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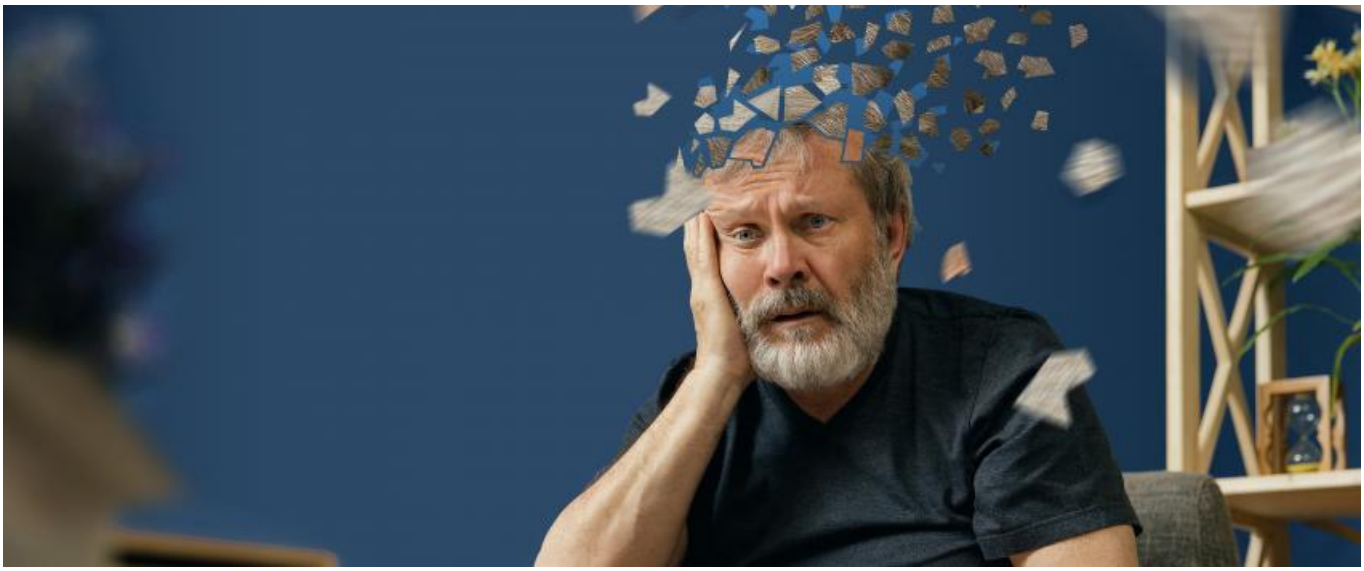
Narrowed label for Biogen’s Aduhelm lays bare FDA’s fail

Amy Brown



In an unprecedented situation Biogen sought to restrict the use of Aduhelm weeks after the drug’s approval. And the FDA said yes.

A few weeks after Aduhelm’s controversial approval Biogen released a statement that read like an argument for a narrower label. That discussion was apparently already happening behind the scenes: the FDA has today authorised a new label that effectively restricts the Alzheimer’s drug to early-stage patients.

The fact that the FDA capitulated so swiftly to widespread criticism of the drug's green light shows just how badly this situation was handled. And, while it was Biogen that filed an sBLA seeking to restrict use, it is not immediately clear which party first pushed for the change and it seems clear that both were amenable.

That Biogen, Aduhelm's biggest proponent, felt it needed clear limits on the drug’s use makes the situation even more astounding. Not that the company is covered in glory. Many consider the $56k price tag for a product backed by scant evidence of effectiveness to be abhorrent, particularly as the US taxpayer will be picking up most of the bill.

By initially granting such a broad label, the FDA was seen as facilitating this excess. And while the row-back will go some way towards appeasing critics, in reality payers had already looked likely to restrict the drug to the sort of patients enrolled in Aduhelm’s pivotal programme. These had mild cognitive impairment or mild dementia, the population the new label specifies for treatment initiation.

Originally the label stated that Aduhelm was approved “for the treatment of Alzheimer’s disease”. This raised concerns about huge demand from more advanced patients, in whom Aduhelm and other beta-amyloid antibodies have failed to show any benefit.

Floodgates open

The FDA has also been maligned for its use of the accelerated approval pathway to get Aduhelm on the market. This saw the MAb approved on the surrogate endpoint of beta-amyloid reduction – with the flimsiness of the evidence supporting dementia and functional endpoints dismissed.

With the bar for approval dramatically lowered, developers with similarly acting projects are already preparing submissions. Lilly has said that it will file donanemab later this year, and Roche is also thought to be considering seeking approval for gantenerumab.

The Swiss pharma giant has not officially confirmed this, despite the prospect being raised by several sellside analysts. Umer Raffat from Evercore ISI said in a recent podcast that Roche was telling investors that gantenerumab would be filed “as soon as possible”.

The company expects data from two ongoing phase 3 trials in the second half of next year, setting up an approval submission in 2023. But Mr Raffat believes that a biomarker study with a high dose could be enough to bring filing forward to this year, which could allow approval in the second half of 2022.

Whatever timelines emerge from Lilly, Roche or other Alzheimer’s developers, the FDA has made it perfectly clear it is amenable to granting early access to beta-amyloid therapies, despite the widespread criticism elicited, much of it from the medical profession.

The longer-term implications of this unprecedented situation are also worth considering. While it could be argued that Aduhelm’s approval confirms that the FDA is in an indulgent phase, it could trigger a change in stance.

The identity of the new FDA commissioner remains unknown. But whoever gets the job is surely going to be determined that such overt condemnation of the agency never happens again. Could the Aduhelm debacle come to mark the beginning of the end of the era of FDA leniency?