National Pharmaceutical Council®

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The Honorable Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

Submitted Electronically via: IRARebateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair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

Dear Deputy Administrator Seshamani:

The National Pharmaceutical Council (NPC) appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS) Guidance, *Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair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* (Guidance or the Guidance).

NPC is a health policy research organization dedicated to the advancement of good evidence and science and to fostering an environment in the United States that supports medical innovation. We have rich experience conducting research and disseminating information about the critical issues of evidence, innovation and the value of medicines for patients. Our research helps inform important healthcare policy debates and supports the achievement of the best patient outcomes in the most efficient way possible.

NPC's research and that of others have found that public policies that reduce the incentives to invest in research and development result in less innovation, fewer treatment options, and lower life expectancy.[1] The Inflation Reduction Act (IRA or the Act) creates a new price-setting mechanism that will change the economic incentives for bringing new medicines to market, and evidence shows manufacturers are already responding to those incentives.[2] There are growing concerns about the potential unintended

[1] Ciarametaro M and Buelt L. Assessing the effects of biopharmaceutical price regulation on innovation. 2022. https://www.npcnow.org/resources/assessing-effects-biopharmaceutical-price-regulation-innovation; Thomas A. Abbott & John A. Vernon, 2007. "The cost of US pharmaceutical price regulation: a financial simulation model of R&D decisions," Managerial and Decision Economics, John Wiley & Sons, Ltd., vol. 28(4-5), pages 293-306.; Leonard D. Schaeffer Center for Health Policy & Economics. Annual Report 2020. https://healthpolicy.usc.edu/wp-content/uploads/2021/03/Schaeffer-Center- 2020-Annual-Report.pdf

[2] Grogan J. (2022) The Inflation Reduction Act Is Already Killing Potential Cures. WSJ. https://www.wsj.com/articles/the- inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira- manufacturers-11667508291 Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: https://catalyst.phrma.org/wtas-inflation-reduction-act-

consequences of the IRA and the Medicare “Drug Price Negotiation Program” (DPNP). Using the term "negotiation" in this statute and Guidance is misleading because there is not a genuine opportunity to negotiate (quotation marks around the words “negotiate” and “negotiation” to specify that these are terms used by the agency in their publications). NPC research highlights that these consequences will likely include delay of access to new medicines, and fewer diseases getting additional approved treatment options.[3]

An important goal in implementation of the Act should be to set guidance that, to every extent possible, minimizes the deleterious impact of the IRA on the incentives for the development of innovative therapies as well as patient access. In its second year of issuing guidance on the DPNP, CMS continues to take steps that do the opposite.

The price-setting mechanism described in the Guidance, incorrectly portrayed as “negotiation,” lacks clear standards for the evidence that will be used in the process and the transparency necessary for the public to reproduce or evaluate CMS’s process and decisions. Although CMS has recognized the need to improve the approach to its patient-focused listening sessions, we remain concerned that even with the specific recommendations we outline below for patient engagement that this process minimizes the opportunity for patients, providers and other clinical experts to continuously inform and participate. Furthermore, the effectuation of the Maximum Fair Price (MFP) and Part D formulary inclusion of selected drugs are built on a chassis ripe with perverse incentives and opportunities for fraud and abuse and provide minimal opportunity to prevent and detect unsavory activities.

The importance of implementing the price-setting provisions of the IRA in a manner that accurately values medicines and maintains patient access cannot be overstated. This process forces manufacturers to accept CMS’s final price, face an unreasonable excise tax, or exit the market – all of which threaten the development of, and patient access to, new treatments or cures.

We understand that CMS has a statutory requirement to implement the IRA. We also note that many NPC members have long argued that the underlying structure of the “negotiation” program, as set forth by the statute and implemented here by CMS, is legally flawed. In review of the punishing penalties for non-compliance, and the general inflexibility of the process for product selection and maximum fair price (MFP) implementation, these legal flaws cannot be overcome through general guidance clarity at this stage.

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already-impacting-rd-decisions; Powaleny, Andrew. (2023). IRA Impacts: Cancer treatment research and development. PhRMA. Available at: https://catalyst.phrma.org/ira-impacts- cancer-treatment-research-and-development; Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions; IRA survey: Biotechs bracing for impact. Biocentury. March 16, 2023. Slabdokin, Greg. IRA Drives Pfizer’s Decision to Focus on Biologics, Not Small Molecules. BioSpace. March 4, 2024. Available at: https://www.biospace.com/article/ira-drives-pfizer-s-decision-to-focus-on-biologics-not-small-molecules/. US IRA May Weigh on Long-Term Global Pharma Growth. FitchRatings. September 2023. https://www.fitchratings.com/research/corporate-finance/us-ira-may-weigh-on-long-term-global-pharma-growth-22-09-2023.

[3]Patterson J, Motyka J, O’Brien JM. Unintended Consequences of the Inflation Reduction Act: Clinical Development Toward Subsequent Indications *Am J Manag Care. 2024;30(2):82-86. https://doi.org/10.37765/ajmc.2024.89495*

"How The IRA Could Delay Pharmaceutical Launches, Reduce Indications, And Chill Evidence Generation", Health Affairs Forefront, November 3, 2023. DOI: 10.1377/forefront.20231101.123865

Nevertheless, NPC appreciates the opportunity to provide input and provides herein several suggestions for CMS to consider that might be helpful to the agency as it implements this program. None of these resolve the more fundamental legal infirmities of the overall program, nor could they, but they can improve transparency and incorporation of the patient perspective. NPC's recommendations are summarized on the following pages:

I. Improving Transparency in the Implementation Process

- The implementation of the Inflation Reduction Act (IRA) is being closely followed by those who invest in, research, and develop new cures. Though the IRA text permitted implementation of the price-setting process via guidance, this Guidance opens CMS to criticism for creating an opaque process giving the agency maximum flexibility and latitude while failing to provide adequate clarity and details about how it will implement important provisions. We urge CMS to make comments in response to this Guidance publicly available, as it did for IPAY 2026 guidance.

II. (Section 40) Requirements for Manufacturers of Selected Drugs

- Address concerns related to manufacturer effectuation of MFP, and ensure processes are in place to prevent MFP-340B duplication of discounts. Manufacturers should not be the only stakeholders (e.g., pharmacies, mail order services, and other dispensers) in the supply chain responsible if an MFP is not made available to beneficiaries. Without CMS intervention to rectify these serious operational issues, manufacturers must have flexibility to compliantly implement MFP effectuation.
- Abandon the burdensome and unworkable Primary/Secondary Manufacturer policy.

III. (Sections 50 and 60) Negotiation Factors and Process

- Implement these sections with maximum transparency to provide manufacturers and other stakeholders the opportunity to inform, evaluate, and predict CMS's process and priorities in the overall negotiation process and the individual negotiations for selected drugs.
- Provide clarity on the choices of therapeutic alternative for each approved indication of selected drugs and ground those choices in current, evidence-based clinical practice. CMS should focus on clinical benefits and cost offsets when comparing treatments and determining value, and not reduce the preliminary price by information unrelated to the value of a treatment (e.g., cost-recovery, remaining exclusivity, etc.).
- Develop, communicate, and more clearly define the factors CMS considers when determining unmet need consistent with relevant patient populations' needs for each indication of selected drugs.
- Engage with patients and caregivers throughout the process to gain insights into the value, preferences for appropriate treatment, and the indirect costs that patients and their families bear, to inform the evaluation of the clinical benefit of a selected drug (evaluation process). It is essential to gain patient input to identify unmet needs, therapeutic alternatives, clinical and humanistic benefits.

- Create and implement a consistent framework that provides more information about how CMS will make decisions during the negotiation process, including the identification of therapeutic alternatives, stakeholder involvement, and the evidence used to support CMS decisions. While CMS did not create and implement a framework with more information for IPAY 2026, CMS can improve upon the process for IPAY 2027 by establishing this framework.
- Apply well-established best practices for evidence evaluations from organizations including the Innovation and Value Initiative and ISPOR, the Professional Society for Health Economics and Outcomes Research. Provide clarity into the evidence standards that CMS will use at all steps of the process, including when working with external organizations.

IV. (Section 110) Part D Formulary Inclusion of Selected Drugs

- While we appreciate CMS's inclusion of additional detail regarding what the agency will monitor with regard to formulary compliance, we remain concerned that patient formulary access may be reduced as a result of IRA implementation and urge CMS to implement additional safeguards and improved oversight and standards for Part D formularies to protect patient access and prevent discriminatory behavior.

V. General Comments

- Encourage CMS to broadly interpret the IRA statute to exclude orphan drugs from negotiation and when determining the number of designations and indications that exempt an orphan product from selection.
- Incorporate the value of novel formulations in its price determination and negotiation process.

I. Improving Transparency in the Implementation Process

The implementation of the Inflation Reduction Act (IRA) is the most significant prescription drug pricing intervention in the history of the Medicare program. As we approach the announcement of set prices for IPAY 2026, it is being closely followed by those who invest in, research, and develop new cures. It is also being closely watched by health policy experts, pharmacoeconomic researchers, patient advocates, and others. CMS has a long history of publishing and responding to information provided by stakeholders when implementing new policies. This Guidance opens CMS to criticism for creating an opaque process giving the agency maximum flexibility and latitude while failing to provide adequate clarity and details about how it will implement important provisions (e.g., identification of therapeutic alternatives, weighting of factors for initial offer, etc.). We appreciate that CMS made comments on the IPAY 2026 guidance publicly available and urge CMS to continue this approach for IPAY 2027 as an important step in maintaining transparency.

II. (Section 40) Requirements for Manufacturers of Selected Drugs

A. Decreasing the Potential for Payment Errors, Fraud, and Perverse Incentives

CMS should also provide flexibility for manufacturers with MFP agreements to provide access to the MFP, particularly given the new systems needed to effectuate MFP. As CMS heard in comments provided in response to the Office of the Inspector General's regulations to remove the safe harbor protection for prescription drug rebates, it is important to contemplate the workability of these new mechanisms.

NPC has a deep understanding of the pharmaceutical supply chain. As such, we have concerns and suggestions about the flow of funds and lack of data described in Section 40.4. The Guidance robustly describes manufacturer noncompliance yet offers nearly no information about dispenser noncompliance.

While CMS is requiring the use of the Medicare Transaction Facilitator (MTF) data exchange, which is intended to facilitate the exchange of claims-level data and payment elements for selected drugs, manufacturers should not be the only stakeholders (e.g., pharmacies, mail order services, and other dispensers) in the supply chain responsible if an MFP is not made available to beneficiaries. As CMS is requiring manufacturers to submit plans for effectuating MFP, supply chain entities should be required to participate in the process laid out by manufacturers. If CMS does not fix the critical issues outlined below in advance of January 1, 2026, CMS must allow manufacturers maximum flexibility to maintain compliance with MFP effectuation requirements. Additionally, CMS should monitor compliance across supply chain entities as it proceeds with establishing its intake system for receiving complaints and disputes (Section 90.2.2).

i. Manufacturer Effectuation of MFP

The pharmacy's actual acquisition cost is not known to or controlled by manufacturers, and the existing chargeback payments and rebate mechanisms are currently inadequate to effectuate the MFP. As such, NPC supports CMS's proposed Standard Default Refund Amount (SDRA) of Wholesale Acquisition Cost (WAC) – MFP. However, while CMS asserts that the MTF is intended to support verification that the selected drug was dispensed to an MFP-eligible and to facilitate this process, NPC remains concerned about the potential for errors. If a prescription was filled, billed, and returned to stock within the 14-day time frame proposed by CMS, the Part D plan would have the information necessary to reverse their payment to the pharmacy, but the manufacturer would not be aware of the need to reverse the MFP effectuation payment. This creates a significant economic incentive that could encourage inadvertent duplicate discounts or outright diversion or fraud that threatens the integrity of IRA implementation. While CMS notes that it is considering how to address claim adjustments and reversals (Section 40.4.1), NPC is concerned that no solution has been put forth yet for manufacturer and supply chain stakeholder feedback, particularly as we approach IPAY 2026. Moreover, manufacturers of selected drugs for IPAY 2026 will be required to submit their plans to make MFP available by June 1, 2025, six months sooner than announced in the Revised Guidance for IPAY 2026. Manufacturers need sufficient time to make their plans, which could be better informed with information on how CMS plans to address claims adjustments and reversals.

NPC is also concerned about the potential for perverse incentives associated with CMS's Guidance on scenarios where SDRA may be inappropriate. In Guidance, CMS asserts that the SDRA might be unsuitable when a dispensing entity's acquisition cost exceeds the WAC for a drug and in such scenarios,

the SDRA payment "would not be sufficient to make the MFP available to the dispensing entity." We believe this may compromise the program's integrity and foster behaviors among dispensers and other supply chain participants to inflate profits via mechanisms that spuriously raise MFP refund amounts. This issue arises in part because manufacturers do not control the prices at which dispensers obtain drugs from supply chain middlemen, including wholesalers. We urge CMS to implement safeguards to protect against these issues.

ii. Verification of 340B Discounts and 340B Nonduplication

Numerous factors create a significant potential for MFP and 340B duplicate discounts. These include a lack of transparency in the 340B Drug Pricing Program, the potential for mixing mechanisms of chargebacks and rebates of 340B and MFP on the same National Drug Code (NDC), and the inconsistent timeframe and methods by which pharmacy claims are determined as 340B eligible. Without additional verification from CMS, manufacturers will be required to validate that 340B entities are only providing the MFP to eligible individuals, without standard processes to do so or the required participation of 340B covered entities (or entities acting on their behalf) to provide sufficient information to determine whether a 340B or MFP discount is owed.

To avoid duplication of 340B and MFP prices, one option is for CMS to require identification of 340B units at the point of sale at the time of dispensing (when the claim is created) and prohibit identification of 340B units after that point for MFP drugs. If this approach is used, we ask the agency to develop a cutoff for 340B identification to avoid duplicates. As part of this, the agency should also commit to ensuring that providers report a "minimally necessary" data set to the manufacturer or its vendor to be entitled to access the MFP and for the purposes of validating their right to access in a timely manner, according to standard business practices and consistent with non- duplication requirements. While the MTF will provide some of this data, NPC remains concerned about the limited information required from dispensing entities, and the data burden required of manufacturers in this scenario.

Given the complex interactions of the processes described above, CMS should establish a 340B clearinghouse, which would act as a claims verifier, reviewing Part D PDE data as well as data submitted by 340B covered entities (or entities acting on their behalf) to confirm whether a claim is subject to a 340B agreement, similar to the role played by 340B third-party administrators (TPAs) and split-billing vendors today.

If this clearinghouse is not established, at minimum, CMS should incorporate 340B-related transaction data from 340B covered entities or their third-party administrators into the MTF for IPAY 2026, rather than in the future as it suggests in the guidance. In the guidance, the agency itself notes that the process of facilitating access to the lesser of MFP or the 340B ceiling process will involve using data from multiple stakeholders, and providing this information via the MTF could improve this process if a clearinghouse is not used. For drugs dispensed to 340B-eligible patients, the use of a 340B identifier should be mandatory to facilitate the provision of this data. Additionally, CMS should also consider aligning data elements used in this process with data elements from CMS guidance on avoiding duplicate discounts for

Medicaid.[4] CMS should also expressly acknowledge that manufacturers will establish, receive, review, and, as necessary, audit MFP validation data to ensure MFP access is provided in accordance with the statute. If CMS does not establish a clearinghouse, manufacturers may need to collect data from covered entities to validate 340B status and avoid duplicates and will need accurate PDE data to confirm this information.

B. Primary/Secondary Manufacturer Definition

NPC maintains, as it commented last year, that CMS should abandon the Primary/Secondary Manufacturer policy. The primary and secondary manufacturer concept developed by CMS is unworkable, impractical, and not supported by the statute. Requiring one manufacturer to enter into an agreement with CMS that holds them responsible for the actions of another manufacturer (and potentially a competitor) unnecessarily complicates implementation and exposes manufacturers to potentially significant burden.

III. (Sections 50 and 60) Negotiation Factors and Process

As stated earlier, many stakeholders are closely watching CMS's IRA implementation process. The price-setting process is being studied not just by manufacturers, but by the broader pharmacoeconomic, health policy, and patient advocacy communities. The credibility of CMS's process will be judged by the agency's use of good evidence and appropriate methods in a transparent and patient-centered process.

CMS has described a domestic reference price-setting mechanism that begins by identifying a therapeutic alternative and using its price as an initial starting point. This initial starting point is then adjusted for clinical benefits to achieve a preliminary price that is further adjusted by a variety of other factors unrelated to the value of a treatment.

We do not believe the Guidance describes a satisfactory process to determine the value of a medicine or set its price and note that it resembles, with less transparency, processes used by countries outside of the United States that face significant delays in accessing innovation. We believe that only clinical benefit, health improvement, including public health and societal benefits, and cost offsets associated with the treatment may be used to determine the value of a medicine. Adjusting reimbursement by the elements described in the manufacturer data elements, which are unrelated to drug benefits, (e.g., R&D costs, cost of production, prior Federal financial support) ignores the complexity of drug development and the multitude of costs across the pharmaceutical supply chain for patients to receive their medicines. Doing so will have disastrous effects on innovation and deny patients future treatments or future indications for existing treatments. Beyond our concerns about potential adjustments to the initial starting point based on factors unrelated to the value of a medicine, NPC is concerned about CMS's definition of the starting point itself. CMS's decision to use the net price of therapeutic alternatives, incorporating discounts paid under the Medicare Part D Manufacturer Discount Program, is an inappropriate metric to use for the Medicare population. It is not a standard price reporting measure

[4] Lynch, C. CMCS Informational Bulletin. SUBJECT: Best Practices for Avoiding 340B Duplicate Discounts in Medicaid. January 8, 2020. Available at: https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_252.pdf

found elsewhere, which will increase burden, and Discount Program payments are highly variable and depend on the mix of drugs patients are taking.

The statute requires CMS to use a "consistent methodology and process" for negotiation.[5] More clarity is needed than is provided in the Guidance to achieve that goal, especially related to the identification of therapeutic benefit and the weighting of factors used to determine the preliminary price and initial offer. Only when such clarity is provided can manufacturers and external stakeholders build their own models to anticipate, inform, and evaluate the process CMS operationalizes. Manufacturers in particular need more clarity to accurately prepare their submissions and meaningfully participate in the process. Clarity has not been provided to manufacturers for the first round, which does not allow manufacturers subject to subsequent rounds of negotiation to apply lessons learned based on experience. While CMS will publish a narrative explanation of the negotiation process and MFP of selected drugs for IPAY 2026 and share non-proprietary information, including information submitted by other interested parties and related to the selected drug and its therapeutic alternatives, this information will not be published until after comments are due for the IPAY 2027 draft guidance and may not be published until manufacturers must sign agreements to participate in the Negotiation Program for IPAY 2027 or face steep "excise tax" penalties. The deadline by which CMS must publish these explanations and by which manufacturers and the public must submit data to CMS for consideration in the negotiation process are the same day. Both sets of stakeholders will need to submit information without understanding what CMS valued in the price-setting process for IPAY 2026. This delay in information hinders manufacturers' ability to comment more granularly on the information that should be included in CMS's public rationale for each MFP and to leverage insights from the first cycle of the price-setting process as it enters its second cycle. Our specific recommendations are below.

A. Development of a Transparent and Rigorous Evaluation and Price-Setting Process

NPC encourages CMS to implement a transparent and inclusive evaluation process to promote credibility and support for their price-setting and counteroffer process. The agency is introducing comparative effectiveness to the Medicare program and making value determinations when establishing a "preliminary price" for selected drugs, yet provides limited, far from sufficient transparency or predictability around this process. Transparency and methodological rigor are paramount during value assessment.[6]

CMS should pursue analytic transparency by carefully considering data assumptions and highlighting the limitations and uncertainties of analyses to the public. By providing robust information about its evaluation criteria and the factors considered during the price-setting process, CMS can help build trust with all stakeholders and allow others to evaluate their process. Specifically, NPC encourages:

[5] SSA § 1194(b)(1).

[6] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

- **Engagement with key stakeholders throughout the assessment process** to ensure all perspectives are considered and have the opportunity to inform the assessment.[7] CMS should specifically seek and incorporate stakeholder feedback about their choice of therapeutic alternatives for each selected drug; the benefits of a selected drug to each stakeholder (including patients, clinicians, caregivers, manufacturers and other scientists); the meaning of unmet need to each stakeholder and the extent to which a selected drug meets that unmet need.

  CMS should seek patient input via a variety of mechanisms and tailor requests to facilitate this input. CMS has recognized that the Information Collection Request (ICR) form and patient-focused listening sessions for IPAY 2026 were not organized to best collect stakeholder input. NPC will review the revised ICR and appreciates CMS intends to take additional steps to improve it, but the ICR process in general may not be the best way to reach this important stakeholder community. It is vital that CMS improve its patient engagement strategy based on participation and engagement in the patient-focused listening sessions for IPAY 2026. The structure CMS used did not promote quantity or quality of engagement, as we will detail further below. For quantity, notably, out of an anticipated 200 speaker slots, there were 106 total speakers, indicating that CMS must change its approach to maximize participation.[8] Given the important perspectives of patients and caregivers, we provide additional recommendations on meaningful patient input to the CMS process determining clinical benefit throughout this comment. Furthermore, manufacturers should be able to inform the selection of evidence about their products and verify information provided about their products from others; to do this, we recommend that CMS issue a confidential report to the manufacturer regarding evidence from stakeholders about the selected drug either with or prior to the initial offer.

- **The use of transparent and reproducible methods and results to the extent possible**, given the confidentiality required for proprietary information, methods, models (including all calculations). Assumptions should be transparent to interested stakeholders. This transparency, combined with the ability to reproduce results, are prerequisites to building credibility and trust in the process.[9] NPC reiterates that CMS should create and publish any decision-making framework it develops– both generally and for selected drugs – which should include, at a minimum, information on:

  1. the therapeutic alternative(s) considered for each indication for selected drugs and the rationale for selection;

[7] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

[8] Patterson J, Wagner T, Salih, K, Shabazz G, Campbell, D. Breadth of Patient and Stakeholder Input in CMS's Drug Price Negotiation Program: A Content Analysis of the 2023 Patient-Focused Listening Sessions. Available at: https://www.npcnow.org/sites/default/files/2024-05/Poster_ISPOR%202024%20Patient-Focused%20Listening%20Sessions%20FINAL.pdf

[9] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

2. the definition(s) of unmet need for each indication of selected drugs;
3. the full range of benefits and impacts considered for each indication;
4. the internal process and rationale for determining which benefits and impacts were included;
5. a list of each stakeholder consulted;
6. the source(s) of evidence considered, particularly clinicians and patients;
7. how each benefit and impact considered influenced the final MFP, to include any algorithms, calculations, or modeling that related to MFP determination, as well as rationale for evidence that was not considered; and
8. the limitations of the data collected and uncertainties in CMS's decision-making. As is common in any rigorous, evidence-based process, this information should also be made clear when reported to the public.

These elements of CMS's evaluation and MFP determination should be made public at distinct phases of evaluation. First, this draft framework should be made public as a scoping document prior to initiating stakeholder engagement and beginning data collection for CMS's evaluation process. Secondly, preliminary results should be shared with manufacturers of selected drugs at least 60 days prior to when CMS issues its initial offer. Finally, results of this framework should be revealed to the public to explain the final MFP. While these comments are for the IPAY 2027 draft guidance, it would be valuable to have this information for the IPAY 2026 MFP explanations before the IPAY 2027 negotiations begin.

- **Robust engagement with manufacturers,** consistent with the practices and policies of other payers and regulators.[10] Given their vast knowledge of their products and therapeutic areas, pharmaceutical manufacturers and their pharmacoeconomic researchers are critically important sources of information on the value of treatments for payer decision-making. Recognizing this, Congress and the U.S. Food and Drug Administration (FDA) have provided guidelines on how healthcare economic information (HCEI) can be provided to payers' pharmacy and therapeutics committees.[11] We encourage CMS to similarly provide opportunities for meaningful engagement with manufacturers.

  While CMS currently offers a maximum of three meetings between the manufacturer of the selected drug and CMS, CMS is requesting feedback on whether three meetings are necessary and if it would be preferable to have an additional written offer in lieu of one or more meetings.

[10] Smith JC, Snider DE, Pickering LK; Advisory Committee on Immunization Practices. Immunization policy development in the United States: the role of the Advisory Committee on Immunization Practices. Ann Intern Med. 2009 Jan 6;150(1):45-9.; Payer Engagement in HEOR. Ispor.org. Available at: https://www.ispor.org/strategic-initiatives/payer-engagement-in-heor

[11] Section 3630, "Facilitating Exchange of Product Information Prior to Approval" of H.R. 2617, Consolidated Appropriations Act, 2023; FDA. Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities Questions and Answers Guidance for Industry and Review Staff.; 2018. Available at: https://www.fda.gov/media/133620/download.

NPC urges the agency to, at minimum, maintain three meetings, though existing industry best practices suggest a minimum level of engagement would extend beyond three meetings, to include meetings at: 1) after drug selection but prior to initiation of the price-setting process; 2) prior to CMS presenting the initial offer; and 3) the three meetings described by CMS as occurring after CMS presents the initial offer. Additional written offers and clear communication surrounding next steps will enhance the "negotiation" process. However, if CMS moves forward with adding an additional written offer, such offer should not be in lieu of live meetings, and must promote the transparent exchange and evaluation of evidence on the value and clinical benefit of selected drugs.

i. *Evaluation of data on product value for quality, particularly information on patient experience*

The Guidance states that CMS will accept information on the benefits of selected drugs from the public and conduct its own literature reviews and database analyses. While laudable and helpful, public submission comes with a cost of sorting through and identifying studies that are both high quality and relevant to the therapeutic alternatives and patient population.[12]

The results of an assessment depend on the evidence that underlies it, and the burden is on CMS to use and develop evidence in a systematic, transparent, and robust manner. To maximize credibility and trust in the assessment process, the procedures by which evidence is identified and included in the assessment should be objective, systematic, transparent, robust, reproducible, and made public as part of the scoping process. Not following widely accepted scientific best practices erodes trust in the process.

Accordingly, we encourage CMS to develop robust, transparent standards for both submitted and internally generated data to ensure that evidence is methodologically rigorous and apply these same rigor and transparency standards to the agency's internal claims analysis and review when adjusting the MFP initial starting point based on clinical evidence. These standards can be informed by using accepted rubrics for evaluating study quality[13] that are fit for purpose and most appropriate for the type of evidence (e.g., clinical vs. economic data).[14] Procedures for evaluating evidence quality should be included in scoping documents, and the results should be made available through the value assessment.

[12] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

[13] Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health. 2022 Jun;25(6):1060.; von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)statement: guidelines for reporting observational studies. Lancet. 2007 Oct 20;370(9596):1453-7.; The GRACE Checklist: A Validated Assessment Tool for High Quality Observational Studies of Comparative Effectiveness. J Manag Care Spec Pharm. 2016 Oct;22(10):1107-13;

[14] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

We encourage CMS to follow and tailor as necessary consensus guidance on the conduct and evaluation of comparative effectiveness research (CER) that is both submitted and internally conducted, and to adopt elements as high-quality research methods, aligned with principles of good CER.[15]

ii. Inclusion of Treatment Costs and Cost Offsets

Costs should be representative of the net price most relevant to the user. Cost offsets are a driving component of drug value and actual transaction costs, and care should be taken to ensure that costs are as representative of the actual net cost to the payer and net revenue realized by the manufacturer as possible in order to achieve an accurate assessment. For biopharmaceuticals, following ISPOR good research practices for measuring drug costs can help achieve this objective.[16] In the case of MFP, CMS must ensure that cost data reflects discounts and rebates provided to Medicare and recognize that the net cost to the payer does not always represent the net revenue realized by the manufacturer.

We encourage CMS to also include comprehensive assessments of the economic benefits of selected drugs, in addition to the costs of the treatments themselves. In any assessment of the value of medical treatments, all healthcare costs and cost offsets should be included.[17] Treatments may have up-front costs that lead to long-term improvements in patient health.

Those improvements may yield "cost offsets," or savings due to reductions in healthcare resource needs, such as reduced hospitalizations, or societal gains (e.g., improved productivity, reductions in caregiver burden). The full value of treatment can only be assessed by including both the treatment costs and other associated cost offsets it may produce, while also including clinical benefits of drugs without discretely quantifiable impacts on costs (e.g., improvements in the overall care of the patient). Only considering the treatment costs but not the potential cost offsets would lead to an incomplete assessment of value. NPC appreciates that this draft guidance now states that CMS may also request evidence related to "healthcare resource utilization and usage patterns" of the selected drugs and its therapeutic alternatives. Reviewing data related to healthcare resource utilization and usage, with consideration of evidence-based medicine, will provide insight into the economic benefits of selected drugs and their impacts on patient health. However, it remains unclear how CMS will use this information, the methods they will employ to analyze it, and how it will inform their evaluations, and transparency on these points is necessary to evaluate whether this evidence will be used appropriately.

When evaluating cost data, the time horizon should be long enough to incorporate the benefits of the treatment and the lower costs of medications when they become generic. Many of the cost-offset

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[15] Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value Health. 2017 Sep;20(8):1003-1008.; Dreyer NA, Bryant A, Velentgas P. The GRACE Checklist: A Validated Assessment Tool for High Quality Observational Studies of Comparative Effectiveness. J Manag Care Spec Pharm. 2016 Oct;22(10):1107-13; National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

[16] Hay JW, Smeeding J, Carroll NV, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: the ISPOR drug cost task force report – Part I. Value Health 2010;13:3-7.

[17] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf

benefits of treatment, such as costs of avoided hospitalizations, show up in the longer-term. To measure the full value of a treatment, the time horizon for costs should be long enough to capture these cost offsets,[18] and to account for the lower costs of medications when generics and biosimilars are introduced.

iii. Utilization of Best Practices Relevant to CMS's Proposed Evidence Evaluation

We have cited in this response several publications on research best practices relevant to the agency's evidence evaluation proposed in the Guidance. We encourage CMS to review and, wherever possible, utilize the guiding principles listed below to ensure the transparency, validity, and credibility of the annual price-setting process. In our foregoing recommendations, we have emphasized methodological issues that are relevant to the price-setting process proposed by CMS. We encourage CMS to consider these tools to the extent that the principles are appropriate for Medicare. For example, NPC has developed or recommends the following resources:

- NPC's Guiding Practices for Patient-Centered Value Assessment includes 33 specific elements surrounding six key aspects of value assessment, including the assessment process, scientific methodology, benefits, costs, evidence, and dissemination and utilization.[19]
- The Myth of Average: Why Individual Patient Difference Matter, published by NPC, provides recommendations for ways improving the patient-centeredness of value assessment.[20]
- ISPOR and the International Society for Pharmacoepidemiology (ISPE) have published good practices for real-word data studies of comparative effectiveness with the goal of providing a trustworthy foundation for use of RWE in decision-making.[21]

ISPOR, the Innovation and Value Initiative, PhRMA, and the National Health Council (NHC) have also developed resources related to the patient perspective, value assessment, and comparative effectiveness research that we ask CMS to incorporate into its process.[22]

[18] Hay JW, Smeeding J, Carroll NV, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: the ISPOR drug cost task force report – Part I. Value Health 2010;13:3-7.
[19] National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2024. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20PatientCentered%20Value%20Assessment%20January.pdf
[20] National Pharmaceutical Council. The Myth of Average: Why Individual Patient Differences Matter. 2022. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2022-01/The_Myth_of_Average_01.2022.pdf
[21] Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value Health. 2017 Sep;20(8):1003-1008.
[22] Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value Health. 2017 Sep;20(8):1003-1008.; Innovation and Value Initiative. Principles for Value assessment in the US. https://thevalueinitiative.org/principles-for-value- assessment-in-the-us/; PhRMA. (2016). Principles for Value Assessment Frameworks. Available at: https://phrma.org/resource-center/Topics/Cost- and-Value/Principles-for-Value-Assessment-Frameworks; National Health Council. Domains of Patient Centeredness in Value Assessment. 2020. Available at: https://nationalhealthcouncil.org/wp-content/uploads/2020/03/NHC-One-Pagers_Domains.pdf; National Health Council. (2016). The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric. Available at: https://nationalhealthcouncil.org/wp-content/uploads/2020/11/20160328-NHC-Value-Model-Rubric- final.pdf; National Health Council. (2021). Value Classroom. https://nationalhealthcouncil.org/education/value-classroom/

B. *Identification of Therapeutic Alternatives*

The IRA instructs CMS to consider "the extent to which [a selected drug] represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives"; however, it does not suggest that the cost of those alternatives should be used as a benchmark for an initial offer. The Guidance diverges from the statute because CMS intends to rely on the lower of either: 1) the Net Part D Plan Payment and Beneficiary Liability, which reflects Total Gross Covered Prescription Drug Costs (TGCPD) net of direct and indirect remuneration (DIR) and Coverage Gap Discount Program (CGDP) payments, or (2) the MFP for initial price applicability year 2026 selected drugs, if applicable, "to determine a starting point for developing an initial offer."[23]

In any assessment of the relative clinical or economic benefits of a drug, the choice of the comparator is a fundamental driver in the outcomes and validity of the assessment with significant implications for patients, payers, and prescribers.[24] NPC recommends that the choice of comparators/therapeutic alternatives be driven by clinical appropriateness, informed by current treatment practices among a relevant patient population, and selected from potential comparators with the same treatment modality and class, rather than be dictated by cost, other concerns or implicit goals.[25] The draft guidance states that for its purposes "the term 'therapeutic alternative' may refer to one or more therapeutic alternative(s) or a subset of therapeutic alternatives that are clinically comparable," without further defining the type and volume of evidence used to define "clinically comparable." CMS changed this language from the IPAY 2026 guidance, which stated that "therapeutic alternative" may refer to "a subset of the most clinically comparable therapeutic alternatives." This is a change in the wrong direction, away from what is most clinically appropriate. The selection of a less-costly therapeutic alternative that is "clinically comparable" but not in the subset of "most clinically comparable" and lacks the safety, efficacy, and other clinical benefits of a selected drug – solely to lower the initial starting point of the price-setting process – fails to recognize the value of modern treatments and threatens to reverse the incentives that currently encourage innovation and access.

The use of a comparator that is not consistent with current clinical practice for given patients injects significant biases into the results and recommendations of a comparative assessment. Real world treatment decisions are based on numerous factors associated with the underlying disease and its severity, general health status or frailty, quality of life, and patient preferences.

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[23] SSA § 1194(e)(2)(A).

[24] Berger ML, Sox H, Willke RJ, et al. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value in Health. 2017;20(8):1003-1008.

[25] Jaime Caro J, Eddy DM, Kan H, Kaltz C, Patel B, Eldessouki R, Briggs AH; ISPOR-AMCP-NPC Modeling CER Task Forces. Questionnaire to assess relevance and credibility of modeling studies for informing health care decision making: an ISPOR- AMCP-NPC Good Practice Task Force report. Value Health. 2014 Mar;17(2):174-82.; Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA, Sculpher MJ, Trikalinos TA, Russell LB, Siegel JE, Ganiats TG. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. JAMA. 2016 Sep 13;316(10):1093-103.

The Agency for Healthcare Research and Quality's (AHRQ) Effective Health Care Program has produced guidance that may be helpful for CMS regarding comparator selection in observational CER.[26] AHRQ details how treatment selection bias (i.e., confounding by indication) may arise when there are differences between patients prescribed the drug being evaluated and the drug used as a comparator. Bias can be minimized by choosing a comparator that has the same indication, similar contraindications, similar adverse effects, and the same treatment modality, class, and mechanism of action.

AHRQ also notes that selection of a comparator of the same treatment modality and class may result in less bias than comparison across modalities or classes.[27] We appreciate CMS's intent to begin identifying therapeutic alternatives within the same drug class based on chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other classes, and encourage CMS to prioritize reducing bias in treatment comparisons by identifying therapeutic alternatives from potential comparators with the same treatment modality, class, and mechanism of action.

In the IPAY 2027 draft guidance, CMS uses the term pharmacological class whereas it previously used the term drug class in identifying therapeutic alternatives. Certain drugs are included in multiple pharmacological classes which may add complexity to the process, and we caution CMS to not let this change further detrimentally affect it.

NPC cautions against using cost to determine a selected drug's therapeutic alternative(s). Rather, during selection of therapeutic alternatives, we encourage CMS to:

- Publicly communicate proposed therapeutic alternatives and solicit feedback from manufacturers, clinicians with specific expertise in the treating the disease, patients and caregivers, and other stakeholders before proceeding with comparative effectiveness analyses that inform the initial offer.
- Ensure guidelines used in identifying therapeutic alternatives are up-to-date and incorporate the latest evidence.[28]
- Include patient preferences and priorities that inform shared decision-making between appropriate treatment options.[29]
- Invite manufacturers of the selected drug to proactively present clinical information focused on the relative clinical benefit of their products compared to therapeutic alternatives during the process of comparator selection and give manufacturers the opportunity to respond to CMS's choices of therapeutic alternatives. Early manufacturer communication is also consistent with practices employed by state Medicaid agencies, other federal agencies and commercial payers.

[26] AHRQ. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide. Content last reviewed March 2021. Effective Health Care Program, Agency for Healthcare Research and Quality, Rockville, MD. https://effectivehealthcare.ahrq.gov/products/observational-cer-protocol

[27] AHRQ. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide. Content last reviewed March 2021. Effective Health Care Program, Agency for Healthcare Research and Quality, Rockville, MD. https://effectivehealthcare.ahrq.gov/products/observational-cer-protocol

[28] National Health Council. A Dialogue on Patient-Centered Value Assessment: Overcoming Barriers to Amplify the Patient Voice. December 2018. Available from: https://www.nationalhealthcouncil.org/dialogue-patient-centered-value-assessmentovercoming-barriers-amplify-patient-voice

[29] Schmidt T, Valuck T, Riposo J, et al. Impact of Shared Decision-Making and Patient Decision Aids on Health Care Cost and Utilization in the US: A Systematic Review. J Clin Pathways. 2022;8(8):33-43. doi:10.25270/jcp.2022.12.0

- Seek input from clinicians with specific expertise in treating the indication of the selected drug to define appropriate therapeutic alternatives among Medicare patient sub-populations, including patients with multiple comorbidities and varying levels of disease severity. There is a long history of guidance to gain this information, including NIH's National Center for Advancing Translational Sciences.[30]
- Limit the choice of therapeutic alternative to drugs and biologics with FDA-approved indications and exclude off-label use from being compared to FDA-approved indications of selected drugs.
- Consider the use of comparative effectiveness studies and real-world evidence to support the selection of therapeutic alternative.

C. Prioritize Patient and Caregiver Input

Patients' and caregivers' view of the drugs they take and the benefits they receive is essential to understanding "the full range of clinical and patient-centered outcomes",[31] as PCORI stated in their recent multi-stakeholder research initiative. The centrality of direct patient input is echoed in best practices for comparative effectiveness research and value assessment that underpin the concept that the price of pharmaceuticals should be based on the value they provide to patients, caregivers, healthcare systems, and society. Value encompasses the balance of benefits and costs experienced by patients and society over time. There are a multitude of specific benefits that constitute "value," from reducing mortality and improving patient functioning, quality of life, and productivity to outcome equity and societal value of scientific innovation, among others.[32]

Measures of "indirect costs" such as patient productivity, caregiver time, and treatment burden (such as travel times for repeated hospitalization) are very important to patients and their families but are often poorly captured in administrative claims databases. This misalignment between patient concerns and priorities surrounding the impact of a disease or its treatment and the outcomes data collected in research and care is well documented.[33] As stewards of the Medicare program accountable to the health of people with Medicare, CMS should include these issues throughout discussions with patients and patient groups and seek and utilize observational studies or real-world evidence that includes these outcomes.

Systematically and rigorously incorporating patient perspectives on the value of selected drugs is essential to ensure that patients have a voice in decisions that affect their health and wellbeing.[34] We are mindful of the federal prohibition on CMS's use of QALYs in coverage and reimbursement decisions. We

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[30] Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. BMJ. 1999 Feb 27;318(7183):593-6. NIH National Center for Advancing Translational Sciences. Toolkit for Creating Clinical Care Guidelines: https://toolkit.ncats.nih.gov/module/after-fda-approval/creating-clinical-care-guidelines/guideline-development-process/

[31] Patient-Centered Outcomes Research Institute (PCORI). Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. https://www.pcori.org/resources/landscape-review-and-summary-patient- and-stakeholder-perspectives-value-health-and-health-care

[32] Neumann PJ, Garrison LP, Willke RJ. The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. Value Health. 2022 Apr;25(4):558-565.

[33] Perfetto, E.M., Oehrlein, E.M., Love, T.R. et al. Patient-Centered Core Impact Sets: What They are and Why We Need Them. Patient 15, 619–627 (2022). https://doi.org/10.1007/s40271-022-00583-x

[34] Oortwijn W, Husereau D, Abelson J, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. Int J Technol Assess Health Care. 2022;38(1).

also emphasize that direct engagement with patients identifies the measures of treatment benefit that patients and their families value, and therefore can avoid the potentially discriminatory nature of aggregate and limited measures such as the QALY. Thus, CMS should take tangible steps to capture the patient voice with validity and fidelity, engaging with patient groups directly to understand their perspective on the value of different pharmaceuticals throughout the negotiation process, particularly when defining unmet need, selecting therapeutic alternatives, and determining clinical benefit.

NPC appreciates CMS's intent to improve upon the design of patient-focused listening sessions used for IPAY 2027 and has conducted research on the patient-focused listening sessions from IPAY 2026, focusing on the breadth of patient and stakeholder input in these sessions. We believe CMS should continue to evolve towards best practices for patient engagement[35] and prioritize opportunities to hear a greater amount of patient-centered evidence directly from patients and their advocates, caregivers, and providers. Our recommendations are below:

- **Improve transparency around how patient input would be utilized in the price determination process, communicating that impact back to patients.** Patient engagement may have been hampered by a lack of transparency surrounding how input would be used in the price determination process. As CMS considers new approaches to patient engagement for IPAY 2027, we encourage CMS to delineate the process by which clinical benefits and patient impacts would be considered and influence MFPs, and to promote transparency surrounding the patient perspective CMS gleans from these listening sessions and how it is incorporated in CMS's MFP offers for each selected drug.[36] While the agency was able to obtain some perspective consistent with the intent of the sessions, the opportunity for patients to provide meaningful feedback on patient experience, including unmet need, drug benefits, and patient access, was hampered by the shortcomings outlined below. Future evolutions of patient engagement in the DPNP should prioritize opportunities for CMS to hear a greater amount of patient-centered evidence directly from patients and their advocates, caregivers, and providers.[37] For example, speakers often focused their time on patient experience and evidence; still, the median duration of input on patient-focused evidence about therapeutic alternatives per drug listening session was less than 15 minutes. A median of only 2.5 patients participated per session, providing CMS with a total of

[35] Harrington RL, Hanna ML, Oehrlein EM, Camp R, Wheeler R, Cooblall C, et al. Defining Patient Engagement in Research: Results of a Systematic Review and Analysis: Report of the ISPOR Patient-Centered Special Interest Group. [cited 2024 Mar 12]; Available from: https://doi.org/10.1016/j.jval.2020.01.019; Innovation and Value Initiative. Principles for Value Assessment in the U.S. [Internet]. 2021. Available from: https://thevalueinitiative.org/wp-content/uploads/2021/01/2021-IVI-Principles-of-VA_FINAL.pdf; National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment [Internet]. 2024. Available from: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20Patient-Centered%20Value%20Assessment%20January.pdf

[36] Patterson J, Wagner T, Salih, K, Shabazz G, Campbell, D. Breadth of Patient and Stakeholder Input in CMS's Drug Price Negotiation Program: A Content Analysis of the 2023 Patient-Focused Listening Sessions. Available at: https://www.npcnow.org/sites/default/files/2024-05/Poster_ISPOR%202024%20Patient-Focused%20Listening%20Sessions%20FINAL.pdf

[37] Patterson J, Wagner T, Salih, K, Shabazz G, Campbell, D. Breadth of Patient and Stakeholder Input in CMS's Drug Price Negotiation Program: A Content Analysis of the 2023 Patient-Focused Listening Sessions. Available at: https://www.npcnow.org/sites/default/files/2024-05/Poster_ISPOR%202024%20Patient-Focused%20Listening%20Sessions%20FINAL.pdf; National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

only seven total minutes of patient input per selected drug.[38] The duration of input received from the sessions was likely attenuated because only approximately half of the anticipated speaker slots (106 of 200) were filled. The agency reported that it used a "process to randomly select" speakers from those who registered.[39] However, given that no session featured the full 20 anticipated speaker slots, and three sessions included fewer than 10 participants, uncertainty remains as to whether fewer than 20 speakers registered or whether the Agency selected only a subset of registered individuals. CMS's extension of the initial registration window by nearly two weeks suggests recruitment and registration requirements may have presented challenges.[40] Clearly specifying the purpose of patient and stakeholder engagement and how evidence provided by participants will be used in CMS's price determination process could further strengthen the sessions.

- **Prioritize diversity and a multi-modal approach in outreach.** NPC and others have emphasized the need for CMS to prioritize diversity and a multi-modal approach in outreach at all phases of the DPNP implementation.[41] Robust engagement with underrepresented communities through outreach and ongoing dialogue is needed to promote an equity-focused implementation process.[42] Documented heterogeneity in treatment preferences[43] and effects,[44] as well as disparities in health status and access to care, further underscore the need for diverse patient voices in informing CMS's price determinations. CMS should account for this heterogeneity in its feedback to manufacturers in addition to integrating it into the process for seeking patient input. Technological barriers to registration (e.g., requiring an email address for an online-only

[38] Patterson J, Wagner T, Salih, K, Shabazz G, Campbell, D. Breadth of Patient and Stakeholder Input in CMS's Drug Price Negotiation Program: A Content Analysis of the 2023 Patient-Focused Listening Sessions. Available at: https://www.npcnow.org/sites/default/files/2024-05/Poster_ISPOR%202024%20Patient-Focused%20Listening%20Sessions%20FINAL.pdf

[39] Centers for Medicare & Medicaid Services. Medicare Drug Price Negotiation Program Patient-Focused Listening Sessions [Internet]. [cited 2024 Mar 18]. Available from: https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation-program-patient-focused-listening-sessions

[40] Karlin-Smith S. As Medicare Drug Negotiation Patient Sessions Kick Off, Advocates Already Eyeing Improvements. Pink Sheet. 2026.

[41] National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf; Miller M, Sara Van Geertruyden B;, Saxton ; M Claire, Courtney ;, Savage Y, Weir D, et al. A summit on amplifying voices of patients, caregivers, and people with disabilities in Inflation Reduction Act drug price negotiations. J Manag Care Spec Pharm. 2024;30:1–5.; National Organization for Rare Disorders. NORD Recommendations: Future Medicare Drug Price Negotiation Program Patient and Provider Listening Sessions [Internet]. 2024. Available from: https://rarediseases.org/wp-content/uploads/2024/01/NORD-Recommendations-for-CMS-Listening-Sessions_vf.pdf; Innovation and Value Initiative. Policy Symposium: Ensuring Equity in Implementation of IRA Drug Price Negotiations [Internet]. 2023. Available from: https://thevalueinitiative.org/wp-content/uploads/2024/02/2023-IRA-Policy-Symposium-Proceedings-Report_FINAL.pdf

[42] Innovation and Value Initiative. Policy Symposium: Ensuring Equity in Implementation of IRA Drug Price Negotiations [Internet]. 2023. Available from: https://thevalueinitiative.org/wp-content/uploads/2024/02/2023-IRA-Policy-Symposium-Proceedings-Report_FINAL.pdf

[43] Hollin IL, González JM, Buelt L, Ciarametaro M, Dubois RW. Do Patient Preferences Align With Value Frameworks? A Discrete-Choice Experiment of Patients With Breast Cancer. MDM Policy Pract. 2020;5:238146832092801; Groothuis-Oudshoorn CGM, Flynn TN, Yoo H Il, Magidson J, Oppe M. Key Issues and Potential Solutions for Understanding Healthcare Preference Heterogeneity Free from Patient-Level Scale Confounds. The Patient - Patient-Centered Outcomes Research. 2018;11:463–6.; Whitty JA, Fraenkel L, Saigal CS, Groothuis-Oudshoorn CGM, Regier DA, Marshall DA. Assessment of Individual Patient Preferences to Inform Clinical Practice. The Patient - Patient-Centered Outcomes Research. 2017;10:519–21.

[44] National Pharmaceutical Council. The Myth of Average Why Individual Patient Differences Matter [Internet]. Washington, DC; 2022 Jan. Available from: https://www.npcnow.org/sites/default/files/2022-01/The_Myth_of_Average_01.2022.pdf

registration),[45] a lack of accommodations for patients with disabilities,[46] and English-only materials may have further reduced participation among patients who were older and/or members of underrepresented or disadvantaged communities.

- **Strive to establish a partnership with patients, their families, and their advocates, including ongoing and two-way dialogue with critical stakeholders.** The patient-focused listening sessions were designed to provide an opportunity for one-sided communication rather than robust, two-way dialogue between CMS, patients, caregivers, providers, and patient advocacy organizations.[47] Patient engagement should communicate clear goals and strive to establish a partnership[48] with patients, their families, and their advocates, including ongoing and two-way dialogue[49] with these critical stakeholders. For example, despite CMS's initial intentions to draw lessons from the FDA's patient-focused drug development meetings[50] – which feature semi-structured, large-group facilitated discussion, follow-up questions, and polling among groups of patients, caregivers, and patient representatives[51] – it is not clear whether such methodologies informed the development of the listening session format. Patient experience dossiers have been proposed as one way to provide consolidated patient-centered evidence that informs more specific, meaningful, and two-way engagement with stakeholders during the evaluation process.[52] Future changes to the DPNP implementation process should prioritize more robust and meaningful engagement beyond time-limited, one-sided listening sessions to improve the patient-centricity of the DPNP.
- **Optimize event logistics.** For IPAY 2027, event logistics should be improved to promote patient engagement and minimize confusion, including the disclosure and registration processes. The disclosure process for IPAY 2026 may have negatively impacted participation. Stipends from patient organizations were listed in the same manner as funding from pharmaceutical

[45] National Organization for Rare Disorders. NORD Recommendations: Future Medicare Drug Price Negotiation Program Patient and Provider Listening Sessions [Internet]. 2024. Available from: https://rarediseases.org/wp-content/uploads/2024/01/NORD-Recommendations-for-CMS-Listening-Sessions_vf.pdf; Karlin-Smith S. As Medicare Drug Negotiation Patient Sessions Kick Off, Advocates Already Eyeing Improvements. Pink Sheet. 2026.

[46] National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

[47] Harrington RL, Hanna ML, Oehrlein EM, Camp R, Wheeler R, Cooblall C, et al. Defining Patient Engagement in Research: Results of a Systematic Review and Analysis: Report of the ISPOR Patient-Centered Special Interest Group. [cited 2024 Mar 12]; Available from: https://doi.org/10.1016/j.jval.2020.01.019; Innovation and Value Initiative. Principles for Value Assessment in the U.S. [Internet]. 2021. Available from: https://thevalueinitiative.org/wp-content/uploads/2021/01/2021-IVI-Principles-of-VA_FINAL.pdf; National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment [Internet]. 2024. Available from: https://www.npcnow.org/sites/default/files/2024-01/2024%20Guiding%20Practices%20for%20Patient-Centered%20Value%20Assessment%20January.pdf

[48] Harrington RL, Hanna ML, Oehrlein EM, Camp R, Wheeler R, Cooblall C, et al. Defining Patient Engagement in Research: Results of a Systematic Review and Analysis: Report of the ISPOR Patient-Centered Special Interest Group. [cited 2024 Mar 12]; Available from: https://doi.org/10.1016/j.jval.2020.01.019

[49] Miller M, Sara Van Geertruyden B;, Saxton ; M Claire, Courtney ;, Savage Y, Weir D, et al. A summit on amplifying voices of patients, caregivers, and people with disabilities in Inflation Reduction Act drug price negotiations. J Manag Care Spec Pharm. 2024;30:1–5.

[50] Seshamani M. Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 [Internet]. 2023. Available from: https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf

[51] Chalasani M, Vaidya P, Mullin T. Enhancing the incorporation of the patient's voice in drug development and evaluation. Res Involv Engagem. 2018;4:10.

[52] Oehrlein EM EHHTVJ. Listening Sessions Can Help CMS Become More Patient-Centered. Here's How The Sessions Could Be More Effective. Health Affairs Forefront. 2023

companies, which was viewed as perpetuating unfair stereotypes of patient organizations.[53] Because members of the public are often not accustomed to reporting conflicts of interest and were unclear as to whether and how these conflicts would be publicly communicated,[54] the process by which CMS defined, collected, and communicated COIs may have further deterred participation. Additional consideration may also be warranted in optimizing patient-friendly language during the speaker registration process.[55] For example, one page of the registration form asked patients if they would include real-world evidence or data in their spoken remarks, with definitions of these terms that may have lacked clarity for patients unfamiliar with them (e.g., "real-world data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources").[56] These definitions may have also conveyed to patients that CMS was not interested in qualitative accounts surrounding their lived experiences.[57]

NPC also supports CMS revising questions in the Negotiation Data Elements and Drug Price Negotiation Process ICRs when it is issued for IPAY 2027 to include "the factors a patient cares most about when assessing the value of a drug," but reiterates that the value of a drug should underpin the entire price-setting process, not only in this context.

Below, we provide considerations and best practices for patient input and value assessment when defining unmet need, selecting therapeutic alternatives, and determining clinical benefit.

i. Defining Unmet Need

In the revised guidance for IPAY 2026 and in this draft guidance, CMS defines unmet medical need as "a circumstance in which the relevant disease or condition is one for which no other treatment options exist, or existing treatments do not adequately address the disease or condition" and notes that it will consider *the extent to which* the selected drug addresses an unmet medical need [emphasis added]. This was a change from the initial IPAY 2026 guidance under which the evaluation of unmet need was dichotomous: "*whether* the selected drug meets an unmet medical need" [emphasis added]. NPC appreciates that CMS has revised this definition to align with a definition promulgated by FDA and that it will consider the nonbinding recommendations in FDA guidance when considering the extent to which a drug addresses an unmet medical for the purposes of the Negotiation Program, and notes that manufacturers will utilize this definition in communicating the scope of unmet need met by innovative

[53] National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

[54] National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

[55] National Organization for Rare Disorders. NORD Recommendations: Future Medicare Drug Price Negotiation Program Patient and Provider Listening Sessions [Internet]. 2024. Available from: https://rarediseases.org/wp-content/uploads/2024/01/NORD-Recommendations-for-CMS-Listening-Sessions_vf.pdf

[56] StopAfib.org. ACTION REQUESTED: Make Your Voice Heard by Medicare [Internet]. 2023 [cited 2024 Mar 12]. Available from: https://www.stopafib.org/afib-news-events/news/action-requested-make-your-voice-heard-by-medicare/

[57] National Health Council. Amplifying the Patient Voice: Roundtable and Recommendations on CMS Patient Engagement [Internet]. 2024. Available from: https://nationalhealthcouncil.org/wp-content/uploads/2024/03/Amplifying-the-Patient-Voice-Roundtable-and-Recommendations-on-CMS-Patient-Engagement.pdf

products. However, NPC remains concerned that a lack of transparency surrounding what specific factors related to unmet need that CMS will consider will result in an approach that is too narrow.

The FDA's definition of unmet need, as outlined in its guidance for expedited programs, includes improved efficacy, reduced toxicity and/or potential drug-drug interactions, and improvements in other benefits such as adherence.[58] Notably, the FDA definition of unmet need also highlights conditions for which there is significant heterogeneity in response to existing treatment options. Patients may respond differently to available treatment options due to pharmacologic differences, genetic risk, or social determinants of health, creating unmet need despite existing treatments.[59] NPC requests CMS clarify what elements of the FDA guidance it considers when determining unmet need, if they are weighted differently, and how these factors play a role in the price-setting process.

We believe assessments of unmet medical need should include a multifaceted definition informed by the patient perspective. Rigorous methods can be used to elicit consensus from clinician experts and have been used to identify unmet medical needs to achieve optimal treatment goals throughout the natural history of a disease.[60] These methods have identified patient-centered unmet needs, including patient quality of life, poor adherence, severe stages of a disease that are hard to treat, and patient preferred routes of administration.[61] Failure to capture the value of treatments that address patient-centered unmet needs disincentivizes innovations that meet those needs, in turn exacerbating disparities in health outcomes among patients receiving treatments less effective in their subgroups and/or unaligned with their preferences.

ii. Selecting alternatives

As discussed above**,** the choice of comparator is the fundamental driver of any value assessment and its implications for patients and caregivers. Accordingly, patient preferences and priorities that inform shared decision-making between appropriate treatment options should be incorporated into CMS's process for selecting treatment alternatives.[62] Prioritizing the patient voice in defining unmet medical need promotes patient access to not only *any* treatment alternative but *satisfactory* and *appropriate* treatment options aligned with patient preferences.[63] While CMS may take steps to further gather information that is important to patients when revising questions in the Negotiation Data Elements and Drug Price Negotiation Process ICRs for IPAY 2027 through questions related to patients' conditions and requesting a description about what it is like to live with a medical condition treated by the selected drug

[58] Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. U.S. Department of Health and Human Services. May 2014. Silver Spring, MD. Available at: https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

[59] National Pharmaceutical Council. The Myth of Average: Why Individual Patient Differences Matter. 2022. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2022-01/The_Myth_of_Average_01.2022.pdf

[60] Danese S, Allez M, Van Bodegraven AA, et al. Unmet Medical Needs in Ulcerative Colitis: An Expert Group Consensus. Digestive Diseases. 2019;37(4):266-283. doi:10.1159/000496739

[61] Danese S, Allez M, Van Bodegraven AA, et al. Unmet Medical Needs in Ulcerative Colitis: An Expert Group Consensus. Digestive Diseases. 2019;37(4):266-283. doi:10.1159/000496739

[62] Schmidt T, Valuck T, Riposo J, et al. Impact of Shared Decision-Making and Patient Decision Aids on Health Care Cost and Utilization in the US: A Systematic Review. J Clin Pathways. 2022;8(8):33-43. doi:10.25270/jcp.2022.12.0

[63] Zhang K, Kumar G, Skedgel C. Towards a New Understanding of Unmet Medical Need. Appl Health Econ Health Policy. 2021;19(6):785-788. doi:10.1007/s40258-021-00655-3

or therapeutic alternatives, NPC urges CMS to be transparent in informing patients and healthcare stakeholders of how this information is specifically used and weighted within the negotiation process.

iii. Determining clinical benefit

We encourage CMS to make use of resources to capture the patient's voice when selecting outcomes for evaluation of relative clinical benefit and to emphasize patient-centered benefits throughout its evaluation process. People with Medicare may prioritize different outcomes, such as symptom relief, improved quality of life, or indirect benefits such as reduced caregiver burden, compared to clinical outcomes like survival or disease progression.[64] Subgroups of people with Medicare may also have different priorities. Our research has identified heterogeneous patient preferences for both treatment characteristics and outcomes,[65] demonstrating the benefits associated with novel drugs and formulations that provide patients and providers with preference-aligned treatment options. Accordingly, patient preferences regarding the benefits and risks of a product, its available dosage forms, and any innovative delivery systems should be included early in the assessment. Patient preference information can inform many aspects of evaluation of benefit in value assessment, including defining what benefits are most important to patients, selecting measures to quantify benefits, and supplementing health state utilities.[66] The FDA has created useful backgrounders and issued guidance on collection and use of patient preference information.[67]

In evaluating relative clinical benefit, we encourage CMS to consider patient-reported outcomes that are complete, comprehensive, and fit for purpose, as opposed to limited, QALY utility-based approaches, including QALYs in or outside of a life-extension context.[68] Fit-for-purpose tools may include disease-specific measures in addition to overarching measures, as well as other outcomes that are meaningful to patients, including productivity, treatment and caregiver burden, and downstream healthcare utilization. Societal benefits, including scientific spillover, limiting the fear and risk of contagion for infectious diseases, and increasing equity have also been recognized as important elements of value.[69] Comprehensive approaches to measuring patient-centered value, including incorporation of factors beyond effectiveness and side effects, will result in more meaningful comparisons.[70]

CMS has a longstanding commitment to beneficiary engagement. By engaging with patients through multiple forms of direct engagement, CMS can ensure that it is receiving comprehensive and representative information directly from patients. We also encourage CMS to emphasize its commitment to patient engagement by including, in its initial offer and price justification, how the patient experience

[64] Ciarametaro M, Buelt L, Dubois RW. Getting Value Right: The Case For Indirect Benefits. Published online 2020. doi:10.1377/forefront.20200310.267867
[65] Hollin IL, González JM, Buelt L, Ciarametaro M, Dubois RW. Do Patient Preferences Align With Value Frameworks? A Discrete- Choice Experiment of Patients With Breast Cancer. MDM Policy & Practice. 2020;5(1). doi:10.1177/2381468320928012
[66] Marsh K, de Bekker-Grob E, Cook N, Collacott H, Danyliv A. How to integrate evidence from patient preference studies into health technology assessment: a critical review and recommendations. International Journal of Technology Assessment in Health Care. 2021;37(1).
[67] FDA. Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities Questions and Answers Guidance for Industry and Review Staff.; 2018. Available at: https://www.fda.gov/media/133620/download
[68] Brown J, Cryer DR. Is the QALY Fit for Purpose? Am J Accountable Care. 2021;9(2):8-13.
[69] Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. Value Health. 2018 Feb;21(2):131-139. doi: 10.1016/j.jval.2017.12.007.
[70] Westrich K, Lisabeth Buelt M. Current Landscape: Value Assessment Frameworks. Washington, DC: National Pharmaceutical Council; 2016.

was considered in the evaluation of unmet need, selection of treatment alternatives, and evaluation of clinical benefit.

IV. (Section 110) Part D Formulary Inclusion of Selected Drugs

The IRA requires Part D plan sponsors to include on their formularies drugs for which an MFP is available. However, the perverse incentives that remain in the ecosystem could be exacerbated because the MFP process will occur concurrently with Part D redesign; more so if selected drugs are in competitive classes and may be priced below the ceiling price. This could lead to adverse tiering impacting patient copayments and/or formulary-driven switching, increased utilization management, or other reductions in beneficiary access thwarting the intent of the MFP process and undermining the competition that has made Medicare Part D a success. What a patient pays for a medicine is a function of the insurance card in their pocket. Insurers also determine whether patients must navigate barriers such as prior authorization or step therapy. Right now, seniors have excellent access and experience few barriers to many of the first ten drugs selected — but that may change. Increased utilization management requirements, which are likely in response to the IRA, could reduce patient access — exactly the opposite of what the program intends to do.[71]

Experts have already warned that the intersection of MFP and Part D redesign provisions are likely to increase formulary exclusions.[72] The revised guidance for IPAY 2026 and this draft guidance for IPAY 2027 includes additional information about CMS's formulary review process and how it will monitor instances where Part D sponsors place selected drugs on non-preferred tiers, instances where a selected drug is placed on a higher tier than non-selected drugs in the same class, any instances where Part D sponsors require utilization of an alternative brand drug prior to a selected drug with an MFP, or any instances where Part D sponsors impost more restrictive utilization management for a selected drug compared to a non-selected drug in the same class. While we appreciate CMS's inclusion of additional detail regarding what the agency will monitor with regard to formulary compliance, we remain concerned that patient formulary access may be reduced as a result of IRA implementation and urge CMS to implement additional safeguards to protect patient access and prevent discriminatory behavior for IPAY 2026, 2027 and beyond. NPC and others will be closely monitoring changes to patient access as a result of IRA and encourages the agency to do the same.

V. General Comments

A. (Section 30.1.1) Orphan drug development

People with rare diseases face significantly higher health care costs,[73] and these patients and their families highly value the current and future treatments that meet their needs. Furthermore, the small

[71] Patterson JA, Wagner TD, O'Brien JM, Campbell JD. Medicare Part D Coverage of Drugs Selected for the Drug Price Negotiation Program. *JAMA Health Forum*. 2024;5(2):e235237. doi:10.1001/jamahealthforum.2023.5237

[72] Kelly C. Medicare Part D Redesign Could Expand Rebate-Driven Formulary Exclusions in Program. The Pink Sheet. January 26, 2023. https://pink.pharmaintelligence.informa.com/PS147634/Medicare-Part-D-Redesign-Could-Expand-Rebate-Driven- Formulary-Exclusions-In-Program

[73] Tisdale, A., Cutillo, C.M., Nathan, R. et al. The IDeaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. Orphanet J Rare Dis 16, 429 (2021). https://doi.org/10.1186/s13023-021-02061-3

patient populations for which orphan drugs are indicated are highly sensitive to changes in the research and development landscape, and the companies that develop orphan drugs are additionally highly sensitive to changes in the reimbursement landscape – especially those that threaten their ability to bring new orphan treatment to market and conduct post-approval research and development. NPC performed a study assessing the research and develop timelines of all small molecule drugs in the top 50 of 2020 Medicare Part D spending and found that all six drugs in its study that were initially approved for an orphan indication had subsequent indications, including 18 subsequent orphan-designated indications. The IRA's single orphan indication exclusion disincentives research towards these additional orphan-designated indications, likely resulting in fewer treatment options for patient with rare diseases.[74] The impact of the DPNP was recently acknowledged by FDA's deputy center director for strategy, policy, and legislation, Julie Tierney, who noted that the program could discourage companies from seeking approval of orphan drugs for multiple rare diseases.[75]

In our comments on the IPAY 2026 guidance, we encouraged CMS to broadly interpret the IRA statute to exclude orphan drugs from negotiation and when determining the number of designations and indications that exempt an orphan product from selection. We believe that CMS should work to preserve incentives for orphan-drug research and development, consistent with Congress's mandate, for example, clarifying that for orphan drugs, the 7- of 11-year period that must elapse before a drug can be considered for negotiation begins upon the date that the orphan drug exclusion no longer applies.

We continue to advocate for this outcome, acknowledging that CMS has taken the position that it lacks the statutory authority to implement it and that a change in legislation might be the path forward. We also note concerns that CMS's reliance on the databases mentioned in Guidance may not always provide an accurate reflection of whether a drug's indication falls within the scope of the orphan drug designation.

B. (Section 30.1) Identification of Qualifying Single Source Drugs for IPAY 2027

CMS takes a broad and sweeping approach to defining qualifying single-source drugs in Section 30. This definition ignores the value of novel formulations and delivery systems, which should be considered at the selection phase of the process not the MFP application phase. We hope that in permitting comments on Section 30 for IPAY 2027 CMS will change this approach.

C. (Section 60) Negotiation Process (MFP Calculations)

[74] Patterson, J, Motyka, J, O'Brien, J.M. Unintended Consequences of the Inflation Reduction Act: Clinical Development Toward Subsequent Indications. February 2, 2024. https://www.ajmc.com/view/unintended-consequences-of-the-inflation-reduction-act-clinical-development-toward-subsequent-indications

[75] https://insidehealthpolicy.com/daily-news/cber-s-tierney-ira-could-impact-rare-disease-small-molecule-development; Chambers JD, Clifford KA, Enright DE, Neumann PJ. Follow-On Indications for Orphan Drugs Related to the Inflation Reduction Act. JAMA Netw Open. 2023;6(8):e2329006. doi:10.1001/jamanetworkopen.2023.29006

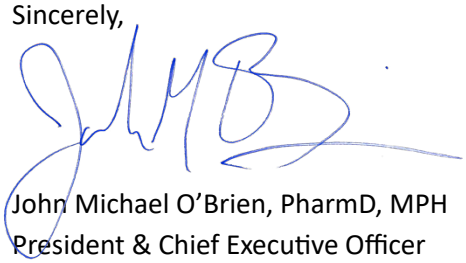
Our research demonstrates how novel formulations provide patients and providers with treatment options that account for heterogeneous patient preferences[76] and promote medication adherence through reduced regimen complexity.[77] Given the documented value of dosage form innovation on patient-centered care and outcomes, NPC encourages CMS to incorporate the value of novel formulations in its price determination and negotiation process. CMS provided additional detail about the calculation of 30-day equivalent supply in this draft guidance, however, we remain concerned about how calculation and implementation of MFP will incorporate and effect the use of loading doses and severity-based dosing, common clinical practices that result in the amount of medicine being used by one patient being different than that used by others. We appreciate CMS stating it will as feasible share inputs behind its methodology with the Primary Manufacturer during the negotiation process and urge CMS to ensure it is feasible for all selected drugs, as open communication about the agency's estimation of a 30-day equivalent supply is vital for manufactures.

CMS has noted it may use an alternative methodology for calculating a 30-day equivalent supply as appropriate for the therapeutic alternative(s) and suggests it may use this methodology for therapeutic alternative(s) covered under Part B. NPC asks CMS to provide examples of where an alternative methodology might be used for Part D drugs, given that IPAY 2027 will be for Part D drugs only (Section 60.3.2).

Conclusion

The National Pharmaceutical Council appreciates the opportunity to submit comments in response to this Guidance and looks forward to additional opportunities to engage with CMS as it implements the second cycle of the Medicare Drug Price Negotiation Program. Please contact me at john.obrien@npcnow.org or (202) 827-2080 if we may provide any additional information.

Sincerely,



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President & Chief Executive Officer

[76] Hollin IL, González JM, Buelt L, Ciarametaro M, Dubois RW. Do Patient Preferences Align With Value Frameworks? A Discrete- Choice Experiment of Patients With Breast Cancer. MDM Policy & Practice. 2020;5(1). doi:10.1177/2381468320928012
[77] Wertheimer AI, Santella TM, Finestone AJ, Levy RA. Drug delivery systems improve pharmaceutical profile and facilitate medication adherence. Adv Ther. 2005 Nov-Dec;22(6):559-77. doi: 10.1007/BF02849950.