Aduhelm: Noncoverage Unless Clinical Trial Enrollee

CED Very Restrictive, Agency Has Health Equity Concerns, Neg for mAbs

- **CMS's recommendation narrows Medicare coverage only for Aduhelm (BIIB) clinical trial participants, a worst-case outcome.** Today's Coverage with Evidence Decision (CED) (here) means BIIB must submit more robust data that includes Black and Hispanic clinical trial participants to maintain Medicare coverage. Specifically, BIIB must conduct CMS approved randomized controlled trials that are conducted in a hospital based outpatient setting, and that are supported by the NIH. CMS recommends coverage for one beta amyloid positron emission tomography (PET) scan if a patient requires it for trial participation, but only if they haven't already had one.

- **BIIB's 50% price cut may have swayed CMS's CED**. Becerra will ask CMS to lower the Part B premium given the price hike was 50% due to Aduhelm. The drug was originally priced at $56K per year. BIIB announced a priced reduction to $28K per year at the end of December 2021. While BIIB states their initial price was based on real world evidence, the company acknowledges virtually no one agreed with the price. Their decision to slash the price may have moved the needle on their "second chance" from CMS.

- **The CMS proposed CED covers an entire class of drugs, not only Aduhelm (BIIB, LLY).** CMS's CED covers all antiamyloid-beta monoclonal antibodies (antiamyloid mAbs), laboratory-made proteins designed to act as binders that activate the body's immune system. Scientists design mAbs as treatments for clearing amyloid plaque accumulation in Alzheimer's patients. Aduhelm is the first and only antiamyloid mAb with FDA approval. This CED is a positive for companies with Alzheimer's treatments leveraging mAbs in the pipeline (see below for details on LLY's donanemab)

- **FDA has given BIIB a 2030 deadline to submit confirmatory trial data.** We think that the data will come in a lot sooner. BIIB will initiate further trials in May 2022, and aims to submit data by 2026. Recall both FDA and BIIB came under fire for the controversial approval for the exorbitantly priced treatment amid a series of questions BIIB's insufficient clinical trial design and Aduhelm's actual safety and efficacy. The drug was granted accelerated approval by FDA, as it was deemed to be a product addressing unmet need, where benefit outweighs risk. See here for full details of the BLA accelerated approval.

- **Health equity concerns: CMS lays out specific criteria mandating inclusion of underrepresented populations in subsequent trials.** According to the Alzheimer's Association, Alzheimer's and other dementias cost the US ~$355 B in 2021, disproportionately impacting Asian American, Black, Hispanic and Native American populations, Full report is here. Specially, CMS requires BIIB include patients with Alzheimer's and amyloid plaques in their study. Patients not meeting this criteria will not be covered. Furthermore, BIIB must submit statistically significant data proving improved cognition in trial participants and a detailed record of any adverse effects. If BIIB's post trial data does not show efficacy in these populations, he FDA has the authority to remove Aduhelm from the market.

- **NEXT UP: A final CMS coverage determination comes in April.** BIIB stated it anticipates H1 2022 accelerated approval for its anti-amyloid product Lecanemab under Breakthrough Designation, but it could face pushback similar to Aduhelm's.We note that LLY and other competitors may surpass BIIB as the company struggles to maintain its position as a leader in Alzheimer's care. Notably LLY has set up a head to head trial comparing its donanemab with BIIB's Aduhelm to test both drugs' abilities to clear amyloid plaques and improve cognition in Alzheimer's patients. Data to date shows LLY's donanemab outperforms Aduhelm. FDA has already granted donanemab Breakthrough Therapy designation, paving the way for timely approval once the company submits comprehensive clinical trial data. LLY may learn from BIIB's hubris and price donanemab more reasonably, sparing itself regulatory headaches.

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Background

- **CMS's decision mandates BIIB share data proving efficacy in under-represented populations.** According to the Alzheimer's Association, Alzheimer's and other dementias cost the US ~$355 B in 2021, disproportionately impacting Asian American, Black, Hispanic and Native American populations, Full report is here. If BIIB's post trial data does not show efficacy in these populations. the FDA has the authority to remove Aduhelm from the market.

- **Aduhelm's approval undermined confidence in FDA's integrity.** In November 2020, FDA statisticians called out BIIB and other FDA officials involved in Aduhelm's approval process for greenlighting the drug's approval based on inconclusive clinical trial results. Specifically, FDA statistician Tristan Massie cited the trials in questions for showing a "lack of substantial evidence, no replication, highly conflicting results in two studies, conflicting subgroup results." See presentation here, slide 3.

- **CMS designed the CED mechanism to expedite access to innovative technologies. BIIB must prove Aduhelm's efficacy in subsequent trials?** An ICER clinical review found that dosing did not impact the results in BIIB's trials, despite the company's claims. BIIB based its efficacy statement on extrapolating dosing from an earlier trial into a later trial. Susan Kremen (Cedars Sinai, and notably a PI for one of Aduhelm's trials) stated that the drug's approval was based on an amyloid pathology, a clinical biomarker that is NOT an indication of efficacy in preventing Alzheimer's.

- **Becerra advised CMS to reconsider increases to Medicare Part B premiums and deductibles since BIIB slashed Aduhelm's price in half.** Becerra issued a statement yesterday stating that BIIB's 50% price cut warranted a reconsideration of its increases to Part B premiums (+ $21.60 monthly) and deductibles ($30 annually) to cover possible costs to the Medicare system posed by Aduhelm. Note ~50% of the $21.60 monthly premium increase is allocated to the Supplementary Medical Insurance Trust Fund (SMI) for contingencies covering Aduhelm and other Alzheimer's treatments. 80% of patients eligible for Aduhelm will be Medicare beneficiaries. Recent reports show Aduhelm alone could double Part B annual drug spend.

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