



The professional society for health economics and outcomes research

Improving healthcare decisions

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Rob Abbott
ISPOR
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Dear The Centers for Medicare & Medicaid Services (CMS):

ISPOR – The Professional Society for Health Economics and Outcomes Research - is pleased to respond on behalf of its membership to your consultation entitled “**Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair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.**”

ISPOR is a scientific and educational society with many of our members engaged in evaluating health technologies, including pharmaceuticals, medical devices, and other interventions. We have a large membership living and working in over 100 countries globally, across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

The response to this consultation was led by the ISPOR Institutional Council. We solicited comments from the entire ISPOR membership. The attached document provides a summary based on their comments. We hope they prove useful.

ISPOR would be happy to answer any questions about our response, to serve as a partner, or to participate in any follow-up consultations on the relevant program items mentioned within the report.

Sincerely,

Robert Abbott
CEO & Executive Director
ISPOR

Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair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

Clear and transparent communication. Maintaining transparency throughout the negotiation process is critically important. Transparent negotiations that incorporate considerations of alternative treatments and comprehensive manufacturer data have the potential to reduce costs for Medicare beneficiaries and create secondary effects for commercial markets. However, it is essential to strike a balance between transparency and confidentiality; without proper safeguards, there is a risk of compromising proprietary information, which could stifle innovation in drug development. All stakeholders want to make progress against diseases with high unmet need for patients.

Evidence about alternative treatments. Clarification is needed regarding the process of analyzing drugs with multiple indications (and potentially different treatment alternatives for said indications). Products with multiple indications will almost certainly be selected for drug price negotiations. The need for clarification will increase as more products with multiple indications are selected leading to major analytical challenges to define a negotiated price. For example, a weighting method could be applied to address the challenge of assessing multiple indications. If indication weighting is pursued for high-volume indications, we request that CMS also consider selecting smaller indications that address high unmet need when considering the selection of alternative treatment comparators. For example, incentives to invest in research and development for pediatric oncology indications should be maintained. For all indications, we encourage CMS to consider comparator treatments that are currently considered the best standard of care.

When selecting a set of alternative therapies, it is also important to consider the stage of the product's lifecycle. At launch, products are often compared to placebo or the current standard of care. For example, comparing apixaban to warfarin reflects the previous standard of care. In health economics and outcomes research (HEOR), apixaban would be compared with other Factor Xa Inhibitors. When the approved therapy represents a major advance or new standard of care, the appropriate alternative can be determined by evaluating clinical guidelines (if available) or by asking manufacturers to provide indirect comparison data against appropriate comparators. These approaches are prevalent in health technology assessment (HTA) bodies globally.

ISPOR's membership would be pleased to help CMS with identifying methods to determine appropriate treatment alternatives.

Unmet medical need. It remains unclear how CMS is applying the definition of unmet medical need. Unmet medical need is a subjective term that lacks consensus.

Unmet medical need is dynamic and may change based on the stage of the product's lifecycle. Unmet need will decrease as the approved therapy is adopted and becomes the new standard of care.

In some cases, unmet medical need is addressed by providers through the use of drugs off-label. We request clarification as to how CMS will consider off-label indications. Questions related to off-label indications will increase as CMS approaches the 2028 implementation of Part B drug Negotiations.

The degree and context of unmet medical need may also differ based on a person's socioeconomic background and disease status. We propose the development of a "whole health" approach to quantifying unmet medical need. ISPOR defines whole health as "the collective impact of physical, behavioral, spiritual, and socioeconomic factors on one's health. It prioritizes enhancing health outcomes and the coordination of health and social service systems through a personalized and team-based approach, while promoting overall

well-being, disease prevention, and equitable and accessible care.”¹ Individuals diagnosed with conditions for which there are no approved medications can experience negative whole health effects. HEOR uses data from a variety of sources, such as electronic medical records, claims data, patient surveys, and economic models to develop a comprehensive value assessment.

Furthermore, ISPOR seeks clarification regarding a potential premium for products with new indications addressing unmet medical need. For example, Japan provides about an 8% premium on pricing for drugs that meet unmet medical needs.² We ask that CMS consider a similar approach when assessing the current and future value of a product as there is a risk of disincentivizing new indication development.

Assessment of value. ISPOR recommends that a comprehensive value assessment should be the main focus of setting prices, as opposed to drug development and manufacturing costs. Data that manufacturers are currently required to submit includes information on financial costs (eg, research and development, production costs) and revenue. The CMS guidance should reflect broader aspects of value, such as clinical benefit, improvements in patient reported outcomes, reduction in toxicity, systemic cost offsets, functional status, and caregiver spillover effects. We recommend investigating elements of value in the ISPOR Value Flower.³ It will be important to consider the value proposition of a drug relative to the three different patient groups that Medicare serves: Adults aged 65 and older; individuals diagnosed with end-stage renal disease (ESRD); and dual eligible (Medicare and Medicaid). ISPOR members have the methods and experience to build comprehensive value assessments based on these different patient populations.

Use of real-world data in decision making. CMS has mentioned that the gold standard of evidence is randomized controlled trials (RCTs) and that real-world evidence (RWE) will be used as secondary evidence. RCTs may not provide the most relevant evidence for today’s decisions. For example, RCTs that support older indications and products that have been on the market for 7+ years often have RCTs that no longer reflect the current state of medicine and clinical care management. As we noted in [our 2023 response to CMS’s guidance document](#), we recommend the use of both comparative effectiveness and RWE to inform decisions. RWE has been shown to appropriately complement RCT data.⁴⁻⁵ ISPOR has issued several good practice guidance reports on the use and grading of RWE and comparative effectiveness.⁶⁻¹⁴ We also strongly encourage using Hypotheses-Evaluating Treatment Effect (HETE) RWE studies, whose study protocols are provided as a part of the Real-World Evidence Registry, and standardized matrix has been used for its reporting.¹⁵⁻¹⁷

Patient engagement. We are encouraged by CMS’ request for assistance to establish best practices for engaging patients in the drug price negotiation process. We ask CMS to consider using studies that genuinely engage patients in research. An ISPOR working group defined patient engagement in research as, “the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients’ contributions as partners, recognizing their specific experiences, values, and expertise.”¹⁸

We encourage CMS to consider two recent publications by experts in the field (and active ISPOR members) about frameworks for patient-centered research.¹⁹⁻²⁰ We also encourage CMS to refer to the US Food and Drug Administration (US FDA), especially their experiences with the patient-focused drug development (PFDD) program, for examples of best practices in engaging patients in decision making.²¹ ISPOR has also partnered with Health Technology Assessment international (HTAi) to publish good practices in stakeholder engagement in deliberative processes.²² The National Health Council (NHC) and the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) also have recommended resources and expertise with engaging patients in discussions in the United States.²³⁻²⁴

ISPOR would be happy to help collaborate with CMS as a neutral third party to facilitate engagement with

patient representatives for a systematic and scalable discussion framework.

PICOs. We recommend the development of a clear scoping framework so manufacturers can estimate the resources required to generate and submit relevant information. We then propose that the scope for PICOs (**P**opulation, **I**ntervention, **C**omparator, **O**utcomes) for each relevant indication for each product under consideration should reflect a mutual consensus between the manufacturer and CMS. The finalization of the PICOs ideally would incorporate robust input from patient and provider organizations.

Ensuring safeguards for patient access. A review of the CMS Prescription Drug Plan Formulary and Pharmacy Network information files analysis found that access to protected class drugs placed on specialty tiers of prescription drug plans and Medicare Advantage prescription drug plans, was heavily restricted due to utilization management tools (eg, prior authorization, step edits). These restrictions may impede patient access and affordability.²⁵⁻²⁶ If evidence-based safeguards are not established for drugs selected under the program, patients might experience similar hurdles for drugs under price applicability year 2026, 2027 and beyond.

Current Part D policy requires sponsors to include all drugs within 1 of the 6 protected classes (ie, antiretrovirals) without prior authorization and step therapy. This approach ensures that patients have unimpeded access to necessary medications without lengthy delays and affordability concerns. Therefore, we urge CMS to incorporate similar safeguards across selected drugs within the program to prevent potential barriers that could hinder patient access.

Medicare Transaction Facilitator. With respect to CMS plans to develop a Medicare Transaction Facilitator (MTF) to assist with data facilitation in a retrospective rebate model, ISPOR anticipates a great deal of planning and dialogue will be required to facilitate an efficient exchange of data between pharmaceutical supply chain entities and Medicare. ISPOR can organize and manage meetings of this size and complexity and as well as develop specialized training programs to support MTF implementation. ISPOR would look forward to further dialogue with CMS on this topic.

In conclusion, ISPOR welcomes further conversations with CMS about best practices in using evidence to make decisions. Evidence-based value assessments conducted using rigorous HEOR scientific practices are critical to make sound decisions. As the leading global Society, we have many experts and years of experience that we can provide CMS to help make these decisions. We welcome the opportunity to continue the policy dialogue for many years to come.

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