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DEFINING "UNMET MEDICAL NEED" IN THE INFLATION REDUCTION ACT FOR THE MAXIMUM FAIR PRICE: REFLECTING PATIENT INPUT

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Assessing Unmet Medical Need: Defined by Patients for Their Health

Executive Summary

Patients, people with disabilities, and their caregivers want their experiences and outcomes that matter to them to be considered when the government or other payers make decisions about their treatments. The Inflation Reduction Act (IRA) directs the U.S. Federal government to establish the price for some of the highest selling drugs in the Medicare program based on a number of factors including whether the drug serves an “unmet medical need” relative to other therapeutic options. This report highlights the perspectives of the patient community on “unmet medical needs” based on survey research and public comments from patient advocacy groups and compares those findings to the government’s proposed approach to consider unmet medical needs under the IRA.

This research surveyed 300 patients who were at least 65 years old, taking a medicine at least once a week and had at least one chronic health condition. The views expressed in the patient survey do not align with the government’s proposed definition and process for assessing the value of a drug in addressing unmet medical need in the IRA. Patients and their advocates want a process that is transparent and considers important attributes of a drug such as the reduction in side effects relative to other options, the ability to take the medicine at home, and the extension of life so that another treatment could be developed. Specifically, this research found:

- Patients and their advocates consider the following factors as top priorities to include in the definition of unmet medical need and its assessment: underserved groups, patients who have tried and failed on certain treatments, treatment toxicity or side effects, and ease of treatment administration such as having a pill form rather than shot or infusion.
- Nearly 9 in 10 patients feel strongly that a drug addresses an unmet medical need if there are no or limited treatment options or if it offers benefits over existing treatment options such fewer side effects, can be taken at home instead of delivered by a physician, or helps the person to work or care for others.
- Approximately 75-80% of patients reported improved symptoms (e.g., fatigue, mobility), ability to extend life long enough for a better treatment to become available, and reduced costs not related to medical care as addressing important unmet medical needs. Among Black patients, these priorities ranked even higher.
- Only about one-third of Black patients (33%) and patients with incomes below $40,000 (29%) reported that their health needs were treated extremely well, compared with 53% of white patients.
- 57% of Black patients reported being hospitalized one or more times in the past year, while only 25% of white patients reported being hospitalized in the past year.
- 39% of patients worried that their insurance would deny payment for important tests or treatments, however, among Black respondents, this number grew to 45%.
- Almost all patients (91%) felt that health insurers should ask patients for input on unmet medical needs and only 18% of patients report that they think the government is well positioned to identify unmet medical needs when they evaluate medicines.

Patient preferences overall were more closely aligned with the approach the Food and Drug Administration (FDA) uses to consider whether a drug addresses an unmet medical need, which is more inclusive of patient input and more transparent than the process proposed for the IRA. As the U.S. government takes steps to

implement the IRA, it should revise the proposed approach to defining “unmet medical need” to meaningfully engage a diverse and representative group of patients, caregivers, and advocacy organizations throughout the entirety of the process to help ensure: 1) the definition is comprehensive and equitably meets the needs, preferences, and priorities of all people whose treatment, experience, and outcomes may be impacted, and 2) transparency of the type and source of evidence sought, collected, considered, and incorporated in the final definition.

Introduction

The Inflation Reduction Act (IRA) directs the U.S. Federal government to establish the price for some of the highest selling drugs in the Medicare program. When determining the price, the Centers for Medicare and Medicaid Services (CMS) is required to consider, in addition to other factors, whether the drug they are evaluating serves a critical “unmet medical need” relative to other therapeutic options. CMS is asked to consider not just the availability of other treatments when assessing the value of a drug, but also to consider if those other treatments are “adequately” addressing patient needs for treatment and diagnosis[1]. This is a challenging task as it is well established that defining “unmet medical need” for medicines is difficult; health technology assessment agencies worldwide have raised issues about the lack of agreement on a useful single overarching definition that also considers individual patient needs. Nevertheless, it is critical that CMS does not take this task lightly and inadvertently make the same mistakes of international health technology assessment agencies that have adopted overly narrow definitions of “unmet medical need” that fail to reflect the perspectives and myriad needs of individual patients.

The process that CMS adopts and implements to assess a drug’s value, including how the drug addresses unmet medical needs adequately for patients and how that assessment informs the price, will send signals to biopharmaceutical investors about what types of drug innovations are valued. Addressing unmet medical needs is not just addressing today’s health but it is also setting the path for therapeutic advance. For example, a drug that is targeted to a specific gene is a therapeutic advance, but may or may not be considered as addressing an unmet medical need if there are already drugs that treat the condition untargeted. If CMS does not account for “unmet medical needs” as seen through the lens of patients when establishing price, then investments that are meaningful to patients may, inadvertently, be discouraged.

In this whitepaper, we present perspectives from the patient community on the definition of unmet medical need proposed by CMS in their March 2023 guidance. This is based on 1) feedback on the proposed definition to CMS from several U.S. patient advocacy organizations and 2) results of a survey of 300 people over the age of 65 reporting their viewpoints on what qualifies as an “unmet medical need”. We find that those surveyed believe that the accurate definition of unmet medical need is far broader, more engaging of patients, and more nuanced than the definition CMS has proposed. They also raised the importance of attributes of medicines that have value for patients to treat unmet medical needs that are not typically reported in easy to collect data such as drug FDA approved labels or published literature. These findings indicate that CMS should engage the patient community more directly to ensure the approach adopted, including the factors considered in determining price, adequately reflects patient needs, preferences, and priorities. At a minimum, CMS should adopt a broader definition of “unmet medical need” than that proposed in their initial guidance.

[1] Specifically, “The extent to which such drug and therapeutic alternatives to such drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.”

Overview of the IRA Provisions to Determine a Maximum Fair Price

The IRA directs CMS to select and set the maximum fair price (MFP) for a growing number of drugs in Medicare parts D (typically drugs taken orally, like pills) and B (physician administered drugs, such as an infusion) each year beginning in 2025. This action will have direct implications for seniors and people with disabilities who receive their medication(s) through Medicare. The MFP ceiling is set by a formula in the IRA. CMS may make additional price reductions below the ceiling at their discretion, and in fact, the statute requires CMS to achieve the lowest possible MFP for a selected drug.

In order to determine a drug’s MFP, CMS is required to consider a list of factors. One factor CMS must consider is whether the drug addresses an unmet medical need when the condition is not adequately treated or diagnosed by other available treatment options. But the term “unmet medical need” is not defined in statute. There is a myriad of definitions of “unmet medical need” and treatment “adequacy” CMS could consider: the availability of another treatment for the disease, the burden of the disease, the urgency to treat (such as an infectious disease), drug delivery (such as in a pill or injection) and patient characteristics (such as the higher prevalence or morbidity of the disease in children or others who may be disadvantaged in the social system). [2] Defining “unmet medical need” at a population level can obscure important differences between individuals who have different experiences with a disease and variable access to care.

On March 15, 2023, CMS issued initial, draft guidance on how they would establish the MFP including how the agency will assess whether a drug addresses an unmet medical need[3]. CMS states that it “intends to define [unmet medical need] as treating a disease or condition in cases where very limited or no other treatment options exist.” CMS will consider the effects on individuals with disabilities, the elderly, terminally ill, children, and other patient populations (not defined in the guidance). CMS offered limited specificity on issues of importance to patients such as what data will be considered (e.g., published literature only, patient surveys, registries), how they determine the value of having multiple therapeutic options for people for whom some drugs don’t work, subgroup analysis of effect on different groups such as by age, race/ethnicity, or gender. Furthermore, CMS does not describe how different types of evidence would be evaluated (e.g., compendia vs. clinical trials vs real-world evidence) or how new information would be considered. They do not indicate that their assessment will be made available publicly and, accordingly, open to public comment.

Federal Government Assessments of Unmet Medical Need

Unmet medical need is a concept already in use in drug development and approval for use in patients. Specifically, the FDA has a definition that is different from what CMS has proposed for the IRA. In considering expedited review for the approval of novel drug treatments or new indications, the FDA has an established definition of unmet medical need[4] . The FDA definition and approach explicitly considers heterogeneity of treatment effects and is more inclusive of diverse patient experiences. The definition that CMS proposes does not explicitly consider any of these attributes of a drug therapy. The FDA first considers if there is an existing therapy or not. Then when there is an available therapy, relative to the existing therapies, the FDA considers if the new drug:

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[2] ZHANG K, KUMAR G, SKEDGEL C. TOWARDS A NEW UNDERSTANDING OF UNMET MEDICAL NEED. APPL HEALTH ECON HEALTH POLICY. 2021 NOV;19(6):785-788. DOI: 10.1007/S40258-021-00655-3. EPUB 2021 JUN 18. PMID: 34143420; PMCID: PMC8545781.

[3] CENTERS FOR MEDICARE AND MEDICAID SERVICES, GUIDANCE ISSUED MARCH 15, 2023 ACCESSED HTTPS://WWW.CMS.GOV/FILES/DOCUMENT/MEDICARE-DRUG-PRICE-NEGOTIATION-PROGRAM-INITIAL-GUIDANCE.PDF

4 GUIDANCE FOR INDUSTRY EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS – DRUGS AND BIOLOGICS, 2014 HTTPS://WWW.FDA.GOV/DRUGS/GUIDANCE-COMPLIANCE-REGULATORY-INFORMATION/GUIDANCES-DRUGS

- yields an outcome or have a side effect profile that is significantly superior to the existing therapy,
- has meaningfully superior tolerability or less toxicity for all or some patients,
- yields better health outcomes in people who are not helped by the existing therapy,
- has an ability to be used in combination with other exiting agents for better health outcomes,
- has similar outcomes but a superior mode of administration (oral vs iv) that is expected to reduce poor outcomes,
- addresses an emerging public health need such as a shortage
- when the other available therapy was approved on a surrogate endpoint and has not been verified in follow on studies in primary endpoints

Patient Perspective on Unmet Medical Need, Response to the CMS Guidance

This whitepaper is written in partnership with several patient advocacy organizations[5]. Many of these organizations offered feedback to the guidance on MFP in letters to CMS. We examined the comments to CMS from letters that represent more than 100 patient organizations focusing on their comments related to CMS on their proposed definition of “unmet medical need”. These comments are summarized in the table below:

Process for Determining Whether a Drug Meets an Unmet Medical Need	How to ***Define*** Unmet Medical Need
• Solicit input from patient organizations including surveys and particularly other information they may have that is not typically collected for clinical trials or published research. • Share the methodology used to assess unmet medical need, as well as any evidence or analysis (e.g., a description of models). • Provide clear and evidence-based definitions for the standards of evaluation including how clinical benefit or unmet need will be translated into a price for a medicine. • Establish and publicize the process for evaluating potential bias in the evaluation. • Specifically define the term related to the consideration of “other factors” they used in the guidance. • Consider evidence that is relevant to health but not often captured in healthcare delivery data (e.g., caregiver burden, patient preferences and societal and economic impact of the treatment).	• Recognize that unmet medical need is not an assessment of the average benefit for all people and consider and put value to the needs of specific subpopulations. • Consider the need for treatment for people with complex medical conditions, who have tried and failed on the ‘standard of care’, and this may include people with multiple chronic conditions who may experience drug-drug interactions or for other reasons need treatment options. • Evaluate how the medicine addresses the needs of people who are typically not well served by the U.S. healthcare system, this includes racial and ethnic minorities, LGBTQ, women, low-income people, people with lower levels of education and people living in rural communities. • Assess the value of treatment attributes that are not directly related to the primary outcome of the drug including having fewer side effects, more manageable modes of administration (e.g., pill vs injection) or frequency of administration.

5 Partnership For Chronic Disease, Alliance For Aging Research, Autoimmune Association, Cancer Care, Cancer Support Community, Health Hiv, Partnership To Improve Patient Care, Preparedness And Treatment Equity Coalition And Tigerlilly

	• Avoid reliance on cost effectiveness metrics such as QALYs in any way.

Some patient groups suggested that CMS could use a process that more closely mimics the FDA approach to considering unmet medical need and its definition. This includes recommendation to convene a patient focused externally led meeting to transparently review information related to treatment attributes. These letters also encourage CMS to support patient organizations in the process of offering feedback with financial and logistical help, and by soliciting input in a two-way communication process. Finally, they encourage CMS to follow up and evaluate the impact of the MFP on access to medicine and patient costs.

Five patient advocate organizations responded to our survey in May 2023 on the attributes that are important to include in a definition of unmet medical need. Every organization surveyed noted that it was a top priority to assess unmet medical need in typically underserved groups including specific races or ethnicities, age, gender, sexuality or living in a rural area. They also indicated it is a top priority to consider unmet medical need in people who have tried and failed on certain treatments. All surveyed indicated that considering toxicity or risk associated with a medication such as the risk of blood clots or falls, evaluating side effects that can interfere with health and well-being such as nausea or fatigue, and ease of administration such as having a drug in a pill form rather than a shot or infusion should be a top priority or at least a useful addition to CMS consideration. Opinions were mixed on the utility of CMS considering the value of a drug to address an unmet medical need when used in combination with other drugs, for certain genetic subtypes or the effect of the drug on the use of non-medicine alternatives such as decreased reliance on a wheelchair.

Results of a Survey of Patient Perspectives on Factors Constituting Unmet Medical Needs

A survey was administered to seek input directly from patients regarding what factors should be considered in defining unmet medical need. It was completed by 300 people through an internet survey platform in May 2023. Respondents selected were at least 65 years old, currently taking a medicine at least once a week that is prescribed by a healthcare professional and had at least one common chronic healthcare condition. The survey included quotas to reflect the demographics of the Medicare population[6]. Similar to other surveys of the Medicare population the most common conditions were heart disease, diabetes, respiratory disease and 25% of those surveyed had been in the hospital at least once in the last year[7]. While 50% felt that their healthcare needs were treated extremely well by their current medications, 23% had symptoms that bothered them or limited their daily activities. (Tables 1-4 appendix)

Key findings from the survey show that most individuals define “unmet medical need” far more broadly than CMS has proposed to do in the initial guidance document and much closer to the FDA definition. When queried on their definition of unmet medical need, respondents highest rated attributes reflected a desire for having multiple treatment options, offers additional benefits relative to an existing treatment. Findings include:

[6] 55% of people over 65 in the U.S. are women, 20% are racial or ethnic minority 2021 PROFILE OF OLDER AMERICANS, Administration for Community Living, U.S. Department of Health and Human Services

[7] CHRONIC CONDITIONS AMONG MEDICARE BENEFICIARIES 2012 CHARTBOOK (MOST RECENT), CENTERS FOR MEDICARE AND MEDICAID SERVICES

Table A

Rate the importance of a new treatment that addressed the following indirect clinical need(s)		Percent rated important or extremely important
A new drug meets an unmet medical need when there are very limited or no other treatment options for the medical condition	260	*87%*
A new drug meets an unmet medical need when some treatments are available, but it offers additional benefits (for example, is safer or more effective, reduces side effects, or can be taken at home instead of a doctor's office)	265	*89%*
A new drug meets an unmet medical need when some treatments already are available, but it better addresses a patient's specific needs, preferences, and treatment goals (e.g., such as returning to work faster, or better managing their symptoms)	258	*87%*

When considering what is important from a new treatment option, the attributes rated as important or extremely important reflected a desire for improved symptom control, fewer side effects, and provided a treatment option for people who don’t have other options. More than three in four also value innovation represented by the ability of a treatment to extend life long enough for a better treatment to become available. Respondents also highly rated attributes that are related to ease of administration and quality of life such as ease of administration or ability to be productive in work and life.

Table B: important treatment attributes for unmet medical need

Rate the importance of a new treatment that addressed the following clinical need(s)		Percent rated important or extremely important[8]
Improved symptoms related to a disease or condition (such as reducing pain, fatigue, or nausea or improving mobility)	237	*80%*
Reduced side effects compared to other available treatments	240	*81%*
Extended life long enough for a better treatment to become available	225	*76%*
Provided treatment for a group of people, or for a particular condition, that otherwise had few treatment options	211	*71%*

Rate the importance of a new treatment that addressed the following indirect clinical need(s)		Percent rated important or extremely important

[8] 70% or more rated as important or extremely important

Allows patients to be able to take the medicine at home	271	*91%*
Improves productivity for patients or caregivers, for example helps people do better at work or school, miss fewer days of work or school, or helps caregivers better care for family, etc.	224	*75%*
Reduces costs due to illness not related to medical care	226	*76%*

Respondents were queried on their viewpoint related to how well an insurance company or the government could assess their unmet medical needs. In this, survey respondents indicated what they want their insurers to consider as it relates to their unmet medical needs. This included seeking input from patients about their specific needs and explaining how they used patient input to make their coverage decisions. They had concerns about their insurance covering the treatments they needed. They had low confidence in the ability of the government to adequately assess their unmet medical needs.

Table C: Questions Related to Insurance and Definition of Unmet Medical Need

Question	% agree or strongly agree	% disagree or strongly disagree
Patient Input		
When my health insurance considers unmet medical need in making decisions, they should consider patients with a variety of health needs, such as: need for a new treatment when an old one stops working; reduced side effects; improved quality of life; more convenient or less painful ways to take the medicine; etc.	90%	0%
My health insurance should ask patients like me for our input on our unmet medical needs before making decisions. When they make decisions, they should explain how they took our input into consideration.	*90%*	*0%*
Confidence in Insurer		
I worry my health insurance will deny, or has denied, payment for tests or treatments that are important to me and recommended by my doctor.	39%	40%
I can rely on my health insurance to consider my unmet medical needs when making coverage and payment decisions.	71%	9%
Confidence in Government		
Government bureaucrats are well positioned to identify unmet medical need.	*17%*	*53%*

Health Disparities and Health Equity: Considering Unmet Medical Need and Health in Typically Underserved Patient Populations

There were notable differences in the underlying health and perceptions of unmet medical need among survey respondents that identified as Black relative to those who identified as white and for people in the lowest

income groups. For Black respondents, 57% had been hospitalized one or more times in the past year, compared to 15% for white respondents and 25% on average[9]. Twenty-seven percent of people in the lowest income group had been hospitalized one or more times, similar to the group average. Only 33% of Black respondents agreed that their health conditions were treated extremely well; 29% of people with annual incomes below $40,000 per year agreed with that statement compared to 53% of whites and 50% overall.

In their assessment of what is important when considering unmet medical need 90% of Black respondents (vs. 72% for whites) rated as extremely or very important that a treatment extended life long enough for another treatment to become available, and 71% gave the extremely or very important rating to a medicine that makes it so patients can take it less frequently (vs. 57% for whites). The differences in these assessment for various income groups were not as significant.

Addressing health equity in the implementation of the IRA, in particular the MFP program and its associated impact, aligns with CMS Framework for Health Equity 2022-2023. The agency released a document describing how it has challenged itself to “to incorporate health equity and efforts to address health disparities as a foundational element across all our work, in every program, across every community.” The agency recognizes that unmet social needs are also a contributor to poor health, as such attributes such as ease of administration and access to a medication for a person who has tried and failed on other options should be prioritized. Furthermore, in this framework, the agency outlines five key priorities including one to “increase all forms of accessibility to healthcare services and coverage”. With this priority, CMS should explicitly consider the effect of how they evaluate unmet medical need in the value assessment process.

Conclusion

The vast majority of patients surveyed felt strongly that a drug addresses unmet medical needs if it offers benefits over existing treatment options such as fewer side effects, can be taken at home instead of delivered by a physician, or allows for returning to work faster. These findings corroborate formal feedback from patient advocacy groups to CMS arguing that CMS’ proposed definition of unmet medical need would exclude many needs that are important to patients. In particular, patients report reduced side effects, improved symptoms, options in mode of administration, and treating select subgroups in need as highly important in defining unmet medical need. Additionally, 9 in 10 patients felt that insurers should incorporate those same factors in coverage decision making. More than half of patients disagree that the government is well positioned to identify unmet medical needs.

As CMS implements the provisions of the IRA to determine drug prices, they should revise the proposed definition and process and take steps to engage patients directly for their perspectives in the assessment of a drug’s clinical benefit and adopt a broad and flexible definition of “unmet medical need” that reliably reflects the diverse needs of all patients. The survey of patient groups and their advocates indicates that the type of attributes and process used by the FDA to define when there is unmet medical need is much more reflective of their preferences and health requirements. CMS should assure the patient community that the process to determine a drug’s clinical benefit and ability to address unmet medical need is transparent, clear, relies on relevant data, and adequately addresses all patients’ health needs, particularly those underserved by the U.S. health system. To help achieve this end, CMS must affirmatively seek the engagement of a diverse and

[9] In this whitepaper we separate responses for Black respondents relative to white and for the lowest income group <$40,000 per year. Those segments both had a relatively large sample size.

representative group of patients, caregivers, and advocacy organizations throughout the entirety of the process, facilitate the collection and consideration of meaningful patient input, and incorporate that patient input.

Patient organizations and people surveyed reflected an appreciation for attributes of medications that meet an unmet medical need that CMS did not explicitly include in their proposed definition under the MFP guidance. This includes having medications available for specific subpopulations, ease of use and a superior side effect profile. People surveyed did not agree that the government is ideally suited to assess their unmet medical needs and both patient organizations and people surveyed indicated that patients should be engaged and asked about their unmet medical needs to inform the process. As the federal government and CMS, the implementing agency, roll out the Inflation Reduction Act Maximum Fair Price setting, accommodating patient preferences will need to evolve to represent values important to beneficiaries of the program. This will require a process that relies on a broader set of variables to assess value, considers differences in needs between different people and their circumstances with health and life, addresses the particular challenges faced by underserved populations, and engages the people the Medicare benefit is designed to serve for this information.

Appendix

Table 1 Basic Demographics

	#	%
Total Qualified Respondents	**300**	**100%**
Gender		
Men	135	*45%*
Women	165	*55%*
Race and Ethnicity		
Asian / Pacific Islander	10	*3%*
Black or African American	42	*14%*
Hispanic or Latino	6	*2%*
Native American	5	*2%*
White / Caucasian	230	*77%*
Multiple ethnicity	7	*2%*
Other or prefer not to answer	0	*0%*
Annual Income		
<$40k	91	*30%*
$40-100k	141	*47%*
$100k+	68	*23%*

Table 2 Health Conditions

	N	%
Rate of Hospitalization	**300**	**100%**
I have not been hospitalized	225	*75%*
I was hospitalized once in the past year	59	*20%*
I was hospitalized more than once in the past year	16	*5%*
Health Conditions	**300**	**100%**
Heart Disease	206	*69%*
Diabetes	67	*22%*
Arthritis	66	*22%*
Respiratory Disease	52	*17%*
Pain management	39	*13%*
Stroke or stroke prevention	37	*12%*
Cancer	32	*11%*
Mental Health	30	*10%*
Other / Prefer not to say	27	*9%*
Vision deterioration	24	*8%*
Kidney Disease	22	*7%*
None of these	7	*2%*
A Rare Disease not fitting into one of these categories	2	*1%*
Alzheimer's or Dementia	1	*0%*

What types of medications and medical services have you, or those you know, used to manage your health? Please select all that you or someone you know have used within the last five years.	**N**	%
Oral (pills) or topical (creams) medications	291	*97%*
Physical Therapy	40	*13%*
Surgery or Therapeutic Operations	42	*14%*
Injections or infusions administered by a healthcare professional such as a doctor or technician	64	*21%*
Self-injectable medications (with needles you give yourself e.g., insulin)	66	*22%*
Counseling	23	*8%*
Other	7	*2%*
Unsure or Don't Know	3	*1%*

Table 4

How effectively do your current medications work to manage your health? Please select the statement that best applies.	**N**	**%**
Treated Extremely Well	150	*50%*
Treated adequately; my health usually does not limit my daily activities.	77	*26%*
Treated adequately; I have symptoms related to my health that bother me	53	*18%*
Poorly treated. My health limits my activities.	14	*5%*
Does not apply	6	*2%*