

VIA ELECTRONIC SUBMISSION

Coverage and Analysis Group, CMS
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244
August 21, 2023

RE: Proposed Clinical Endpoints Guidance: Knee Osteoarthritis

Dear Coverage and Analysis Group,

The Robert J. Margolis, MD Center for Health Policy at Duke University (“the Duke-Margolis Center” or “the Center”) appreciates the opportunity to comment on the Proposed Clinical Endpoints Guidance: Knee Osteoarthritis, published on June 22, 2023.

The Duke-Margolis Center generates and analyzes evidence across the spectrum of health policy and supports the triple aim of better care, better health, and lower cost. The Center focuses on transforming health care delivery and increasing the value of biomedical innovation through evidence-based solutions to the most pressing, relevant health care delivery and payment policy questions. Center experts are engaged in policy research and development efforts to improve both care delivery and the processes and infrastructure needed at the Centers for Medicare and Medicaid Services (CMS) to ensure efficient access to new and innovative technologies.

The comments below describe opportunities for strengthening the Clinical Endpoints Guidance: Knee Osteoarthritis to more closely align with CMS’s goals for the guidance to provide a framework for more predictable and transparent evidence development. These comments are informed by the Center’s independent analysis of the guidance document and engagement with a diverse group of stakeholders, including manufacturers, real-world evidence experts, providers, researchers, and payers. The Duke-Margolis Center is supportive of the direction of the Clinical Endpoints Guidance: Knee Osteoarthritis document. To further strengthen this guidance document and future guidance, the Center recommends that CMS:

- Clarify the circumstances under which CMS would facilitate broader stakeholder engagement for determining clinical endpoints of interest for emerging therapeutic areas;
- Include guidance on the types of data sources and data collection strategies that would generate data on the outcomes of interest identified; and
- Clarify how they will prioritize the selection of therapeutic areas in which to develop Clinical Endpoints Guidance and clarify if forthcoming guidance can inform evidence generation efforts for existing CED requirements; and
- Consider aligning the recommended outcome domains with existing performance and quality measures that CMS already collects to inform quality and performance metrics in the same therapeutic areas.

Background

Clinical evidence that supports a coverage determination must show that an item or service is reasonable and necessary for the Medicare beneficiary population. For a product to be “reasonable and necessary,” it must be: (1) safe and effective, (2) not experimental or investigational, and (3) appropriate for use in Medicare beneficiaries.¹ An item or service is “appropriate” in this context if it is furnished according to the medical practice standards for the diagnosis or treatment of a condition, in a setting of care that can meet patient needs, by a qualified provider, whether a product meets the medical needs of the patient, and whether it is as least as beneficial as an existing alternative. Medicare beneficiaries tend to be older, with multiple comorbidities, and are often underrepresented or not represented in many clinical studies. CMS thus looks to the evidence supporting FDA market authorization and product indications for evidence generalizable to the Medicare beneficiary population, data on improvement in health outcomes, and durability of those outcomes. In cases in which the evidence is promising, but does not necessarily show that an item or service is appropriate for the intended Medicare populations, CMS can offer Coverage with Evidence Development (CED) as sponsors collect supplementary data in the post-market setting. The benefit of these CED studies is they often offer a larger, more diverse cohort can provide key insights into what constitutes “appropriate” use of a product by allowing investigators to observe how a product performs in different patient populations, with different provider experience or site capacity.

The Clinical Endpoints Guidance not only reflects CMS’s current view on health outcomes for the treatment of Knee Osteoarthritis, but also illustrates the methodology that CMS uses to identify clinically meaningful endpoints within a disease area when determining a National Coverage Determination. This is the first of a series of guidance documents that will review the clinical outcomes for treatments in different disease areas. In turn, these are the types of endpoints that could be used in both investigational clinical trials and post-market studies, such as those designed to support Medicare coverage. Through this guidance, CMS is aiming to:

- Provide a framework for more predictable and transparent evidence development by demonstrating how CMS assesses health outcomes and clinically meaningful endpoints and evidence thresholds to support Reasonable and Necessary coverage; and to
- Illustrate the types of evidence CMS intends to review.

The first part of this comment letter will analyze how the process described in the guidance document supports these aims, as well as CMS’s overarching goals for Medicare coverage. The second portion of the comments will address opportunities for greater alignment with broader Medicare reforms, especially how these clinical endpoints could align with existing quality and performance measures.

Strengthening Guidance to Support CMS Goals

In the Clinical Endpoints Guidance, CMS outlines the framework that they use for determining clinical endpoints of interest through a systematic literature review imbedded in a Technology Assessment (TA). TAs involve a systematic evaluation of the available evidence on a given technology to determine the effect of a technology on patient health outcomes. The TA includes a systematic literature review with specific inclusion and exclusion criteria, including date and language of publication, reporting on appropriate outcome measures for managing knee osteoarthritis (KO), and methods for evaluating and

developing consensus on outcomes of interest. The evidence was then appraised to assess its validity (credibility), usefulness (clinical applicability), and importance (magnitude of effect).

CMS also reviewed society consensus statements and core outcome sets, noting overlap between these sets of outcomes and endpoints commonly used in the existing literature. From this data, CMS was compiled a list of prioritized outcome domains for researchers to consider for future studies that would be particularly relevant and meaningful for evaluating medical technologies to treat KO. CMS does identify the most commonly used instruments in the literature for supporting the priority domain outcomes, but does not necessarily make recommendations about which instruments would be most valuable in trials. Rather, CMS recommends that clinical studies prioritize validated endpoints and instruments to ensure that CMS can more easily interpret study results.

CMS's description of this methodology and its resulting recommendations do push CMS closer to meeting its goals of providing a predictable framework and illustrating the types of evidence CMS intends to review. Importantly, for emerging therapeutic areas where there are no existing frameworks for interventions, there may not be enough directionally aligned literature to determine or prioritize a list of relevant and meaningful clinical endpoints. In the event that there are not validated endpoints or instruments to measure outcomes for a given therapeutic area, a systematic literature review may not reveal clear outcome domains. CMS could call on the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) panel or engage with a variety of stakeholders, including patients, providers, and specialty societies to better prioritize and align on outcomes of interests.

Recommendation: CMS should clarify the circumstances under which CMS would host a MEDCAC and facilitate broader stakeholder engagement for determining clinical endpoints of interest for emerging therapeutic areas.

Prioritizing Therapeutic Areas

Knee Osteoarthritis was an illustrative disease area to develop a proposed clinical endpoints guidance. We note that while there may be ongoing medical innovations in this therapeutic space, KO has well established reimbursement structures that may preclude the need for formal coverage processes for new innovations. As CMS considers developing internal processes to develop clinical endpoints guidance documents, they should clarify how they will prioritize the selection of therapeutic areas. CMS could additionally clarify if they will develop clinical endpoints guidance for therapeutic areas with no pre-existing coverage policies, or if forthcoming guidance can support evidence generation efforts for existing NCDs with CED requirements.

Recommendations: CMS should clarify how they will prioritize the selection of therapeutic areas in which to develop Clinical Endpoints Guidance and clarify if forthcoming guidance can inform evidence generation efforts for existing CED requirements.

Another way that CMS can add additional transparency and predictability to the clinical endpoint guidance documents—and thus add further clarification to Medicare coverage pathways—is to include guidance on the types of data, potential data sources, and evidence generation strategies that would

best support collection of the identified clinical endpoints throughout different stages of evidence development. Different types of data may be more effective for determining the clinically meaningful differences in outcomes over others. Guidance on data sources that are most rigorous, high-quality, and least burdensome need not limit studies, but guidance may help sponsors use existing data infrastructures or plan for new infrastructures when applicable. This will help support the updated CED guidance and timely access to novel technologies if manufacturers are able to more quickly and confidently develop evidence development plans or study designs.

Recommendation: CMS should include guidance on the types of data, data sources, and data collection strategies that would best support data collection for the identified clinical endpoints.

Alignment with Broader Medicare Measures

Although the clinical endpoints guidance documents are a summation of what CMS may be looking for when reviewing devices within a therapeutic area, there is an opportunity to align these guidance documents with broader Medicare performance or quality measures to provide greater consistency in reimbursement for Medicare items and services.

For example, through the Quality Payment Program (QPP) CMS collects data on some of the recommended outcome domains identified in the proposed clinical endpoints guidance on KO. For example, Merit-Based Incentive Payment System (MIPS) measure #217: “Functional Status Change for Patients with Knee Impairments” captures a risk-adjusted change in functional status using a patient-reported measure of the FOTO Lower Extremity Physical Function (LEPF). Functional status is also further captured in MIPS measure #470: “Functional Status After Primary Total Knee Replacement” through either the Oxford Knee Score or the KOOS, JR. tool. In the Clinical Endpoints Guidance, there are recommended outcome domains of physical function and function/functional ability, though it is not immediately clear in the guidance how CMS is differentiating these domains, and how either may be different from the intended meaning of “functional status” in existing MIPS measures.

Additionally, although CMS states that this guidance document does not specifically endorse or recommend any particular instrument to measure outcome domains, only one instrument listed in the guidance document is also currently collected in CMS quality measures and in the Comprehensive Care for Joint Replacement model measures, namely the KOOS tool. CMS also noted that function/functional ability may be already captured in instruments that are used in other outcome domains, including the 12-item short-form health survey (SF-12), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), both of which are surveys used to measure patient quality of life. The SF-12 focuses more on patient quality of life holistically through measuring physical functionality, bodily pain, general health, social functioning, and mental health,² while the WOMAC focuses more on joint pain, stiffness, and function.³ However, neither of these tools appear to be regularly collected by CMS. Thus, there are opportunities to foster alignment between what is regularly used in the literature in the KO space, what CMS will evaluate to determine appropriateness of a product or service, and what is collected by CMS to incentivize providers and health systems. Greater alignment in these related areas—data collection to support Medicare coverage and data collection to support quality and performance measures—could support CMS’s goals to minimize provider and patient burden of data

collection. Aligning outcome domains and instruments to quality and performance measures would allow the clinical endpoints guidance document series to apply more holistically to disease spaces. This would in turn ensure that incentives across care delivery and evidence development for novel products are working in tandem, providing clear signals for technological innovation that can address CMS quality goals.

Recommendation: When prioritizing outcome domains of interest, CMS should consider aligning the recommended outcome domains with existing performance and quality measures (or vice versa) that CMS already collects to inform quality and performance metrics.

Conclusion

The Duke-Margolis Center supports CMS's efforts to publish a series of guidance documents on clinical endpoints of interest for different disease areas. The Center encourages CMS to consider the importance of additional elements that encourage early stakeholder engagement, innovative study designs, and alignment across broader Medicare quality improvement efforts. The Duke-Margolis Center appreciates CMS's consideration of our comments, and the Administration's support for advancing high-value, affordable healthcare.

Sincerely,

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Hannah Graunke – Senior Policy Analyst, Duke-Margolis Center
Mark McClellan – Director, Duke-Margolis Center

References

¹ Centers for Medicaid & Medicare Services, “Medicare Program Integrity Manual, Ch 13” (CMS, February 12, 2019), <https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/pim83c13.pdf>.

² Kate E. Webster and Julian A. Feller, “Comparison of the Short Form-12 (SF-12) Health Status Questionnaire with the SF-36 in Patients with Knee Osteoarthritis Who Have Replacement Surgery,” *Knee Surgery, Sports Traumatology, Arthroscopy* 24, no. 8 (August 1, 2016): 2620–26, <https://doi.org/10.1007/s00167-015-3904-1>.

³ “Western Ontario and McMaster Universities Osteoarthritis Index,” Shirley Ryan AbilityLab, July 26, 2016, <https://www.sralab.org/rehabilitation-measures/western-ontario-and-mcmaster-universities-osteoarthritis-index>.