

Business

Canadian regulators wade into Alzheimer's drug controversy

By **Noel Courage and Iris Cheung**

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(September 14, 2022, 1:29 PM EDT) -- In June 2022, neuroscience firm Biogen withdrew its Canadian drug submission for approval of aducanumab, which is a monoclonal antibody drug for the treatment of Alzheimer's disease (AD). The company's statement said, "... based on the review to date, the agency [Health Canada] indicated that the data provided would not be sufficient to support a marketing authorization in Canada." Biogen's withdrawal of the drug submission did not come as a surprise, since the drug application was withdrawn in Europe.

The U.S. market approval of Aduhelm (aducanumab) by the United States Food & Drug Administration (FDA) was also controversial. Subsequent to the Centers for Medicare & Medicaid Services' final National Coverage Policy that limited Medicare coverage of Aduhelm to individuals with Alzheimer's enrolled in FDA or National Institutes of Health approved clinical studies, Biogen substantially scaled back its commercial infrastructure for Aduhelm. It has been reported that Biogen does not have a sales team for the drug anymore and only maintains access for those who have already begun treatment.

Aducanumab in the U.S. and Europe

In June 2021, the FDA approved the marketing of Aduhelm for treatment of AD. The approval was exciting news for AD patients dementia advocacy groups, as there had not been any new treatment approved for AD since 2003. As a monoclonal antibody drug, aducanumab also represents first-of-the-kind treatment for AD.

The approval process for the Aduhelm, however, has been controversial. Concerns with regards to the efficacy of the drug have been raised by many. In fact, 10 of 11 members of the FDA advisory committee voted against approval of the drug and the 11th member was undecided, because they alleged there was not strong enough evidence that the drug

improves cognitive outcome of AD patients.

The FDA was also criticized for approving the drug using the accelerated approval pathway and giving Biogen until 2030 to complete a study to confirm the drug's beneficial effects. A month after approving the drug, the FDA requested an independent investigation into its own approval process of Aduhelm, stating that independent investigation is called for to maintain public confidence in view of the concerns over interactions between Biogen representatives and FDA staff during the reviewing process. Two committees in the House of Representatives also launched an investigation into the price of the drug and the process that led to the drug's approval. That is not all: in its regulatory filing, Biogen disclosed that the company has received a civil investigative demand from the Federal Trade Commission and an inquiry from the Securities and Exchange Commission relating to Aduhelm's approval and marketing.

In Europe, the European Medicines Agency (EMA) issued an opinion in December 2021 recommending the refusal of the marketing authorization for Aduhelm. Biogen initially requested a

re-examination of the opinion, but subsequently withdrew its application in April 2022.

Aducanumab in Canada

In Canada, Biogen filed an application in May 2021 to Health Canada for approval of aducanumab. In response to the application, a group of Canadian clinical dementia experts published a consensus statement stating that it would be premature for Health Canada to approve aducanumab for the treatment of AD.

In the consensus statement, the group alleged that the relevant data supporting the FDA's decision were not published or otherwise made available to the public. Based on the limited data available, the group raised the concern that the surrogate measure of amyloid levels in the brain has not been demonstrated as acceptable to indicate dementia progression and/or reversal. The fact that the FDA's own advisory committee did not support the approval was considered a major "red flag." Furthermore, only one of the two phase three trials met endpoint. The group concluded that the threshold for clinically relevant benefit was not met. The group cautioned that premature approval could have detrimental effects, including setting a bad precedent "by establishing such a low bar for therapeutic success" and loss of confidence in the drug regulatory system if it is later found that the drug is not effective.

The group also pointed out that the health-care systems in Canada are not ready for the enormous changes that will be needed to accommodate disease-modifying therapies for AD such as aducanumab. For example, capacity for the evaluation of amyloid status as part of diagnostic assessment and for monthly intravenous infusions is limited. In addition, regularly scheduled access to MRI will be required as therapeutic follow-up for safety reasons. Another important consideration raised is the value of investment, as the cost of the drug and implementation of the therapy must be balanced against other potential uses of public resources and must be aligned with the drug's clinical benefits.

Biogen has continued to stand by the safety and efficacy of its drug in the face of criticism. A Phase IV clinical study to verify the clinical benefit of aducanumab is underway. The estimated completion date of the clinical study is in 2026. In the meantime, it will be interesting to see the outcome of the various clinical investigations around Aduhelm.

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