CAPITOL STREET

July 5, 2023

Leqembi FDA Approval: Slow Uptake To Follow

Clinical Protocols & CMS Coverage with New Registry

Relevant Companies

Our Take & Next Up

Assuming traditional FDA approval by the end of the week Leqembi (Eisai/Biogen) uptake will be slow as neurology clinics and academic medical centers establish internal patient selection & treatment protocols, while learning to manage a new national registry required for Medicare coverage. While the FDA is not required to follow committee recommendations, we expect Leqembi to receive full approval by its PDUFA date of July 6.

Leqembi treatments are expected to start within weeks in patients with MCI and mild AD and will be administered every two weeks via intravenous infusion ($26,500 annual cost). Neurologists will administer treatment and eventually clinics, geriatric and family health centers, as well as traditional physician offices will have the ability to provide Leqembi with necessary clinical follow-up.

Due to Leqembi's CMS registry requirements for all mAbs, along with launch dynamics, patient selection & follow-up, it will take weeks-then-months before the drug becomes more widely disseminated. We explore the next steps for Alzheimer's approvals, including the tau hypothesis, below.

Key Points

FDA

On June 9, FDA's Peripheral and Central Drugs Advisory Committee voted 6-0 that a Phase 3 study of Leqembi confirmed its clinical benefit for those with early-stage Alzheimer's disease and recommended full FDA approval of the drug. Link to meeting details here. We expect full FDA approval to occur by July 6th, the given PDUFA date, and CMS coverage to be available upon traditional approval.

Phase 3 data for the 1800-patient study of Leqembi used "clear and robust" evidence to demonstrate statistical significance and clinically meaningful endpoints. This is in contrast to the more divided nature of Aduhelm (BIIB) data that resulted in FDA approval but limited CMS coverage/uptake. The results of the trial indicate a 27% slowed rate of cognitive decline over an 18-month period, a percentage that the committee believes is meaningful to AD patients and caregivers. Concerns raised by the committee: study inclusion, drug efficacy, potential drug side effects. They may be addressed through label restrictions and pre-screening requirements.

Label restrictions and/or testing recommendations are likely to mitigate safety concerns. Despite confirming clinical benefit on June 9, Ad comm advisors voiced concerns related to the safety of the drug class. Side effects include amyloid-related imaging abnormalities (ARIA) which can be detected by PET imaging and adverse events like cerebral hemorrhaging. There is an increased risk of adverse effects for patients who are genetically apolipoprotein (ApoE) ε4 homozygotes, patients on anticoagulants, and patients with cerebral amyloid angiopathy (CAA). Testing for ApoE ε4 genotype is not a current standard practice, and the drug label may be stricter on testing due to the higher risk for ApoE ε4 homozygotes. The final label will also likely recommend closer monitoring for patients on anticoagulants and restrict access for patients with CAA-related inflammation.

PRICING & COVERAGE

The estimated wholesale acquisition cost (WAC) for Leqembi is $26,500 per year. ICER calculated the health-benefit price benchmark for Leqembi to be between $8,900 and $21,500. Due to the unmet need in AD, as well as the uncertain risks and limited benefits of the drug, ICER determined that the co has exceeded the health-benefit price benchmark. The treatment will only be available to those who undergo the complex diagnosis process (including amyloid PET scans, lumbar puncture) and those who are available to see specialists for MRI imaging and the bi-weekly infusions. Eisai/BIIB have encountered some pushback on the drug's pricing, particularly from Sen. Bernie Sanders (I-VT) who asked HHS to use the full extent of their authority (including March-in rights) to address the pricing of Leqembi in June.

Medicare coverage is expected to be more accessible upon FDA approval as CMS has indicated. On June 22, CMS reaffirmed its intentions to provide Part B coverage for monoclonal antibodies (mAbs) in treating Alzheimer's disease, under the requirement of a patient registry for data collection purposes. CMS's new coverage framework is much broader than the prior Coverage with Evidence Development (CED), but the data requirements remain in place. The new registries will be submitted through a CMS-facilitated portal that will be launched after FDA traditional approval. The "easy-to-use" format of the portal will enable clinicians to submit their data collected from routine patient assessments and follow-ups directly to CMS. Information required includes clinician demographics, patient demographics, and patient clinical information i.e. clinical diagnosis, anticoagulation/antiplatelet drug history, results of PET scans, CSF tests, and amyloid tests, evidence of ARIA-E, and overall cognitive function results.

A national registry can be burdensome, especially to smaller providers in rural areas, but could be modified / removed over time. CMS is trying to make the registry platform as accessible as possible and will require no additional fees. CMS is also expected to cover PET Aβ scans under specific patient requirements. We expect slower uptake in 2023, but we expect to improve as CMS works through registry implementation and potentially the eventual removal of the registry requirements in the future.

The U.S. Veterans Health Administration will provide full coverage for Leqembi under certain criteria, commercial coverage will likely follow suit. The VHA announced the intention to provide all necessary coverage for Leqembi assuming the patient follows the criteria of both the FDA label and the VHA exclusion list. Commercial insurance companies have not provided statements on intention to cover the cost of Leqembi or any added costs for pre-screening requirements. Due to potential mistrust after Aduhelm's failed experiment, insurance companies are relying on the FDA to make a confident and well-informed decision on Leqembi. We expect companies to determine coverage policy soon after the FDA final decision.

NEXT UP: MAB & TAU

Eli Lilly's donanemab (mAb) is expected to be considered for traditional approval in Q3. In January 2023, the FDA denied accelerated approval of donanemab, requiring that the Phase three TRAILBLAZER-ALZ trial 2 of the drug include at least 100 patients receiving treatment for 12 months. In trial 2, Lilly reported that all primary and secondary endpoints have been meant with statistical significance and clinical benefits. Patients on donanemab experienced a 35% slowing of disease progression. LLY is anticipating reconvening with the FDA this quarter. In the case that the FDA grants traditional approval to donanemab, we expect the same coverage requirements as Leqembi to be provided.

Pending AD treatments are not curative per se but rather therapies to slow disease progression. Research for AD is far from over but innovation such as Leqembi and donanemab are promising for the future of Alzheimer's treatment. Both are monoclonal antibodies that target and breakdown beta-amyloid proteins in the brain. In a patient with AD, these proteins accumulate into plaques surrounding nerve cells, inhibiting the cell's ability to communicate and eventually slowing all brain function.

Tau – the next frontier? Unfortunately, beta-amyloid protein is just one piece of the puzzle. Another major contributor to the rise of dementia and AD is the tau protein. Like beta-amyloid, tau proteins are natural and necessary to all functioning brains. In AD patients, these proteins begin to overproduce and form "tau-tangles" that block the communication between the synapses and receptors on a neuron. Some researchers believe that these proteins have a bigger role in Alzheimer's Disease development, however, they are much more difficult to target in treatment. Tau protein treatments are in earlier stages of development. Companies exploring tau protein treatments include ABBV/VYTauRX, TAK, RHHBY, JNJ, and LLY.

Ipsita Smolinski
Managing Director | Capitol Street

ipsita@capitol-street.com

900 19th Street, NW 6th Fl
Washington DC 20006

202.250.3741

www.capitol-street.com