

February 10, 2022

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue SW
Washington, DC 20201

Re: CAG-00460N

Dear Ms. Brooks-LaSure:

The Medicare Payment Advisory Commission (MedPAC) welcomes the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS's) proposed national coverage determination (NCD) decision memorandum entitled "Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease." Although the Commission does not normally comment on coverage decisions, we have chosen to do so in this case because of its significance, including the potential fiscal implications, and because the decision invokes coverage with evidence development (CED), which we have discussed in the context of our prescription drug work. The proposed NCD would cover Food and Drug Administration (FDA)-approved monoclonal antibodies that target amyloid for the treatment of Alzheimer's disease through CED. We appreciate your staff's ongoing efforts to establish an evidence-based process to develop and refine coverage determinations that ensures beneficiaries' access to high-quality care, particularly considering the competing demands on the agency.

As we detail below, the Commission supports CMS's proposal to implement an NCD that applies CED to cover available anti-amyloid monoclonal antibody drugs, including Aduhelm. Given the limited, conflicting evidence on Aduhelm's clinical effectiveness and the potential for significant side effects, CMS should ensure that the use of this product is appropriate for Medicare beneficiaries. Although Medicare does not consider spending implications as part of its coverage process, the Aduhelm case has highlighted the broader challenges Medicare faces in paying for high-cost products with limited clinical evidence. Our letter also discusses these broader spending and payment challenges.

CMS's NCD would apply CED to cover anti-amyloid monoclonal antibody drugs for the treatment of Alzheimer's disease

Alzheimer's disease (AD) is a fatal neurodegenerative brain disease characterized by the progressive accumulation of beta-amyloid protein plaques and neurofibrillary tangles; these are

hypothesized to damage neurons and lead to the loss of cognition and physical functioning.¹ Conventional treatment of AD is focused on supportive care, which may include treatment of dementia symptoms with medications that do not alter the course of the disease.²

Aduhelm is a first-in-class anti-amyloid monoclonal antibody drug that the FDA has approved for the treatment of AD.³ According to its FDA label, Aduhelm is indicated for patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.⁴

In the proposed NCD to cover Aduhelm and other FDA-approved products in its class, CMS noted that although there was insufficient evidence that this therapeutic class is reasonable and necessary for the treatment of AD, the condition is a particularly important disease that affects many beneficiaries. Consequently, the agency stated that “the CED paradigm provides the most appropriate pathway to provide Medicare coverage while additional evidence is developed.”⁵

Under its proposal, Medicare would cover FDA-approved anti-amyloid monoclonal antibody drugs, including Aduhelm, in CMS-approved randomized controlled trials and in trials supported by the National Institutes of Health (NIH) for beneficiaries with mild cognitive impairment due to AD or mild AD dementia with evidence of amyloid pathology consistent with AD (which is consistent with the participants of the manufacturer’s Phase III trials).⁶ The CED trials would evaluate the health outcomes of beneficiaries, focusing on changes in the decline of cognitive function and any adverse events associated with these new drugs and specifically addressing these research questions:

- Does use of monoclonal antibodies directed against amyloid for the treatment of AD result in a statistically significant and clinically meaningful difference in decline in cognition and function?
- What are the adverse events associated with the use of monoclonal antibodies directed against amyloid for the treatment of AD?⁷

¹ Institute for Clinical and Economic Review. 2021. *Aducanumab for Alzheimer’s disease: Effectiveness and value*. Boston, MA: ICER. [*ICER_ALZ_Final_Report_080521.pdf](#)

² Institute for Clinical and Economic Review. 2021, *op. cit.*

³ This product is administered via intravenous infusion every four weeks. Consequently, it is covered and paid for under Part B, rather than through a Medicare Part D drug plan.

⁴ Food and Drug Administration. 2021. Label medication guide for Aduhelm. July. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761178s003lbl.pdf.

⁵ Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2022. *Proposed National Coverage Determination memorandum: Monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease*. CAG-00460N. January 11. <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=305>.

⁶ According to the proposed NCD, beneficiaries not permitted to participate in the clinical trials include those: (1) with any neurological or other medical condition (other than AD) that may significantly contribute to cognitive decline; (2) with medical conditions, other than AD, likely to increase significant adverse events; or (3) whose expected death from any cause is anticipated during the duration of the study. The NCD proposes to cover one beta amyloid PET scan per patient, if the patient did not previously receive a beta amyloid PET scan.

⁷ Centers for Medicare & Medicaid Services. 2022, *op cit.*

In addition, all CED trials would have to be: (1) representative of the national population diagnosed with AD and (2) conducted through hospital outpatient departments.

After reviewing comments submitted by the public, CMS will issue a final national coverage determination policy by April 11, 2022. In the absence of a national coverage policy, the Medicare Administrative Contractors, which are local contractors that pay Medicare claims, decide whether the drug is covered for a beneficiary on a claim-by-claim basis.

Medicare's coverage of and payment for a drug with a limited, conflicting evidence base

Observers have noted several concerns about Medicare's coverage of and payment for a service like Aduhelm. First, some have raised concerns about the evidence base developed through the FDA approval process, including limited and conflicting evidence on Aduhelm's efficacy and the potential for serious side effects demonstrated during clinical trials. Second, although Medicare's determination of payment for an item or service is outside the scope of an NCD, some have warned of the implications of this new drug for Medicare spending, as well as the potential impact on beneficiary out-of-pocket spending and Part B premiums, given that Medicare's Part B drug payment system pays the price set by the manufacturer without regard for the clinical effectiveness of the product. Lastly, some have voiced concern about the underrepresentation of individuals at high risk for developing AD—including individuals 85 years and older, Blacks, and Hispanics—in Aduhelm's Phase III clinical trial population.

Limited, conflicting evidence on Aduhelm's clinical effectiveness

The two Phase III double-blind clinical trials (EMERGE and ENGAGE) of 18 months duration randomly assigned 3,285 patients (from 20 countries) with mild cognitive impairment or mild Alzheimer's dementia and a baseline PET scan revealing amyloid plaques to receive low-dose or high-dose Aduhelm or placebo.⁸ Both trials' primary clinical end point was a change in the Clinical Dementia Rating Sum-of-Boxes (CDR-SB) score, an 18-point scale measuring cognition (memory, orientation, judgment, and problem solving) and function (community affairs, home and hobbies, personal care). In March 2019, the independent data monitoring committee stopped both studies prior to their completion after an analysis found that pre-specified futility criteria were met based on pooled data from both trials (i.e., the futility analysis found that the trials were not able to achieve their efficacy objectives).

After the studies were unblinded, subsequent analyses of EMERGE data showed a small positive treatment effect (i.e., a slowing of AD progression) in the mean CDR-SB score among high-dose Aduhelm patients compared to placebo (but not the low-dose arm). By contrast, neither low- or high-dose Aduhelm arms of the ENGAGE trial demonstrated a statistically significant change in their mean CDR-SB score compared to placebo. Based on subsequent analyses, in July 2020,

⁸Haeberlein, S.B., C. von Hehn, Y. Tian, et al. 2020. EMERGE and ENGAGE topline results: Two phase 3 studies to evaluate aducanumab in patients with early Alzheimer's disease. April. <https://investors.biogen.com/static-files/f91e95d9-2fce-46ce-9115-0628cfe96e83>.

Biogen announced it had completed submission of a Biologics License Application to the FDA for Aduhelm.⁹

None of the members of FDA’s Peripheral and Central Nervous System Advisory Committee (a group of independent, outside clinical experts that advise the FDA on issues related to drugs, biological products, medical devices, and food) voted for approval of Aduhelm. Members of the advisory committee noted that:

“We agreed nearly unanimously that the [trials’] results provide a signal that the drug might have a clinical effect—but are equally consistent with the conclusion that it does not affect disease progression. We concluded that the positive signal from Study 302 [EMERGE], when considered with the totality of the evidence, did not amount to the substantial evidence of efficacy from adequate, well-controlled trials that the law requires, and that patients and physicians should expect for traditional approval.”^{10,11}

In June 2021, the FDA approved the product using an accelerated approval pathway based on its effect on a surrogate endpoint: reductions of amyloid beta plaque in the brain. In explaining its decision, the Director of the FDA’s Center for Drug Evaluation and Research stated: “Although the Aduhelm data are complicated with respect to its clinical benefits, FDA has determined that there is substantial evidence that Aduhelm reduces amyloid beta plaques in the brain and that the reduction in these plaques is reasonably likely to predict important benefits to patients.”¹² The FDA is requiring Aduhelm’s manufacturer to conduct a new randomized, controlled clinical trial to verify the drug’s clinical benefit within a nine-year timeframe. If the trial does not confirm the product’s benefit, the FDA can withdraw approval.¹³

Partly because of the uncertainty surrounding the clinical evidence, the approval of Aduhelm has been met with scrutiny and debate. For example:

- The Institute for Clinical and Economic Review (ICER) concluded that “...the evidence is *insufficient* to conclude that the clinical benefits of [Aduhelm] outweigh its harms or, indeed, that it reduces progression of AD in patients with [mild cognitive impairment] and

⁹Biogen. 2020. Biogen completes submission of biologics license application to FDA for aducanumab as a treatment for Alzheimer’s disease. July 8. <https://investors.biogen.com/news-releases/news-release-details/biogen-completes-submission-biologics-license-application-fda>.

¹⁰ Members of FDA’s Advisory Committee also noted that, before Aduhelm’s approval, “...the FDA had not indicated that it considered beta-amyloid a valid pharmacodynamic biomarker, much less an acceptable surrogate end point for clinical trials.” See Alexander, G. C., D. S. Knopman, S. S. Emerson, et al. 2021. Revisiting FDA approval of aducanumab. *New England Journal of Medicine* 385 (August 26): 769–771. <https://www.nejm.org/doi/full/10.1056/NEJMp2110468>

¹¹ Among the FDA’s advisory panel, 10 of 11 members recommended that the FDA not approve Aduhelm; one member was “uncertain.” See J. Stephenson. 2022. Medicare to cover controversial Alzheimer disease drug only in clinical trials. *JAMA Health Forum* 3(1):e220048. doi:10.1001/jamahealthforum.2022.0048. <https://jamanetwork.com/journals/jama-health-forum/fullarticle/2788405>

¹² Cavazzoni P. 2021. FDA’s decision to approve new treatment for Alzheimer’s disease. June 7. <https://www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease>

¹³ Food and Drug Administration. 2021. BLA accelerated approval letter for Aduhelm. June 7. https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2021/761178Orig1s000ltr.pdf.

mild AD.”¹⁴ ICER’s independent committee of medical evidence experts voted unanimously that the evidence is not adequate to demonstrate that Aduhelm is superior to supportive care. Further, it was noted that the relationship between beta-amyloid clearance and clinical benefit has yet to be demonstrated. ICER has also raised methodological concerns about the analyses of the clinical trial results, such as carrying out multiple post-hoc analyses to explain the findings from the conflicting studies.¹⁵

- The Veterans Affairs (VA) Pharmacy Benefit Management Services stated that “...we recommend against offering this agent [Aduhelm] to patients with Alzheimer’s dementia (mild or otherwise) or mild cognitive impairment. However, recognizing that there is an accelerated FDA approval, we also recommend that if it is to be used by exception then it should be utilized only in highly selected patients by experts and centers that have the necessary diagnostic and management expertise—and only by those with the needed resources for close monitoring to assure safety. As such, any use should be governed by stringent regulation, and safety and appropriateness of use monitored real time by the VA Center for Medication Safety.”¹⁶
- CMS, ICER, and others have noted that the modest, statistically significant improvement in patients’ functional score found in one of the two clinical trials for a subset of the population may not be clinically meaningful. Although statistically significant, CMS concluded that the change in CDR-SB score (the trials’ primary outcome) in the high-dose group (0.39) was less than the 1 to 2 point change that has been suggested as a minimal clinically important difference. CMS also noted that: “[it] is unclear what the baseline CDR-SB scores, or the changes, were in the EMERGE and ENGAGE trials because to date there has not been peer-reviewed publication of the trial design, results or secondary analyses.”¹⁷

Aduhelm’s potential for significant side effects

In multiple clinical studies of anti-amyloid monoclonal antibody drugs, including Aduhelm, in patients with AD, researchers have reported MRI findings of brain swelling and bleeding as adverse effects of treatment. These adverse events are referred to as amyloid-related imaging abnormalities (ARIAs) that can manifest as brain edema or sulcal effusion (ARIA-E) or as hemosiderin deposits resulting from hemorrhage in the brain parenchyma or on the pial surface (ARIA-H). To monitor for ARIAs, Aduhelm’s FDA label recommends an MRI before the start of therapy, and prior to the 7th and 12th infusions.

¹⁴ Institute for Clinical and Economic Review. 2021, *op. cit.*

¹⁵ Institute for Clinical and Economic Review. 2021, *op. cit.*

¹⁶ VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives. 2021. *Aducanumab-avwa (ADUHELM) national drug monograph*. July.

https://www.pbm.va.gov/PBM/clinicalguidance/drugmonographs/Aducanumab_ADUHELM_monograph_508.pdf

¹⁷ Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2022, *op. cit.*

Pooled data from both Aduhelm Phase III clinical trials show that high-dose patients experienced ARIA at a greater frequency than placebo patients:¹⁸

- Overall, 41 percent of high-dose Aduhelm patients experienced any ARIA compared with 10 percent of placebo patients.
- Brain edema (ARIA-E) was the most common side effect, affecting 35 percent of Aduhelm patients compared to 3 percent of placebo patients. Brain microbleed was observed in 19 percent of Aduhelm patients compared to 7 percent of placebo patients, and brain bleeding (superficial siderosis) was observed in 15 percent of Aduhelm patients compared to 2 percent of placebo patients.

Although the majority of patients were asymptomatic or had symptoms such as headache, confusion, or dizziness that resolved with temporary stoppage of the drug, 6 percent of participants receiving the high dose of Aduhelm discontinued the drug due to ARIA, compared to 0.6 percent of placebo patients.^{19, 20}

Aduhelm exemplifies the challenges Medicare faces from high-priced services with a limited evidence base

Although Medicare payment implications are outside the scope of an NCD, Aduhelm has highlighted the broader challenges Medicare faces in paying for high-cost products with limited clinical evidence. Though there is only limited, conflicting data on Aduhelm's clinical effectiveness, Medicare would pay a high price for the product under its Part B payment system. (Because this biologic is administered in a physician's office or hospital outpatient department, it is paid for under Medicare Part B, rather than through a Medicare Part D drug plan.) For Part B-covered single-source drugs and biologics, manufacturers effectively determine Medicare's payment rate because Medicare generally pays 106 percent of the manufacturer's average sales price. As of December 20, 2021, the manufacturer has set Aduhelm's price for a one-year supply at \$28,200.²¹

At this price, spending implications for the Medicare program could be very large if there is significant uptake of Aduhelm. An estimated 6.2 million adults ages 65 and older have Alzheimer's dementia.²² Though it is unknown what share of this population is likely to receive Aduhelm, its manufacturer (Biogen) has stated that the product is appropriate for between one million to two million individuals. At the current price of \$28,200 for a year of maintenance therapy, Medicare Part B FFS spending and beneficiary cost sharing could total \$1.5 billion

¹⁸ Salloway, S., S. Chalkias, F. Barkhof, et al. 2022. Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease. *JAMA Neurology* 79, no. 1 (November 22): 13–21. <https://jamanetwork.com/journals/jamaneurology/fullarticle/2786606>

¹⁹ Salloway et al. 2022, *op. cit.*

²⁰ Institute for Clinical and Economic Review. 2021, *op. cit.*

²¹ Biogen. 2021. Biogen announces reduced price for Aduhelm® to improve access for patients with early Alzheimer's disease. December 20. <https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelmr-improve-access-patients>

²² Alzheimer's Association. 2021. *2021 Alzheimer's disease facts and figures*. Chicago, IL: Alzheimer's Association. <https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf>

annually if 50,000 FFS beneficiaries received the product and \$15 billion annually if 500,000 FFS beneficiaries received the product. Thus, with substantial uptake, the product has potential to swamp current Part B drug spending, which totaled \$39 billion in 2019.

In addition to spending on Aduhelm, use of the product is likely to increase use of, and therefore spending on, MRIs (which FDA recommends be done at certain intervals to monitor for brain swelling) and potentially PET scans (which Medicare currently covers under a national coverage determination (NCD) to diagnose Alzheimer's disease in limited circumstances). Higher spending on Aduhelm and related services also has implications for Medicare Part B premiums and deductibles and Medigap premiums for beneficiaries with supplemental coverage. It could also have substantial spending implications for Medicare Advantage plans, which generally must cover the Part A and Part B services covered by traditional FFS Medicare (including following NCDs and, in some cases, local coverage determinations). Indeed, CMS has indicated that one of the factors contributing to the increase in the Part B monthly premium for 2022 was the need to create contingency reserves due to uncertainty over the potential use of Aduhelm.²³

Lack of diversity among clinical trial participants

Although AD's prevalence is higher among Blacks and Hispanics, there was a lack of racial and ethnic diversity in Aduhelm's Phase III clinical trial population. Out of 3,285 total participants of ENGAGE and EMERGE, 0.6 percent were Black and 3 percent were Hispanic.²⁴ By contrast, a study that estimated the size of the Medicare FFS population with Alzheimer's disease and related dementias in 2014 using Medicare claims data found Blacks accounted for 9.7 percent and Hispanics accounted for 5.7 percent of FFS beneficiaries ages 65 years and older with dementia that year.²⁵

The clinical trial population was limited to individuals between the ages of 50 to 85 years, with the age of the clinical trial population averaging about 70 years old.²⁶ Thus, the clinical trials excluded the over age 85 population, a group that has a high prevalence of Alzheimer's disease. Roughly one-third of individuals ages 85 and older have Alzheimer's dementia, according to data from the Alzheimer's Association.²⁷ ICER concluded that with higher prevalence of AD among Blacks and

²³ Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2021. Medicare program; Medicare Part B monthly actuarial rates, premium rates, and annual deductible beginning January 1, 2022. Notice. *Federal Register* 86, no. 219 (November 17): 64205–64214.

²⁴ Clinical trial participants included individuals ages 50 to 85 years; information on race was not reported for 13 percent of trial participants, and information on ethnicity was not reported for 9 percent of trial participants. MedPAC analysis of data available on [clinicaltrials.gov](https://www.clinicaltrials.gov) for the EMERGE ([221AD302 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111518)) and ENGAGE trials ([221AD301 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111518)).

²⁵ Matthews K.A., W. Xu, A.H. Gaglioti, et al. 2019 racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015–2060) in adults aged ≥65 years. *Alzheimer's & Dementia* 15, no. 1 (January): 17–24.

²⁶ EMERGE ([221AD302 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111518)) and ENGAGE trials ([221AD301 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111518)).

²⁷ Alzheimer's Association. 2021, *op. cit.*

Hispanics, and among the over age 85 population, a lack of representation of these groups in the trial population could limit the generalizability of the results to the broader US population.²⁸

Other criteria used to select clinical trial participants might affect whether the trial population is representative of the Medicare population. For example, the trials excluded potential participants with impaired renal or liver function; a history of unstable angina, myocardial infarction, or advanced chronic heart failure; HIV infection; clinically significant unstable psychiatric illness in past 6 months; and alcohol or substance abuse in the prior year.²⁹

Comment

Given the limited, conflicting evidence on Aduhelm's clinical effectiveness and the potential for significant side effects, CMS should ensure that the use of this product is appropriate among Medicare beneficiaries. To this end, the Commission supports CMS's proposal to implement an NCD that applies CED to cover available anti-amyloid monoclonal antibody drugs, including Aduhelm. Under CED, beneficiaries have access to medical services while clinical evidence is being collected and analyzed. Because CED provides Medicare the opportunity to generate clinical evidence that otherwise might not have been collected, it enables the program to ultimately develop better, more evidence-based policies.³⁰ Second, given these evidentiary concerns, we are especially concerned about the implications of this new drug for Medicare spending, and its cost impact on all Medicare beneficiaries and taxpayers. Although Medicare does not consider cost as part of its coverage process, Aduhelm has highlighted the broader challenges Medicare faces in paying for high-cost products with limited clinical evidence.

Medicare's coverage process should use tools including CED to address items and services of potentially low value

Many new services disseminate quickly into routine medical care in FFS Medicare with little or no knowledge of whether or to what extent they outperform existing treatments. At FDA approval, evidence on new medical products is not always complete, particularly on products approved under expedited approval pathways. With Aduhelm, we are concerned about the evidence base, including limited and conflicting evidence on Aduhelm's efficacy and the potential for serious side effects demonstrated during clinical trials.

Therefore, the Commission supports CMS's use of CED in the NCD for Aduhelm as a means to generate additional clinical evidence on the drug's effectiveness and safety specific to the Medicare population. Importantly, CED in CMS's proposed NCD would permit the Medicare

²⁸ Institute for Clinical and Economic Review. 2021, *op. cit.*

²⁹ EMERGE ([221AD302 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111558)) and ENGAGE trials ([221AD301 Phase 3 Study of Aducanumab \(BIIB037\) in Early Alzheimer's Disease - Study Results - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02111558)).

³⁰ Medicare Payment Advisory Commission. 2018. *Report to the Congress: Medicare and the health care delivery system*. Washington DC: MedPAC.

program to provide beneficiaries access to Aduhelm while assessing the product's effectiveness in reducing progression of AD specific to the Medicare population.³¹

More systematic use of CED for drugs paid under FFS is an approach that could generate clinical evidence to cover potentially beneficial services (including drugs and devices) that lack clear evidence showing their clinical effectiveness in specific patient populations.³² Benefits of applying CED include improving post-market evidence development, providing important new knowledge for care decisions, and clearer understanding for patients, providers, and payers regarding the risks and benefits of a new intervention. CED could help support, and be reinforced by, other efforts to improve the post-market data infrastructure.³³ In addition, CED would provide an opportunity for generating evidence on Aduhelm's safety and effectiveness for individuals who were underrepresented in the product's clinical trials.

The Medicare program should adjudicate coverage and spending determinations based on the specific needs of the Medicare population

The Commission does not support the use of FDA approval (under either the traditional or expedited pathways) for qualification for Medicare coverage unless the drug in question also meets the standards that Medicare uses to determine national or local coverage. That is, CMS should not use any of FDA's approval processes as sole proxy for Medicare coverage. We reiterate our comments on the IPPS proposed rule for FY 2020, the IPPS proposed rule for FY 2021, and Medicare coverage of innovative technology (2021); in these comment letters we said that:

- The Medicare program, not the FDA, should adjudicate coverage and spending determinations based on the specific needs of the Medicare population. CMS's evidence base for a coverage determination should rely on the ability of the item or service to specifically address the needs (diagnosis and treatment) of Medicare beneficiaries.
- The FDA's role in the drug and device development process as a regulator is distinct and separate from the role of CMS as a payer. The FDA regulates whether a device or pharmaceutical product is "safe and effective" for its intended use by consumers. The FDA

³¹ Medicare Payment Advisory Commission. 2021. Comment letter on CMS's proposed rule entitled "Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2022 Rates; Quality Programs and Medicare Promoting Interoperability Program Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Changes to Medicaid Provider Enrollment; and Proposed Changes to the Medicare Shared Savings Program." June 25. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/comment-letters/06252021_fy_2022_ipps_ltch_medpac_comment_sec.pdf

³² Medicare Payment Advisory Commission. 2010. *Report to the Congress: Aligning incentives in Medicare*. Washington DC: MedPAC.

³³ McClellan, M. B. 2012. *Coverage with evidence development: Where do we go from here?* Engelberg Center for Health Care Reform at Brookings. Washington DC: Brookings Institution.

approval process may or may not include the pharmaceutical product's or new device's safety or effectiveness with regard to the Medicare population.^{34,35,36}

Conclusion

To summarize, the Commission supports CMS's proposal to apply CED to cover anti-amyloid monoclonal antibody drugs, including Aduhelm, given the uncertainty of the clinical benefit of Aduhelm, as concluded by CMS, ICER, and others, and the potential for serious side effects. More systematic use of CED for drugs, including Aduhelm, is an approach that could generate clinical evidence to cover potentially beneficial services that lack clear evidence showing their clinical effectiveness and safety in specific patient populations, particularly drugs approved under FDA's expedited pathways. Although Medicare's determination of payment for an item or service is outside the scope of an NCD, the Commission is concerned about the implications of this new drug for Medicare spending and its cost impact on all beneficiaries and taxpayers, given that Medicare's Part B drug payment system pays the price set by the manufacturer without regard for the clinical effectiveness of the product. In addition, the Commission maintains that the Medicare program, not the FDA, should adjudicate coverage and spending determinations based on the specific needs of the Medicare population. Lastly, CED would provide Medicare an opportunity to collect effectiveness and safety evidence for groups that were underrepresented in Aduhelm's clinical trials, including beneficiaries who are age 85 years and older, Blacks, and Hispanics.

³⁴ Medicare Payment Advisory Commission. 2019. Comment letter on CMS's proposed rule entitled "Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2020 Rates; Proposed Quality Reporting Requirements for Specific Providers; Medicare and Medicaid Promoting Interoperability Programs Proposed Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Rule." July 21. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/comment-letters/06212019_medpac_2020_ipps_ltch_comment_v3_sec.pdf.

³⁵ Medicare Payment Advisory Commission. 2020. Comment letter on CMS's proposed rule entitled "Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2021 Rates; Proposed Quality Reporting Requirements for Specific Providers; Medicare and Medicaid Promoting Interoperability Programs Proposed Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Rule." July 7. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/comment-letters/07072020_fy2021_ipps_medpac_comment_v2_sec.pdf.

³⁶ Medicare Payment Advisory Commission. 2021. Comment letter on CMS's interim final rule entitled "Medicare Program; Medicare Coverage of Innovative Technology (MCIT) and Definition of "Reasonable and Necessary"; Delay of Effective Date; Public Comment Period." April 13. https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/comment-letters/04132021_mcit_medpac_comment_with_2020_letter_sec.pdf.

Chiquita Brooks-LaSure

Administrator

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MedPAC appreciates the opportunity to comment on this proposal. The Commission values the ongoing cooperation and collaboration between CMS and MedPAC staff on technical policy issues. We look forward to continuing this productive relationship. If you have any questions, or require clarification of our comments, please feel free to contact James E. Mathews, MedPAC's Executive Director at (202) 220-3700.

Sincerely,

A handwritten signature in black ink, appearing to read "m. chernew", with a horizontal line extending to the right from the end of the signature.

Michael E. Chernew, Ph.D.

Chair