July 2nd, 2024

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

Meena Seshamani, M.D., Ph.D.
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Dear Administrator Brooks-LaSure and Deputy Administrator Seshamani,

On behalf of the more than 30 million Americans living with one of the over 10,000 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 Initial Pay Applicability Year (2027) Medicare Drug Price Negotiation Program (MDPNP) guidance. Millions of Medicare beneficiaries are living with a rare disease, and many struggle with high out-of-pocket prescription drug costs.[1] Implementations of the MDPNP and related programs have the opportunity to dramatically reduce patient out-of-pocket costs for rare disease patients. However, without careful consideration and intentional implementation, NORD is concerned about potential unintended consequences.

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 more than 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 MDPNP will bring significant changes that are likely to impact rare disease patients in several complex ways, in particular given CMS' narrow interpretation of the orphan drug exclusion in the Inflation Reduction Act (IRA).[2,3] We greatly appreciated CMS' efforts to engage patients and health care providers as part of the 2026 MDPNP. We value the opportunity to recommend further changes and improvements to the solicitation and consultation processes with

[1] *Prescription Drug Affordability among Medicare Beneficiaries*. HHS- ASPE Office of Health Policy. (19 January, 2022). https://aspe.hhs.gov/sites/default/files/documents/485edf2a2d4870f88a456df61c8ff471/prescription-drug-affordability.pdf

[2] *Inflation Reduction Act of 2022*, P.L. 117-269.

[3] *Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections1191-1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair Price (MFP) in 2026 and 2027.* Section 30. CMS. (3 May, 2024). https://www.cms.gov/files/document/medicare-drug-price-negotiation-draft-guidance-ipay-2027-and-manufacturer-effectuation-mfp-2026-2027.pdf

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patients and health care providers through listening sessions and the Information Collection Request (ICR) for the 2027 MDPNP.

However, we remain deeply concerned about the smooth implementation of other key provisions of the MDPNP that are likely to have significant direct impacts on rare disease patients and their families. These include: formulary enforcement procedures and education; outreach efforts to ensure patients understand their co-pay liability (including their financial responsibility at the pharmacy counter and any rebates that may be applied retrospectively); and ensuring patients have the information they need to choose the Medicare plan that is right for them. Recognizing the crucial role of patient and health care provider engagement in assessing the impacts of the MDPNP on patients and families, we are pleased to also provide specific recommendations for successful engagement around program implementation. We realize the unique challenges of CMS simultaneously implementing two MDPNP years (currently for Initial Pay Applicability Years 2026 and 2027) and urge CMS to continue to prioritize assessment and evaluation as the first MDPNP program is implemented to allow for the collection of lessons learned and continuous program improvement and refinement.

Recommendation 1: Make the solicitation and consultation process with patients, caregivers, and health care providers more transparent, predictable, and inclusive and streamline the process to build and refine year-over-year capacity (Section 50).

NORD appreciated that the patient and health care provider listening sessions for the 2026 MDPNP were livestreamed and available for the public to view. Our recommendations are based on learnings from these sessions, as well as our extensive patient engagement experience and informed by a review of the relevant literature.[4] These recommendations are intended to be complementary to recommendations provided previously, including in a recent National Health Council (NHC) white paper to which NORD was honored to contribute.[5]

Our recommendations to strengthen the solicitation and consultation processes are primarily informed by three main findings with the 2026 MDPNP listening sessions:

1. The format of the listening sessions inadvertently left out some important voices in our community (*e.g., because the public format was uncomfortable for many patients; because of language, logistical, and technology barriers; because many patients were not aware of the listening sessions; because the ICR closed before the listening sessions and patients had no opportunity to submit written comments <u>after</u> the listening session, and because of questions about who was eligible to participate*).

[4] *Three Ways to Improve the Patient-Focused Listening Sessions In The Medicare Drug Price Negotiation Program.* Vandigo et. Al. Health Affairs (24 June, 2024). https://www.healthaffairs.org/content/forefront/three-ways-improve-patient-focused-listening-sessions-medicare-drug-price-negotiation

[5] *Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement.* National Health Council. (24 March, 2024). https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

2. Patient listening sessions provided limited data to directly inform the negotiation process and maximum fair price calculation (*e.g., because the 3-minute speaking slots were very short; because patient, caregivers, and health care providers lacked guidance on what insights would be most informative; and because the ridged session format prevented dialogue or clarifying questions*).

3. Patient listening sessions lacked standardization and were very heterogenous, generating inconsistent and widely varying outputs even for products in the same therapeutic area (*e.g., because listening sessions were organized by product rather than indication; included variable mixes of patients, caregivers, and providers; and because they lacked a standard set of questions*).

NORD recognizes the challenges of effective and inclusive patient engagement, exacerbated by the short timelines of MDPNP implementation and the logistical challenges of hosting the listening sessions shortly after the selected drug list is published. NORD recognizes and commends CMS' intent to host patient-focused events to seek input from patients and other interested parties and is encouraged by CMS' commitment to the most effective design and format for these sessions.

To ensure the listening sessions can help inform CMS about the true value of the selected therapies to the patient community and other select stakeholders, NORD is pleased to offer specific recommendations around three key priorities:

1. Start preparing for the listening sessions ahead of time; be transparent and standardize the outreach and engagement processes; maximize patient engagement including from historically underserved and other harder to engage communities; build long-term relationships, capacity and support in communities that are likely impacted in this and future plan years; and smooth out agency activity and workload on patient engagement over the plan year.

a. Identify therapeutic areas that are likely impacted by the selected drugs (e.g., oncology, lung, cardiovascular, diabetes); proactively begin outreach activities to these communities now; intentionally engage harder-to-reach communities; and with a goal of building long-term partnerships.

One of the most crucial elements of a successful and inclusive public participation campaign is to begin early; partnering with trusted community voices, proactively messaging important timelines, and explaining the information to be gathered (and why) as early as possible is vital to broader participation. While we commend CMS for implementing last year's iteration of the listening sessions on a tight timeline, the reality is that limited runway in advance of the listening sessions resulted in suboptimal patient and provider representation.

Although we recognize the logistical challenges CMS faces regarding proactive patient engagement, we believe this is a largely solvable problem. By the nature of the diseases that are prevalent in the Medicare population, and considering long-standing Medicare spending patterns, it appears almost certain that a limited number of therapeutic areas, including for instance oncology, lung, cardiovascular, and diabetes and related comorbidities, will likely be disproportionately represented amongst the selected products in the 2027 MDPNP as well as in future plan years.[6] CMS should proactively engage now with key stakeholder groups representing patients impacted by these diseases, and develop these relationships as long-term engagements to leverage in this year as well as future plan years.

Starting now and building out the engagement over time will allow CMS to engage a broader spectrum of diverse stakeholder groups, and to create sustainable, trusting, and fruitful partnerships over time. Moreover, approaching patient engagement by therapeutic area, rather than product, may lead to more diverse stakeholder engagement; for instance, while a given product may not be used by a specific patient group (e.g., because of label restrictions), that patient group may have valuable insights for this and future plan years. In addition, early and sustained partnerships with patient groups can have additional downstream benefits, such as helping to increase written comments and more robust participation in focus group sessions as the community builds capacity and individuals develop levels of familiarity and comfort with the process.

To ensure representation from patients, advocates, providers, and industry leaders from across the country, we encourage CMS to utilize their regional offices and ties to local communities to ensure appropriate patient engagement across different geographic regions. One effective way to do this is through in-person meetings; this would ideally include in-person outreach and education (e.g., at regional patient summits or health care provider meetings) and in-person listening sessions (e.g., at regional offices). While we recognize engaging individuals living in rural areas poses particular challenges, regional education and outreach will allow for richer, and more inclusive engagement than focusing outreach primarily nationally or on those located in, or able to travel to, the DC metro area. This is another area where year-over-year capacity building will be particularly valuable.

b. Develop educational and patient engagement materials that can be leveraged across products, therapeutic areas, and plan years; refine and revise these materials with input from the stakeholder community; and begin publicizing the listening sessions as early as possible BEFORE the selected drug list for negotiation is released.

CMS should begin developing and deploying educational materials and tools now to facilitate effective patient engagement in the drug price negotiation and refine and revise them with input from trusted partners (e.g., patient groups or providers with vested interest in the patient

[6] *Drugs likely subject to Medicare negotiation, 2026-2028.* Dickson, Sean and Hernandez, Inmaculada. National Library of Medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10387900/

populations utilizing the likely selected therapies). This should include outreach materials in languages other than English, and particular care should be given to ensure these materials are linguistically and culturally appropriate. These activities can and should start long before the announcement of the MDPNP 2027 selected products and build on learnings and successes year over year. Because these materials can be reused in future plan years, we urge CMS to create a feedback process that can be used to refine and revise these materials over time.

We encourage CMS to be as specific as possible in the materials about the logistics of the sessions to maximize transparency and give stakeholders a clear understanding of expectations. This transparency is vital to building trust and will mean more participants may be inclined to share their information and provide more meaningful responses. Specifically, in the lead up to the public listening sessions, we encourage CMS to be transparent with participants about how their data will be used and if / how they will be identified. Moreover, CMS should clarify how information from different population subgroups may be considered; for instance, patients who were formerly on a therapy may have inherently different experiences than the patients who are currently on it, and different patient populations may have different therapeutic alternatives available.

Information about how CMS intends to handle real or perceived conflicts of interest will be equally important. The lack of standardized processes or the required disclosure of professional or personal affiliations with interest groups led to inconsistent conflict of interest interpretation and implementation last year, which threatens to undermine trust in the process. We strongly recommend implementing a standardized mandatory disclosure process for professional or personal affiliations as a prerequisite for session participation.

Moreover, while CMS may not be able to release the names of the selected drugs until February 1, the agency can and should proactively set dates, times, structures, and locations (virtual and/or in person) for each listening session, focus group, or other engagement opportunity (preferably by therapeutic area). Scheduling these sessions early will make it easier for patients, caregivers, and providers to participate, and provide community partners more time to advertise the sessions and prepare their communities for the sessions. CMS should publicize the date and format (including speaker type) for the public engagement sessions even BEFORE the drug negotiation list is published. We encourage CMS to publish whether the sessions will include indication specific reviews, and if so, which of the sessions will be reserved for less common indications (including rare diseases).

A common challenge in the rare disease space is small patient populations. In addition, many rare disease patients experience several comorbidities which can make it harder to travel or rearrange pre-planned health care appointments. Announcing which sessions will be reserved for less common indications will make it easier for rare disease communities to plan, maximizing the chance of robust participation. This will allow for tailored outreach based on the therapeutic area and speaker type and allow umbrella organizations and other key stakeholders to begin socialization of the sessions as early as possible to maximize awareness.

2. Reconsider the session format; provide more options to meet patients where they are; include opportunities for patient engagement that protect patients' privacy and make it easier for all relevant patient populations to engage; better integrate the written and verbal opportunities for feedback and make the written process easier to navigate.

Following the success of the first year, we hope CMS will develop a process to continue to identify incremental improvements for future years. To ensure success of the program in future years, we encourage CMS to create a variety of virtual and in-person engagement opportunities, including smaller focus group style sessions targeted at both patients and caregivers and health care providers (we recommend separate focus groups for health care providers and for patients/caregivers); provide opportunities for more meaningful engagement between CMS staff and participants during the listening session; and provide opportunities for anonymous or closed-door engagement to lower the bar to participation for patients or caregivers who do not feel comfortable sharing their information with the public; provide opportunities for engagement specifically for patients or caregivers whose primary language is not English and those that need other types of accommodations (including opportunities for asynchronous input for those in our community who cannot take off time from work or school to participate during the scheduled times).

a. Streamline the public comment opportunities; provide opportunities for audio-only participation and for patients whose primary language is not English (e.g., Spanish-language listening sessions or real-time translation services); work with the patient advocacy groups and other key stakeholders to prepare patients better for the sessions; and continue to refine and revise the format for the listening sessions year over year.

As last years' experience clearly showed, not all patients feel comfortable sharing highly personal information about their disease or other aspects of their daily life on camera in publicly recorded settings. Furthermore, providing English-only engagement opportunities threatens to leave out important parts of the community. Establishing a system where participants can provide responses that will be deidentified and/or aggregated before being publicly posted has been shown to improve the quality of responses.[7] We urge CMS to continue to work with the affected communities to provide options that meet their needs.

b. Simplify and better integrate the written and verbal comment process to provide patients with a range of options to engage and share feedback without having to engage publicly.

After last year's data submission process, we are pleased to see there will be additional opportunities to strengthen written public comment. To ensure the public data submission process is captured in a meaningful way, we encourage CMS to increase timelines for

[7] *How Transparency Affects Survey Responses.* Connors, et. Al. Public Opinion Quarterly. (18 June 2019). https://academic.oup.com/poq/article/83/S1/185/5520299

participation, standardize the data capture process, and increase accessibility for patients with lower literacy comprehension and/or who need other accommodations to navigate the process (e.g., because of chronic diseases or physical or mental disabilities). Specifically, in our opinion, last year's public written comment process was terminated prematurely by closing it before the listening session. By failing to leave the written comment process open throughout the duration of the listening sessions, patients were forced to comply with tight timelines and opportunities for engagement were missed. Although we recognize that CMS was given a herculean task to accomplish within a short period of time, the short process was a significant barrier to participation for many patients, together with the complexity of navigating the process.

For this upcoming year, we recommend clearly publishing the timeline for public participation well in advance of the opening, alongside the questions that will be asked during the submission process. To our point on transparency above as well, we encourage CMS to share how the written submission will be considered differently than or in addition to the oral participation.

Moreover, we urge CMS to simplify and streamline the data submission process. Last year's data submission process included a complex series of mandatory forms with complicated and potentially concerning language utilizing terms that were not patient friendly. We encourage CMS to use short, simple forms at no greater than an eighth grade reading level to ensure language comprehension is less of a barrier. We view the written submission as a vital opportunity to supplement and complement the other engagement methods, including the collection of information from patient groups who may have difficulty (or wish not to) participating in oral sessions, such as individuals who speak English as a second language, or those who are impacted by audio-visual or physical challenges. All forms should be read with this in mind, and we strongly urge CMS to make the forms available in languages other than English.

To better understand who leverages the written process for future years we encourage CMS to collect voluntary demographic information from participants and/or to collect some of this information from stakeholder partners as appropriate. Moreover, we recommend streamlining the data collection process and prioritizing the information that is most important to CMS. Specifically, NORD recommends prioritizing the collection of plain-language information on:

- Demographic information, such as age, gender, race/ ethnicity, zip code
- Diagnosis and time since diagnosis
- Degree of disease progression
- If the information is provided by a patient or a caregiver
- What therapies the patient uses to manage their disease and for how long
- If the patient has tried other therapies in the past
- Degree of disease progression on treatment
- Most significant challenges in accessing medications
- How the patient feels and functions on the disease, and what symptoms remain unaddressed

- Challenges patient experienced associated with switching from one therapy to another
- What therapeutic alternatives the patient may have considered or may consider

It is also important for CMS to be clear about how written and oral submissions will be analyzed. For a variety of reasons, some patients may prefer submitting a written statement over participating in a live session. CMS may also not be able to find representatives for each of the indications that a selected product covers and the written responses may provide meaningful ways to substantiate and expand upon the data collected in the listening sessions. However, without clarification on how patient and stakeholder submission will be analyzed, we are concerned that components of the patient populations that are more difficult to survey may fall through the cracks during the negotiation process, and that the written submission form will not be used to its maximum extent. Certain types of patients, such as those with psychiatric conditions, cognitive limitations, and sight deficiencies, are often particularly difficult to include in surveys; specific, intentional efforts will be required to allow for meaningful inclusion of these populations.[8]

Additionally, we are concerned that without clarification of how the oral and written submissions are processed, patients could feel that submitting written comments would be a less valuable contribution. Establishing a system where participants are assured that their (deidentified) responses will be publicly posted has been shown to improve the quality of responses.[9] Even if exact weights for each of the types of responses relative to other factors cannot be shared or may vary by drug and indication, simply sharing the types of analysis used (i.e. quantitative vs. qualitative), will be helpful in how patients may structure their responses to be maximally beneficial.

c. Provide opportunities for more direct interaction with CMS through focus-group sessions in addition to the public listening sessions; this will allow the agency to ask clarifying questions and better understand varied patient perspectives on the most influential aspects of the MDPNP calculations including nuanced thinking around appropriate therapeutic alternatives (in particular in therapeutic areas like oncology or immunology where switching among products may have significant and hard-to predict impacts on long-term patient outcomes).

In our prior experience hosting patient listening sessions, NORD has found smaller focus-group listening sessions to be most effective to gain granular and nuanced input. These closed-door sessions make it more comfortable for patients to share personal details about their disease and how it impacts their daily life. We recommend sessions to be limited to five to 10 participants and set between 60 and 90 minutes. Each session should be limited to patients, providers, or caregivers, depending on the focus of the specific session – and may be further tailored (e.g., by

[8] *Barriers to Participation in a Patient Satisfaction Survey: Who Are We Missing?* Gayet-Ageron, et. Al. National Library of Medicine. (26 October, 2011). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3202588/

[9] *How Transparency Affects Survey Responses.* Connors, et. Al. Public Opinion Quarterly. (18 June 2019). https://academic.oup.com/poq/article/83/S1/185/5520299

geographic area, population subgroup, or to explore specific questions such as patients' experience switching across therapeutic alternatives).

Maintaining independence of each of the sessions and limiting them to a single stakeholder type will allow participants to develop a greater level of trust, both with one another and with the moderator, and help guard against issues like halo and bandwagon effects. Including different stakeholder types risks changing the power dynamic, where some participants feel their commentary is less worthy than others, or may become more deferential, rather than all participants viewing each other as equals. In addition, we recommend each focus group to be facilitated by a skilled facilitator knowledgeable in appropriately handling group dynamics in scientifically rigorous ways.

After participants have been selected for each of the respective sessions, we encourage CMS to proactively communicate expectations and solicit requests for accommodations. Some individuals may require additional time to process the questions in advance; sending around what each of the participants will be asked is helpful in ensuring all are able to respond on time and feel comfortable doing so. We also encourage CMS to ensure the participants understand what expectations for timing are, and to help stakeholders navigate the timekeeping requirements. While the first year of the listening sessions successfully kept the conversation within the confines of time requirements, the abrupt cut off while patients were telling their stories and no response permitted from CMS staff was suboptimal. Informing participants of the time limits and setting expectations for types of follow-up questions from CMS staff will be crucial in improving the quality of responses from participants moving forward.

We also encourage CMS to consider protecting participant privacy by exclusively releasing a redacted transcript after the conclusion of these focus group sessions. Potential participants may feel dissuaded from taking part in the sessions, or not feel comfortable fully participating in the session, if their identifiable information were to be released to the general public. As we saw in the first sessions, some patients are willing to share sensitive information, and we commend the patients who were willing to share their stories. To encourage participants to share their perspective, however, and to provide more granular responses with the nuance necessary to ascertain the true value of the selected products, extending privacy protections is crucial.

3. <u>Develop a standardized set of questions that are most relevant to CMS; develop a process to tailor these questions to each given therapeutic area, product, or patient group as needed; and focus on the key insights CMS needs most to inform the MDPNP; partner with key stakeholders to optimize the phrasing of these questions for clarity and consistency and explain how this data informs the negotiation process.</u>

We urge CMS to introduce more structure into the sessions compared to last year. While last year's sessions included some general guidelines for how participants should respond to questions, we encourage much more specificity to standardize the feedback the agency receives and ensure the agency can utilize participant answers.

a. Determine which data elements are most meaningful to CMS (e.g., therapeutic alternatives, remaining unmet medical need), both in general and specific to each therapeutic area; prioritize the written and verbal data collection for these critical data elements, and partner with relevant patient groups and other stakeholders to educate the patient community and collect the most meaningful input on these negotiation factors.

Not all data elements that can be informed by patients, caregivers, and health care providers will be equally important to CMS or have the same impact on the negotiation or maximum fair price calculation. Given the large number of products and indications CMS must consider, we strongly urge CMS to prioritize what insights will be most impactful and to be clear and transparent in communication and education to targeted stakeholders. We encourage CMS to clearly communicate how patient experience data informed the drug price negotiation and the final offer for each negotiated product.

b. Standardize the data collection efforts to ensure robustness and comparability across products and plan years while providing for sufficient flexibility to address the unique aspects of each product, therapeutic area, or patient population.

We encourage CMS to consider consistently asking questions specific to three thematic areas: 1. how the patient feels, functions and survives (on the treatment, an alternative treatment, or without any therapy); 2. cost and access; and 3. therapeutic alternatives. We recognize that these questions cannot be meaningfully answered in three minutes and appreciate CMS' flexibility to reconsider the session format. We also recognize that some of these questions may vary in pertinence based on therapeutic area, patient population, or other factors, and we encourage CMS to work with the relevant stakeholder community to prioritize and refine these questions as needed; however, we believe that this is a useful starting point for CMS' listening sessions.

Thematic area 1: How the patient feels, functions and survives:

- How does this disease impact you?
- How has your disease changed since you have been using this treatment?
- How long have you been using this treatment?
- What side effects have you been experiencing with this treatment?
- What formulation do you use for this treatment (if applicable)?
- Does this formulation best fit your needs?
- Rank the importance of the different characteristics of the treatment?
- What symptoms remain unresolved, and how is this impacting your day-to-day life?
- How does this product impact your social and emotional well-being?
- What would it mean to your daily life to no longer have access to the therapy?

Thematic area 2: *Cost and access:*

- Do you find this medication to be affordable? What does affordable mean to you?
- How much do you pay out of pocket annually for this medication?
- Did your insurance company make you try any other medications before agreeing to pay for this medication? If so, how many alternative medications were you required to try?
- Has this medication caused you any financial problems?
- Have you ever skipped a dose of this medication because you could not afford it?
- Have you ever skipped a dose of another medication because this medication was too expensive?
- What would cause you to stop taking this medication?
- Does your insurance company require prior approval before you fill this medication?

Thematic area 3: Therapeutic alternatives:

- What would you consider a therapeutic alternative to your current therapy? What characteristics make it a therapeutic alternative?
- Have you tried using any other medication to treat your condition? What has been your experience?
- How have you felt or functioned on the other therapy, and how does that differ from how you feel or function on the current therapy? Has that changed over time?
- Why did you switch / stop using that medication? Or why have you not tried other therapeutic options?
- How effective do you feel this other medication was compared to the medication you are using now?
- How does the price of your other medication compare to the medication you are using now?
- How were the side effects of the other medication compared to the medication you are using now?
- Did you find the other product(s) easier or harder to use than your current medication?
- What was your experience switching from one product to another?
- Would you consider switching products? Why or why not?

To further refine these questions, we encourage CMS to work with the impacted patient communities, as well as FDA and other stakeholders who have conducted successful patient engagement sessions to identify strategies best able to accomplish the goals of the patient listening sessions. FDA's Voice of the Patient Sessions are a crucial component of FDA's Patient Focused Drug Development (PFDD) sessions. To date, over 200 sessions have been completed on a wide variety of conditions, including both rare and non-rare conditions, and may

be a strong resource to supplement listening sessions and focus groups, particularly for rare conditions where participants may be more challenging to source.

Part of FDA's success with the Voice of the Patient Sessions derives from individual modifications made to each session reflective of each of the diseases under consideration. We encourage CMS to individualize each of the patient listening sessions towards both the indications under consideration and the population involved in the sessions. Tailoring individual indications under consideration while adhering to a common structure will allow patients to speak directly to their own experience and provide valuable feedback on the product's value for patients in specific situations.

We urge CMS to further refine and revise these questions with input from key stakeholders for future plan years and to establish a process to consistently learn from and revise these questions with each subsequent plan year. We are particularly concerned about how CMS will select therapeutic alternatives for consideration. As CMS considers how to best identify therapeutic alternatives, it is crucial to solicit information from patients, caregivers, health care providers, and other key stakeholders on when, and when not, certain therapies can be identified as an alternative. We also want to raise two areas of concern regarding information gathering on therapeutic alternatives: prohibitions on medical switching and off-label use of products.

As the listening sessions last year clearly showed, for many diseases, particularly immune conditions and cancers, the use of a treatment can have significant impacts on the effectiveness of other treatments, because of, for instance, emerging tumor resistance or a secondary loss of response due to antibody formation to the drug.[10,11] This raises concerns about the prospect of therapeutic alternatives. Although there may be alternatives available on the market, if they are not available to the patient for medical reasons, they should be given consideration independent of therapeutic alternatives for other indications.

Due to the lack of treatment options available for so many rare diseases, both providers and patients frequently rely on prescription medications without an FDA-approved indication for their condition on the label, known as off-label use. Physicians frequently rely on clinical compendia to make decisions about whether treatment options would be appropriate for their patients. Off-label use accounts for up to one third of all prescriptions, and up to 97% in certain populations.[12] We recognize that CMS has indicated their intent to conduct literature reviews on therapeutic alternatives for each of the selected products in the past; to ensure all relevant

[10] *What to Do When Biologic Agents Are Not Working in Inflammatory Bowel Disease Patients*. Dalal, et. Al. National Library of Medicine. (October, 2015). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4849518/

[11] *Clone Wars: Quantitatively Understanding Cancer Drug Resistance.* Yates, et. Al. JCO Clinical Cancer Informatics. (28 October, 2020). https://ascopubs.org/doi/10.1200/CCI.20.00089

[12] *Off-Label Use vs Off-Label Marketing of Drugs.* Van Norman, Gail. National Library of Medicine. (27 February, 2023). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9998554/#:~:text=Off%2Dlabel%20use%20of%20drugs%20is%20common%2C%20constituting%20up%20to,off%2Dlabel%20use%20of%20drugs.

therapeutic alternatives, we strongly recommend CMS consider including off-label uses of products.

Recommendation 2: Prioritize monitoring of unintended consequences associated with the MDPNP implementation; engage patients, caregivers, and health care providers in this monitoring activity; and refine and revise the monitoring activity over time (Section 110).

NORD appreciates CMS' commitment to monitoring plan formularies to ensure negotiated products are kept accessible to patients. Since plans benefit from drugs with higher rebates, for products with therapeutic alternatives, manufacturers may be incentivized to seek better formulary tier placement by offering increased rebates. When rebates are reduced, plan sponsors may increase the formulary tier, increasing patient cost sharing and decreasing access. Therefore, we have concerns that without requiring plans to place negotiated products on a preferred formulary tier, plans may place these products on a less preferred tier, and/or erect additional utilization management barriers, resulting in higher patient cost sharing for negotiated products.

Rare disease drugs are frequently already placed on the non-preferred or specialty tiers of Medicare Part D plan formularies, resulting in increased patient out-of-pocket liability and access delays. A 2020 study found that 85% of orphan drugs on a Part D formulary were placed on the highest cost-sharing tier.[13] A KFF analysis of 2023 Medicare Part D plans found that in 12 of the 16 national prescription drug plans, co-insurance amounts for non-preferred drugs range from 40-50 percent, with similar trends in prior plan years.[14] While we recognize that patient out-of-pocket costs for Medicare Part D are set to be capped at $2,000 beginning in 2025, high out-of-pocket costs remain a barrier for many patients, particularly those just above the qualification level for the low-income subsidy, and the MPNPP is expected to have far-reaching implications beyond Medicare plans.

We encourage CMS to think critically about how best to balance patient out-of-pocket cost and access with potentially misaligned incentives. While 95 percent of rare diseases have no FDA approved treatment, some rare disease areas, such as rare cancers, have more than one treatment available. Certain therapies, particularly those that have been on the market for a significant number of years, may not be as clinically applicable as newer therapies, which may provide more benefit, a preferable route of administration, or fewer or lesser side effects. Inadvertently incentivizing physicians and patients to choose an inferior therapy due to cost and ensuring patient access to necessary medication is a delicate balance for which there is no easy solution.

[13] *Predictors of Orphan Drug Coverage Restrictions in Medicare Part D.* Yehia, et. Al. American Journal of Managed Care. (September, 2020). https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d

[14] *Medicare Part D: A First Look at Medicare Drug Plans in 2023.* Cubanski et. Al. KFF. (10 November, 2022.) https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/

NORD believes health care providers, and their patients, are best positioned to choose the medication that is right for them. Yet, patients trying to access medications on higher formulary tiers frequently run into utilization management barriers, such as prior authorization and step therapy. A 2020 study found that 76 percent orphan drugs on Medicare Part D formularies were subject to prior authorization.[15]

To rectify these cost and access issues for rare disease patients trying to access medications, we encourage CMS to consider implementing a requirement that significantly reduces or eliminates step therapy and prior authorization requirements for negotiated products. Additionally, we recommend requiring that formularies place negotiated therapies on more preferential tier, to reduce patient cost and access burdens.

However, we also realize that monitoring and surveillance of formulary placement and utilization management will be key. We urge CMS to work with the patient, caregiver and provider communities to understand trends and changes in formulary placement, the use of utilization management, or other ways that may impact availability and access to these products.

Recommendation 3: Reconsider CMS' interpretation of orphan drug exclusion provision (Section 30.1.1).

Although we recognize that CMS has established their interpretation of the orphan drug exclusion set forth in accordance with Section 1192(e)(3)(A), we remain greatly concerned that the agency's narrow interpretation could have significant negative ramifications for the future of rare disease drug development. Today, about 60 percent of all orphan drugs have a single FDA-approved orphan indication, whereas only about 20 percent are FDA-approved for both orphan and non-orphan indications.[16] Among the drugs that only have orphan indications, fewer than a 25 percent have more than one FDA-approved indication and fewer than 10 percent have three or more approved indications.[17] Similarly, among the drugs that have both orphan and non-orphan indications, less than 20 percent have three or more orphan indications.

Still, developing already-approved therapies to treat additional rare diseases is a critical strategy to address the rare disease community's significant unmet need because these drugs have already proven to be safe for humans. In fact, according to a recent analysis, over 3,000 unique drugs have been FDA designated as rare disease drugs and studied, with about a 25 percent of these

[15] *Predictors of Orphan Drug Coverage Restrictions in Medicare Part D.* Yehia, et. Al. American Journal of Managed Care. (September, 2020). https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d

[16] *Orphan Drugs in the United States.* IQVIA. (2019). https://rarediseases.org/wp-content/uploads/2022/10/orphan-drugs-in-the-united-states-NRD-2020.pdf

[17] Ibid

drugs being designated for more than one rare disease.[18] Serial innovation and the investigation and development of multiple rare disease indications of use is an increasingly important dimension of orphan drug development, making the preservation of incentives to further develop drugs to treat additional orphan diseases after they have entered the market particularly important.

Orphan drug development is a lengthy and difficult process. Due to the complexity and long timeline from initial drug discovery and early research and development to FDA approval, drug sponsors are making decisions today that will impact their investments and drug development pipeline for decades to come. A typical orphan drug takes over 15 years to go from first patent filing to product launch, 18% longer than the average time for all new drugs.[19] Another study found that drugs with an orphan designation take over 550 days longer than drugs without an orphan designation.[20] Remaining uncertainty about if, when, and how rare disease drugs will become negotiation eligible creates strong disincentives to develop drugs for the limited populations impacted by rare diseases. Therefore, as part of the negotiation process, NORD urges CMS to make clear that research and development efforts in support of orphan therapies that address unmet needs will be treated favorably in the price negotiation process.

We again urge CMS to consider the language in Section 1192(e)(3), "the drug or biological drug must (1) be designated as a drug for only one rare disease or condition under section 526 of the FFD&C Act and (2) be approved by the FDA for only one or more indications within such designated rare disease or condition" as a two-prong test, rather than considering each clause independently. This interpretation is consistent with Congressional intent and has more limited implications for research and development into the rare disease space. Considering each of the two clauses independently inadvertently disincentivizes manufacturers of rare disease products and reduces incentives in repurposing products, an effort the Biden administration granted $50M through ARPA-H to support earlier this year.[21]

Disincentivizing manufacturers to seek additional designations has the unintended consequence of pushing manufacturers to pursue research into new molecular entities (NMEs) rather than

[18] Miller, KL, Kraft, S, Ipe, A, and Fermaglich, L. Drugs and biologics receiving FDA orphan drug designation: an analysis of the most frequently designated products and their repositioning strategies. Expert Opin Orphan Drugs. 2022 Mar 1;9(11-12):265-272. doi:10.1080/21678707.2021.2047021.

[19] *Facing Many Challenges, Orphan Drugs Take 18% Longer to Develop.* Tufts. (14 May, 2018). https://www.centerwatch.com/articles/12603-tufts-facing-many-challenges-orphan-drugs-take-18-longer-to-develop

[20] *Clinical development times for innovative drugs.* Brown, et. Al. National Library of Medicine. (1 November, 2023). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9869766/

[21] *ARPA-H awards AI-driven project to repurpose approved medications.* ARPA-H. (28 February, 2024). https://arpa-h.gov/news-and-events/arpa-h-awards-ai-driven-project-repurpose-approved-medications

repurposing additional products.[22] Though NMEs play a crucial role in identifying treatments and cures for rare diseases, drug repurposing is a crucial part of the treatment ecosystem. Drug repurposing takes less time, is less expensive for the manufacturer and the system, and is successful in bringing a treatment to market more frequently than NME development.[23] CMS' current interpretation of the orphan drug exclusion runs contrary to the intent of the Medicare drug price negotiation program, as it may result in increased systemic costs and increased patient out of pocket costs. As such, we urge CMS to reconsider their interpretation of the orphan drug exclusion to protect incentives to continue innovation for existing products.

We thank CMS again for the opportunity to comment on this guidance and look forward to working with CMS to ensure rare disease patients can fully participate in and benefit from the Medicare Drug Price Negotiation Program. For questions related to this letter, please contact Karin Hoelzer, Director of Policy and Regulatory Affairs at KHoelzer@rarediseases.org or Mason Barrett, Policy Analyst at MBarrett@rarediseases.org.

Sincerely,

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[22] *Does Therapeutic Repurposing in Cancer Meet the Expectations of Having Drugs at a Lower Price?* Fierro et., al. National Library of Medicine. (8 March, 2023). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10097740/#:~:text=The%20total%20cost%20of%20bringing,repurposing%20averages%20US%248.4%20million.

[23] Ibid