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Alzheimer's: yet another unwelcome drug

A drug that is effective in Alzheimer's disease? There can be no doubt that such a drug would be more than welcome for a large number of patients, their families and friends, and healthcare professionals. And yet, the announcement by the US Food and Drug Administration (FDA) that marketing authorisation (MA) had been granted for what it called *"the first therapy to target and affect the underlying disease process of Alzheimer's"* has been met with much criticism (1).

No clinical proof. The story of *aducanumab* (Aduhelm°) is relatively recent, but highly eventful. After failing to demonstrate efficacy in terms of disease progression, the company discontinued the two initial phase 3 clinical trials (2). However, it then reanalysed the data and submitted a request for MA to the FDA, based primarily on a reduction in amyloid plaques (2-4).

In 2020, the FDA's advisory committee for nervous system diseases issued a nearly unanimous negative opinion regarding this request. Yet the FDA nevertheless granted an accelerated MA for all patients, supported by the reduction in amyloid plaques, a non-clinical endpoint which has not been shown to be linked to disease progression in numerous studies (1,3,4). In addition, the FDA has given the company 9 years in which to carry out another comparative trial using clinical endpoints (3).

While the clinical efficacy of this drug in terms of progression of Alzheimer's disease has not been demonstrated in clinical trials, it is indeed active on amyloid plaques, to such an extent that it caused cerebral œdema in about one-third of patients (4).

This MA has sparked much criticism and led to the resignation of three members of the expert advisory committee (2-4).

A promising commercial future. With a treatment price of 56 000 dollars per year, the company will certainly find ways to fuel demand for this drug between now and 2030, through investment in advertising in the press and publicity aimed at affected individuals, as well as financial incentives to prescribing doctors, and the funding of continuing medical "education".

Publications continue to confirm the high effectiveness of pharmaceutical marketing. For example, one study showed that advertisements in a Danish medical journal in 2015 mainly involved drugs which had no added therapeutic value and which were more expensive than comparator drugs (5). One study carried out in the USA showed a link between the payments received by doctors between 2016 and 2017 and their prescriptions for the most expensive insulins (6). The founder of the DC Center for Rational Prescribing argues that *"industry-funded medical education is always promotion"* (7).

In summary, despite *aducanumab*'s lack of demonstrated efficacy in Alzheimer's disease, the scene is set to raise the hopes of patients and those close to them, and above all to promote the interests of the company and its shareholders.... once again.

► Translated from *Rev Prescrire* October 2021 Volume 41 N° 456 • Page 774

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