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December 24, 2025

Mehmet Oz, MD, MBA, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

RE: **Drug Price Negotiation for Initial Price Applicability Year 2028 under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849) - (IRA)**
OMB Control Number: 0938-1452
ICR Reference Number: 202511-0938-003

Dear Administrator Oz:

The Protecting Innovation in Rare Cancers (PIRC) coalition appreciates the opportunity to submit feedback, including input from our patient communities, on the above-referenced Information Collection Request for initial price applicability year 2028 (the ICR).

PIRC is a collaborative, multi-stakeholder, advocacy coalition focused on improving access to and affordability of existing treatments while preserving incentives to advance future innovations in rare cancers. The coalition was convened in 2023 to fulfill an important role in exchanging information, identifying, and resolving barriers to access and innovation, and educating both our rare cancer communities and policymakers on the Inflation Reduction Act (IRA) and its impact on rare cancer patients.

PIRC recognizes that the Medicare Drug Price Negotiation Program (MDPNP) has become a key factor as investors and manufacturers calculate the feasibility of pursuing a particular drug candidate for a specific indication. Our rare cancer patient communities remain concerned that investors and manufacturers have viewed MDPNP implementation as tipping

the scales away from innovation in cancers that impact too few patients to ensure a rapid return on investment and potential revenue in proportion to risk. The recent refinements in the orphan drug exemption and the Administration's statements encouraging repeal of the differential timeline to negotiation eligibility disfavoring small molecules are cause for optimism among rare cancer patient communities. Unfortunately, the MDPNP refinements to date have not resolved the high potential for unintended consequences likely to disproportionately hinder research in rare and ultra-rare disease treatments with high unmet need.

PIRC's comments provide a brief discussion of the challenges to research and development (R&D) in rare cancers. We highlight aspects of the MDPNP and/or CMS' implementation of the negotiation program that have already disrupted the oncology R&D paradigm to the disproportionate detriment of rare cancer patients. Our concerns and recommendations are intended to help CMS maintain a post-MDPNP access and innovation landscape that does not leave rare cancer patients with fewer new treatment advances and constricted access to existing therapies. PIRC and its rare cancer communities:

- Urge CMS to utilize its administrative discretion (and work with Congress to expand that discretion) on renegotiation selection to deter monopolistic behaviors while protecting innovation in rare cancers.
- Request that CMS resolve the lack of transparency and asymmetry in how it determines the extent to which a manufacturer has recouped its investment in a selected drug.
- Urge CMS to acknowledge and respond to the fact that the combination of IRA's Part D redesign and impending implementation of MFPs has led to payer utilization management strategies that are based on differential plan financial incentives rather than evidence.
- Highlight PIRC's significant concerns that mechanisms for effectuating the MFP for Part B drugs could have unintended consequences for providers and patients.
    - *We recommend that CMS engage a broad set of stakeholders and focus on minimizing provider burden as it considers this aspect of the MDPNP*.
- Appreciate CMS' continuing efforts to gather meaningful information from non-manufacturer stakeholders and ask that the mechanism for soliciting feedback account for patient advocacy organization input.
- Reiterate our request that CMS align its stakeholder engagement approach with the Cancer Support Community's (CSC's) *Principles for Patient-Centered Engagement*.

Background:

Over the initial two years of MDPNP implementation, five oncology drugs have been selected for negotiation, two of which are indicated for chronic lymphocytic leukemia (CLL) and functioned as "therapeutic alternatives" for each other. We expect that as Part B drugs become eligible for selection, the proportion of oncology agents subject to negotiated prices will put pressures on manufacturers and investors to re-evaluate whether, how, and when to direct funds toward cancer research and development.

While we may never have a clear line of sight into rare cancer research programs that are abandoned early due to MDPNP-related financial uncertainties, the August 2023 announcement that was considering delaying its ovarian cancer indication for a small molecule until it could simultaneously submit an NDA for its larger-population prostate cancer indication. The manufacturer cited its consideration of the "nine years of Medicare sales for both ovarian and prostate cancer" at full price, versus losing a few years on the prostate cancer indication. While this disincentive for orphan indications as a "first approval," has been resolved through a statutory expansion of the orphan drug exemption, it illustrates how MDPNP implementation can serve as a powerful disincentive for investment in R&D programs with small addressable populations. If, for example, a treatment gains its first approval in prostate cancer, new investment in follow-on rare cancer indications will depend on the likely timeline to MDPNP selection, the R&D risk, and the adequacy of the addressable population(s).

We are also concerned that since cancer treatments are far less likely to have generic competition than treatments for more common conditions, these treatments are more likely to be subject to serial selection and the eventual punitive pricing for "long monopoly" status. The combined effect of emerging follow-on indications and lack of generic competition creates a landscape that is not only burdensome but either an added "value" to patients (follow-on indications) or outside the direct control of manufacturers (lack of generic market interest). PIRC has previously noted a recent study that compared generic competition for oncologic drugs with that of cardiovascular treatments.

- A smaller proportion of oncologic products have generics (49% vs. 80%).
- For off-patent drugs, the median time from approval to the first generic approval is longer for oncologic products compared to cardiovascular products (15.4 years versus 12.3 years).

- Factors impeding generic development in oncology include product dosage form and FDA recommendations requiring patient enrollment for cancer treatment bioequivalence studies.

Availability of generic competition may also be less effective in reducing healthcare costs in cancer than in nonmalignant conditions. This is because newer versions of older cancer drugs often offer improvements in progression-free survival and/or overall survival and become replacements for, rather than alternatives to, older treatments. Moreover, once a cancer drug is subject to an MFP, the lower price point for the innovator product makes investment in developing a generic alternative proportionately less attractive.

PIRC urges CMS to utilize its administrative discretion (and work with Congress to expand that discretion) on renegotiation selection to deter monopolistic behaviors while protecting innovation in rare cancers.

Manufacturers and investors have started to reprioritize their portfolios in ways that signal a clear threat to future innovation in rare and ultra-rare diseases and rare cancers. Selecting drugs for renegotiation based solely upon new uses opens the potential that a drug would be subject to renegotiation multiple times over a short period – due to both new indications and changes in monopoly status to an extended- and then a long-monopoly drug. Although competition from a generic or biosimilar would end this cycle, manufacturers cannot facilitate generic market entry without the risk that its actions would deem the generic an authorized generic with no impact on renegotiation eligibility.

For patients with rare and ultra-rare cancers, follow-on indications are not incremental commercial opportunities; they are often the *only* pathway to improved outcomes for biologically distinct subtypes, biomarker-defined populations, or lines of therapy without a standard of care capable of delivering a durable clinical benefit. Generating the evidence to support these new uses frequently requires substantial post-approval investment, including confirmatory trials, registries, and long-term follow-up—obligations that are often conditions of FDA approval, particularly under the Accelerated Approval pathway. Treating the pursuit of additional indications as a trigger for renegotiation risks creating a disincentive to generate exactly the evidence that rare cancer patients depend upon for access to new, potentially life-extending therapies.

Notably, even organizations that are highly skeptical of drug price increases have acknowledged that new clinical evidence and expanded uses can represent added value to

the health system. For example, the Institute for Clinical and Economic Review's (ICER's) "unsupported price increase" framework has distinguished between price increases that occur absent new evidence and those associated with new clinical data or additional indications, recognizing that expanded benefits may be relevant to assessments of value. This distinction underscores an important principle: new indications can reflect increased patient benefit, not merely increased utilization. Using new indications as a basis to seek additional price cuts acts would create an unpredictable incremental risk that, considering the cost and logistic hurdles associated with evidence generation in rare cancers, risks undermining patient access and discouraging continued research in areas of high unmet need.

We urge CMS to carefully consider the impact any renegotiation selection might have on future innovation and to use its selection discretion only when manufacturer behaviors run counter to the interests of patients and the health system. We also strongly recommend that CMS engage Congress to remove the mandatory renegotiation selection provision for change in monopoly status and, if warranted, replace it with a provision that punishes behavior rather than "status." In the interim, CMS should select drugs for renegotiation in a manner that does not impose a financial penalty for manufacturer investments in repurposing drugs to new indications.

PIRC asks that CMS resolve the lack of transparency and asymmetry in how it determines the extent to which a manufacturer has recouped its investment in a selected drug.

Patient communities remain confused on how R&D costs vs. revenue impact price negotiations.

PIRC understands that manufacturer R&D costs and analyses on cost recoupment may provide relevant information as the Agency calculates an initial offer and establishes a Maximum Fair Price (MFP). There is, however, a lack of transparency between CMS and the patient community on how this information impacts the negotiation process. Similarly, there does not appear to be any clear contingency for addressing situations where costs have not been recouped – either within the initial negotiation or a renegotiation. We urge CMS to include in its MFP summaries a clear discussion on how this data was used and the impact it had on the initial offer as well as the MFP.

Failure to consider global R&D costs while including global revenue disproportionately disadvantages rare and ultra-rare disease development.

CMS's continued reliance on global revenue data, without a parallel and systematic accounting of global regulatory and development costs, risks producing distorted assessments of a drug's economic context. To the extent that recoupment of investment has a tangible impact on MFP, this asymmetry is particularly consequential for rare cancers, where global development and regulatory strategies are often necessary to make research feasible. Multi-site, global studies support **both** U.S. and global commercialization; without international sites it is often all but impossible to recruit a sufficient participation population to enable meaningful data analysis. If global revenue is considered relevant to negotiation, then the associated global costs required to achieve that revenue must also be considered to avoid penalizing evidence generation and access.

Disincentives for rare cancer R&D are magnified when follow-on rare cancer indications are pursued under Accelerated Approval with confirmatory obligations—because those obligations are costly, long-duration, and often global by necessity.

For rare oncology products, FDA approval is often contingent upon the completion of post-marketing requirements and commitments, including confirmatory clinical trials, patient registries, REMS programs, and long-term safety follow-up. These obligations frequently extend for years or even decades after initial approval and require substantial, ongoing investment. Importantly, these costs are not discretionary; they are conditions of continued approval and are often incurred during years in which Medicare price negotiation or renegotiation may occur. CMS's evaluation of R&D and approval-related costs should explicitly recognize FDA-mandated post-approval obligations, including those incurred in future years, to avoid understating the true cost of developing and maintaining access to therapies for rare cancers.

In addition, rare cancer confirmatory studies are extremely difficult—if not impossible—to conduct solely within the United States once the product is commercially available (either as off-label, compendia-listed uses or through Accelerated Approval). Ethical considerations, patient access to approved therapy, and small patient populations often make global enrollment and multi-regional trial designs the only real option. These confirmatory studies are undertaken to satisfy U.S. regulatory requirements and frequently also support international regulatory approvals. These costs, however, could be ignored within the MDPNP process because they are associated with non-US studies and may be incurred in the future. In that context, a pricing framework that counts global revenue while discounting the global costs of evidence generation can further erode the business case for follow-on indications in rare cancers.

Viewed holistically, the MDPNP's selective data consideration and lack of clear pricing "upside" when R&D costs are not recouped, combined with renegotiation triggers can all but eliminate any business case for pursuing follow-on rare cancer indications.

For rare oncology therapies with ongoing FDA-mandated post-approval evidence obligations, repeated and foreseeable price resets (initial MFP plus renegotiation triggers such as new indications and monopoly-status changes) can create a cumulative incentive problem. Over time, this can make continued U.S. commercialization economically irrational for some products with small treated populations—risking reduced investment in confirmatory evidence generation and new accelerated approvals.

***Hypothetical**:* A targeted therapy initially approved for a non-orphan oncology indication receives accelerated approval for an ultra-rare cancer subtype based on a surrogate endpoint. FDA requires a large confirmatory RCT that cannot be completed without global enrollment and long follow-up. The drug is later selected for negotiation and receives an MFP beginning IPAY 2028. Post-MFP, the sponsor considers investing in a second ultra-rare indication (or biomarker-defined subset) that would require additional trials/registry work and would likely be pursued under accelerated approval or with major postmarketing commitments. If that new indication makes the drug renegotiation-eligible—and when, separately, the drug experiences a monopoly status change—CMS's IPAY 2028 approach signals that renegotiation becomes highly likely (and increasingly punitive) despite manufacturer behavior aligning with patient interests.

In this setting, a rational board and shareholders could view the decision to pursue the second rare cancer follow-on indication investment as value-destructive: the company assumes the cost and risk of additional R&D and FDA obligations while facing a predictable "price reset" that limits the potential to recoup high R&D costs within a small patient population.

The combination of IRA's Part D redesign and impending implementation of MFPs has led to payer utilization management strategies that are based on differential plan financial incentives rather than evidence.

PIRC understands that the MDPNP is just one part of a broader set of changes to the Part D program. Part D redesign has shifted a greater share of prescription drug costs onto Part D plans. Most payers are acutely aware of the increased liability for Part D plans due to the IRA's redesign provision. Over the past 2 years, CMS has recognized the potential for patient access constrictions and increased provider burden due to increased utilization management among

plans. While PIRC appreciates CMS' intention to monitor plan activities, our patient and provider communities report increasing, and increasingly restrictive/onerous sets of coverage criteria, prior authorization and documentation requirements, and, more recently, step therapy protocols that run counter to NCCN guidelines.

PIRC is increasingly concerned that by simply "monitoring" plan activities CMS will fail to sufficiently protect Medicare beneficiaries. Without CMS intervention and/or oversight, it is likely that plans will continue to determine which drug(s) are associated with the lowest financial liability and steer patients toward that drug through formulary inclusion/exclusion, tier placement, and/or utilization management tools.

The simplest, most pragmatic recourse for CMS is to reinforce the protected classes framework and require that Part D plans, including MA-PD plans, include all available treatment options within the protected classes on their formularies, without imposing step therapy protocols. We have previously conveyed our concerns about the year-over-year erosion of protections for Part D drugs within the six "protected" classes, i.e., immune-suppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics. CMS' designated these classes of drugs to require that plans include all or substantially all drugs within the class. The rationale --to ensure that formulary designs do not disadvantage and discriminate against vulnerable patients requiring access to specific drugs or combinations of drugs -- is as valid today as it was when the protected classes were created.

In addition, we urge CMS to:

- Increase Agency oversight to ensure that plan formularies include all necessary medications, base all utilization management strategies on clinical evidence, and maintain expedited formulary exception and claim denial reconsideration processes so vulnerable patients, including those with rare cancers, can get the treatment they need when they need it.
- Provide Part D plans with clear guidance on what they can and cannot do with respect to coverage, formulary tiers and utilization management (UM) tools.
- Proactively monitor the impact of the Manufacturer Discount Program, the MDPNP, and other D redesign provisions on formulary decisions and UM practices.
- Identify and mitigate any access constrictions, on the plan and sponsor levels as well as program wide.

- Establish a formal mechanism for patients and patient advocacy organizations to communicate their experiences, including any barriers to getting their prescribed medications when they need them, directly with CMS. We urge the Agency to create a dedicated communication channel as well as a set of proactive forums for patients and clinicians.

This will ensure that patient treatments are aligned with NCCN guidelines and shared decision making, not Part D plan economics.

PIRC has significant concerns that mechanisms for effectuating the MFP for Part B drugs could have unintended consequences for providers and patients. We recommend that CMS engage a broad set of stakeholders and focus on minimizing provider burden as it considers this aspect of the MDPNP.

Implementing the MFP discounts for Part B drugs will entail new administrative and logistical processes that could burden healthcare providers and, indirectly, patients. Providers administering Part B drugs subject to an MFP will be receiving significantly lower reimbursement and, as the MFP is renegotiated to lower levels, these cuts could tip the scales for some clinicians and centers and reduce the set of willing providers for negotiated Part B drugs. Rural patients with rare cancers could face access constrictions requiring them to either travel to distant academic medical centers or switch treatment regimens. We also expect that hospitals relying on 340B discounts to maintain their cancer infusion capabilities will find any incremental burden that accompanies a cut in revenue to be unacceptable. We urge CMS to keep this reality top of mind as it considers options for effectuating the MFP for Part B drugs.

CMS has previously outlined mechanisms to ensure manufacturers provide the negotiated price to "dispensing" providers. Both approaches, however, have drawbacks when applied to Part B drugs that could dramatically change how and where rare cancer patients receive infused treatments. These options can be broadly categorized below:

- Prospective Price Reduction Model: Providers would acquire the drug upfront at or below the MFP for their Medicare patients.
    - This alleviates the burden of purchasing drugs at full price and waiting for a rebate
    - Clinics would likely need to maintain separate stock for MFP-eligible Medicare patients

    - Inventory segregation is not only complex logistically but it could require additional storage space and staff
    - These issues are compounded for biologics requiring refrigeration or special handling.

- Retrospective Rebate (Reconciliation) Model: Under this model, providers continue purchasing drugs at normal prices, administer the therapy, and receive reimbursement based on the MFP. The manufacturer would then refund the difference between the purchase price and the MFP.
    - Although this approach avoids multiple inventories, it shifts a financial burden onto providers.
    - If the transaction is processed in the same manner as a Part D refund, a provider could have a 6-8 week wait for each dispensed dose.
    - Small practices and providers with thin cashflow margins will struggle to absorb this financial strain or, alternatively, have to borrow funds to bridge the gap.
    - Providers could also have significant administrative overhead associated with implementing new tracking systems, contracting facilitators or distributors for support, and ensuring compliance with CMS's requirements.

PIRC's patient communities fear that the burdens of MFP effectuation, combined with the reduced revenue due to an MFP well below the ASP, will push some practices out of Medicare participation and lead others to refer Part B drug administration patients to hospitals. For patients, the administrative complexities could lead to inconveniences or delays. For example, clinics maintaining separate inventories might decide to simplify their procedures by reserving doses for Medicare patients and setting up administration on specific days. Under the retrospective model, provider financial strain could lead to delays reordering costly medications and disrupt patient treatment cycles.

We urge CMS to reach out to provider stakeholders to assess the impact the MFP and its effectuation will have and craft a process or set of processes that preserves, to the extent possible, the status quo for patients relying on Part B drugs for rare cancers and other serious conditions. Stakeholders should include:

- Community oncologist offices
- Independent infusion clinics
- Teaching hospitals
- 340B covered entities.

- Community cancer centers
- Rural oncologists
- Rural hospitals
- Hospitals, infusion centers, and providers in medically underserved areas

PIRC appreciates CMS' continuing efforts to gather meaningful information from non-manufacturer stakeholders.

PIRC appreciates that CMS responded to feedback from the patient and caregiver community and:

- Removed the need to "email register" to access Section I through the HPMS portal.
- Expanded and refined the information requested from patients, clinicians and researchers. PIRC particularly appreciates that CMS has included inquiries on:
    - access to the selected drug and therapeutic alternatives.
    - factors impacting choice of treatment
    - how clinicians assess whether a patient is tolerating and/or responding to the selected drug or therapeutic alternatives and when discontinuation or treatment change might be considered

PIRC is, however, concerned that the narrative descriptions of what constitutes a "therapeutic alternative" does not align with cancer care and NCCN guidelines. CMS noted that therapeutic alternatives in oncology must be indication and line of therapy specific. While these are important "requirements" for therapeutic alternatives, agents can differ by biomarker, subtype, prior therapy, tolerability, and combination use. Moreover, products within the same class that share an indication are not always clinically comparable or interchangeable. We ask that CMS use its stakeholder engagement events to gain a clear understanding of each selected drug and the set of therapeutic alternatives as informed by patient experience and defined by disease-specific experts.

Finally, we note that the form design and inquiries contemplate one submission per interested part per drug. We provided feedback through the HPMS portal in both negotiation cycles and found that the process within the first year (IPAY 2026) was easy to access and complete, and sufficiently flexible to enable patient advocacy organization responses to all questions on which the stakeholder chose to provide information. The questions, however, were extremely broad. The IPAY 2027 form, like the IPAY 2028 form, was sufficiently detailed to

generate relevant information with the detail CMS likely requires. Unfortunately, PIRC found that:

- The ”deadline” for submission changed multiple times from 11:59 ET to 11:59 PT and back again. This likely caused confusion from stakeholders and may have impeded responses.
- The HPMS system tended to “freeze” from time to time, requiring re-entry of information. CMS should consider prompting stakeholders to “save” their responses as they move from one question to the next.
- PIRC and participating patient organizations found the “screening” questions in each section might have precluded responses to any questions from a stakeholder not identifying as a patient/caregiver, clinician, researcher, or manufacturer. We note that CMS has specifically acknowledged the value of patient advocacy organization feedback. Our organizations serve patient communities and actively seek feedback from patients and caregivers, and often have medical advisory panels comprised of researchers and treating clinicians. We strongly urge CMS to incorporate a work-around into HPMS so that patient advocacy organizations can provide relevant feedback by answering questions directed to patients/caregivers, clinicians and researchers.

PIRC re-emphasizes its request that CMS align its stakeholder engagement approach with the Cancer Support Community’s (CSC’s) *Principles for Patient-Centered Engagement*.

PIRC has previously emphasized that stakeholder engagement activities related to the MDPNP should be accessible to patients and caregivers and invite dialogue among participants and between participants and CMS staff. We have also urged the Agency to continue engaging patients beyond the negotiation process to ensure that any unintended consequences from the MDPNP are quickly identified and resolved.

Last year, the Cancer Support Community (CSC) collaborated with other stakeholders to establish a set of recommendations for patient-centered engagement within the MDPNP process and to guide and support subsequent policy efforts to ensure patient access to necessary medications. These recommendations include:

- "Engage patient advocacy organizations, patients, and caregivers in structured, meaningful ways throughout the MDPNP process."[1]
- Define clinical benefit to prioritize evaluations around endpoints, patient reported outcomes, patient experience data including impact on quality of life, and preferences that matter most to patients living with cancer and other complex conditions. This includes both qualitative and quantitative measures such as clinical endpoints, patient preference data/models, patient reported outcomes, and social impacts.
- Develop critical infrastructure necessary to educate the patient community and facilitate meaningful feedback that prioritizes patient definitions of value, including feedback on the evidence being considered by CMS and whether it reflects patient experiences and preferred outcomes.[2]
- Refer to patient navigators to provide information to patients about the impact of these policies and to receive feedback from patients, with an explicit goal to identify any changes in utilization management practices as a result of IRA implementation.
- Develop a monitoring and evaluation platform and reporting framework surrounding the MDPNP and its impacts on patients to support continuous improvement in ongoing implementation.
- Collect and report specifically on access challenges facing patients as a result of the IRA to allow for continuous improvement of the MDPNP process and lessen the unintended consequences of this process on patients.
- Collect and incorporate meaningful data and real-world evidence that amplifies patient values and input within the MDPNP implementation process, including patient reported outcomes, patient experience data, impact to quality of life, and models that capture the dynamic and varied preferences of patients.
- Prioritize outreach to patients, people with disabilities, and people living in rural communitiesto ensure that the MDPNP supports all patient populations and does not threaten healthcare access.
- Consider the groups and populations that have not already engaged in defining patient-focused clinical benefit and impact of the MDPNP process and determine how best to activate those individuals.[3]

PIRC urges CMS to align its ongoing MDPNP efforts with these principles.

[1] *Patient-Centered Engagement*, https://www.cancersupportcommunity.org/sites/default/files/file/2025-03/Option%202%20-Principles%20for%20Patient-Centered%20Engagement%20for%20CMS.pdf.
[2] Id.
[3] Id.

Conclusion

PIRC appreciates the opportunity to contribute the rare cancer patient perspective as CMS implements the drug price negotiation provisions of the IRA. We look forward to a continuing dialogue throughout the IRA implementation process and welcome the opportunity to discuss our comments or the experience of rare cancer patients generally.

Association of Cancer Care Centers
Biomarker Collaborative
Cancer*Care*
Cancer Support Community
Cactus Cancer Society
Chondrosarcoma CS Foundation, Inc.
CLL Society
Cutaneous Lymphoma Foundation
Exon 20 Group
FORCE: Facing Our Risk of Cancer Empowered
Haystack Project
Histiocytosis Association
Hope for Stomach Cancer
ICAN, International Cancer Advocacy Network
MET Crusaders
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