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Removing CMS Constraints and Going Beyond the NCD Approach A Broader Set of Congressional Legislative Action and Policy Reforms to Address Increase in Prescription Drug Spending and Improve Medicare Beneficiary Access to New Drugs

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Introduction

Prescription drug spending is one of the fastest areas of spending growth in the US healthcare system, and a key driver of increased overall healthcare costs especially within Medicare. Increase in the Medicare beneficiary population, increase in drug prices and an increase in the number of more expensive drugs entering clinical practice has exacerbated this in recent years. The FDA regulates the review and approval of new drugs based on an empirical evaluation of the risk benefit profile of new drugs. Once approved by the FDA, CMS then determines whether the newly approved drug will be covered and accessible to Medicare beneficiaries. This two-step independent process has created an uneasy tension between these two government agencies both of which reside within the Department of Health and Human Services. FDA approval of a new life-saving drug must align with the ability of CMS to pay for it. This is most pronounced for expensive drugs with a large beneficiary target and that fall under Medicare Part B coverage - the focus of this paper.

The recent FDA approval of a new biologics drug for the treatment of Alzheimer's Disease under an expedited process has further illustrated this chasm and surfaced this underlying tension. In the absence of broader legislative actions and policy reform, CMS has limited options to manage prescription drug spending for Medicare beneficiaries. This paper further expands on this issue and proposes reforms needed to address the issue of access and spending on Medicare Part B drugs. Part I of this paper provides a background on Medicare and increase in Part B prescription drug spending. Part II provides an overview of the FDA review process in contrast to the CMS review standards and the CMS NCD process. Part III provides an overview and analysis of the recent CMS NCD process for anti-amyloid therapeutics for AD. Finally, Part IV proposes congressional legislative actions and policy reforms that should be considered to address the increase in drug spending while maintaining access to innovative life-saving drugs.

Part I - Medicare and Prescription Drug Spending Overview

1. Medicare Overview

Medicare provides health insurance for individuals over the age of 65, some younger individuals living with disabilities,[1] and patients with two specific diseases: end-stage renal disease (ESRD) and amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease).[2] The total number of Medicare beneficiaries in 2020 exceeded 61 million.[3] A quarter of Medicare beneficiaries are in fair or poor health, and a fifth have five or more chronic conditions.[4] They have modest incomes, limitations in their ability to independently conduct daily living activities, with nearly one-third having one functional impairment.[5] A segment of the population with high per capita health costs.

Medicare insurance is organized in four basic parts that include coverage for hospital care, doctor visits, prescription drugs and other health services. Medicare Part A covers inpatient hospital stays, care in skilled nursing facilities, hospice care and some home health care. Medicare Part B covers certain doctors' services, outpatient care, medical supplies, preventive services and prescription drugs administered intravenously by a physician. Part C refers to Medicare Advantage program through which beneficiaries can enroll in a private health plan such as a health-maintenance organization (HMO) and receive all Medicare-covered benefits. Medicare Part D is a voluntary, subsidized prescription drug benefit that covers the cost of prescription drugs.[6]

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[1] Juliette Cubanski, Tricia Neuman and Meredith Freed, *The Facts on Medicare Spending and Financing*, August 2019), accessible at https://www.kff.org/medicare/issue-brief/the-facts-on-medicare-spending-and-financing/ (last accessed May 1, 2022).
[2] Louise Norriss, *Medicare eligibility for ALS and ESRD patient*, July 2021, accessible at https://www.medicareresources.org/medicare-eligibility-and-enrollment/medicare-eligibility-for-als-and-esrd-patients/, (last accessed May 1, 2022).
[3] Kaiser Family Foundation, *An Overview of Medicare*, February 2019, accessible at https://files.kff.org/attachment/issue-brief-an-overview-of-medicare (last accessed May 1, 2022).
[4] *Id*.
[5] Kaiser Family Foundation, *supra* note 3, at 1.
[6] Medicare.gov, *What's Medicare?*, accessible at https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare (last accessed May 15, 2022).

Medicare has relatively high cost-sharing requirements, no limit on out-of-pocket spending, and a coverage gap or "donut hole" in the prescription drug benefit.[7] Medicare does not pay for many critical services such as long-term care, dental or vision. Medicare is financed by a combination of payroll taxes, general revenue, beneficiary premiums, interest and other sources.[8]

Prescription drugs covered under Part B are physician-administered infusion or injectable drugs, the majority of which are biologics and specialty drugs. Biologics include a wide range of drugs such as vaccines, blood and blood components, gene therapy, and recombinant therapeutic proteins.[9] Specialty drugs are high-cost prescription drugs to treat complex, chronic conditions like cancer, rheumatoid arthritis, and multiple sclerosis and are administered via injection or infusion.[10] There are no formulary, utilization controls, or a separate drug plan under Medicare Part B.[11] Beneficiaries receive coverage for drugs under the general umbrella of their Medicare Part B coverage.[12] Enrollees pay a monthly premium, an annual deductible and Medicare pays 80% of an approved expense. Patients are responsible for 20% of the remainder costs, giving patients a significant out-of-pocket expense.[13] In contrast, the Medicare Part D prescription program for self-administered drugs is managed by private prescription drug plans, who negotiate pricing and may

[7] Medicare.gov, *Costs in the coverage gap*, accessible at https://www.medicare.gov/drug-coverage-part-d/costs-for-medicare-drug-coverage/costs-in-the-coverage-gap (last accessed May 1, 2022).
[8] Kaiser Family Foundation, *supra* note 3, at 6.
[9] *See* U.S. Food and Drug Administration, *What Are "Biologics" Questions and Answers*, February 2018, accessible at https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers (last accessed May 1, 2022).
[10] *See* HealthInsurance.gov, *What is a specialty drug*, accessible at https://www.healthinsurance.org/glossary/specialty-drug/ (last accessed May 1, 2022).
[11] Medicare.gov, *Prescription drugs (outpatient)*, accessible at https://www.medicare.gov/coverage/prescription-drugs-outpatient (last accessed May 1, 2022).
[12] *Id*.
[13] Cubanski et al., *supra* note 1.

condition formulary placement on the availability of manufacturer discounts.[14] The focus of this paper is on biologics and specialty drugs covered under Medicare Part B.

2. Prescription Drug Spending Increase in the US

Medicare spending is projected to grow from $583 billion in 2018 to $1,260 billion in 2028.[15] The aging of the population, increase in the volume of health care services used, price increases especially of prescription drugs, growth in Medicare enrollment and increase in per capita health care costs are key drivers of overall Medicare spending.[16]

Prescription drug spending is projected to be the fastest growing health category over the next decade and will consistently outpace other health spending.[17] Rising drug costs are a pressing concern for the U.S. health care system especially for Medicare beneficiaries. Nearly 80 percent of Americans said that prescription drug prices were unreasonable in 2019, about a quarter said that it is difficult to afford their prescription drugs, and one in ten said that it is "very difficult" to afford them.[18] Congress has held many hearings on drug pricing in recent years and advanced drug pricing bills, however no legislation has been passed to enact the structural changes necessary to rein in drug prices and control U.S. drug prescription spending.

[14] CMS.gov, *Part D Information for Pharmaceutical Manufacturers*, accessible at https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/Pharma (last accessed May 1, 2022).
[15] Kaiser Family Foundation, *supra* note 3, at 5.
[16] *Id*.
[17] American Academy of Actuaries, *Prescription Drug Spending in the U.S. Health Care System*, March 2018, accessible at https://www.actuary.org/sites/default/files/files/publications/PrescriptionDrugs.030718.pdf (last accessed May 1, 2022).
[18] Ashley Kirzinger, Lunna Lopes , Bryan Wu , and Mollyann Brodie, *KFF Health Tracking Poll – February 2019: Prescription Drugs*, March 2019, accessible at https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/ (last accessed May 1, 2022).

Between 2013 and 2015, the price of biologics and specialty drug increased 12.5 % a year, more than six times the annual inflation rate.[19] From 2010 through 2015, high priced biologics and specialty drugs accounted for a growing share of new drugs, leading to a disproportionate increase in prescription drug spending in Medicare Part B, which increased from $13.4 billion in 2005 to $39 billion in 2019.[20] Spending on biologics and specialty drugs accounted for 92% of all Medicare Part B drug spending growth.[21] Per beneficiary Medicare Part B spending increased 8.1% between 2006 and 2017, more than twice as high compared to Medicare Part D (3.4%).[22] While biologics and specialty drugs represent a small proportion of claims (25% in 2016), they accounted for majority of the spending (88%).[23] The top 50 drugs in Part B which are mainly biologics and specialty drugs, accounted for 80% of total Medicare Part B spending in 2019, while the bottom 485 drugs accounting for 7% of spend.[24] The disproportionate growth in Medicare Part B drug spending, driven by an increased spend on biologics and specialty drugs, and the increase in the number of such drugs entering the clinic means that Medicare Part B drug spending remains a fertile ground and primary focus for legislative and policy reform to control overall healthcare costs.

[19] Inmaculada Hernandez, Chester B. Good, David M. Cutler, Walid F. Gellad, Natasha Parekh, and William H. Shrank, *The Contribution Of New Product Entry Versus Existing Product Inflation In The Rising Costs Of Drugs*, 38 Health Affairs 79 (2019).
[20] MedPAC, *A Data Book: Health care spending and the Medicare program, Section 10 Prescription Drugs*, July 2021, accessible at https://www.medpac.gov/wp-content/uploads/2021/10/July2021_MedPAC_DataBook_Sec10_SEC.pdf (last accessed May 1, 2022).
[21] *Id*.
[22] https://www.jmcp.org/doi/pdf/10.18553/jmcp.2021.27.5.565 Alvaro San-Juan-Rodriguez, et al., *A decade of increases in Medicare Part B pharmaceutical spending: what are the drivers?*, 27 J Manag Care Spec Pharm. 568 (2021).
[23] MedPAC, *supra* note 20.
[24] Juliette Cubanski and Tricia Neuman, *Relatively Few Drugs Account for a Large Share of Medicare Prescription Drug Spending*, April 2021, accessible at https://www.kff.org/medicare/issue-brief/relatively-few-drugs-account-for-a-large-share-of-medicare-prescription-drug-spending/ (last accessed May 1, 2022).

Part II - FDA Drug Approval and Relation to CMS Access

1. Overview of the FDA Review and Expedited Processes

The Food and Drug Administration (FDA) is a federal regulatory agency within the Department of Health and Human Services (HHS) that enforces the Federal Food, Drug and Cosmetic Act (FDCA) and has the responsibility to determine whether drugs and medical devices are "safe and effective" for their intended use.[25] A new drug application under the FDCA follows a well-defined path of oversight and review during drug development.[26] These phases include preclinical *in vitro* (laboratory) and *in vivo* (animal) testing, safety studies, clinical testing in human volunteers and patients, FDA review of the application and post marketing clinical studies.[27] On average, it takes at least ten years for a new drug to go from initial discovery to approval at an average cost of between $1.3 billion[28] and $2.6 billion.[29]

Congress has created several programs to expedite the development time of new drugs that are intended to treat serious or life-threatening conditions and provide substantial improvement over existing treatments. These programs include, "accelerated approval"[30], "priority review",[31] "fast-track"[32] and "breakthrough therapy."[33]. Once an expedited designation is granted to a new drug, the FDA takes an "all hands-on-deck" approach and maintains ongoing interactions with the

[25] Kenneth R. Pina and Wayne L. Pines, *A Practical Guide to FDA's Food and Drug Law and Regulation*, 39 (5th ed. 2014).
[26] 21 U.S.C. § 301 (1938).
[27] Pina *et al.*, *supra* note 25.
[28] Olivier J. Wouters, Martin McKee and Jeroen Luyten, J. *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018,* 323 JAMA 844 (2020).
[29] Joseph A DiMasi, Henry G Grabowski and Ronald W Hansen, *Innovation in the pharmaceutical industry: New estimates of R&D costs,* 47 J Health Econ. 20 (2016).
[30] 21 U.S.C. §314.500 (1992).
[31] Pina *et al.*, *supra* note 25.
[32] 21 U.S.C. §312.80 (2012).
[33] 21 U.S.C. 356 (2012).

sponsor providing guidance and feedback throughout the process.[34] The establishment of these pathways has resulted in drug approvals occurring at record speed. In 2018 and 2019, more than 65% of new drugs were approved in an expedited manner.[35] Development times for drugs in an expedited pathway were just over four years compared to eight years for drugs not in any expedited program.[36] Many of the drugs that are in the FDA expedited programs are high priced biologics and specialty drugs that fall under Medicare Part B coverage.[37]

The "accelerated approval" program expedites the approval of drugs for serious or life-threatening diseases with unmet medical need.[38] The FDA can authorize a drug for marketing approval, if the drug demonstrates evidence of efficacy from a change in a surrogate biomarker as a primary efficacy endpoint as long as the biomarker is "reasonably likely" to predict clinical benefit.[39] As part of the "accelerated approval", the FDA requires the sponsor to conduct post-approval "confirmatory" clinical trial to demonstrate direct clinical benefit of the drug.[40] Once clinical benefit is confirmed, the FDA may then convert the approval to a "full approval" denoting that efficacy based on a direct measure of clinical benefit has been established. If the confirmatory trial fails, then the FDA may withdraw approval of the product using expedited procedures.[41] The FDA has approved 278 drugs under the "accelerated approval" pathway.[42] Nearly half of the drugs

[34] Pina *et al.*, *supra* note 25.
[35] Erin A Ferries, William K Fleming, and William H Shrank, *FDA expedited approval and implications for rational formulary and health plan design*, 27 J Manag Care Spec Pharm, 682 (2021).
[36] Thomas J. Hwang, Jonathan J. Darrow, and Aaron S. Kesselheim, *The FDA's Expedited Programs and Clinical Development Times for Novel Therapeutics, 2012-2016*, 318 JAMA 2137 (2017).
[37] *Id.*
[38] *Id.*
[39] Bishal Gyawali, Joseph S. Ross, and Aaron S. Kesselheim, *Fulfilling the Mandate of the US Food and Drug Administration's Accelerated Approval Pathway*, 181 AMA Intern Med. 1275 (2021).
[40] 21 U.S.C. §356 (c)(3) (2012).
[41] 21 U.S.C. §356 (a) (2012).
[42] https://www.fda.gov/media/151146/download U.S. Food and Drug Administration, *CDER Drug and Biologic Accelerated Approvals Based on a Surrogate Endpoint*, December 2021, accessible at https://www.fda.gov/media/151146/download (last accessed May 1, 2022).

authorized have not been confirmed as clinically effective, while only 16 drugs approved through the pathway have ever been withdrawn.[43] The accelerated pathway program has come under increased intense scrutiny especially since many drugs approved through this pathway are expensive biologics or specialty drugs, and they stay on the market despite limited clinical evidence that they work.[44]

In addition to the shortened development timelines, the number of expensive biologics and specialty drugs that the FDA has approved in the last ten years has increased. Between 2012 and 2021, the FDA approved 104 such drugs compared to only 46 from 2002 to 2011.[45] CMS has become increasingly concerned with the disproportionate growth rate of biologics and specialty drugs spend under Medicare Part B, and especially those drugs that are approved via the FDA's expedited "accelerated approval" pathway. In 2020, the top five CMS outlays for drug spending under Medicare Part B were biologics including Keytruda ($3.5 billion), Eylea ($3 billion), Prolia ($1.6 billion), Opdivo ($1.6 billion) and Rituxan ($1.3 billion).[46]

2. CMS and FDA Review Standards for Drugs

The Centers for Medicare & Medicaid Services (CMS) is the agency also within the U.S. Department of Health and Human Services (HHS) that administers Medicare and other federal healthcare programs including Medicaid. CMS is the largest single health payer in the United States and over 148 million Americans rely on CMS programs for health coverage including prescription drug coverage.

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[43] https://www.bmj.com/content/374/bmj.n1898 Elisabeth Mahase, *FDA allows drugs without proven clinical benefit to languish for years on accelerated pathway*, 374 BMJ 1898 (2021).
[44] *Id.*
[45] Asher Mullard, *2021 FDA Approvals*, 21 Nature Reviews Drug Discovery 85 (2022).
[46] CMS.gov, *Medicare Part B Spending by Drug*, 2020, accessible at https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-b-spending-by-drug/data (last accessed May 1, 2022).

Both the FDA and CMS play a critical role in determining access to new drugs. The FDA approves drugs based on evidence that the product is "safe and effective". FDA approval of a drug means that data on the drug's effects have been reviewed by the FDA and the drug is determined to provide benefits that outweigh the risks for the intended population.[47] As a science-based organization, the FDA uses empirical evidentiary information to make decisions through a deliberative process. No information on the proposed pricing of the drug is part of the FDA review process and the FDA is prohibited from considering a cost benefit analysis.[48]

Once a new drug is approved for marketing by the FDA, CMS makes reimbursement coverage determination for Medicare beneficiaries based on whether a drug is "reasonable and necessary" as per the Social Security Act that established Medicare.[49] Amid escalating costs and rapidly evolving expedited drug approvals by the FDA, CMS has struggled to apply the "reasonable and necessary" standard consistently to new services and drugs, especially the application of cost as a factor in determining access. In 1989, CMS published a proposed regulation defining "reasonable and necessary" that included cost-effective as a factor.[50] This sparked wide criticism from industry and medical professionals and this proposal was subsequently withdrawn.[51] The role of cost-effectiveness in any coverage analysis remains unresolved as the Medicare statute is silent on the role of cost as a factor, and Medicare has not explicitly considered costs in making coverage decisions.[52] While the FDA evaluates a new drug data file with relatively well established evidence requirements in determining "safe and effective", the CMS in contrast must account for additional

[47] U.S. Food and Drug Administration, *Development & Approval Process*, April 2022, accessible at https://www.fda.gov/drugs/development-approval-process-drugs (last accessed May 1, 2022).
[48] 21 U.S.C. §355 (2012).
[49] 42 U.S.C. §§ 1395 (1965).
[50] Peter J. Neumann and James D. Chambers, *Medicare's Enduring Struggle to Define "Reasonable and Necessary" Care*, 367 N Engl J Med 1775 (2012).
[51] *Id.*
[52] *Id.*

benefit-risk trade-offs and less clear statutory and more ambiguous guidelines in applying the "reasonable and necessary" standard.[53]

Coverage analysis of FDA approved drugs between 1999 and 2011 showed that CMS covered 100% of new drugs approved by the FDA.[54] However, 25% of FDA-approved medical devices were not covered by CMS suggesting the underlying friction between the FDA "safe and effective" standard and the CMS "reasonable and necessary" standard.[55]

Under long-standing CMS guidance in the Medicare Program Integrity Manual (MPIM), CMS evaluates whether a therapy is "reasonable and necessary" by assessing whether it is, (1) safe and effective; (2) not experimental or investigational (except certain routine costs in clinical trials); and (3) appropriate for Medicare beneficiaries in accordance with accepted standards of medical practice.[56] Attempts by CMS to codify the "reasonable and necessary" standard have failed legislatively, including most recently under the Medicare Coverage of Innovative Technology and Definition of "Reasonable and Necessary" (MCIT/R&N) rule published in January 2021.[57] After intense debate, CMS repealed the MCIT/R&N rule in November 2021[58] and stated that it intended to explore coverage process improvements that will enhance access to innovative and beneficial technologies in a way that will better suit the healthcare needs of people with Medicare.[59] Repeal of the MCIT/R&N rule further illustrated the underlying friction that exists between the FDA and

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[53] James D. Chambers, Katherine E. May, and Peter J. Neumann, *Medicare Covers The Majority Of FDA-Approved Devices and Part B Drugs, But Restrictions And Discrepancies Remain*, 32 Health Affairs 1109 (2013).
[54] *Id.* at 1111.
[55] *Id.* at 1112.
[56] CMS, *Medicare Program Integrity Manual, Ch. 13*, 2019, accessible at https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/pim83c13.pdf (last accessed May 1, 2022).
[57] https://public-inspection.federalregister.gov/2021-24916.pdf
[58] CMS.gov, *CMS Repeals MCIT/R&N Rule; Will Consider Other Coverage Pathways to Enhance Access to Innovative Medical Devices*, November 12, 2021, accessible at https://www.cms.gov/newsroom/press-releases/cms-repeals-mcitrn-rule-will-consider-other-coverage-pathways-enhance-access-innovative-medical#:~:text=Today%2C%20the%20Centers%20for%20Medicare,sufficient%20to%20protect%20Medicare%20patients (last accessed May 1, 2022).
[59] *Id.*

CMS. With no statutory definition, CMS relies on the guidance in its MPIM to determine if a therapeutic is "reasonable and necessary".

3. CMS National Coverage Determination (NCD)

Responsibility for Medicare coverage determinations for new drugs is split between CMS and regional contractors known as Medicare Administrative Contractors (MACs). For the majority of coverage decisions, the decision is made locally by the MACs and applied regionally. However, when there are large cost, quality or safety implications for the Medicare population, or when a request is made by an interested party, CMS may issue a coverage position on access which is applied nationwide and supersedes any local decisions.[60] National coverage determination is a nine-to-twelve-month process which starts with CMS opening a National Coverage Analysis (NCA). After a 30-day public comment period, CMS publishes a draft proposal outlining the coverage decision and allows for a 30-day public comment period. CMS announces the final National Coverage Determination (NCD) within 90 days of the initial proposed draft decision.[61] CMS has stated that as a matter of policy, NCD is made through an "evidence-based process" and cost is not an explicit factor in determining coverage.[62] The new drug or service should provide adequate evidence that intervention compared to alternatives would result in clinically meaningful improvement in health outcomes. While comparative effectiveness is a factor in determining coverage, cost effectiveness is not part of the CMS analysis.[63]

[60] Elizabeth Richardson, *Aligning FDA and CMS Review*, 10 Health Affairs 1 (2015).
[61] Medicare Program; Revised Process for Making National Coverage Determinations, 78 Fed. Reg. 152, 48164 (Aug. 7, 2013).
[62] Centers for Medicare & Medicaid Services, *Medicare Coverage Determination Process*, August 2013, accessible at https://www.cms.gov/Medicare/Coverage/DeterminationProcess (last accessed May 14, 2022).
[63] *Id.*

As the output of a NCD, CMS may approve nationwide coverage in all cases, deny coverage in all cases, defer the decision to MACs, or provide coverage only in specific circumstances where the evidence supports its use, also known as coverage with evidence development (CED).[64] Since 1999, there have been 191 NCD decisions issued by the CMS, approximately 10 to 15 each year.[65] A meta-analysis NCDs suggested that the evidentiary bar for coverage has gone higher and coverage decisions have become more restrictive in recent years.[66]

4. Coverage with Evidence Development (CED)

Coverage with evidence development (CED) is one of the outcomes from an NCD. This is a utilization management tool used by CMS to attempt to limit coverage of a new drug or service and indirectly achieve cost avoidance to the Medicare program. CMS issued guidance to its staff on CED in 2014 when it began implementing this additional outcome from an NCD.[67] Under a CED, Medicare covers a medical service or drug only on the condition that they are used in the context of an approved clinical study and the collection of additional clinical data is concomitant to use and access for Medicare beneficiaries. CMS cited sections of the Social Security Act[68] as the basis of the CED policy. CMS views CED as an important tool designed to provide limited access to new expensive drugs and services while more robust clinical effectiveness and safety

[64] *Id*.
[65] Tufts Medical Center, *CEVR Value Databases*, 2003, accessible at https://www.tuftsmedicalcenter.org/research-clinical-trials/institutes-centers-labs/center-for-evaluation-of-value-and-risk-in-health/cevr-value-databases (last accessed May 7, 2022).
[66] James D. Chambers, Matthew Chenoweth, Michael J. Cangelosi, Junhee Pyo, Joshua T. Cohen, and Peter J. Neumann, *Medicare Is Scrutinizing Evidence More Tightly For National Coverage Determinations*, 34 Health Affairs 253 (2015).
[67] Centers for Medicare & Medicaid Services, *Guidance for the Public, Industry, and CMS Staff: Coverage with Evidence Development*, November 2014, accessible at https://www.cms.gov/medicare-coverage-database/view/medicare-coverage-document.aspx?MCDId=27 (last accessed May 7, 2022).
[68] 42 U.S.C. § 1395y (1965).

evidence is collected.[69] CMS states that a CED provides complementary medical evidence and does not undermine the FDA's authority in assuring the safety and efficacy of drugs.[70]

Until recently, a final CED requirement decision had never been issued as an outcome of a NCD for an on-label usage of an FDA-approved drug. CMS has covered and reimbursed all Part B drugs upon FDA approval.[71] CMS did previously in one instance attempt to use the CED option for the first FDA approved gene therapy drugs, which were priced at over $400,000 for a one-time treatment.[72] CMS proposed to cover these drugs under a CED paradigm in the draft NCD issued. Following strong opposition from industry groups and community oncologists,[73] CMS removed the CED requirement in its final NCD.[74] Affordability of gene therapies and other expensive biologics and specialty drugs is a central issue for CMS. Recent developments in Alzheimer's Disease has brought more attention to the CMS NCD and CED paradigm and shifted this debate into higher gear.

[69] CMS, *supra* note 67.
[70] *Id*.
[71] Shaw, Daniel L., *Coverage Of Novel Therapeutic Agents By Medicare Part D Following FDA Approval*, January 2018, accessible at https://elischolar.library.yale.edu/ymtdl/3447 (last accessed May 7, 2022).
[72] Institute for Clinical and Economic Review, *Chimeric Antigen Receptor T-Cell Therapy for BCell Cancers: Effectiveness and Value, March* 23, 2018, accessible at https://icer.org/wp-content/uploads/2020/10/ICER_CAR_T_Final_Evidence_Report_032318.pdf (last accessed May 15, 2022).
[73] Kelsey Waddill, *Finalized CMS Rule Supports Medicare Coverage for Gene Therapy*, August 2019, accessible at https://healthpayerintelligence.com/news/finalized-cms-rule-supports-medicare-coverage-for-gene-therapy (last accessed May 7, 2022).
[74] Centers for Medicare & Medicaid Services, *Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers*, August 7, 2019, accessible at https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&NCAId=291 (last accessed May 7, 2022).

Part III - Alzheimer's Disease and Anti-Amyloid Antibody Drugs

1. Alzheimer's Disease

Alzheimer's Disease (AD) is the third leading cause of death after cancer and heart disease, and the leading cause of dementia in older Americans.[75] It is an irreversible, progressive brain disease that degrades memory, cognitive function, and ability to carry out tasks of daily living. An estimated 6.5 million Americans aged 65 and older are living with AD in 2022. Barring the development of medical breakthroughs to prevent, slow or cure AD, the number of AD patients is expected to double over the next decade.[76] Significant emotional, physical and financial stress is placed on individuals with AD, their family members and care takers. Care costs for dementia patients ranged from $75,000 - $83,000 per patient per year in 2010.[77] Costs to the healthcare system due to AD are expected rise to more than $355 billion over the next two decades as the US population ages.[78]

President Obama signed into law the National Alzheimer's Project Act (NAPA) in January 2011.[79] The law required the HHS to establish the National Alzheimer's Project to accelerate the development of treatments that would prevent, halt or reverse the course of AD. In December 2021, in response to NAPA, the HHS issued an updated policy proposal titled: "*National Plan to Address Alzheimer's Disease: 2021 Update*".[80]

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[75] Alzheimer's Association, *2022 Alzheimer's Disease Facts and Figures*, 2022, accessible at https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf (last accessed May 7, 2022).
[76] *Id.* at 19.
[77] *Id.* at 38.
[78] *Id.* at 61.
[79] 42 U.S.C. § 11201 (2011).
[80] U.S. Department of Health and Human Services, *National Plan to Address Alzheimer's Disease: 2021 Update*, December 2021, accessible at https://aspe.hhs.gov/sites/default/files/documents/66904c18bb1f0843c3c113d7099e98c1/napa-national-plan-2021-update.pdf (last accessed May 7, 2022).

2. Anti-Amyloid Antibody Drugs and *Aducanumab*

Until recently, there were no FDA approved drugs that could slow the progression of AD and modify the disease trajectory. Accumulation of abnormal amyloid plaques and tangled bundles of fibers are the main pathological features of AD.[81] On June 7, 2021, the FDA granted regulatory approval to *Aducanumab* - the first drug approved that addresses the pathophysiology of AD. *Aducanumab* is a monoclonal antibody shown to bind and reduce amyloid plaques in the brain in AD patients.[82] The drug developed by Biogen had been designated as a "breakthrough therapy" by the FDA and approved under the "accelerated approval" pathway based on the amyloid reduction surrogate biomarker.[83] As part of this approval, the FDA required the company to conduct confirmatory clinical trials to show evidence of clinical benefit.[84] There are three other anti-amyloid antibody (AAA) drugs in late-stage clinical development for AD including *Lecanemab* (Eisai), *Donanemab* (Lilly) and *Gantenerumab* (Roche).[85]

Aducanumab and the other AAA drugs are administered in a doctor's office via an intravenous infusion and therefore fall under Medicare Part B coverage. Until recently there were no AD drugs covered by Medicare under Part B. The only other FDA-approved AD drugs are self-administered pills that manage AD symptoms and are covered under Medicare Part D. These AD drugs include cholinesterase inhibitors (*Donepezil*, *Galantamine* and *Rivastigmine)* and glutamate regulators

[81] Eric Karran and Bart De Strooper, *The amyloid hypothesis in Alzheimer disease: new insights from new therapeutics* 21 Nat Rev Drug Discov. 306–318 (2022).
[82] US Food & Drug Administration, *FDA's Decision to Approve New Treatment for Alzheimer's Disease*, June 7, 2021, accessible at https://www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease (last accessed May 7, 2022).
[83] *Id.*
[84] US Food & Drug Administration, *BLA Accelerated Approval*, June 7, 2021, accessible at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/761178Orig1s000ltr.pdf (last accessed May 7, 2022).
[85] Karran et al., *supra* note 81 at 307.

(*Memantine*) all of which are now available as generics.[86] The total spending for all these four AD drugs by CMS in 2020 was approximately $500 million dollars.[87]

Biogen initially priced *Aducanumab* at $56,000 annually and subsequently reduced the price to $28,000 a year.[88] Given that the vast majority of AD patients that would potentially benefit from *Aducanumab* are age 65 and older and therefore covered by Medicare, the drug can have profound financial impact on Part B drug spending.[89] If only one million Medicare beneficiaries (of the 6 million AD patients) were to receive *Aducanumab* or one of the other AAA drugs, the cost to Medicare from these drugs alone could exceed $25 billion.[90] In November 2021, CMS announced a historic 15% increase to 2022 Medicare Part B monthly premiums due to the "significant uncertainty regarding the potential for future coverage of clinician-administered Alzheimer's drugs, requiring additional contingency reserves."[91] The Department of Veterans Affairs (VA)

[86] Alzheimer's Association, FDA-approved treatments for Alzheimer's, 2021, accessible at https://www.alz.org/media/documents/fda-approved-treatments-alzheimers-ts.pdf, (last accessed May 7, 2022).
[87] Centers for Medicare and Medicaid Services, *Medicare Part D Spending by Drug*, accessible at https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug, (last accessed May 7, 2022).
[88] Biogen, *Biogen Announces Reduced Price for ADUHELM® to Improve Access for Patients with Early Alzheimer's Disease*, December 20, 2021, accessible at https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelmr-improve-access-patients (last accessed May 7, 2022).
[89] Juliette Cubanski and Tricia Neuman, *Medicare's Coverage Decision for the New Alzheimer's Drug and Why It Matters*, January 14, 2022, accessible at https://www.kff.org/policy-watch/medicares-coverage-decision-for-the-new-alzheimers-drug-and-why-it-matters/ (last accessed May 7, 2022).
[90] Juliette Cubanski and Tricia Neuman, *FDA's Approval of Biogen's New Alzheimer's Drug Has Huge Cost Implications for Medicare and Beneficiaries*, June 10, 2021, accessible at https://www.kff.org/medicare/issue-brief/fdas-approval-of-biogens-new-alzheimers-drug-has-huge-cost-implications-for-medicare-and-beneficiaries/ (last accessed May 7, 2022).
[91] Centers for Medicare and Medicaid Services, *CMS Announces 2022 Medicare Part B Premiums*, November 12, 2021, accessible at https://www.cms.gov/newsroom/press-releases/cms-announces-2022-medicare-part-b-premiums (last accessed May 7, 2022).

decided not to add the drug to its formulary.[92] Adding *Aducanumab* would have cost VA more than $4 billion a year which is 40% of the total VA pharmacy budget.[93]

Medicaid programs are required to cover nearly all FDA approved drugs, even drugs that Medicare chooses not to cover.[94] Medicare's restrictive coverage of *Aducanumab* and other AAA drugs could potentially leave states fully responsible for the drug's costs which could cost Medicaid more than $2 billion a year, which is 7% of the Medicaid current drug spend.[95] The fiscal implications for states are serious. Unlike the federal government, states can't run budget deficits which means that they would need to raise taxes or find other sources of funding to pay for expensive drugs like *Aducanumab*. The interdependencies of a Medicare NCD and Medicaid reimbursement of FDA-approved drugs is another complex issue patients face and not the subject of this paper.[96]

3. Draft CMS NCD for Anti-Amyloid Antibody Drugs for AD

On July 12, 2021, the CMS took the unusual and unprecedented step of opening a NCA for not only *Aducanumab* but for all antibodies being developed to target amyloid in AD to determine Medicare national coverage.[97] In a draft NCD issued on January 11, 2022, CMS proposed to cover FDA approved AAA drugs under CED in CMS approved randomized controlled trials (RCT)

[92] Joseph Walker, *VA Health System Won't Cover Biogen's Alzheimer's Drug*, The Wall Street Journal, August 12, 2021), accessible at https://www.wsj.com/articles/biogens-alzheimers-drug-wont-be-covered-by-va-health-system-11628803740 (last accessed May 14, 2022).
[93] Adrian D. Haimovich *et. al.*, *Estimated Veterans Health Administration costs for Alzheimer's disease treatment with aducanumab*, July 30, 2021, accessible at https://www.medrxiv.org/content/10.1101/2021.07.24.21261063v1.full.pdf (last accessed May 15, 2022).
[94] Kaiser Family Foundation, *Medicaid's Prescription Drug Benefit: Key Facts*, May 1, 2019, accessible at https://www.kff.org/medicaid/fact-sheet/medicaids-prescription-drug-benefit-key-facts/ (last accessed May 7, 2022).
[95] Rachel Dolan and Elizabeth Williams, *How Might the FDA's Approval of a New Alzheimer's Drug Impact Medicaid?*, July 13, 2021, accessible at https://www.kff.org/medicaid/issue-brief/how-might-the-fdas-approval-of-a-new-alzheimers-drug-impact-medicaid/ (last accessed May 7, 2022).
[96] *Id.*
[97] Centers for Medicare & Medicaid Services, *CMS Opens National Coverage Determination Analysis on Treatment for Alzheimer's Disease*, July 12, 2021, accessible at https://www.cms.gov/newsroom/press-releases/cms-opens-national-coverage-determination-analysis-treatment-alzheimers-disease (last accessed May 7, 2022).

conducted in a hospital setting. This was an unprecedented outcome for three reasons. First, CMS provided an extremely narrow coverage for an FDA-approved drug by only paying for patients in a CED RCT setting. Second, the NCD was to apply to all drugs in the class both approved and those in clinical development. Third, the NCD did not differentiate between drugs approved via the "accelerated approval" pathway from those that may be received "full-approval" by the FDA.[98]

While acknowledging that there are no effective treatments for AD, CMS concluded that there remained significant doubts about the potential clinical benefits of AAA drugs and whether benefits outweigh the risks. No clinical trial has yet demonstrated a meaningful improvement in health outcomes for patients treated with anti-amyloid antibodies in AD and more trials were needed to show clinical benefit or harm of these antibodies.[99] CMS viewed the safety profile of treatment and the risk-benefit profile as not attractive for Medicare beneficiaries. CMS argued that Medicare funding for such drugs may divert investment away from approaches that may be more beneficial. The CMS also implied that while oncology drugs approved under the "accelerated pathway" are used only for a limited time and by a narrow group of Medicare beneficiaries, AAA drugs for AD will have very broad and chronic use in the Medicare beneficiary population. Finally, CMS made the argument that the Phase 3 clinical trials conducted for *Aducanumab* did not include sufficient ethnic and age diversity, and that patients over the age of 85 years were excluded, and therefore the trial population was not a reasonable representation of Medicare beneficiaries.[100] For these reasons, the CMS stated that a CMS approved RCT is needed to generate the evidence that

[98] Centers for Medicare & Medicaid Services, *Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, January 11, 2022, accessible at https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=305 (last accessed May 7, 2022).
[99] *Id*.
[100] *Id*.

is currently lacking to establish whether AAA drugs are "reasonable and necessary" for the treatment of AD for Medicare beneficiaries.[101]

During the 30-day public comment period following the draft NCD, the CMS received over 10,000 comments on the draft NCD including from manufacturers Biogen, Lilly, Eisai, Roche and other stakeholders including MEDPAC[102], Duke Margolis Center for Health Policy[103], and CIDSA[104]. Additional comments were submitted by Alzheimer's Disease Task Force[105] (an aggregation of 18 patient advocacy groups), and a group of 75+ House Republicans.[106]

Former FDA commissioner, Scott Gottlieb commented that the CMS was setting an "unwelcome precedent" by rejecting the analysis of the FDA and conducting a separate analysis. He added that CMS took an unprecedented position by suggesting that if a drug is approved "under accelerated approval, it didn't necessarily prove an advantage and didn't necessarily need to be covered."[107]

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[101] *Id*.
[102] Medicare Payment Advisory Commission, *MedPAC comment on CMS's proposed NCD decision memorandum on monoclonal antibodies that target amyloid for the treatment of Alzheimer's disease*, February 10, 2022, accessible at https://www.medpac.gov/wp-content/uploads/2022/02/Feb22_NCD_Monoclonal_Alzheimers_MedPAC_comment_v2_SEC.pdf (last accessed May 7, 2022).
[103] Duke Margolis Center for Health Policy, *National Coverage Analysis (NCA) Tracking Sheet for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, August 11, 2021, accessible at https://healthpolicy.duke.edu/sites/default/files/2021-09/Duke%20Margolis%20Comments_CAG-00460N.pdf (last accessed May 7, 2022).
[104] Council for Informed Drug Spending Analysis, *Proposed National Coverage Determination "Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, February 1, 2022, accessible at https://global-uploads.webflow.com/5e59d7f99e288f91abe20b9f/620178784ff0847ee04a32d8_CIDSA%20Aduhelm%20Letter.pdf (last accessed May 7, 2022).
[105] Alzheimer's Disease Task Force, *Proposed National Coverage Determination for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, February 10, 2022, accessible at https://www.agingresearch.org/app/uploads/2022/02/Alzheimers-Disease-Policy-Task-Force-CMS-Comment-Sign-on-Letter-2.10.22-1.pdf (last accessed May 7, 2022).
[106] Cathy McMorris Rodgers *et. al*, *Letter to Secretary Becerra and Administrator Brooks-LaSure*, February 8, 2022, accessible at https://republicans-energycommerce.house.gov/wp-content/uploads/2022/02/02.08.22-Letter-to-Becerra-re-CMS-NCD.pdf (last accessed May 7, 2022).
[107] Paul Schloesser, *Scott Gottlieb criticizes CMS in feud over Aduhelm coverage, calls out their lack of expertise*, January 27, 2022, accessible at https://endpts.com/scott-gottlieb-criticizes-cms-in-feud-over-aduhelm-coverage-calls-out-their-lack-of-expertise/ (last accessed May 7, 2022).

4. Final CMS NCD for Anti-Amyloid Antibody Drugs for AD

On April 7, 2022, CMS released the final national policy for coverage of all AAA drugs currently approved by the FDA and future AAA drugs to be approved by the FDA. In its final NCD report, CMS reiterated that it ran a transparent, evidence-based NCD process that incorporated more than 10,000 stakeholder comments and more than 250 peer-reviewed documents into determination.[108]

In its final guidance, CMS acknowledged the unprecedented and unique approach of the NCD. For the first time ever, the CED requirement was retained for an FDA approved drug and in this case for all FDA approved and future drugs for an entire class of drugs.

On April 8, 2022, CMS administrator Chiquite Brooks-LaSure and FDA Commissioner Robert Califf issued a joint statement. The statement reiterated that the two agencies play an important, related, but different roles. The "FDA's decision to approve a new medical product is based on a careful evaluation of the available data and a determination that the medical product is safe and effective for its intended use."[109] Whereas the CMS "can conduct its own independent review to determine whether an item or service should be covered nationally by Medicare, including examining whether it is reasonable and necessary for use in the Medicare population."[110] The statement emphasized that while the agencies shared a common goal advancing the development

[108] Centers for Medicare & Medicaid Services, *CMS Finalizes Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, April 7, 2022, accessible at https://www.cms.gov/newsroom/press-releases/cms-finalizes-medicare-coverage-policy-monoclonal-antibodies-directed-against-amyloid-treatment#:~:text=Today%2C%20the%20Centers%20for%20Medicare,use%20in%20treating%20Alzheimer's%20disease (last accessed May 7, 2022).

[109] U.S. Food and Drug Administration, *Joint Statement from CMS Administrator Chiquita Brooks-LaSure and FDA Commissioner Robert M. Califf, M.D., on Ensuring Access to Safe and Effective Treatments*, April 8, 2022, accessible at https://www.fda.gov/news-events/press-announcements/joint-statement-cms-administrator-chiquita-brooks-lasure-and-fda-commissioner-robert-m-califf-md (last accessed May 7, 2022).

[110] Centers for Medicare & Medicaid Services, *Joint Statement from CMS Administrator Chiquita Brooks-LaSure and FDA Commissioner Robert M. Califf, M.D., on Ensuring Access to Safe and Effective Treatments*, April 8, 2022, accessible at https://www.cms.gov/newsroom/press-releases/joint-statement-cms-administrator-chiquita-brooks-lasure-and-fda-commissioner-robert-m-califf-md (last accessed May 7, 2022).

and availability of innovative medical products, the two agencies "remain committed to using our distinct set of authorities to ensure the continued availability of medical products that meet our respective standards to care for the people we serve."[111]

There were four key updates between the draft and final NCD guidance. First, CMS differentiated access between AAA drugs receiving FDA approval via the "accelerated approval" pathway and those that receive "full approval". AAA drugs approved via the "accelerated approval" pathway may be covered in a CED paradigm and only for patients in a RCT. AAA drugs receiving "full approval' will have more expanded coverage but still within the CED paradigm but not necessarily in a RCT. The RCT may be replaced with a CMS-approved study design ranging from prospective longitudinal comparative studies to pragmatic clinical trials and study data may be collected in a patient registry.[112] In a departure from previous standards, CMS also stated that even FDA approval and determination that a drug or biologic demonstrates efficacy from a direct measure of clinical benefit (full approval), would not necessarily meet the statutory "reasonable and necessary" standard and therefore the CED paradigm will still apply for coverage.[113]

Second, CMS removed the requirement of a "CMS-approved trial" language for the RCT and not require a separate RCT that duplicates the FDA requirement of a confirmatory trial for drugs approved under an "accelerated approval" pathway. Therefore, patients on a AAA drug approved via the "accelerated approval" pathway and in the FDA required and approved confirmatory clinical trial would be eligible for coverage. CMS clarified that it would not need to approve the trial protocol already approved by the FDA, but would need to coordinate the CMS payment

[111] *Id.*
[112] Centers for Medicare & Medicaid Services, *Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, April 7, 2022, accessible at https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305 (last accessed May 7, 2022).
[113] *Id.*

operationally, to ensure that payment is administratively feasible for a patient in a double-blind, placebo-controlled study, so that a "statement of benefits" does not inadvertently unblind patients and compromise the integrity of the trial.[114]

Third, while patients in the RCT will be limited to a hospital-based outpatient center to ensure integrated and coordinated care, access to AAA drugs receiving "full-approval" will not be limited to a hospital setting. To removed access barriers, they would be covered in care settings including outpatient department, infusion centers and community clinics to remove barriers to access.[115]

Fourth, CMS in its final NCD provided clarity on coverage for dual eligible and Medicaid only beneficiaries. For Medicaid beneficiaries, CMS noted that states are required to cover a drug if the manufacturer has a National Drug Rebate Agreement with HHS and when the drug is used for a medically accepted indication, subject to any permissible restrictions or limitations on coverage applied by the state, for example prior authorization.[116] However, state Medicaid programs could subject the drug to utilization management techniques, such as prior authorization, and medical necessity criteria.[117] Essentially, the NCD pushed the final coverage decision to the states. Implications and application of the CMS decision and the NCD for Medicaid beneficiaries for AAA drugs remain largely unresolved. Medicaid access is not the focus of this paper.

5. Legal, Administrative and Operational Issues with the CMS NCD

While the CMS made reasonable adjustments to the final NCD decision, there remain a number of legal, administrative and implementation challenges with the CED requirement for AAA drugs.

[114] *Id*.
[115] *Id*.
[116] *Id*.
[117] *Id*.

The NCD Does Not Support HHS AD Action Plan

The HSS National Plan on AD as part of the 2011 NAPA legislation called for among other things for the HSS to create and maintain an integrated national plan to overcome AD, provide information and coordination of AD research across all Federal agencies, and accelerate the development of treatments for AD.[118] The NCD challenges the analysis of the FDA, and creates additional clinical requirements which appear to contradict the NAPA intent of Congress and the goals of the HHS. The NCD suggests that the FDA and CMS, two agencies within the same HHS department did not coordinate their approach to AD.

The NCD Negates Congressional mandates to implement expedited drug reviews by FDA

Congress has been modernizing the FDCA to allow for faster review and approval of drugs for serious and progressive conditions so that patients can have access sooner.[119] The CMS decision to limit access to drugs because they were approved through the "accelerated approval" pathway contradicts the analysis of the FDA and negates Congress's mandate to accelerate access to certain life-saving treatments. CMS covers many drugs that were approved under the "accelerated approval" pathway, which is no less scientifically rigorous. FDA can only grant approval if the same evidentiary standards of safety and efficacy are met compared to "full approvals".[120]

There is no legal basis for the CED Paradigm in the NCD

The CED construct does not have a basis in law and CMS lacks statutory authority to impose a CED requirement. When the CMS first issued CED guidance[121], CMS stated that its statutory

[118] U.S. Department of Health and Human Services, *supra* note 80.
[119] Janet Woodcock, *Expediting drug development for serious illness: Trade-offs between patient access and certainty*, 15 Clinical Trials 230–234 (2018).
[120] *Id.*
[121] Centers for Medicare & Medicaid Services, *supra* note 67.

authority for CED was based on the Social Security Act.[122] Neither of the SSA provisions cited authorizes CMS to establish a CED program. Section 1862(a)(1)(E) authorizes CMS to conduct research under the guidance of Agency for Healthcare Research and Quality (AHRQ) for a limited scope.[123] CMS does not have the authority to oversee any clinical trials except for certain research exceptions under the oversight of AHRQ. The RCT and prospective clinical studies in the CED are not a "research" requirement and are without AHRQ sponsorship.[124]

When CMS issued its proposed CED guidance in 2014, the agency did not properly go through notice and comment rulemaking process. In *Azar v. Allina Health Services*[125], the Supreme Court has ruled that because the HHS had neglected its statutory notice-and-comment obligations when it revealed a new policy that dramatically and retroactively reduced Medicare payments to hospitals serving low-income patients, its policy must be vacated. Even in circumstances in which the Administrative Procedure Act (APA) does not otherwise require such rulemaking, under Section 1871(a)(2) of the SSA[126], any Medicare policy that establishes or changes a "substantive legal standard" governing the scope of benefits, payment for services, eligibility of individuals to receive benefits, must be promulgated through notice-and-comment rulemaking.[127]

The NCD Is Arbitrary and Capricious in Violation of the Administrative Procedure Act (APA)

The proposed application of CED to approved uses of an FDA-approved drug is unprecedented and arbitrarily holds FDA-approved AAA drugs for AD to a higher standard than drugs in any

[122] 42 U.S.C. § 1395y (1965).
[123] 42 U.S.C. § 1320b (1944).
[124] Cathy Kelly, *Medicare's CED For Alzheimer's Drugs May Exceed Statutory Authority, Former HHS Attorneys Say*, February 10, 2022, accessible at https://pink.pharmaintelligence.informa.com/PS145677/Medicares-CED-For-Alzheimers-Drugs-May-Exceed-Statutory-Authority-Former-HHS-Attorneys-Say (last accessed May 7, 2022).
[125] *Azar v. Allina Health Services*, 139 S. Ct. 1804, 1810 (2019).
[126] 42 U.S.C. § 1395hh (1965).
[127] Azar, *supra* note 125.

other therapeutic area. The anti-amyloid class NCD is inconsistent with how CMS has treated all other FDA approved drugs in its history, including hundreds of other drugs approved under the "accelerated approval" pathways. CMS has never before made a final determination to require a CED for an entire class of drugs. CMS has indeed never before applied CED to the on-label use of a single FDA approved drug. There is no precedent for CMS imposing CED restrictions on a labeled indication of a drug that FDA has approved and deemed "safe and effective".[128] CMS has consistently rejected the idea of imposing CED restrictions for an FDA approved drug use. In the 2011, NCD for a prostate cancer immunotherapy, the CMS guidance rejected use of CED restrictions for FDA approved uses of the drug. CMS determined that the therapy was "reasonable and necessary" for its FDA-approved use.[129] CMS also recently rejected CED restrictions for gene therapy drugs in its final decision. While CMS acknowledged that gene therapies are known to have a significant risk for toxicity, the agency nonetheless rejected the need for CED in light of FDA's prior evaluation of safety and effectiveness and authorized coverage for all FDA approved indications.[130] CMS is holding FDA-approved AAA drugs for AD to a different standard than it has previously applied to drugs for any other disease, including other "accelerated approval" drugs. A fundamental rule of administrative law is that agencies must treat similarly situated entities the same. A long line of precedent has established that an agency action is arbitrary and capricious

[128] Biogen, *Proposed Decision Memorandum for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)*, February 10, 2022, accessible at https://investors.biogen.com/static-files/48bc8500-bf36-4be1-ae87-81d4bab2d05f (last accessed May 7,2022).
[129] Centers for Medicare & Medicaid Services, *Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer*, June 30, 2011, accessible at https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=247&keyword=%22coverage+with+evidence+development%22&keywordType=starts&areaId=all&docType=NCA%2cNCD&contractOption=all&sortBy=relevance&bc=1 (last accessed May 7, 2022).
[130] Centers for Medicare & Medicaid Services, *Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers*, August 7, 2019, accessible at https://www.cms.gov/medicare-coverage-database/view/ncacal-decision memo.aspx?proposed=N&NCAId=291 (last accessed May 7, 2022).

when the agency offers insufficient reasons for treating similar situations differently.[131] The broad scope of the NCD for an entire class of drugs, makes it arbitrary and capricious under APA.[132]

The RCT for AAAs Effectively Denies Coverage

The largest late-stage clinical trials in AD have recruited no more than a few thousand patients. Requiring a patient to be on a RCT for access to a therapeutic is essentially a non-coverage decision given that the vast majority of AD patients will not be in the RCT. The RCT will require a placebo arm to the clinical study, as such even of those few thousand that would be part of a RCT, half of the patients with AD will be on placebo. Patients on placebo may have to pay the 20% deductible under Medicare Part B coverage for the drug in the amount of $5,600 a year to receive placebo only. It is medically unethical to charge patients receiving a placebo for a marketed drug.[133]

While there are legal and other challenges with the NCD for AAA drugs and the CED requirement, CMS has no other mechanisms available to manage access to new expensive drugs that have yet to be fully proven. A high-priced drug, with potential for broad and chronic use ought to have a higher evidentiary bar. CMS has therefore reasonably determined based on the "reasonable and necessary" standard, that this bar has not been achieved by the AAA drugs, and therefore before access can be provided to Medicare beneficiaries, additional clinical evidence under the CED paradigm should be evaluated.

[131] *County of Los Angeles v. Shalala*, 192 F.3d 1005 (D.C. Cir. 1999).
[132] 5 U.S.C. § 706 (1946).
[133] Alzheimer's Disease Task Force, *supra* note 99.

Part IV - Congressional Legislative Actions and Policy Reforms to Address Underlying Issue

The unspoken underlying rationale for CMS to provide such a restrictive access for AAA drugs is the potential financial impact of the drugs on Medicare Part B given the large qualifying beneficiary population in Medicare and potential chronic use of these drugs. Although Medicare payment implications are outside the scope of an NCD, the approval of *Aducanumab* has highlighted the broader challenges Medicare faces in paying for high-cost biologics and specialty drugs.[134] With almost no policy and legislative tools to manage this issue, CMS has attempted to employ the only tool in its armamentarium to manage overall drug spending under the programs it manages by issuing an extraordinary and restrictive access position. Congressional legislative actions and policy reforms are needed that can manage the increase in drug spend while maintaining access to innovative lifesaving treatments for Medicare beneficiaries.

1. Allow HHS to Negotiate Drug Prices with Manufacturers

The U.S. is the only country in the 34-member Organization for Economic Co-operation (OECD) that lacks government regulation of prescription drug prices. All other high-income countries employ use of centralized drug price negotiations, coverage determination, and drug value to control drug prices and spending.[135] The HHS and CMS has few administrative tools to influence utilization management or product selection once Medicare approves coverage for a drug. While at the same time, Medicare is the largest payer for pharmaceuticals in the U.S. as measured by total spending. The CBO has estimated that the federal government could save $456 billion over

[134] Medicare Payment Advisory Commission, *supra* note 105.
[135] Daniel Hilary, *Stemming the Escalating Cost of Prescription Drugs: A Position Paper of the American College of Physicians* 165 Annals of Inter Med. 50-52 (2016).

10 years by establishing direct drug price negotiation with manufacturers on the costliest drugs.[136] Two bills have been introduced recently to address this issue.[137]

On April 22, 2021, the chairs of the Ways and Means and the Education and Labor committees reintroduced H.R. 3—the Elijah E. Cummings Lower Drug Costs Now Act.[138] Under current law, a provision known as the "noninterference" clause, stipulates that the HHS cannot interfere with the negotiations between drug manufacturers and pharmacies, may not require a particular formulary nor institute a price structure for the reimbursement of covered drugs.[139] H.R. 3 amends the non-interference clause and would establish a "Fair Price Negotiation Program," that would allow HHS to negotiate lower prices on many of the highest-priced drugs directly with pharmaceutical companies without generic or biosimilar competition. HHS would be required to negotiate a minimum of 25 drugs in 2024 and a minimum of 50 drugs in following years. If pharmaceutical companies refuse to negotiate, they would face civil and tax penalties.[140]

The Build Back Better Act (BBBA) introduced in the Congress and passed by the House of Representatives on November 19, 2021, would also amend the non-interference clause by adding an exception allowing the federal government to negotiate prices with drug companies for a small number of high-cost drugs covered under Medicare Part D and Part B.[141] The negotiation process would apply to a limited number of brand-name drugs or biologics that lack generic or biosimilar competition. These drugs would be selected from among the 50 drugs with the highest total

[136] Juliette Cubanski, Tricia Neuman Follow and Meredith Freed, *Explaining the Prescription Drug Provisions in the Build Back Better Act*, November 23, 2021, accessible at https://www.kff.org/medicare/issue-brief/explaining-the-prescription-drug-provisions-in-the-build-back-better-act/ (last accessed May 7, 2022).
[137] Juliette Cubanski, Tricia Neuman Follow and Meredith Freed, *What's the Latest on Medicare Drug Price Negotiations?*, July 23, 2021, accessible at https://www.kff.org/medicare/issue-brief/whats-the-latest-on-medicare-drug-price-negotiations/ (last accessed May 7, 2022).
[138] H.R.3 — 117th Congress (2021-2022).
[139] 42 U.S.C. § 1395w (1965).
[140] Cubanski, *supra* note 137.
[141] H.R.5376 — 117th Congress (2021-2022).

Medicare Part B and D spending. An excise tax would be levied on drug companies that do not comply with the negotiation process. CBO's estimates that prescription drug policies in the BBBA could provide savings of over $150 billion over ten years from Medicare drug price negotiations, inflation rebates, and commercial drug inflation rebates.[142]

2. Redefine Medicare Part B Incentives and Payment Methodology

CMS is constrained in how it pays for physician administered biologics and specialty drugs that fall under Medicare Part B. Essentially CMS is a "price taker" and in most cases pays 106 percent of the Average Sales Price (ASP) of a drug which is the average manufacturer sales price to all manufacturers in the US, inclusive of rebates and other discounts.[143] Under this "buy and bill" system, a provider first buys and stores covered drugs and then later bills Medicare after the drug has been administered to the patient. This reimbursement structure incentivizes providers to choose higher-priced drugs in two ways. First, providers typically make more revenue on higher-priced drugs because they are often able to negotiate rebates or discounts from manufacturers on these drugs, meaning they pay less for the drug than the average sales price they are reimbursed. Manufacturers are better able to offer large rebates or discounts on higher-priced drugs; generics don't usually pay rebates. Second, the percentage add-on ensures that choosing a higher-priced drug results in a larger add-on payment for the physician.[144] This is an unusual environment in which physicians are in the business of purchasing drugs, administering them, and earning a margin from CMS payments and patient out-of-pocket costs. There are few competitive forces to

[142] Cubanski *et. al*, *supra* note 137.
[143] Department of Health & Human Services, *Report to the White House Competition Council Comprehensive Plan for Addressing High Drug Prices*, September 9, 2021, accessible at https://aspe.hhs.gov/sites/default/files/2021-09/Drug_Pricing_Plan_9-9-2021.pdf (last accessed May 7, 2022).
[144] Department of Health & Human Services, *Medicare Part B Drugs: Pricing and Incentives*, March 8, 2016, accessible at https://aspe.hhs.gov/sites/default/files/migrated_legacy_files/142631/PartBDrug.pdf (last accessed May 7, 2022).

restrain spending for Part B drugs, in contrast to many drugs obtained from pharmacies and financed under Medicare Part D. Even when physicians have a choice among therapeutic alternatives for drugs they administer, under "buy and bill" there are no incentives to choose drugs that are more cost-effective and no tools, such as formularies, to do that. Administrative action by CMS to change the structure of Part B payments to providers and use the Part D pharmacy management approach would allow for better utilization and cost management for high prices biologics and specialty drugs.[145]

3. Pass Legislation to Limit Drug Price Increases

In 2017, Medicare spending for the top ten drugs paid under the ASP system totaled about $13.6 billion, about 43 percent of all Part B drug spending that year.[146] Notably, all the top ten of these products are biologics. The patterns of spending growth within the top ten products illustrate the two factors driving spending growth: new products with high launch prices and existing products with price inflation. In its June 2019 report, the Medicare Payment Advisory Committee found that Medicare Part B drug spending increases between 2009 and 2016 were partially attributable to "increased prices for existing products."[147] Price growth is the largest driver of Medicare Part B spending growth. Nearly two-thirds of the growth in Part B drug spending between 2009 and 2016 was accounted for by price growth, which reflects increased prices for existing products and shifts in the mix of drugs, including the launch of new high-cost drugs.[148] Part B drug spending is concentrated in a small number of expensive products. The HHS report "Comprehensive Plan for

[145] *Id.*
[146] Medicare Payment Advisory Commission, *Medicare payment strategies to improve price competition and value for Part B drugs*, June 2019, accessible at https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/reports/jun19_ch3_medpac_reporttocongress_sec.pdf (last accessed May 7, 2022).
[147] *Id.*
[148] *Id.*

Addressing High Drug Prices" issued in September 2021, called for legislation to permit HHS to negotiate drug prices and limit drug price increases to the rate of inflation.[149]

The federal government could do much more to discourage these drug price increases, such as imposing a penalty on drug companies that increase list prices faster than the inflation rate. This approach would deter drug manufacturers from pushing large price increases.[150] H.R. 3 would require pharmaceutical manufacturers to pay rebates for the amount they raised prices for covered drugs above the rate of inflation.[151] BBBA would require inflation rebates to limit annual increases in drug prices and require drug manufacturers to pay a rebate to the federal government if their prices for biologics covered under Medicare Part B increase faster than the rate of inflation.

4. Bring US Drug Prices in Line with OECD Countries

The United States spends more on prescription drugs on a per capita basis than other countries in the OECD, and drug prices are more than double (2.56 times as high) compared to other members of the OECD. The price gap between the U.S. and other nations is larger for some critical medications.[152]

In November 2020, CMS issued the Most Favored Nation (MFN) Model interim final rule (MFN Rule), to align drug prices in the U. S. with those available in economically similar countries.[153] This reimbursement model was promulgated as a CMS Innovation new payment model which

[149] Department of Health & Human Services, *supra* note 137.
[150] Anna Anderson-Cook, Kevin Love, Andrea Noda and Mark E. Miller, *How A Medicare Part D Inflation Penalty Would Lower Drug Spending for Patients, Taxpayers, And Employers*, February 5, 2020, accessible at https://www.healthaffairs.org/do/10.1377/forefront.20200204.864372/full/ (last accessed May 15, 2022).
[151] Center for American Progress, *H.R. 3 Could Save Patients Thousands of Dollars on Prescription Drugs*, July 20, 2021, accessible at https://www.americanprogress.org/article/h-r-3-save-patients-thousands-dollars-prescription-drugs/ (last accessed May 14, 2022).
[152] Andrew W. Mulcahy *et al.*, *International Prescription Drug Price Comparisons*, 2019, accessible at https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf (last accessed May 7, 2022).
[153] Most Favored Nation (MFN) Model, 85 Fed. Reg. 229, 76180 (Nov. 27, 2020).

permits CMS to test innovative payment models to reduce program expenditures while preserving or enhancing the quality of care furnished to government program beneficiaries.

The MFN Model if finally adopted, would have operated for seven years, from January 1, 2021, to December 31, 2027, and aligned payment for Medicare Part B drugs with international prices.[154] In the MFN Model, Medicare would have paid manufacturers price based on a blended formula based on ASP and the lowest GDP-adjusted price paid by an OECD member country. The MFN Price would have been phased-in gradually over a seven-year period, with the MFN Price model applied to 25 percent of the drug cost in years 1-4 (remainder 75 per cent remaining as ASP) and increasing to 100 percent by year 7. The MFN Model would have been a mandatory, nationwide model and would have focused on approximately 50 Medicare Part B drugs that encompass a high percentage of Medicare Part B drug spending. If the rule had taken effect on January 1, 2021, as contemplated, it would have dramatically reduced Medicare Part B drug reimbursement.

On 23 December 2020, Judge Catherine Blake of the U.S. District Court for the District of Maryland granted the Pharmaceutical Research and Manufacturers of America a 14-day nationwide temporary restraining order, preventing the CMS from implementing and enforcing the MFN Model.[155] On 28 December 2020, the U.S. District Court for the Northern District of California granted California Life Sciences Association a nationwide preliminary injunction, preventing CMS from implementing the MFN Model due to failure to follow notice and comment procedures under the APA.[156] The order vacated the MFN Rule in its entirety pending completion of the notice and comment process under the APA. On December 31, 2020, the U.S. District Court

[154] Centers for Medicare & Medicaid Services, *Most Favored Nation Model*, January 2021, accessible at https://innovation.cms.gov/innovation-models/most-favored-nation-model (last accessed May 7, 2022).
[155] *Id*.
[156] *Id*.

for the Southern District of New York issued a preliminary injunction in Regeneron Pharmaceuticals v. United States Department of Health and Human Services, barring CMS and HHS from applying the MFN Rule to Regeneron's drug EYLEA.[157]

These court actions essentially ended the MFN Model. On December 27, 2021, the CMS announced that it would rescind the MFN Model in a final rule published in the Federal Register.[158] CMS should continue to focus on pricing structures that bring US drug prices closer to comparable payments made by insurers in similarly situated OECD countries.

5. Encourage Adoption of Biosimilars

Some of the highest-priced drugs on the market today are biologics, and most of them have no competition to date. The Affordable Care Act legislation created the first abbreviated pathway in the U.S. for biosimilars.[159] Unlike generic small-molecule drugs, pharmacy-level biosimilar substitution is only permitted with the approval of a physician, or if the biosimilar has received approval from the FDA as interchangeable with the biologic, creating a barrier to more widespread use of biosimilars. Additionally, current reimbursement policy does not sufficiently encourage uptake of biosimilar products over biologics. When a small-molecule generic enters the market, uptake of the generic over the brand happens relatively quickly, and within five years, prices of generic oral medicines drop 80% from their pre-expiry brand prices.[160] However, for biologics, current Medicare reimbursement policies, rewards higher reimbursement for brand reference

[157] *Id*.
[158] *Id*.
[159] Anna Rose Welch, *How Kaiser Permanente Built A Biosimilar Empire — The Inside Story*, February 7, 2020, accessible at https://www.biosimilardevelopment.com/doc/how-kaiser-built-a-biosimilar-empire-the-inside-story-0001 (last accessed May 7, 2022).
[160] *Id*.

biologics than for the available biosimilar competitors, creating an incentive for physicians to continue to prescribe the higher-price product given the ASP payment model for Part B drugs.[161]

A number of policy decisions to incentivize biosimilar use is needed including: adjusting Medicare Part B reimbursement for biosimilars and originator biologic products to incentivize the use of the biosimilar over the originator biologic, creating a shared Medicare Part B reimbursement billing code for both a reference biologic and all corresponding biosimilars, preventing Medicare plans from requiring patients to fail first on the originator biologic before covering the biosimilar, requiring Medicare plans to add FDA-approved biosimilar drugs to their formularies as soon as the biosimilar comes on the U.S. market, making the interchangeable biosimilar the default product chosen first over the reference biologic for Medicare Part B patients starting a biologic regimen.[162]

In July 2018, FDA released the Biosimilars Action Plan (BAP), which applies many of the lessons learned from FDA's experience with generic small molecule drugs to facilitate biosimilar competition.[163] The BAP is based on four key strategies: improving the efficiency of the product development and approval process; maximizing scientific and regulatory clarity for the product development community; developing effective communications to improve understanding among interested parties; and supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay market entry to follow-on versions of biological products.[164] Recently the FDA announced the approval of the first interchangeable biosimilar product for a long-acting insulin. The FDA determined that Semglee (insulin glargine), a long-acting insulin analog, is biosimilar to, and interchangeable with, its reference product (Lantus). States may now

[161] Medicare Payment Advisory Commission, *supra* note 146.
[162] Department of Health & Human Services, *supra* note 144.
[163] U.S. Food & Drug Administration, *Biosimilars Action Plan*, July 2018, accessible at https://www.fda.gov/media/114574/download (last accessed May 14, 2022).
[164] *Id*.

permit a pharmacist to substitute an interchangeable product for the reference product without consulting the prescriber. This pharmacy-level substitution for the first biosimilar will result in further savings and should be further expanded along with other actions to encourage the uptake of biosimilars. Recently the FDA approved a biosimilar for Lucentis which is one of the top spending drugs by CMS in Part B.[165] The top selling Part B drug in 2019 was Eylea, which is also approach patent expiration and biosimilars will enter the market in 2024.[166] Biosimilars can lower spending on biologics between $38.4 billion and upto $124 billion from 2021 to 2025, assuming quicker biosimilar entry, greater biosimilar volume share, and more robust price competition.[167]

6. Improve FDA-CMS Communications

The coverage decision by CMS for AAA drugs underscores the importance of these two HHS agencies working very closely together and coordinating efforts. U.S. Reps. Diana DeGette (D-CO) and Fred Upton (R-MI) in November 2021 introduced the bipartisan Cures 2.0 legislation that addresses how the U.S. should conduct biomedical research going forward. Section 305 of the introduced bill titled "*Improving FDA-CMS Communication Regarding Transformative New Therapies*" proposes that upon designation of a product as a "breakthrough therapy", or a product eligible for "accelerated approval", there should be established an automatic communication requirement between FDA and CMS.[168] The FDA and CMS shall then maintain communications

[165] U.S. Food & Drug Administration, *FDA Approves First Biosimilar to Treat Macular Degeneration Disease and Other Eye Conditions*, September 17, 2021, accessible at https://www.fda.gov/news-events/press-announcements/fda-approves-first-biosimilar-treat-macular-degeneration-disease-and-other-eye-conditions (last accessed May 7, 2022).
[166] Juliette Cubanski and Tricia Neuman, *Relatively Few Drugs Account for a Large Share of Medicare Prescription Drug Spending*, April 19, 2021, accessible at https://www.kff.org/medicare/issue-brief/relatively-few-drugs-account-for-a-large-share-of-medicare-prescription-drug-spending/ (last accessed May 7, 2022).
[167] Andrew Mulcahy *et al*., *Projected US Savings From Biosimilars*, 2021-2025 28 Am J Manag Care. 7 (2022).
[168] Cures 2.0 Act.

with each other regarding approval and coverage decisions with respect to such product; and share information with each other to inform and coordinate such decisions.

Another more formalized way to improve the dialogue between the CMS and FDA is to further expand the use of the "Parallel Review" process. This program was announced jointly by the CMS and FDA in 2016 and allows manufacturers of new devices to interact with both agencies simultaneously during clinical development in order to reduce the time between FDA marketing approval and Medicare coverage of new technologies.[169] This program is intended to ensure prompt and efficient process to allow patient access to new technologies in the Medicare population. The "Parallel Review" program has shown that device manufacturers benefit from engaging both Agencies at the pivotal clinical trial design phase, and the feedback received from both Agencies at the pivotal clinical trial design stage can assist in designing pivotal trials that can answer both Agencies' evidentiary questions. For example, on August 11, 2014, FDA approved a medical device that was part of the Parallel Review program, and only three months later CMS published a favorable final NCD.[170] The Parallel Review program gives stakeholders an opportunity to collaborate early in the process which can be critical to achieve alignment. Manufacturers who design and conduct the clinical trials benefit from early feedback from the FDA and CMS as they develop their plans to conduct clinical investigations to gather valuable clinical evidence. Such an approach has many advantages in addition to timelier access, and lower costs.[171] CMS Deputy Administrator, Dr. Meena Seshamani added that, "[t]hrough parallel review and collaboration, we speed access to innovative diagnostics, so that doctors are better able to

[169] Program for Parallel Review of Medical Devices, 81 Fed. Reg. 205, 73113 (Oct. 24, 2016).
[170] *Id*.
[171] Foley Hoag LLP, *CMS/FDA Parallel Review and Alternative Coverage Pathways*, November 2, 2018, accessible at https://www.pennmedicine.org/cancer/-/media/event%20media/2018/cancer/11%20november/intraoperative%20molecular%20imaging%20for%20cancer%20surgery/schulwolf_cms_fda_parallel_updated.ashx?la=en (last accessed May 7, 2022).

deliver the best quality care to their patients and patients have access to these state-of-the-art tests."[172] A meta-analysis of this parallel review process found that this approach was not very widely used by manufacturers, and only two devices are known to have gone through parallel review process.[173] However, the FDA and CMS Parallel Review remains in effect and is viewed positively by both FDA and CMS officials and reviewers.

Given the increase in the number of expensive to develop biologics and specialty drugs in the FDA review process that could have impact on CMS, it is important to reinvigorate this formal parallel review process and more importantly expand its availability to drugs and encourage a three-way interaction between manufacturer, FDA and CMS as early as possible. This will streamline the process, increase transparency, manage costs and shorten the time between FDA approval and access to new drugs for Medicare beneficiaries.

7. Legislation to Constraint Drugs Approved via the Accelerated Approval Pathway

The FDA approval of *Aducanumab* under the "accelerated approval" pathway based on a surrogate biomarker was one of the rationale cited by CMS to limit coverage by CED with RCT. Recent legislation introduced attempts to put some limitations on drugs marketed under the FDA's accelerated approval pathway. The House Energy and Commerce Committee's Democratic chairman, Frank Pallone, Jr. (D-NJ) and Republican ranking member, Cathy McMorris Rodgers (R-WA) have proposed competing bills in the Health Subcommittee's legislative hearing on March 17, 2022. The Accelerated Approval Integrity Act of 2022[174] introduced by the Democrats significantly enhances FDA's ability to ensure that drugs receiving accelerated approval are

[172] *Id*.
[173] Marta Podemska-Mikluch, *FDA-CMS Parallel Review: A Failed Attempt at Spurring Innovation*, September 2016, accessible at https://www.mercatus.org/system/files/podemska-mikluch-fda-cms-parallel-review-v1.pdf (last accessed May 7, 2022).
[174] H.R.6963 — 117th Congress (2021-2022).

providing a clinical benefit by way of new expedited procedures to remove drugs if such benefit is not demonstrated through post-approval studies. The bill would impose a five-year limit for drugs to stay on the market without confirming clinical benefit. The FDA could withdraw a drug if the sponsor fails to conduct post-approval testing, or if the sponsor fails to achieve agreed upon study targets or fails to confirm clinical benefit. If enacted, the legislation would also require that prior to FDA granting accelerated approval, manufacturers enter into an agreement with FDA explaining how post-approval studies will be conducted and require manufacturers to provide the FDA quarterly updates on post-approval studies. The bill would also make it easier for FDA to take drugs off the market if they don't show benefit.[175]

The Accelerating Access for Patients Act of 2022[176] introduced by the Republicans would grant the FDA the authority to use "expedited procedures" to withdraw a grant of accelerated approval for products that are not demonstrating clinical benefit to patients. The bill would require FDA to establish procedures regarding the requirement that drug sponsors develop a plan detailing how they will comply with accelerated approval requirements, and grant FDA the authority to use expedited procedures to withdraw accelerated approval status if post-approval testing requirements are not satisfied. While the expedited review process for new biologics and specialty drugs and approved via the "accelerated approval" program by the FDA is an important driver of innovation, legislation that puts additional levels of FDA controls on such drugs once they are in the market is an important step in the right direction. This will also ensure that there are guardrails in place for access as well, and CMS can rely on such FDA imposed guardrails on these drugs and would avoid the CMS adding duplicative clinical trial requirements on sponsors.

[175] *Id*.
[176] H.R.6996 — 117th Congress (2021-2022).

CONCLUSION

The recent NCD process for anti-amyloid antibody drugs strongly suggests the need for the FDA, CMS, Congress and other stakeholders to collectively and proactively look for solutions to counter the ever-increasing costs of prescription drug spending especially within the Medicare population while at the same time ensue that life-saving treatments are available to Medicare beneficiaries in a timely manner. *Aducanumab* was approved by the FDA in June 2021, and it was not until April 2022, more than ten months later when patients, physicians, families and all patient stakeholders were able to obtain clarity on the level of access for an FDA approved drug. This experience highlights the importance of coupling scientific and regulatory innovation with innovative coverage and payment policies. While both the FDA and CMS are aligned that new life-saving drugs should reach Medicare patients as soon as possible, the friction between the two agencies would have been far more subdued if the drugs was more affordable to Medicare. It is time to move from finger-pointing to collaborating and implementing real legislative reform and implement policy actions to ensure that the system works better in the future for patients, payers, drug developers, physicians and all parties involved.