Dear CMS Review Committee,

Arnold Ventures welcomes the opportunity to provide comments to the Centers for Medicare and Medicaid Services (CMS) on the *Proposed National Coverage Decision (NCD) for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease* published on January 11, 2022.

Arnold Ventures is a philanthropy dedicated to building evidence and developing policy solutions that maximize opportunity and minimize injustice. Arnold Ventures' goal is to promote evidence-based policy solutions that comprehensively lower drug prices while maintaining incentives for meaningful biopharmaceutical innovation.

Arnold Ventures is writing in support of CMS's proposed NCD with Clinical Evidence Development (CED).

The Food and Drug Administration (FDA) approved aducanumab despite evidence of severe clinical harms such as brain swelling and bleeding, and without clear evidence of clinical improvements in patient cognition. Further, an FDA advisory committee overwhelmingly rejected the premise that the data collected in clinical trials using a surrogate endpoint of amyloid reduction on brain scans could be extrapolated to drug effectiveness in slowing cognitive decline. Major hospital systems such as Mount Sinai and the Cleveland Clinic announced they would not administer aducanumab even though it is approved by the FDA given the lack of clarity that amyloid reduction was reasonably likely to predict such benefit.

Although the FDA's decision-making has been called into question, it still may result in the accelerated approval of similar drugs using the same types of flawed surrogate endpoints that led to aducanumab's approval. Aducanumab's approval, including the process of decision making to change from endpoints measuring direct patient benefit on cognition to a surrogate endpoint late in the development process, undermines FDA's credibility.

Given the lack of evidence of a reasonable likelihood of patient benefit, and documented harms pointed out by the advisory committee, we believe CMS has a clear basis to deny coverage of aducanumab as not being reasonable and necessary. That said, given the cruel impact Alzheimer's disease has on patients and families, we understand why CMS is taking the proposed approach. CMS has chosen to cover the drug for beneficiaries who join qualified clinical trials. The objective is to use representative clinical trials to determine whether the drug is effective (improving patients' cognition) and that these direct benefits on patient cognition outweigh potential patient harms. With that information, CMS would then be in an informed position to make a final coverage decision. It is unfortunate that the FDA has put CMS in the position of having to build the relevant clinical evidence post-approval that is needed to determine the appropriate level of coverage.

As noted in a recent Health Affairs article, data collected under the CED could result in more timely clinical data collection than the 9 years required by FDA to complete post-

approval studies of aducanumab. That said, there is no explicit limitation on how long a drug can be provided under a CED arrangement. To that point, we would recommend that the final NCD definitively set a date when coverage under the CED expires – well short of the 9 years required by FDA. As FDA's own regulations note, trials to confirm the patient benefits assumed with a surrogate endpoint should ordinarily be ongoing at the time of approval, a condition not met with adacanumab. Therefore, at that determined point CMS could decide to terminate its provisional coverage, continue with its trials, or make a final coverage determination if the evidence is present.

Additionally, we recommend that CMS require trial sponsors to report progress and interim results to CMS and to the public annually. This will motivate the manufacturer to move through the clinical trial process and ensure that patients, providers, and payers have more complete clinical information to inform their decision-making.

Aducanumab's high price seems entirely untethered and unjustified by the current evidence available. Under the CED, the cost of the drug and services incident to its administration will be borne by Medicare beneficiaries and taxpayers supporting both the Medicare and Medicaid programs for an indefinite period of time. While we understand that CMS cannot consider the cost of treatment in its coverage decision, we would point out that this particular case provides a strong argument for CMS to have such authority. Paying for medications with highly questionable efficacy and documented harms uses taxpayer dollars that could otherwise be directed toward higher value services. Moreover, this case could also be viewed as an excellent example of why Congress should take steps to limit excessive Medicare Part B and D drug prices that bear little relation to the true clinical value of the drug on improving patient outcomes.

Thank you for the opportunity to comment and for your review.

Sincerely,

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