



Canada's dementia experts urge caution in the review of aducanumab, a medication for Alzheimer's disease

SUMMARY

A medication under review

A medication called aducanumab (commercialized under the name Aduhelm™) is in the early stages of review for potential approval in Canada. Aducanumab was recently approved, with conditions, in the U.S., where it can now be prescribed for mild Alzheimer's disease. The cost estimate for this medication is \$56,000 USD a year, per person. Many researchers from around the world, including in the U.S., have raised questions concerning this approval.

Canadian experts coming together

Under the leadership of the Canadian Consortium on Neurodegeneration in Aging (CCNA), six organizations leading research on Alzheimer's disease and dementia (listed below), which include clinical and scientific experts in dementia from across Canada, came together to discuss aducanumab as a treatment for Alzheimer's disease. The experts prepared and submitted a consensus statement to Health Canada in which they shared their concerns and recommendations. The goal of the consensus statement is to inform the review process of this medication in Canada. In addition, these experts volunteered to advise on the potential introduction of this kind of medication in Canada in the future.

This summary was prepared to share the main points of the statement with the public. A group of people living with dementia and family members of people living with dementia reviewed this summary.

The consensus statement

The consensus statement submitted to Health Canada explains the concerns of the Canadian experts. The most important thing to consider is the lack of sufficient scientific evidence that aducanumab is effective in slowing or reversing Alzheimer's disease. **This is the main reason the consensus statement concludes that the approval of aducanumab in Canada cannot be justified**, based on information available today. In addition, there are health risks associated with this medication such as brain swelling and bleeding from small blood vessels in the brain.

Approving aducanumab for use in Canada would also require substantial changes to the health care system. These changes could divert funding from other aspects of Alzheimer's health care

and may delay studies of other medications. Any discussion of approval of this type of medication should include a careful evaluation of the impact on the Canadian health system to ensure appropriate and equal access to it for all Canadians who might need it, regardless of where they live and how much money they have. For all of these reasons, the consensus statement urges Health Canada to approach the review of aducanumab very cautiously.

The experts and organizations who wrote the consensus statement support the need to develop new medications for Alzheimer's disease. The Canadian and international community of researchers continues to work together to find a treatment for dementia. A number of promising experimental medications for Alzheimer's disease are currently under study. Each of these medications aims to slow or reverse the disease progression. Adequate scientific proof that they work must be provided to Health Canada to justify approving each one. It is important not to give false hope to patients and their families, or to approve medications that may not be effective in doing what they are intended to do.

The statement was prepared and endorsed by members of the following organizations:

CCNA (Canadian Consortium on Neurodegeneration in Aging) is a Canadian national umbrella organization for research on dementia funded by CIHR and partners with 350 researchers across Canada.

C5R (Consortium of Canadian Centres for Clinical Cognitive Research) is a not-for-profit research network of 30 academic memory clinics and research sites across Canada that conduct clinical trials in the desire to research and develop treatments for patients with Mild Cognitive Impairment, Alzheimer's disease, as well as other forms of dementia.

CAGP (Canadian Academy of Geriatric Psychiatry) is a national organization of psychiatrists and health professionals dedicated to promoting mental health in the Canadian elderly population through the clinical, educational, research and advocacy activities of its membership.

CGS (Canadian Geriatric Society) is the professional society for Geriatric Medicine specialists and Care of the Elderly specialists, and has over 500 members representing such specialists, along with medical students and residents, as well as other physicians and members of allied health professions with an interest in the health care of older adults.

ONDRI (Ontario Neurodegenerative Disease Research Initiative) brings together Ontario's research scientists and clinicians to tackle the complexity of dementia by studying multiple diseases related to neurodegeneration. ONDRI is funded by the Ontario Brain Institute (OBI).

TDRA (Toronto Dementia Research Alliance) is a University of Toronto collaboration of scientists and clinicians which aims to better understand, prevent, and treat dementia, and embed research into care.

The statement is also supported by:

CIMA-Q (the Consortium for the early identification of Alzheimer's disease) gathers more than 90 Quebec based researchers and clinicians who share the common ambition of advancing knowledge on Alzheimer's disease. More specifically, the aim is to develop tools to detect the very first signs of the disease.

To learn more about the considerations outlined in the consensus statement prepared by the group of experts, please read this list of questions and answers:

- **What is aducanumab and what does it do?**

People with Alzheimer’s disease show an increase of a protein called amyloid in their brain. Aducanumab is a medication that reduces amyloid in the brain (anti-amyloid). It is administered by a monthly intravenous infusion (with a needle into the vein in the arm). There are good reasons to think that reducing amyloid can improve Alzheimer’s symptoms, but to date there is no evidence that this is the case.
- **Should aducanumab be approved for use in Canada?**

Based on the scientific results from the drug trials conducted by Biogen (the pharmaceutical company that developed aducanumab), which are currently available, the experts agree that Health Canada approval of aducanumab cannot be justified at this time. The reasons for this position are described in the questions below.
- **Is aducanumab safe?**

Significant risks such as brain swelling and bleeds were found in studies of aducanumab. It is important to monitor such risks using imaging technology while taking this medication.
- **Is aducanumab effective?**

Biogen has not released enough information from the results of the drug trials they conducted to determine that it is effective. Aducanumab was conditionally approved in the U.S. despite the fact that the scientific advisory committee for the Food and Drug Administration (FDA) did not recommend the approval. An independent review reached the same conclusions.
- **What is missing to show that this medication is beneficial?**

In the U.S., aducanumab was approved by the FDA on the condition that a third study takes place. There are time-tested criteria for medication approval in Canada and in the U.S. This includes showing that the benefits from the medication are greater than the risks. Aducanumab does not appear to meet these criteria. A further large-scale study is needed to understand if the medication is truly beneficial, before any decision on its approval is taken.
- **Why is it dangerous to approve this medication without enough evidence?**

While finding new treatments for Alzheimer’s disease is needed, approving the medication with limited benefits and significant risks could:

 - Set a low bar for success of any other medication studies
 - Slow down studies of other medications, which could turn out to be more effective
 - Lead people to lose trust in the systems that approve medication, if aducanumab is shown to be ineffective later
 - Possibly divert funds away from other aspects of Alzheimer’s disease healthcare
 - Increase the burden on the healthcare system (more specialist visits needed, more MRI scan visits needed than currently sustainable, etc.) in return for little benefit

- **What steps are recommended if aducanumab is approved in Canada?**
If this medication is approved despite the limited scientific evidence, the experts who prepared the statement strongly recommend:
 - Labeling the exact stage of the disease in which it could be given, “mild cognitive impairment due to Alzheimer’s disease” or “mild Alzheimer’s disease dementia”
 - Giving it only to people with abnormal presence of amyloid in the brain
 - Testing people with the use of imaging scans before starting the medication and regularly during the course of treatment, to check for known complications (brain swelling and bleeds)
 - Using this medication only where there is proper access to imaging scans
 - Developing extensive guidelines for clinicians
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- **What should Canada do to prepare for this kind of medication in future?**
Using an anti-amyloid medication for Alzheimer’s disease would require major changes in the delivery of Alzheimer’s disease care in Canada. These changes can and will be made for effective medications for Alzheimer’s disease when they become available, but will require time effort and financial resources from governments. These include significantly increasing capacity for:
 - Specialist care: neurologists, radiologists, geriatricians, geriatric psychiatrists and others
 - Medical imaging technologies to determine medication suitability beforehand and the presence of side effects after
 - Infusion clinics which are needed to deliver aducanumab
- **What are the cost considerations?**
Canada’s public health system has limited funds, and aducanumab is expensive (estimated \$56,000 USD a year per person). It is important to compare treatment and prevention options when considering this type of medication. Given how expensive these medications are, it is critical to establish effectiveness before considering approval. Funding treatments that can also help in preventing dementia – for example, blood pressure control and diabetes prevention – could prove to be more effective. With limited public healthcare funds, relevant choices must be weighed carefully.
- **What should be the next step?**
The expert group of clinicians and researchers in dementia are offering to participate in a working group to advise Health Canada on this matter. They also believe it is essential to involve people who are at risk for dementia and people living with dementia in this work. They are committed to working with health authorities to prepare our healthcare system for the introduction of effective medications for dementia.