Evaluate Vantage

June 12, 2023

Leqembi heads towards full approval

Madeleine Armstrong

Big questions now include details about a US registry and its impact on initial sales.

After a unanimous adcom vote on Friday, Eisai and Biogen's anti-amyloid MAb Leqembi looks set to have its accelerated Alzheimer's nod converted into full approval. The debate now moves on to two big outstanding issues: how the FDA will approach certain patients at high risk of the brain-swelling side effect Aria, and lingering questions around payment.

On the latter point, the Centers for Medicare & Medicaid Services has already said thatMedicare will cover Leqembi on full approval – but also that patients will need to have mild cognitive impairment or early Alzheimer's, and then be followed in a registry. How this will work in practice remains shrouded in mystery.

Eisai itself could not shed any light on the matter, Alex Scott, the group's executive vice-president of integrity, told *Evaluate Vantage* before the adcom. "We don't have details. Registry is a loose term."

The situation should become clearer if and when Leqembi gets full approval, when the CMS will implement its new approach; the drug's Pdufa date is 6 July. "We would expect that it could not be that complex if something's going to be stood up that quickly," Scott added.

At the time of the CMS announcement, Stifel analysts noted that the registry represented "another, even if small, hurdle to the early days of the [Leqembi] launch", but that it should not stop anti-amyloid MAbs from becoming blockbusters eventually.

Sellside consensus compiled by *Evaluate Pharma* puts Leqembi's 2028 sales at around $4.5bn, but the early launch is expected to be slow. Currently Leqembi, like Biogen's Aduhelm before it, is only reimbursed in clinical trial settings.

This is despite Eisai seemingly learning from Biogen's mistakes with Aduhelm; on accelerated approval in January the former priced Leqembi at half Aduhelm's initial cost.

"As a Japanese-origin company, pricing is part of the whole social responsibility interaction between companies and society," Scott said. "We certainly learned: hey, we should be very clear about this. And we were, I think, more public than most companies have been as to their rationale for pricing."

He added that, when discounts were taken into account, Leqembi's actual price fell within the $8,500-20,500 per year range suggested by the US pricing watchdog Icer.

Aria concerns

Assuming that the registry is not too onerous, another potential issue is whether Leqembi might be contraindicated in certain patients, or whether the FDA might tighten monitoring requirements. Under the current label patients receive regular MRIs to check for Aria, the brain swelling that has been seen with anti-amyloid antibodies.

The panel discussion centred around three populations thought to be at particular risk of Aria: ApoE4 homozygotes, patients with cerebral amyloid angiopathy, and those receiving concomitant anticoagulants. Although a few panellists argued for restricting use, sellside analysts agreed that this was ultimately unlikely. And, on monitoring, Stifel wrote that the frequency of MRIs did not seem set to change.

There could be a stronger argument for genetic testing for ApoE4 status, however, which if implemented would put up practical barriers.