Evaluate Vantage

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It’s official: expect near-zero Aduhelm sales for the foreseeable future

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Aduhelm’s status as a commercial nonentity is confirmed, but what does the final coverage decision mean for follow-on amyloid-beta MAbs?

Any glimmer of hope Biogen might have had to reverse the fortunes of Aduhelm, at least in the near term, has been extinguished. The US Centers for Medicare & Medicaid Services (CMS) yesterday upheld the tough proposed restrictions on reimbursing the controversial Alzheimer’s drug that it had laid out in January.

As *Vantage Analysis* had argued at the time, the CMS’s draft national coverage determination was so severe that the agency had left itself very little room to loosen its proposed stance. The bigger question now is what US reimbursement could look like for gantenerumab, lecanemab and the like, as the final document makes it clear that it will apply to these too.

The final determination remains, as in the draft, coverage with evidence development; it applies to all MAbs targeting amyloid-beta for treating Alzheimer’s, meaning not only those with accelerated approval, like Aduhelm, but also any that receive a traditional full green light from the FDA.

In the near term this will affect Biogen/Eisai’s lecanemab, Roche’s gantenerumab and Lilly’s donanemab, each of which is in a phase 3 study designed to demonstrate a benefit on a cognition endpoint. The first two read out in the second half of this year, while the last is expected to yield data in mid-2023.

For Aduhelm itself Biogen expects to begin patient screening next month for a confirmatory trial, Envision. Donanemab is additionally expected to yield data this year from a biomarker study comparing it against Aduhelm, but this will at best provide a means of handicapping its chances rather than backing approval per se.

Any positives?

For Biogen the only positive takeaway is that the CMS, in its requirement that Medicare cover Aduhelm only when given as part of approved clinical trials, relaxed its stance and said these could be carried out beyond the hospital-based outpatient setting stipulated in the draft. In reality this probably makes little difference.

The harshness of the wording confirms the CMS’s coverage determination as a slap on the FDA’s wrists for approving Aduhelm on the basis of flimsy data. The Baird analyst Brian Skorney, long a critic of Aduhelm, tweeted: “Right decision by the wrong agency.”

> Right decision by the wrong agency. https://t.co/x67GGhBblq
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> — Brian Skorney (@BrianSkorney) April 7, 2022

Notably, the CMS states that its coverage determination relates also to amyloid-beta drugs that secure full approval backed by a cognition benefit. These will similarly be subject to the restrictive “coverage with evidence development” requirement.

One concession versus drugs under accelerated approved is that coverage will not be restricted to the clinical trial setting, but would also encompass a patient registry. “Registry data may be used to assess whether outcomes seen in carefully controlled clinical trials are reproduced in the real world and in a broader range of patients,” the CMS says.

In a statement Biogen bemoaned an “unprecedented CMS decision” that it said could “limit coverage for any future approved treatment in the class. These coverage restrictions, including the distinction between accelerated approval and traditional approval, have never been applied to FDA-approved medicines for other disease areas.”

Stifel analysts said the proposed restrictions for fully approved drugs represented a literal reading of the guidance. Instead, they suggested that the CMS was just creating a “bar” for hard clinical outcomes, writing: “We still think if an amyloid drug clearly succeeds CMS would not be in a realistic position to deny coverage.”

Either way, those follow-on drugs still have something to play for. The same cannot be said for Aduhelm, which sold a grand total of $3m in the more than six months that followed its US approval last June.

Evaluate Pharma data suggest that sellside consensus taken before the CMS’s draft decision saw Aduhelm revenues breaching $4bn in 2026. The actual figure now looks set to be rather closer to 2021’s full-year number.