National Down Syndrome Society Comments to the Centers for Medicare & Medicaid Services

Re: NCA – Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)

February 10, 2022

The National Down Syndrome Society (NDSS) is the leading human rights organization for all individuals with Down syndrome. NDSS envisions a world in which all people with Down syndrome have the opportunity to enhance their quality of life, realize their life aspirations, and become valued members of welcoming communities. On behalf of the community we serve, we write today to express grave concern with the decision proposed by the Centers for Medicare & Medicaid Services (CMS) to cover FDA-approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease (AD) under Coverage with Evidence Development (CED). Individuals with Down syndrome deserve coverage for therapies related to Alzheimer's disease as much as anyone else, but the proposed CED process fails to provide meaningful access today and casts doubt on coverage tomorrow.

Summary

In our comments below, it is our intent to convey that the Down syndrome community is relying on CMS to ensure it has access to new and developing treatments for Alzheimer's disease because so many individuals with Down syndrome will develop the disease. The proposed CED process excludes each and every person with Down syndrome in its very design, creating a disparate impact and guaranteeing that physicians will ultimately have less information about how aducanumab and related future treatments will affect their patients with Down syndrome than they have about how it will affect their other patients. NDSS recommends that CMS abandon its plans to move forward with a CED and find an inclusive, nondiscriminatory alternative. We stand ready to assist however we can.

Discussion

This coverage determination – and any related to Alzheimer's disease – has an outsized impact on the Down syndrome community because of the genetic intersection of the two conditions: the amyloid

precursor protein (APP) gene is present on chromosome 21 and is strongly associated with the formation of amyloid peptides and plaques, a hallmark of Alzheimer's disease. Because people with Down syndrome have three copies of chromosome 21 and thus three copies of the APP gene, they are at a higher risk for developing Alzheimer's disease than people in the general population who only have two copies**. In the real world, the somber reality is that individuals with Down syndrome face an estimated lifetime risk higher than 90% for developing Alzheimer's disease, with the onset of symptoms coming earlier and progressing faster than their counterparts in the general public.** With the vast majority of adults with Down syndrome entitled to coverage under Medicare, the agency must not ignore the Down syndrome community now, at this critical moment, with the first of a new class of Alzheimer's treatments starting to become available and subsequent treatments not far behind.

Despite the clear need for information about how forthcoming Alzheimer's treatments will impact the health of people with Down syndrome, the proposed CED protocol categorically excludes patients with "any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline," as well as patients with "medical conditions, other than AD, likely to increase significant adverse events." This proposed CED is the only mode of coverage currently being offered by CMS for this class of drugs, and we believe these exclusion criteria apply to everyone with Down syndrome. This action, therefore, denies all coverage to our community based on the presence of their disability, possibly in violation of Sec. 1557 of the Patient Protection and Affordable Care Act, which states that "an individual shall not be excluded from participation in, be denied the benefits of, or be subjected to discrimination on the grounds prohibited under Title VI of the Civil Rights Act of 1964, 42 U.S.C. 2000d et seq. (race, color, national origin), Title IX of the Education Amendments of 1972, 20 U.S.C. 1681 et seq. (sex), the Age Discrimination Act of 1975, 42 U.S.C. 6101 et seq. (age), or Section 504 of the Rehabilitation Act of 1973, 29 U.S.C. 794 (disability), under any health program or activity, any part of which is receiving federal financial assistance; any program or activity administered by the Department under Title I of the Act; or any program or activity administered by any entity established under such Title." In addition to the CED process itself running afoul of Sec. 1557, it also forces the test sites that would administer the trials into a position where they would similarly discriminate against individuals with intellectual and developmental disabilities. CMS must not make coverage distinctions

between different subpopulations of otherwise-eligible beneficiaries, so this proposed CED is discriminatory and unreasonable, and CMS must change course.

In the context of the near-linear risk factor for members of our community, it becomes clear that exclusion from this coverage process will produce a disparate impact on the entire subpopulation of people with Down syndrome. To ignore the connection between Down syndrome and Alzheimer's disease breaches CMS' own standards of scientific integrity, specifically the requirement that any CMS-approved trials "must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and […] if the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary." Furthermore, "the study protocol explicitly [must discuss] how the results are or are not expected to be generalizable to affected beneficiary subpopulations," and that "separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility." The Down syndrome community is unequivocally an affected beneficiary subpopulation here, and CMS has not addressed any impact in this proposed coverage decision.

CMS has proposed a CED for the specific purpose of developing evidence, noting that "to date, no trial of an antiamyloid mAb has confidently demonstrated a clinically meaningful improvement in health outcomes (i.e., cognition and function) for AD patients." While we appreciate CMS' impetus to ensure that any covered medicines are safe for patients, the CED process as laid out will fail to produce any such evidence with respect to the Down syndrome community because no people with Down syndrome will be a part of any trials. This exclusion will produce negative impacts on our community now and into the future. Aducanumab is only the first in a new family of Alzheimer's treatments, and if people with Down syndrome are denied access to it, there will be no evidence of its effects, no baseline data upon which to make coverage or treatment decisions going forwards, which in turn is likely to affect coverage for related diagnostic and imaging services. If people with Down syndrome are excluded today, there will be no way to determine whether this treatment or any of its progeny will benefit them – or harm them – tomorrow.

CMS has correctly cited that there are questions of equity in the development of treatments for Alzheimer's disease. The decision notes that "significant differences in the prevalence of AD across racial and ethnic groups have previously been reported," and NDSS applauds the agency's efforts to consider the social determinants of health for different groups. We agree that "in order to address these barriers in coverage and care, it is critical that these patients are engaged, recruited, and retained in future trials," but we challenge CMS' conception of diversity as being limited to race and ethnicity. Diversity must include disability. CMS even cites Executive Order 13985 (Advancing Racial Equity and Support for Underserved Communities Through the Federal Government) in the decision – but without full appreciation of its wording. Executive Order 13985 clearly states that the pursuit of equity is not limited to race and must include "individuals who belong to underserved communities […] such as persons with disabilities." In order to be consistent and compliant with the president's order, CMS must include individuals with Down syndrome in the coverage determination. If CMS decides to stay the course and move forward with a process that, by design, will fail to produce "clinically meaningful" health outcome data for individuals with Down syndrome, then the agency must also find another way to ensure timely access to treatment, as delayed access would be yet another inequity.

Conclusion

NDSS strongly urges CMS to strike the proposed CED process. It is critical that people with Down syndrome have access to developments in Alzheimer's care. If the health equity considerations described above are found to be fundamentally incompatible with the CED process, then CMS must identify a different methodology to ensure that people with Down syndrome and other similarly situated disabilities will have meaningful access to current and future advancements in treatments for Alzheimer's disease, and that those treatments are safe and effective. Medicare coverage must ensure patients with Down syndrome – like all other enrolled patients – have access to physicians who are empowered to determine the best course of treatment for them, including through ensuring access to the most current technologies for evaluation of the patient, detection and diagnosis of Alzheimer's disease, and testing for potential adverse events.

The proposed CED process will widen the gap between the quality of care available to patients with Down syndrome and available to others. In the short term, for aducanumab, it openly discriminates against patients with intellectual and developmental disabilities, treating them differently than patients without those disabilities. In the longer term, for developments in Alzheimer's treatments yet to come, the CED would set a public precedent of exclusion that CMS would need to undo. After the completion of the CED, the best-case scenario would be for CMS to provide equitable coverage, but even then the damage from the CED would have already been done, reducing the information available to physicians. For the good of the community, now and into the future, CMS must not proceed with this discriminatory proposal. We thank CMS for the opportunity to comment on this process, and we look forward to working with you to chart an equitable and inclusive path forward. For more information regarding these comments, please contact us at info@ndss.org.

Sincerely,

Kandi Pickard
President and CEO
National Down Syndrome Society