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VIA ELECTRONIC DELIVERY TO: MedCACpresentations@cms.hhs.gov

January 13, 2023

Joseph Ross, MD, MHS
Chair, Medicare Evidence Development and Coverage Advisory Committee (MEDCAC)
Centers for Medicare & Medicaid Services (CMS)
7500 Security Boulevard
Baltimore, Maryland 21244

Re: Medicare Program; Virtual Meeting of the Medicare Evidence Development and Coverage Advisory Committee; Cancellation of the December 7, 2022. Virtual Meeting and Announcement of the February 13 and February 14, 2023 Virtual Meetings

Dear Chairman Ross:

The Biotechnology Innovation Organization (BIO) appreciates the opportunity to comment on MEDCAC's, "Medicare Program; Virtual Meeting of the Medicare Evidence Development and Coverage Advisory Committee; Cancellation of the December 7, 2022 Virtual Meeting and Announcement of the February 13 and February 14, 2023 Virtual Meetings (hereinafter, "Announcement").[i]

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes, but also have reduced healthcare expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO membership includes biologics and vaccine manufacturers and developers who have worked closely with stakeholders across the spectrum, including the public health and advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

According to the Announcement, the February meeting will "examine the general requirements for clinical studies submitted for CMS coverage requiring CED" and that such studies "will produce reliable evidence that CMS can rely on to help determine whether a particular item or service is reasonable and necessary." While the search for reliable evidence is a necessary process for improving our overall health system, we believe that current CMS efforts to apply CED to FDA-approved treatments are against current law,

unnecessarily duplicative, and ultimately thwart, rather than enhance, patient access to needed new therapies.

BIO recommends that on-label uses of drugs and biologicals be excluded from CED restrictions. We believe use of CED for on-label uses drugs and biologicals is contrary to law, as well as the best available evidence and sound public policy.

As MEDCAC knows, CED is used for certain technologies where the Centers for Medicare & Medicaid Services (CMS) does not believe there is sufficient evidence to conclude definitively that the item or service is "reasonable and necessary"[ii] for the Medicare population. When CMS applies CED to a technology, it restricts Medicare coverage nationwide to only a narrow range of circumstances—e.g., coverage as part of clinical trials or registries meeting strict CMS criteria. Historically, CMS has limited use of CED to devices; other non-drug/biological technologies or procedures; or, in rare cases, to off-label uses of drugs or biologicals.[iii] Earlier this year, however, in an unprecedented shift in policy, CMS issued a National Coverage Determination (NCD) that applied CED to the on-label use of an anti-amyloid product approved under a Biologics License Application (BLA).

Application of CED to an on-label use of a drug or biological is contrary to the requirements of the Social Security Act (SSA).

CMS's recent use of CED for an on-label use of a drug or biological is contrary to law. The SSA obligates CMS to cover drugs and biologicals in most settings of care,[iv] unless a particular therapy is not "reasonable and necessary" for diagnosis, treatment, or to improve the functioning of a malformed body member.[v] As CMS itself has historically recognized, Food and Drug Administration (FDA) approval of a drug or biologic demonstrates the reasonableness and necessity of the therapy: "[A]s a matter of national policy," CMS's long-standing position has been that "drugs or biologicals approved for marketing by FDA are safe and effective when used for indications specified in their labeling."[vi]

As such, application of CED to on-label uses of drugs and biologicals is fundamentally arbitrary. CED for on-label uses of drugs and biologicals also subverts the overarching regulatory structure, as it amounts to little more than second guessing the considered judgment of FDA about whether a drug or biological is, in fact, safe and effective for its indicated uses. CMS's role is not to re-arbitrate the conclusive determinations of FDA.[vii] Rather, CMS's role is to defer to FDA's judgment on issues of safety and effectiveness, and it is therefore inherently "arbitrary, capricious, . . . or otherwise unlawful" under statute for CED to be applied to restrict coverage to on-label uses of drugs and biologicals.[viii]

Application of CED to on-label uses of drugs and biologicals is needlessly duplicative.

In the first place, applying CED to on-label uses of drugs and biologicals (or medically appropriate off-label uses) is needlessly duplicative and will impede beneficiary access to medicines that have already proven to be safe and effective. Drugs and biologicals are unique in that they must undergo years of rigorous clinical trials to ensure that the therapies can be safely and effectively used in human patients. Over the last two decades (between 2000 and 2020) nearly 700 new prescription medicines (new molecular entities (NMEs) and original biologic license applications (BLAs) have been approved for use by the

U.S. Food and Drug Administration (FDA), at a potential cost of over two billion dollars[ix] and taking on average 10.5 years.[x] Further, the data and results from such trials are carefully reviewed by FDA prior to approval to ensure their rigor and reliability.[xi] Imposing additional post-approval CED requirements on on-label uses of drugs and biologicals unnecessarily duplicates the careful and thorough work and analysis conducted by FDA.

BIO emphasizes that CED also is duplicative of work already done by FDA for drugs and biologicals approved under the FDA's Accelerated Approval Program. Accelerated approval is a special pathway created by Congress to allow for faster patient access to therapies treating serious conditions and unmet medical needs. Although the accelerated approval pathway involves the assessment of surrogate endpoints rather than clinical endpoints, accelerated approval is no less scientifically rigorous than traditional approvals. The FDA conducts a thorough evaluation of proposed endpoints, all data is gathered under clinical trials demonstrating a drug's safety and effectiveness, a rigorous confirmatory trial is required to assure anticipated clinical benefits, and the therapies must meet the same standards of safety and efficacy as traditional approvals. Further, drugs and biologicals approved under the Accelerated Approval Program are required by FDA to undergo Phase 4 confirmatory trials after approval. Additionally, according to the National Academies of Science, whether or not Phase IV trials are required by FDA, "all drugs are monitored to identify new or delayed toxicity—a process described as post-marketing surveillance."[xii] Accordingly, imposing additional CED restrictions on accelerated approval therapies would be duplicative and wasteful, given that FDA already comprehensively regulates such therapies—including through post-approval studies. Ultimately, CED simply would serve to impede patient access to these important therapies that otherwise could address the critical unmet medical needs of patients across the country as Congress intended when establishing the pathway.

Application of CED to on-label uses of drugs and biologicals restricts patient access, compounding existing inequities.

Imposing CED requirements to on-label uses of drugs and biologicals will compound health inequities by unfairly restricting beneficiary access to needed care. Imposition of CED generally means that Medicare beneficiary access is limited to the small number of patients fortunate enough to have reliable access to a CMS-approved trial or study. All other beneficiaries are de facto denied covered access to the therapy, even though FDA has already approved the therapy and determined it is safe and effective.

In practice, large clinical trials tend to be performed at academic medical centers (AMCs) or other major hospital systems in partnership with community organizations, because these are the facilities with the resources and expertise to conduct such trials. These AMCs are located in a relatively small number of geographic areas. As a consequence, beneficiaries may be restricted in accessing coverage through CED simply as a byproduct of geography. Further, in the past, CED restrictions on access often have proven disproportionately to impact communities of color,[xiii] thereby exacerbating already significant issues of health inequity facing these communities.

Conclusion

BIO appreciates MEDCAC's consideration of these comments. We strongly urge the Committee to recognize that on-label uses of drugs and biologicals should be categorically

excluded from CED restrictions. We look forward to further engagement on these issues in the future.

Sincerely,

/s/
Crystal Kuntz
Vice President
Healthcare Policy & Research
Biotechnology Innovation Organization

/s/
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Senior Director
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Biotechnology Innovation Organization

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[i] *See* Federal Register, Vol. 87, No. 233, p. 74632, December 6, 2022
[ii] *See* Social Security Act (SSA) § 1862(a)(1)(A), (E).
[iii] *See, e.g.*, CMS, Coverage with Evidence Development, https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development (list of current CED NCDs) (last visited Sept. 16, 2022). Since 1999, CMS has issued only 29 NCAs related to drugs or biologicals out of nearly 300 total NCAs. Further, NCAs involving drugs or biologicals often address only off-label coverage or otherwise affirm availability of on-label coverage.
[iv] *See, e.g.*, SSA § 1861(b) (inpatient hospital services includes drugs and biologicals), (s)(2)(A) (incident-to physicians' services includes drugs and biologicals that are not usually self-administered furnished as an incident to a physician's professional service), (s)(2)(B) (outpatient hospital services includes drugs and biologicals not usually self-administered furnished as an incident to a physician's professional service to an outpatient). Limited exceptions to the requirement to cover drugs and biologicals do apply—e.g., most self-administered drugs and biologicals furnished in Part B settings are not covered by Medicare fee-for-service. *See, e.g.*, Decision Memo for Outpatient Intravenous Insulin Treatment (Therapy), CAG-00410N (Dec. 23, 2009); Decision Memo for Blood Brain Barrier Disruption Chemotherapy, CAG-00333N (Mar. 20, 2007); Decision Memo for Extracorporeal Photopheresis, CAG-00324R (Dec. 19, 2006) (first reconsideration).
[v] *Id.* § 1862(a)(1)(A).
[vi] *See* 54 Fed. Reg. 4,384, 4,306 (Jan. 30, 1989), *accord* Medicare Benefit Policy Manual, ch. 15, §§ 50.4.1 and 50.4.2.
[vii] *See, e.g.*, Federal Food Drug and Cosmetic Act (FDCA) § 505.
[viii] 5 U.S.C. § 706(2)(A).
[ix] See, https://www.cbo.gov/publication/57126
[x] See, https://www.bio.org/blogs/how-long-does-it-take-get-drug-approved
[xi] *See generally* BIO, Drug Development and Clinical Trial Process, https://www.bio.org/policy/human-health/drug-development-review-lifecycle-management (last visited Sept. 18, 2022).
[xii] National Academies of Science, ".Medications in Single-Dose Vials: Implications of Discarded Drugs (2021)," http://nap.naptionalacademies.org/25911
[xiii] *See, e.g.*, Individualized Decisions for Endocrine Therapy Alone Study, ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT02400190 (last updated Dec. 21, 2021) (CED IDEAS study participants self-reported as 88% non-Hispanic White/Caucasian. A New IDEAS study was subsequently launched with the specific objective of studying a more diversion population, but the study has had difficulty enrolling the targeted levels of diverse participants).