AmerisourceBergen
Xcenda

Accelerated approval not accelerated access

Clinical trials required for coverage of Alzheimer's treatments

With the Alzheimer's disease drug market expected to increase over the next few years, a dynamic interplay between market and policy has emerged.

This began with the Food and Drug Administration (FDA) approval of Biogen's treatment ADUHELM (aducanumab) under the accelerated approval pathway, finding enough evidence that the drug reduces amyloid beta plaque for the treatment of Alzheimer's disease.[1] The decision was controversial as the FDA's scientific advisory committee recommended against it, challenging the clinical benefit of the treatment. Nonetheless, ADUHELM is the first new therapy approved for Alzheimer's in nearly 20 years, and the first targeting amyloid beta.

Since FDA approval:

- **June 2021:** ADUHELM entered the market at $56,000 per year, with each infusion costing $4,300.
- **November 2021:** The Centers for Medicare & Medicaid Services (CMS) announced a nearly 15% increase in monthly Part B beneficiary premiums for 2022,[2] the largest ever year-over-year increase, based partially on the uncertainty around the cost of ADUHELM. Estimates found Medicare spending of ADUHELM could range from $7 billion to $37.4 billion annually, a severe impact on the Medicare budget.[3]
- **December 2021:** The yearly cost of ADUHELM was reduced to $28,200.[4]
- **January 2022:** In an unprecedented move, Health and Human Services (HHS) Secretary Xavier Becerra instructed CMS to reconsider the 2022 premium increase, citing the price drop of ADUHELM.[5] Several members of Congress have also asked CMS to reconsider the premium increase.[6,7]
- **February 2022:** Uptake has fallen far short of expectations with around $1 million in total revenue reported since launch.[8]

The National Coverage Determination

Scrutiny of the FDA's decision, the product's price point, and the fact that this is for Alzheimer's, a disease that impacts more than 6 million Medicare beneficiaries, has led CMS to open a National Coverage Determination (NCD) analysis. CMS often reserves NCDs for controversial treatments expected to have a large financial impact.

On January 11, CMS proposed to cover ADUHELM and other monoclonal antibodies directed against amyloid plaque for the treatment of Alzheimer's through Coverage with Evidence Development (CED).[9] CED is a standard in which Medicare covers a treatment (or service) on the condition the treatment is furnished in an approved clinical study, to test whether the treatment meaningfully improves health outcomes of the enrolled beneficiaries.

- It is not often an NCD with CED is used for a drug, and even less common for a class of drugs.[10]
- **The proposed coverage policy is expected to apply to all therapeutics in this class, including Alzheimer's medications in development that have not yet been approved**

Accordingly, patient participation in a qualifying randomized clinical trial would be the ONLY pathway to Medicare coverage for this ENTIRE class of Alzheimer's treatments—including future treatments.

To be considered an approved clinical trial under the CED:

- The treatment must be furnished in a CMS-approved randomized controlled trial, **or**
- Furnished in trials supported by the National Institutes of Health (NIH); **and**
- The trial must be conducted in a hospital-based outpatient setting.

The CED limits Medicare beneficiaries eligible for trial enrollment to:

- Patients who have evidence of amyloid plaques; **and**
- Persons with mild cognitive impairment due to Alzheimer's or mild Alzheimer's dementia.

To identify patients who may benefit from therapies targeting amyloid plaque, CMS is proposing to cover 1 beta amyloid positron emission tomography (PET) scan per patient if the patient did not previously receive a beta amyloid PET scan.

Why it matters

Following are potential access challenges from the proposed NCD with CED:

1. Alzheimer's patients who do not live near a hospital outpatient center will encounter a barrier to clinical trial enrollment. This could have a severe impact on underserved, rural populations.
2. Other approved drugs in this class will presumably have their own label, clinical trial design, and clinical results, yet would be blocked from Medicare coverage from the start.
3. With the coverage uncertainty, the CED may impact product development from investment to clinical trial design.
4. Select patients will receive a placebo in the randomized controlled trials.
5. While well-intentioned, a benchmark for diversity in clinical trials may inadvertently restrict patient access.

Generally, an NCD with CED is intended as a middle ground between nationwide coverage and restriction of coverage, but in reality, an NCD with CED is closer to a rejection of coverage.

Next steps

It is common for a CMS coverage decision to change before becoming final, but to what extent is unclear. Stakeholders are looking to a 2019 decision by CMS to remove a CED requirement from the final coverage determination for chimeric antigen receptor T-cell (CAR-T) therapies.[11] Comments to the proposed NCD are due to CMS by **February 10**. CMS will announce its final coverage decision by **April 11, 2022**.

If you are working on an equally complex product within a sensitive policy environment, or have any questions about the impact of this NCD with CED on your next launch, please contact **Daniel Fellenbaum**.

References

1. Dunn B. Accelerated approval of aducanumab NDA for Alzheimer's disease. FDA.gov. 2021. https://www.fda.gov/media/149903/download
2. 2022 Medicare Parts A & B premiums and deductibles/2022 Medicare Part D income-related monthly adjustment amounts. CMS.gov. 2021. https://www.cms.gov/newsroom/fact-sheets/2022-medicare-parts-b-premiums-and-deductibles2022-medicare-part-d-income-related-monthly-adjustment
3. Mafi JN, et al. Estimated annual spending on aducanumab in the US Medicare program. JAMA Health Forum. 2022. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2788098
4. Biogen announces reduced price for ADUHELM® to improve access for patients with early Alzheimer's disease. Biogen. 2021. https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelmr-improve-access-patients
5. HHS Secretary Xavier Becerra instructs CMS to reassess recommendation for 2022 Medicare Part B premium. HHS.gov. 2022. https://www.hhs.gov/about/news/2022/01/10/hhs-secretary-xavier-becerra-instructs-cms-reassess-recommendation-2022-medicare-part-b-premium.html
6. Letter to Sec. Becerra on Medicare Part B premium reconsideration. 2022. https://courtney.house.gov/sites/courtney.house.gov/files/1.1922%20Letter%20to%20Sec.%20Becerra%20on%20Medicare%20Part%20B%20premium%20reconsideration.pdf
7. Senator Sanders comments on proposed NCD for Aduhelm. 2022. https://www.sanders.senate.gov/wp-content/uploads/Senator-Sanders-comments-on-proposed-NCD-for-Aduhelm-1-25-22.pdf
8. Biogen. Fourth quarter. 2021: financial results and business updates. 2021. https://investors.biogen.com/static-files/e4a90dde-5b3a-4167-887b-96267a6550f1
9. Monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease. CMS.gov. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=305
10. Coverage with evidence development. CMS.gov. 2021. https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development
11. Chimeric antigen receptor (CAR) T-cell therapy for cancers. CMS.gov. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=291

AmerisourceBergen
Xcenda