VIA ELECTRONIC SUBMISSION

May 22, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: CMS-10849
Information Collection Request (ICR) for the Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act

Dear Administrator Brooks-LaSure:

Haystack Project appreciates the opportunity to provide comments on the Centers for Medicare & Medicaid Services' (CMS') Information Collection Request (ICR) in connection with the manufacturer counteroffer process under the Inflation Reduction Act's (IRA's) Drug Price Negotiation Program (DPNP).

Haystack Project is a 501(c)(3) non-profit organization enabling our membership of 140+ rare and ultra-rare disease patient advocacy organizations to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for all Americans. We strive to amplify the patient and caregiver voice in disease states where unmet need is high and treatment delays and inadequacies can be catastrophic.

Since its inception, Haystack Project has engaged with CMS through comments on CMMI model proposals, implementation and refinement of the Medicare Quality Payment Program (QPP) and the Affordable Care Act, as well as throughout annual rulemaking cycles refining policies under Medicare Parts A, B, C and D.

Since enactment of the IRA, Haystack Project membership has continued to grow – both in numbers (nearly doubling to over 140 ultra-rare disease advocacy organizations) and in the collective concern that the drug price negotiation program could threaten the fragile balance

that has historically enabled an adequate return on investment for targeted treatments in small population diseases and rare cancers.

Our community of patients and caregivers were initially hopeful that CMS would implement the drug price negotiation program with proactive and intentional consideration of the complex set of incentives and risks associated with developing treatments in the ultra-rare disease space. Our comments (attached) to CMS' Initial Guidance implementing the DPNP articulated our concerns with CMS' approach. Haystack Project restated those concerns within the context of the negotiation data elements ICR, asserting that the sufficiency of the data elements within the ICR and the burden associated with providing that information were inextricably linked to and vastly impacted by the Initial Guidance. Unfortunately, each piece of the process CMS releases has revealed the Agency's adherence to an approach that will unnecessarily, and potentially inextricably, tip the scales away from innovation.

Haystack Project believes it is not only possible, but imperative, that CMS implement the DPNP to align with our shared goal of ensuring that Medicare drug prices reflect treatment value ***without*** disrupting incentives toward innovation in rare disease therapies. We reiterate our recommendations that CMS:

- Reconsider its decision to define qualifying single source drug based on moiety or active ingredient rather than NDA/BLA.

- Replace the Primary/Secondary Manufacturer framework with a more flexible approach that can be adapted to the contours of contractual arrangements when there is more than one manufacturer for a selected drug.

We also provide our comments, concerns, and recommendations specific to the counteroffer process and urge CMS to be more transparent and collaborative with respect to the negotiation process as a whole. Unfortunately, stakeholder input on the counteroffer process is substantially compromised by the fact that the processes leading to and following this phase of negotiation are unknown to the public.

Background: Individuals with Rare and Ultra-Rare Conditions and Rare Cancers will be Disproportionately Impacted by the IRA's Potential to Deter Innovation.

Although countless lives have been improved or saved by new therapies enabled by Congress' set of incentives for orphan drugs, significant unmet need predominates in extremely rare conditions and rare cancers:

- Of the approximately 7,000 rare diseases identified to date, 95% have no FDA-approved treatment option.
- 80% of rare diseases are genetic in origin, and present throughout a person's life, even if symptoms are not immediately apparent.

- Diagnosing a patient with a rare disorder is usually a multi-year process involving a series of primary care clinicians, specialists, and diagnostic testing regimens – extreme rarity of a disorder compounds the resources required for diagnosis.
    - Patients often progress to more serious and more costly disease states by the time they receive a diagnosis.
- If a diagnosed condition has no FDA-approved option, treatment often involves off-label use of existing products.
- Approximately half of identified rare diseases do not have a disease-specific advocacy network or organization supporting research and development, and lack of disease-specific natural history severely complicates research toward new, targeted treatments.

Patients suffering from rare diseases that are currently untreatable have maintained hope that the incentives toward innovation, coupled with increased scientific understanding of disease mechanisms, would stimulate progress toward treatment and, eventually, a cure. For patient populations approaching the 200,000 orphan disease limit, current incentives have proven to be sufficiently robust to mitigate clinical trial and reimbursement risks. As affected populations dwindle below 20,000 or even into and below the hundreds, the balance can be far more tenuous, and risks or uncertainties can discourage the investor interest required to take promising therapeutic candidates from bench to market. The DPNP has the potential to place an abbreviated timeline for recouping return on investment into the already-complex risk/benefit analysis for ultra-rare disease treatments.

Haystack Project urges CMS to reconsider its decision to identify negotiation-eligible drugs based on moiety or active ingredient rather than NDA/BLA.

Haystack Project had anticipated that CMS would identify negotiation-eligible drugs on the basis of NDA/BLA approvals given the statutory reference to NDA/BLA approval date in identifying negotiation-eligible drugs. CMS' decision to broadly define qualifying single source drug' for negotiation eligibility purposes was unexpected and will likely negate existing incentives for securing approvals in small population conditions.

- Under CMS' definition, a drug with an NDA/BLA approval could be negotiation-eligible earlier than the 9 or 13 years outlined in the IRA if a reference drug is negotiation-eligible.

    - CMS has not indicated how it would assess information on multiple NDAs that include one or more orphan indications. Would value in small population indications have a greater or lesser impact on CMS' initial offer compared to uses in more common diseases?

    - It is also unclear whether CMS would subject a subsequently-approved orphan indication to the maximum fair price (MFP).

        - The negotiation data elements ICR indicated that CMS would not take into account any research and development costs associated with indications that had not yet been approved. It is unclear whether CMS would accept this information within the counteroffer process.

        - CMS' definition of qualifying single source drug could increase pressures on manufacturers to sell follow-on NDAs/BLAs and exact artificial negative pressures on the value of those asset(s) that ultimately deter innovation in ultra-rare diseases.

CMS has yet to respond to our concerns that CMS' definition went beyond the type of simple implementation of statutory requirements Congress envisioned the Agency completing without notice and comment. We remain concerned that CMS made a policy decision, and that policy decision has driven a statutory interpretation beyond and in likely conflict with the plain language of the IRA.

- The MFP is a single price for a drug under the Medicare program. The IRA negotiation process outlines considerations such as alternative therapies, unmet need, and the extent to which a treatment represents an advance in therapeutic options.

    - Had CMS adhered to the NDA/BLA driven approach to drug selection outlined in the IRA, data collected on a drug's value to patients would be clearly related to the NDA/BLA and the patients and conditions to which it applies.

    - Aggregating NDAs/BLAs into a single negotiation-eligible drug reduces the nexus between data collected and the true value of the treatment to patients.

        - The value determination will place unwarranted emphasis on large patient populations in disease states with multiple treatment options.

        - Any value in treating rare and ultra-rare patients will be diluted and ultimately rendered irrelevant. This would be the case even if the drug was the only approved option in treating a life-threatening disease.

    - Information on alternative therapies is indication-specific. CMS' decision to utilize costs of alternative therapies in calculating an initial offer does not appear reasonable unless the selected drug is defined by an NDA/BLA rather than moiety or active ingredient.

        - Aggregating NDAs/BLAs with multiple, potential diverse, indications and patient populations would lead to a MFP that aligns with the NDA/BLA with the largest patient population.

        - Haystack Project believes that this result is bad for rare and ultra-rare patients waiting for a treatment to come to market and that the MFP, as applied to that NDA/BLA, would be arbitrary rather than negotiated.

        - Stakeholders cannot contribute meaningful feedback to the counteroffer ICR without further guidance on how CMS would identify a single MFP across NDAs/BLAs in diverse indications with variable unmet needs and no single alternative treatment optioin

- CMS' definition of unmet medical need is narrow and fails to consider unmet needs associated with patient subpopulations, or a general need within a condition that is not adequately addressed by available therapeutic options.
    - Failure to determine unmet need based on NDA/BLA will make it impossible for CMS to incorporate actual, real-world unmet needs across divergent patient populations and disease states. Once again, aggregating unmet need will yield a result that is innacurate and arbitrary if applied equally to indications with and without alternative treatment options.

CMS' Primary/Secondary Manufacturer structures are particularly problematic within the context of the small biotech and pharmaceutical manufacturers that have historically developed rare disease treatments.

Arrangements between an early-stage innovator and a larger manufacturer with commercialization expertise are common in the rare and ultra-rare disease space. Agreements between manufacturers are generally based on contracts negotiated and executed well before the parties perform any manufacturing, distribution, and/or marketing activities, and are based on the laws and regulations in place at the time. Neither the IRA, the ICR, nor CMS' Initial Guidance provide for any mechanism through which a primary manufacturer can secure information required within the ICR from a secondary manufacturer.

The counteroffer process introduces additional wrinkles that CMS may not have considered. The overarching lack of transparency into the entirety of the negotiation process makes it impossible to determine how CMS will accommodate situations in which the BLA holder has contractual arrangements that preclude it from agreeing to an MFP, proposing a counteroffer, or rejecting CMS' initial offer. We strongly urge CMS to engage industry stakeholders to pressure-test the assumption that all NDA/BLA holders will have (1) access to all information CMS needs within the DPNP process; (2) authority to disclose all required information; and (3) authority to agree to or reject an initial offer or propose a counteroffer applicable to all NDAs/BLAs within CMS' definition of a qualifying single source drug selected for negotation.

Haystack Project believes that the most prudent approach would be for CMS to refine its definition of a qualifying single source drug and implement a more flexible mechanism for

obtaining negotiation-relevant information and securing agreement on an MFP. Put simply, the burden associated with providing information a manufacturer has no legal recourse to access, much less disclose, and penalizing entities for failing to act on drug pricing agreements they are contractually prohibited from entering into is both enormous and avoidable.

The information currently available on the negotiation process does not illuminate how non-manufacturer stakeholder input will be incorporated into the initial offer or the counteroffer process.

The negotiation data elements ICR provided for public input into the consideration of alternative therapeutic options. We previously expressed our concerns that the process for submission, limitation of information content and quantity, and certification requirement will substantially deter input from patient advocacy organizations. Haystack Project reiterates those concerns and further urges CMS to outline how input from patients and providers will be incorproated into the initial offer, as well as the extent to which manufacturers will have access to that information as they propose a counteroffer.

In addition, off-label uses in ultra-rare conditions may not be factored into CMS' initial offer. Permitting manufacturers to submit information on unmet needs and other relevant information within the counteroffer process is an important step toward underscoring the relevance of our patient communities to manufacturers and the Medicare program.

- Most patients with rare and ultra-rare conditions have no FDA-approved treatment options and rely on off-label uses of existing treatments. These uses are rarely included within the compendia CMS lists as acceptable sources of information on off-label indications.

- CMS has not articulated how the information and scientific evidence it collects will be used to inform decisions on therapeutic alternatives or what evidence is particularly important in the negotiation process.

- Rare and ultra-rare disease patients will find it difficult to challenge CMS identification of an alternative treatment option unless CMS provides information on the treatments it is considering. For example, CMS may focus on a high-volume indication and identify multiple treatment options that could be substituted for the selected drug.

    - Our patient communities cannot provide information on whether those therapies are, in fact, actual options in treating their condition or contraindicated/ineffective unless we know what those alternatives are.

    - Without that information, patient advocacy organizations may not be able to identify condition-specific options or state that there are no alternative therapies.

The Orphan Drug Exclusion Should be Implemented to Maintain Incentives for Developing New Treatments in Rare Conditions and Expanding Labeled Indications of Existing Therapies

Haystack Project appreciates that CMS recognizes the need to protect access to orphan drugs currently available as well as innovations that have yet to be developed. We fully support CMS' determination to qualify drugs for the exclusion based on whether approved indications are within a single designation. Unfortunately, the policy on defining a qualifying single source drug by active moiety/ingredient discussed above will likely reduce manufacturer interest in pursuing multiple indications within or beyond a single designation.

The initial year(s) for the DPNP will likely shape investory perspectives on the value of pursuing new treatments for ultra-rare diseases and/or seeking FDA approval for new ultra-rare uses of existing drugs. It is, therefore, imperative that CMS take steps toward protecting the incentives currently in place for rare disease product development. Patients with ultra-rare conditions and rare cancers are particularly concerned that:

- Manufacturers will face pressures to focus on an orphan indication with the largest patient population.

- Research and development programs confirming clinical benefit for accelerated approval treatments may be halted and indications withdrawn if those indications fall outside a single orphan drug designation.

- Pressures to focus on larger-population orphan designations/indications could delay product approval and increase initial research and development costs.

- The IRA's chilling effect on research and development will fall disproportionately on patients with ultra-rare diseases and rare cancers.

- Investors and shareholders will seek to ensure that initial price points for newly-approved drugs are sufficient to recoup research and development costs and achieve a profit margin from successful innovations.

Once again, we appreciate that CMS has limited discretion in implementing the orphan drug exclusion. In its Initial Guidance, CMS sought stakeholder feedback on how it might implement the IRA drug price negotiation program without detering access and innovation in rare diseases. We urge CMS to take concrete steps to preserve viability of orphan indications with particular atttention to the unique circumstances within the ultra-rare disease communities, including that it:

- Work with patient and industry stakeholders to remove the single orphan designation requirement from the IRA orphan drug exception.

- Identify qualifying single source drugs by NDA/BLA (as more fully outlined in the preceding sections).

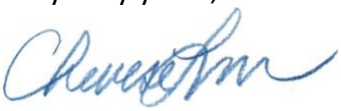
- Engage in meaningful dialogue with Haystack Project and other patient-centered ultra-rare disease organizations to preserve the balance in incentives and risks that has spurred innovation in rare and ultra-rare disease treatments, including through CMMI and CMS' general demonstration authority.

- Implement a transparent process for manufacturers to submit evidence demonstrating that a particular product is eligible for the orphan drug exclusion.

Conclusion

Haystack Project appreciates the opportunity to submit feedback on the counteroffer ICR. Once again, we thank you for your consideration of our comments. If you have any questions, please contact our policy consultant M Kay Scanlan, JD at 410.504.2324.

Very truly yours,



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