INDEPENDENT VOICES FOR SAFE AND EFFECTIVE DRUGS

REPRESENTING CANADIAN ACADEMICS, RESEARCHERS, PATIENT AND CONSUMER ACTIVISTS

September 23, 2021

Dr. Stephen Lucas, Deputy Minister of Health
Canada
stephen.lucas@hc-sc.gc.ca

Dear Dr. Lucas,

As members of Independent Voices for Safe and Effective Drugs (IVSED), we are extremely disturbed by the recent submission of the Alzheimer drug Aduhelm to Health Canada for approval, and the positive publicity created by Alzheimer Society of Canada, a patient advocacy group, asking Health Canada to approve it. We are academics, researchers, and patient and consumer advocates with no ties to the pharmaceutical industry and can therefore speak directly and without bias about this new dementia drug, which the U.S. FDA recently approved.

As a pan-Canadian community-based organization concerned about Canadians' access to safe and effective medications at a reasonable cost, we draw your attention to some contentious issues associated with Aduhelm.

1. This drug was tested in Phase III clinical trials across several Canadian provinces. Many of those enrolled in the Aduhelm clinical trials were diagnosed with Mild Cognitive Impairment (MCI) and not Alzheimer's disease. People with MCI may never develop Alzheimer's disease for various reasons. It is absurd to recruit people into a clinical trial for a disease that may never develop, let alone to rely on the trial results to make policy decisions. Drawing conclusions about benefits of Aduhelm in people with Alzheimer's when the drug was not tested in that population cannot be justified.
2. The period for testing this new drug was too short, only 18 months. In most people Alzheimer's disease progresses very, very slowly, over the course of many years. To properly assess the effects of Aduhelm, the clinical trials should have continued significantly longer.
3. Biogen, the drug's manufacturer stopped the ongoing two Phase III Aduhelm drug trials (Study 301 and 302) in 2015 due to their "futility," their inability to achieve set objectives to demonstrate clinical effectiveness (i.e., they did not improve cognitive functioning or slow disease progression). In fact, in Study 301, the placebo group did better than the group receiving the drug.

4. The FDA approval process was highly questionable, for several reasons.
    - After the clinical trials were stopped, the clinical trial results were so disappointing that Biogen and the FDA conducted a collaborative post hoc analysis. Post hoc analyses may be useful for forming new hypotheses but, should be avoided for reaching conclusions about the efficacy of a drug.
    - A reduction in amyloid plaque in the brain, which is a surrogate endpoint and not evidence of clinical effectiveness, was reviewed in this post hoc analysis. It is generally acknowledged that the pharmaceutical industry has singularly and relentlessly pursued research on reducing amyloid in the brain for over 25 years, yet all clinical trials have failed to demonstrate any meaningful benefits to people with Alzheimer's disease. Unsurprisingly then, the results of the post hoc analysis were no different; and yet, alarmingly, Aduhelm was approved.
    - The FDA's own biostatistical review failed to find that Aduhelm produced positive clinical results in people with Alzheimer's disease.
    - The probability of serious adverse effects from taking this drug is very high. These include brain swelling and bleeding, microhemorrhages, visual and gait disturbance, dizziness, nausea or headaches, diarrhea, confusion, disorientation, higher incidence of falls - terrible prospects for people with Alzheimer's disease who are already struggling with their thinking and having difficulty understanding and recognizing their world.
    - These adverse drug reactions can make the symptoms of an already terrible disease worse or lead to death. Even the process of taking this drug is problematic. Aduhelm must be administered by infusion and special brain scan tests (PET and MRI) are conducted for both for diagnosing the presence of amyloid plaques and to monitor for the side effects from the drug. Infusion is an invasive procedure and scans such as PET and MRIs can be frightening for persons with dementia. The well being of persons with dementia can be detrimentally affected by being diagnosed, by being administered the drug and by monitoring its side effects.
    - Finally, of greatest concern, no independent review of these questionable post hoc analyses conducted by Biogen and the FDA was performed, failing to ensure impartiality, credibility, and public trust. These post hoc analyses were never presented to the Peripheral and Central Nervous System Advisory Committee, an independent advisory committee that the FDA itself created to provide unbiased oversight. After reviewing the original clinical trial results, this committee voted overwhelmingly not to grant Aduhelm's approval (10 against and 1 abstention). Ultimately, the FDA ignored the findings of its own independent advisory Committee and, despite earlier ruling out relying on a surrogate outcome (clearing amyloid plaque), reversed its decision and used its Accelerated Approval mechanism. Three of its members resigned in protest over Aduhelm's approval. One of these members called the approval decision, "The worst drug approval decision in recent U.S. history" and a regulatory failure. In fact, the entire FDA approval process is now under investigation by two U.S. Congressional Committees due to a suspected cozy relationship between Biogen and the FDA.

One of our members has twenty years of experience giving care to both parents affected simultaneously at age 60 by Alzheimer's disease. For many years she worked both professionally, supporting informal caregivers, and as an active volunteer for the Alzheimer Society at the local, provincial, and national levels. She completed a doctoral degree on the educational needs of informal caregivers who care for persons with Alzheimer's disease. As

someone at risk for the disease herself, she is obviously as eager as many Canadian patients, family members, other caregivers are, as well as healthcare providers and society in general for a drug that is proven to be safe and beneficial. Understandably, people with the disease and their families are terribly desperate.

However, desperation is not a basis on which to grant a drug approval. We are deeply troubled that Alzheimer Society of Canada is actively pressing for the approval of Aduhelm. Its American counterpart, the Alzheimer Association, vigorously advocated for the approval of Aduhelm as well. It received financial support from Biogen, the drug's manufacturer, creating a serious conflict of interest that calls into question the group's ability to objectively assess the potential benefits and harms associated with the drug. Canada lacks transparency laws requiring patient organizations with charitable status to detail donations from pharmaceutical companies; furthermore, Alzheimer Society of Canada has not yet released its 2020-2021 financial statements, so whether the organization has financial ties to Biogen is not on the public record. We know, however, that pharmaceutical companies frequently fund relevant Canadian patient groups when they are seeking approval for a new drug.

The costs of this treatment are prohibitive. Aduhelm is going to cost the US Medicare system US$56,000 per person per year. In addition, using the drug commits the patient to the additional expense of PET and MRI scans to diagnose the presence of amyloid plaque and to monitor for side effects from Aduhelm. If Health Canada approves Aduhelm, the negative impact on the Canadian health care system will be significant. If the drug is approved, experience shows that Biogen and desperate patients will aggressively lobby our Canadian provincial health ministers to add it to provincial formularies, which would drain scarce health care dollars without benefits for those suffering from Alzheimer's disease. Approval of Aduhelm would also lead to opportunity costs. We have a dire and urgent need to fund new and better avenues of Alzheimer's research and to increase funding for home care and long term care homes for persons with Alzheimer's disease.

Evidence is the cornerstone of our drug approval process and Canadians rely on Health Canada to uphold scientific integrity. Innumerable scientists and clinicians in the U.S. have deplored the FDA approval, and many Canadian scientists already have asked Health Canada not to approve this drug.

The problems regarding Aduhelm raised in this letter are far from exhaustive but suffice to conclude that the evidence for patient benefit is totally absent. We implore Health Canada to flatly refuse to approve this ineffective, harmful, and costly drug.

Sincerely,

Dr. Linda Furlini, Ph.D., Montreal. Particular expertise on caregivers of persons with dementia and their need for educational support. She is also an advocate for person-centred dementia care. She has worked in the field of research ethics for many years.

Email: furlinil@bell.net

In collaboration with:

Wendy Armstrong, Alberta. Community-based policy researcher and consumer advocate. Focus is on how changing healthcare and societal landscapes influence the safety, effectiveness and pricing of drugs and new medical technologies as well as the importance of tools and strategies to help Canadians negotiate these landscapes.

Dr. Sharon Batt, Ph.D., Halifax. Journalist and qualitative researcher with a focus on health ethics and pharmaceutical policy. Special expertise in breast cancer treatments, breast cancer groups, and how pharmaceutical company funding of patient advocacy groups distorts information and health policies.

Dr. Janet Currie, MSW, PhD. Edmonton and Vancouver. Long term medication safety advocate with specific expertise in drugs used for mental health problems, and of drugs for women and older Canadians. Her PhD, completed in May 2021, focused on the safety issues associated with the widespread use of drugs prescribed off-label (those prescribed by physicians where the particular use is not approved by Health Canada).

Colleen Fuller, Vancouver. Qualitative researcher / writer in health and pharmaceutical policy. Expertise in the development and commercialization of insulin therapy for Type 1 and Type 2 diabetes in Canada and internationally.

Terrie Hendrikson, MPA., Vancouver. Long-time public health and affordable housing advocate. Expertise in non-profit administration, communications and development, including website development.

Erin Little. Ontario. Erin is an undomesticated advocate raising awareness about cystinosis, a rare disease that her daughter lives with. She fights for pharma transparency and to protect parents and caregivers from using unsafe and excessively expensive prescription drugs.

Dr Nancy Olivieri, MD, MA, FRCP(C), Ontario. Is a hematologist, clinical researcher, and professor of paediatrics, medicine, and public health sciences at the University of Toronto. Her experience with a prescription drug in which she had conducted original clinical trials became the focus of one of Canada's most prominent and ongoing medical research scandals, leading to her advocacy in the process of drug evaluation and approval at the regulatory agencies of Canada, the USA and Europe.

cc:

Celia Lourenco, Director General
Biologics and Genetic Therapies Directorate
celia.lourenco@hc-sc.gc.ca

Adrian Dix, Minister of Health
British Columbia
HLTH.Minister@gov.bc.ca

Tyler Shandro, Minister of Health
Alberta
health.minister@gov.ab.ca

Paul Merriman, Minister of Health
Saskatchewan
he.minister@gov.sk.ca

Audrey Gordon, Minister of Health
Manitoba
minhsc@leg.gov.mb.ca

Christine Elliott, Minister of Health
Ontario
Christine.elliott@pc.ola.org

Christian Dubé, Ministère de la Santé
Québec
ministre@msss.gouv.qc.ca

Dorothy Shephard, Minister of Health
New Brunswick
Dorothy.Shephard@gnb.ca

Michelle Thompson, Minister of Health
Nova Scotia
Health.Minister@novascotia.ca

Ernie Hudson, Minister of Health
Prince Edward Island
ehhudsonminister@gov.pe.ca

John Haggie, Minister of Health
Newfoundland & Labrador
hcsminister@gov.nl.ca

Tracy-Anne McPhee, Minister of Health
Yukon
tracy.mcphee@yukon.ca

Julie Green, Minister of Health
Northwest Territories
Julie_green@gov.nt.ca

Lorne Kusugak, Minister of Health
Nunavut
lkusugak@gov.nu.ca

Suzanne McGurn, President & Chief Executive Officer
Canadian Agency for Drugs & Technologies in Health
SuzanneM@CADTH.ca

Dr Colin Dormuth, and Dr. Ken Bassett
Co-Managing Directors
Therapeutics Initiative, University of British Columbia
colin.dormuth@ubc.ca; ken.bassett@ubc.ca