Biogen's Statement on the Draft National Coverage Determination (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

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Alzheimer's patients and their families deserve to have choice and access to FDA-approved treatments.

Biogen believes that the proposed coverage with evidence development (CED) decision for anti-amyloid therapies denies nearly all Medicare beneficiaries from accessing ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use, the first FDA-approved treatment for Alzheimer's disease since 2003, as well as future amyloid-directed therapies.

It is imperative to change this draft decision to be aligned with reimbursement for other therapies for progressive diseases, where patients have immediate and equal access to medicines approved by the FDA. The FDA's accelerated approval was supported by clinical data showing that ADUHELM impacted the underlying pathology of Alzheimer's disease. This includes a robust reduction in pathological hallmarks of Alzheimer's disease, specifically for both amyloid plaques and neurofibrillary tangles in the brain.

It is urgent to act. Thousands of patients progress each day from mild to moderate disease stages, where treatment may potentially no longer be an option. For these patients, each day matters. If a final NCD, expected to be issued in April, continues to require a randomized controlled trial as outlined in this draft, it would likely take in excess of a year to begin enrolling patients, further delaying reimbursement for Medicare beneficiaries. It is also particularly concerning that this draft implies that some Medicare beneficiaries will receive a placebo instead of a treatment they are seeking.

We at Biogen urge CMS to align Medicare coverage for the class of amyloid-directed therapies consistent with the criteria used in the respective clinical trials and guided by expert recommendations for appropriate use.

During the 30-day open comment period, Biogen will make a formal response. CMS' final decision is expected to be issued in April 2022. An outline of the NCD process is available on the CMS website.

The Negative Impact on Patients of a Coverage with Evidence Development

- **This CED requirement would be duplicative of robust efficacy and safety data collection efforts already in place.** Biogen anticipates additional data from both EMBARK and ICARE-AD US and plans to begin patient screening for its post-marketing confirmatory study for ADUHELM® (aducanumab-avwa) in May 2022, with a primary completion date of approximately four years after the study begins. Biogen's confirmatory study aims to enroll more than 1,300 early Alzheimer's disease patients and has a primary clinical endpoint at 18 months after treatment initiation. The trial will also include a long-term extension to collect data for up to 48 months. For the class of anti-amyloid treatments, multiple clinical studies are expected to generate data over the next 12-18 months, and patient registries are also planned.

- **A CED with a randomized controlled trial (RCT) requirement would almost completely remove coverage for Medicare beneficiaries.** Even the largest RCTs in Alzheimer's disease have been limited to a few thousand patients, of which 30-50% have been on placebo. The population with access to reimbursement under such a CED would likely amount to just hundreds of patients, leaving the majority of AD patients to continue to decline without hope of intervention.

- **This CED could severely limit patient access for underserved patients. Any access would be wholly inequitable.** While the draft CED requires a randomized controlled trial to be reflective of the national population, we believe that, in the real-world, such a CED would restrict coverage to Medicare beneficiaries who live close to, or can travel to, participating medical centers, which are typically limited to academic centers or major healthcare systems – exacerbating health inequity in dementia care. Medicare beneficiaries without access to these sites, even if they meet clinical trial criteria, would not have access to the treatment.

- **This CED requirement would significantly restrict and delay patient access to an FDA-approved therapy for a progressive disease.** CED registries or studies can take many months or years to operationalize, and only the limited number of patients enrolled would be eligible to receive treatment. For example, the IDEAS study, in the amyloid PET CED[i], didn't enroll patients until two years after a CED determination. Medicare beneficiaries will not be eligible for coverage for ADUHELM during the period after the final NCD is issued and before the trial is initiated.

About ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use

ADUHELM is indicated for the treatment of Alzheimer's disease. Treatment with ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Aducanumab-avwa is a monoclonal antibody directed against amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. The accelerated approval of ADUHELM has been granted based on data from clinical trials showing the effect of ADUHELM on reducing amyloid beta plaques, a surrogate biomarker that is reasonably likely to predict clinical benefit, in this case a reduction in clinical decline.

ADUHELM can cause serious side effects including: Amyloid Related Imaging Abnormalities or "ARIA". ARIA is a common side effect that does not

usually cause any symptoms but can be serious. Although most people do not have symptoms, some people may have symptoms such as: headache, confusion, dizziness, vision changes and nausea. The patient's healthcare provider will do magnetic resonance imaging (MRI) scans before and during treatment with ADUHELM to check for ARIA. ADUHELM can also cause serious allergic reactions. The most common side effects of ADUHELM include: swelling in areas of the brain, with or without small spots of bleeding in the brain or on the surface of the brain (ARIA); headache; and fall. Patients should call their healthcare provider for medical advice about side effects.

Biogen Safe Harbor
This document contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to: Biogen's strategy and plans; potential of, and expectations for, Biogen's commercial business, including ADUHELM; the potential clinical effects of ADUHELM; the potential benefits, safety and efficacy of ADUHELM; the identification and treatment of Alzheimer's disease; the anticipated benefits and potential of our collaboration arrangements with Eisai; the clinical development program and future clinical trial(s) for ADUHELM; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "possible," "prospect," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including ADUHELM; unexpected concerns that may arise from additional data or analysis obtained during clinical trials; actual timing and content of submissions to and decisions made by the regulatory authorities regarding ADUHELM; the occurrence of adverse safety events, restrictions on use or product liability claims; risks of unexpected costs or delays; the risk of other unexpected hurdles; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; third party collaboration risks; the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition; and any other risks and uncertainties that are described in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

[i] HPMS IDEAS Memo. https://clinicaltrials.gov/ct2/show/NCT02420756?term=ideas