs can bring to specific subsets of the patient population, including rare disease patients who often have few or no therapeutic options. NORD commends CMS' efforts to consider data on clinical benefit, therapeutic alternatives, and unmet medical need in the negotiation process. The agency's stated objective to assess value in an indication-specific manner including some off-label uses, is critical to CMS understanding the complex tradoffs and unmet needs that exist within the rare disease patient community. Moreover, we are encouraged that CMS has explicitly recognized the value of patient experience data, including its nuances, and the expectation that not all patients are necessarily sharing the same views and experiences. For instance, the science of patient engagement has long recognized that patient experience data may reflect differences depending on disease progression or a patient's cultural, geographic, and socio-economic background. While we are grateful CMS recognizes the value of patient experience data, we strongly encourage CMS to expand the opportunities and strengthen the processes for providing such input.

<u>The external data CMS staff plan to rely on in the negotiation often does not exist for most rare diseases, creating an added burden for CMS and the affected community to collect this data.</u> CMS plans to supplement the data submitted by the public through this ICR with relevant published data, relying on such data being readily available to CMS staff through literature searches. Unfortunately, it is a recognized challenge that for many rare diseases, data relevant to determine a negotiated product's clinical benefit, therapeutic alternatives, or unmet medical need often does not currently exist in peer-

reviewed journals or consensus treatment guidelines. FDA's Voice of the Patient (VOIP) reports, which are trying to fill this void, are playing an increasingly important role in patient-focused drug development and frequently collect meaningful information on how patients evaluate therapeutic alternatives or characterize the unmet need and clinical benefit of alternatives. However, these data are not indexed in a way that would clearly find them in a traditional literature search. In addition to ensuring CMS considers all relevant data collected as part of the FDA approval process in the negotiation process, patient and provider engagement will be critical to ensure CMS is aware of and able to leverage all available data. This is particularly important for rare diseases because the lack of disease-specific International Classification of Disease (ICD-10) codes for most rare diseases makes strategies relying on existing real-world data (RWD) from sources such as electronic health records (EHRs) or medical claims data largely infeasible for many rare diseases.

CMS will have to collect data on treatment alternatives, clinical benefit, and unmet medical need for rare diseases *de novo,* including from patients, caregivers, and providers. In fact, patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. For instance, rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families, and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate price on an indication-specific level including certain off-label uses, which are common in the rare disease space albeit notoriously hard to study.[5] Because published data to assess these specific uses remain scarce, patients and providers are often the best experts from which to elicit such information for the rare disease community.

For the reasons outlined above, NORD urges CMS to:

a. **Partner with key stakeholders on externally-led patient listening sessions specific to selected drugs to collect representative data to inform CMS' initial offer for a negotiated price.**

- In planning these sessions, CMS should use FDA patient listening sessions as a roadmap and work closely with the impacted patient communities to develop a representative and meaningful data collection effort. For instance, while we appreciate CMS' intends to only focus on pharmaceutical alternatives and to primarily consider alternatives in the same drug class, we recognize non-pharmaceutical options such as surgery are often the only viable alternative for our patient populations and that therapeutic alternatives in other drug classes and with other mechanisms of actions may be the most appropriate alternatives for some of our patients.

- Engaging the patient community in planning the listening session will help ensure that these alternatives are appropriately considered. Having external groups take a leadership role can

[5] Fung A, Yue X, Wigle PR, Guo JJ. Off-label medication use in rare pediatric diseases in the United States. Intractable Rare Dis Res. 2021 Nov;10(4):238-245. doi: 10.5582/irdr.2021.01104. PMID: 34877235; PMCID: PMC8630459.

help address both CMS staffing shortages and concerns about administrative and logistical issues (e.g., compliance with administrative and legal requirements for federal data collection).

- Logistically, patient listening sessions will likely be most effective if they focus on one negotiated drug and one (or potentially multiple closely related) uses or indications. This may require prioritization among drugs and indications that will be part of the negotiation program and should be guided by considerations such as to what extent the patient listening session will generate unique data to close key data gaps and to what extent the generated data is likely to materially impact the price negotiation. Transparency and engagement of the stakeholder community in this decision-making will be key to success. In fact, pre-meeting community surveys and enrollment strategies such as snowball sampling, when used appropriately, can be effective in helping to ensure the listening sessions will truly reflect the affected community.

- Other considerations include issues such as ensuring appropriate representation and diversity of perspective among the meeting participants; identifying and prioritizing questions for meeting participants ahead of time to provide time to prepare; carefully designing and pre-testing questions with consideration for well-established heuristics and cognitive biases (e.g., anchoring and adjustment, bandwagon effect, availability); and developing tools and approaches to capture the meeting outcomes in a way that is scientifically valid and allows participants to review the summary. Here again, FDA's experience with patient listening sessions and patient-focused drug development meetings will be able to provide valuable lessons learned.

b. **Include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data.** We urge CMS to report a detailed and standardized summary of the data relied upon in the negotiation process including the therapeutic alternatives, clinical benefit, off-label use, and unmet need for each indication and the data sources relied upon. CMS should further break out the use of patient experience data and patient-reported outcomes; list data identified by CMS through literature searches and guideline review as well as primary data, such as claims, EHR, or other real-world evidence (RWE), generated and collated by CMS. This level of transparency will be key to create consistency and trust in the negotiation process. Clearly breaking out the use of different data will also motivate the creation of valuable patient experience data for future negotiation years. In fact, much of the data for rare diseases collected through this process will be unique and useful beyond this specific negotiation process.

3. Engage FDA's and CMS' patient engagement experts as well other relevant government, academic, and private sector experts at every step of the data collection process.

NORD recognizes that the timelines for the IRA implementation are exceedingly short. Fortunately, as CMS engages on capturing patient perspectives in the Negotiation Program, the agency can draw upon a rich set of existing data, relevant scientific knowledge, and experience. For instance, considerable deliberation and research has gone into defining and measuring key concepts such as unmet medical need or therapeutic advantage.[6] Rather than reinventing these concepts, CMS can draw upon decades

[6] https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

of practice in the FDA space to streamline and fast track the process. Similarly, the science of patient engagement has made tremendous progress in the past decade. The academic literature is full of scientific studies seeking to identify best practices, develop tools to streamline the process, and capture the value of patient engagement. In fact, a 2014 systematic review of patient engagement in research identified 142 studies that met the inclusion criteria[7] – and hundreds more studies have been published in the decade since. FDA has made leaps in developing patient engagement best practices and tools that are largely applicable across FDA's product centers and through every step of the product life cycle.

CMS itself has a long history of successfully engaging patients and families. Tools such as CMS' Person and Family engagement strategy[8] have been instrumental in empowering patients and families to be meaningful partners in the design, delivery, and evaluation of their care. NORD also brings a wealth of experience engaging patients in various parts of the drug development and reimbursement space, and a range of other non-profit and academic institutions from the Patient-Centered Outcomes Research Institute (PCORI) and the Milken Institute's FasterCures Center to the Medical Device Innovation Consortium (MDIC) to a range of more disease-specific patient groups and many, many, others will have meaningful advice to offer. Relying on this wealth of experience and tried-and-true best practices, concepts and approaches will prove helpful in ensuring that patients will be meaningfully engaged in this data collection effort – but the right experts will have to be at the table when the data collection strategy for patient experience data is developed, implemented, and assessed.

For the reasons outlined above, NORD urges CMS to:

a. **Engage with CMS and FDA patient engagement experts and other relevant experts within CMS, HHS, as well as government-wide and within the private and non-profit sector.** This will help lay the foundation for a resilient and sustainable patient engagement system to rigorously engage patients and leverage the best practices and approaches to maximize the efficiency and chance of success.

We thank the Agency again for the opportunity to comment and look forward to working with CMS to ensure rare disease patients can fully participate in and benefit from the Negotiation Program.

Sincerely,

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[7] https://bmchealthservres.biomedcentral.com/articles/10.1186/1472-6963-14-89
[8] https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment Instruments/QualityInitiativesGenInfo/Person-and-Family-Engagement