

Aducanumab and Intellectual Disability

Frequently Asked Questions

Q: *What is the connection between Aduhelm (aducanumab) and Down syndrome?*

- A. Aduhelm™ is marketed as a drug that can reduce the amount of beta amyloid in the brain. Beta amyloid is thought to be one reason that persons with Alzheimer's disease lose memory and other general cognitive abilities. Reducing the amount of amyloid beta plaques is believed to minimize the symptoms of Alzheimer's disease and improve cognitive abilities. Adults with Down syndrome have naturally occurring high levels of beta amyloid plaques in their brains and thus it is thought that any drug that reduces these levels can be therapeutic and help them maintain their cognitive abilities.

Q: *What is the difference between Aduhelm™ and aducanumab?*

- A. Aducanumab is the generic term for the medications that target the reduction of beta amyloid plaques. The version developed by Biogen/Eisai Pharmaceuticals is marketed under the trade name Aduhelm.

Q: *What is Aduhelm?*

- A. Aduhelm is a Food and Drug Administration (FDA) approved drug for the treatment of mild cognitive impairment and early-stage Alzheimer's disease. The approval was issued on June 7, 2021. This is the first drug approved by the FDA for the treatment of Alzheimer's disease in almost 20 years. It is a novel medication¹ as it is given in a vein (IV) every 4 weeks. Previous medications approved for use with adults diagnosed with Alzheimer's disease were taken in pill form. It was created to reduce beta amyloid, a protein that builds up in the brain, and is associated with Alzheimer's disease.

Q: *Does Aduhelm cure Alzheimer's disease?*

- A. No, Aduhelm is believed to slow down the progression of the disease. People on the drug will still have symptoms of Alzheimer's, but these symptoms might progress more slowly. While aducanumab doesn't reverse or cure dementia, it may slow the loss of memory and general cognition (thinking ability). Biogen reported that orientation and

¹ According to the FDA, 'novel drugs' are **innovative products that serve previously unmet medical needs** or otherwise significantly help to advance patient care and public health. See: [download \(fda.gov\)](https://www.fda.gov/oc/innovation)

language problems, such as losing track of time and place, and not being able to name well-known objects, improved somewhat in test subjects.²

Q. Does Aduhelm work with mitigating symptoms of dementia from other causes?

- A. Aduhelm is a drug approved for use with persons with mild cognitive impairment and early-stage Alzheimer’s disease and is specifically designed to reduce the amount of beta amyloid in the brain. No information is available as to whether amyloid-targeting therapies might be helpful to adults with dementia stemming from causes such as frontotemporal degeneration, Lewy body disease, vascular stroke/infarction, and other conditions, unless there is co-existing Alzheimer’s disease.

Q: Is Aduhelm taken as a pill like other common drugs?

- A. No, Aduhelm is taken by injection once a month. The medication is injected into a vein (that is, ‘intravenously’ or IV). The total treatment time is approximately an hour. Patients will need to visit their physicians every month to receive their injection or go to an infusion center, like where people with various cancers may go to get their specialized therapies. Such infusion centers are generally located in hospitals and other medical facilities.

Q: Are there side effects to taking Aduhelm?

- A. In the original clinical trials undertaken by Biogen, the most common side effects were abnormal brain changes associated with anti-amyloid treatments. Two common side effects were swelling in the brain (called ARIA-E) and persistent or recurring long-term bleeding (or micro hemorrhage/superficial siderosis) in the brain (called ARIA-H). ARIA can be observed by a brain MRI (magnetic resonance imaging) medical imaging technique. Headache, balance problems leading to falls, stomach issues including diarrhea, and disorientation are also possible side effects.³ The term “ARIA” stands for ‘amyloid-related imaging abnormalities’

Q: What are some considerations about who can be given Aduhelm?

- A. ARIA is a common side effect which is usually monitored with a brain MRI. So, anyone who cannot tolerate the MRI procedure -- which involves loud noises, being in a confined space, and the need to remain still for 40 minutes -- should not be on Aduhelm, unless they can be given a sedative beforehand. To begin receiving the medication, a brain MRI is mandatory to determine the brain’s condition, as well as at least an additional two more times while taking the medication to ensure no significant abnormalities are seen.

² [Aducanumab / Aduhelm: Benefits, Side-Effects, Costs & Medicare Coverage \(dementiacarecentral.com\)](https://dementiacarecentral.com/aducanumab-aduhelm-benefits-side-effects-costs-medicare-coverage)

³ [Aducanumab / Aduhelm: Benefits, Side-Effects, Costs & Medicare Coverage \(dementiacarecentral.com\)](https://dementiacarecentral.com/aducanumab-aduhelm-benefits-side-effects-costs-medicare-coverage)

Currently, the medication is not advised for persons receiving anticoagulants (blood thinners) or who have a clotting disorder due to risk for ARIA.

Q: How often would a person have to be subjected to a brain MRI procedure?

- A. Besides the initial magnetic resonance imaging [MRI]⁴ procedure to provide a baseline during the diagnostic phase, Biogen recommends administering MRI scans that detect ARIA before the 7th and 12th infusions, as the problems typically develop in the first 12 to 16 weeks of treatment and are asymptomatic (meaning a person can't feel them happening).⁵ At this time it is unknown how long an individual may be on Aduhelm and how often further examinations by a brain MRI would be prudent.

Q: Are there other disqualifications for taking Aduhelm at this time?

- A. It has been recommended that persons with neurological disorders that could account for or contribute to the clinical syndrome of the individual not be treated with aducanumab. This would include adults with parkinsonism, evidence of stroke or widespread white matter ischemic changes, or rapidly progressive dementia. Also, those adults with recent major psychiatric illness which may compromise their ability to adhere to therapy and treatment should be deferred until behavioral stability is established. Poorly controlled or serious medical illnesses (e.g., cancer, heart failure) were exclusions for trial participation and if such illnesses are present in an individual being considered for treatment with aducanumab, the medical condition should be managed and stabilized prior to initiating treatment. Evidence of significant brain vascular changes seen on an MRI prior to treatment may also disqualify someone from being able to receive Aduhelm.⁶

Q: Can adults with intellectual disability take Aduhelm?

- A. Adults with intellectual disability were not included in the clinical trials and thus the exclusion rationale noted for persons with neurological disorders would also apply. Special considerations apply to adults with Down syndrome. It has been noted that as individuals with Down syndrome essentially uniformly develop brain amyloid plaques and often have symptoms of dementia in midlife that the presence of the amyloid plaques might suggest that treatment with Aduhelm may be beneficial. However, there are many differences between Down syndrome and late onset dementia of the Alzheimer's type, and an Alzheimer's Disease Expert Panel recommended against treating adults with Down syndrome with Aduhelm until more data are available.⁷ Although the Expert Panel

⁴ Magnetic resonance imaging uses a large magnet and radio waves to look at organs and structures inside the body. Health care professionals use MRI scans to diagnose a variety of conditions, from torn ligaments to tumors. MRIs are very useful for examining the brain and spinal cord.

⁵ [Aducanumab / Aduhelm: Benefits, Side-Effects, Costs & Medicare Coverage \(dementiacarecentral.com\)](https://www.dementiacarecentral.com/aducanumab/)

⁶ Cummings, J., Aisen, P., Apostolova, L.G. *et al.* Aducanumab: Appropriate Use Recommendations. *J Prev Alzheimers Dis* (2021). <https://doi.org/10.14283/jpad.2021.41>

⁷ Cummings, J., Aisen, P., Apostolova, L.G. *et al.* Aducanumab: Appropriate Use Recommendations. *J Prev Alzheimers Dis* (2021). <https://doi.org/10.14283/jpad.2021.41>

did not specifically focus on intellectual disability or Down syndrome, it did consider the effects of Aduhelm on people with Down syndrome.

Q: Should adults with intellectual disability be prescribed Aduhelm?

- A. As adults with intellectual disability were not included in the clinical trials it is unknown whether they would benefit from being administered Aduhelm and whether they may experience any specific adverse effects. As adults with intellectual disability are a diverse and heterogeneous population, with various etiologies, it can be assumed that unless there is a genetic basis for beta amyloid plaque build-up, they might benefit like age peers in the general population once diagnosed with mild cognitive impairment (MCI) of early-stage Alzheimer's disease. The main cautionary considerations would involve tolerance of the brain MRI procedures and the monthly infusion visits. Another factor is ensuring that either appropriate biomarker or other standard disease presence testing validation is available and approved for use. However, until more data are available on benefit and safety, caution would have to be exercised prior to considering adults with intellectual disability for receiving the medication.

Q: Are there any tests that must be done before anyone can get Aduhelm?

- A. At the time of the FDA accelerated approval of Aduhelm on June 7, 2021, confirmation of a biomarker-proven diagnosis of Alzheimer's disease was not included in the labeling with respect to being eligible to receive Aduhelm. It was left up to the prescribing physician to make the determination. The Biogen led research studies that led to the current approval of Aduhelm, however, did require that biomarkers were used to provide proof of the presence of amyloid plaques in the brain (confirmed either by a specialized scan called Amyloid PET scan or by evaluation of cerebrospinal fluid through a spinal tap. These somewhat contradictory messages may be sorted out as the approval and oversight process moves forward in the future.

Q: What are the criteria for eligibility to receive treatment with Aduhelm?

- A. It has been recommended that adults who may be appropriate for treatment with aducanumab have a diagnosis of mild cognitive impairment (MCI) or early-stage Alzheimer's disease established by a diagnostic evaluation that includes: 1) detailed history that is sufficient to establish the nature and time course of cognitive symptoms, functional changes, and behavioral status; 2) objective corroboration of cognitive decline using standardized testing; 3) detailed neurological and physical examination; 4) review of all current medications and supplements; 5) laboratory testing sufficient to exclude other concomitant disorders that can cause cognitive decline including a complete blood count, electrolyte panel, thyroid stimulating hormone, lipids and triglycerides, liver function tests, serum vitamin B12 and folate levels; and 6) magnetic resonance imaging (MRI) of the brain to rule out other conditions that could present with cognitive decline (e.g., normal pressure hydrocephalus, vascular dementia, slow going neoplasm,

subdural hematoma) and to assess possible exclusions for use of aducanumab.⁸

Q: Sedation may be required in some adults with Down syndrome who may be highly sensitive and anxious about the necessary tests and treatments such as IV Aduhelm, MRIs, possibly an initial lumbar puncture (spinal tap), and monthly IV injections of the medication. Will the usage of sedation to reduce anxiousness itself contribute to additional cognitive decline?

- A. Commonly used sedatives and tranquilizers including diazepam and alprazolam can cause confusion and disorientation. The reaction to these medications is variable and the risks would have to be considered in each person. There is insufficient evidence that the occasional usage of these medications would cause long term harm.

Q: Why is the FDA requiring Biogen, the manufacturer, to conduct more research on the efficacy of the drug?

- A. The clinical trial data was promising but not entirely clear as to the ability of the drug to delay the onset or mitigate the symptoms of Alzheimer's disease, such as memory loss. As such, Biogen has been required to conduct another study to determine if this treatment will be effective over time with respect to reducing symptom effects and helping adults living with dementia. The rationale for additional trials is complex and in essence is asking Biogen for more data on efficacy of the drug to reduce beta amyloid and more importantly evidence cognitive improvements. If the trials fail to confirm efficacy, the FDA can revoke the approval of Aduhelm. Biogen is also being asked to extend its trials to a broader sample, as the first lacked sufficient diversity reflective of the population of the United States. Also, there is a need to include neuroatypical groups, such as persons with Down syndrome, to assess safety and utility.

Q: As adults with Down syndrome are at high risk for Alzheimer's disease should they be prioritized for receiving Aduhelm?

- A. Unfortunately, to our knowledge, no person with Down syndrome was included in the clinical trials nor has ever been given Aduhelm. Therefore, we can only speculate as to the efficacy and safety of this drug for people with Down syndrome. It has been recommended that as individuals with Down syndrome tend to develop brain amyloid plaques and often have symptoms of dementia in midlife, that the presence of amyloid plaques might suggest that early treatment with an aducanumab type medication may be beneficial. However, there are many differences between the presence of amyloid in earlier life among adults with Down syndrome and that found in other adults who are diagnosed with Alzheimer's disease later in life. Thus, the Alzheimer's Disease Expert Panel recommended against treating Down syndrome patients with aducanumab until more data are available.⁹ Until further studies are undertaken, it is unknown what

⁸ Cummings, J., Aisen, P., Apostolova, L.G. *et al.* Aducanumab: Appropriate Use Recommendations. *J Prev Alzheimers Dis* (2021). <https://doi.org/10.14283/jpad.2021.41>

⁹ Cummings, J., Aisen, P., Apostolova, L.G. *et al.* Aducanumab: Appropriate Use Recommendations. *J Prev Alzheimers Dis* (2021). <https://doi.org/10.14283/jpad.2021.41>

prophylactic effects the medication might have in slowing the progression of Alzheimer's disease in persons with Down syndrome if taken early in life.

Q: Will people with Down syndrome be included in future Aduhelm clinical trials?

- A. We hope that Biogen, the National Institute of Health, and others will fund and support this important research so that the appropriate use of Aduhelm for persons with Down syndrome can be determined. Important outcomes would include noting the reduction of the level of beta amyloid as well as any notable cognitive impairment reduction.

Q: Are there financial implications for persons with Down syndrome or their families?

- A. Aduhelm is expensive, costing about \$4,312 per infusion or about \$56,000 annually. The Centers for Medicaid and Medicare Services (CMS) has yet to determine how much Medicaid and Medicare will cover for the use of aducanumab. MRI or PET brain scans to detect amyloid beta plaques would probably be necessary to determine aducanumab coverage and those are expensive. It is not yet clear how much of these costs will be covered by insurance. CMS is currently considering this issue and should decide on what they will cover in the coming months. However, as an infusion drug that people with Alzheimer's would need to take in their doctor's office, aducanumab is likely covered by the outpatient care benefit under Medicare Part B, whose standard premium is \$148.50 per month. Enrollees of Medicare Advantage, which pairs the government program with private insurers, also have a cap on expenses that would be significantly less than out-of-pocket costs for Aduhelm. Whether Medicare Part D, which pays for prescriptions, will cover Aduhelm has not been determined yet.¹⁰ Additionally, since most people with Down syndrome may develop Alzheimer's disease prior to age 65, they may not be eligible to receive the benefits of Medicare.

Q: Are their current research studies being conducted now in people with Down syndrome who have Alzheimer's disease?

- A. There are efforts underway to link several sites across the United States and internationally where research can be done to determine if Aduhelm is safe in people with Down syndrome who are diagnosed with Alzheimer's disease. Details will be forthcoming soon. Additional information about other types of research can be found through:
- i. **Alzheimer's Biomarkers Consortium-Down Syndrome (ABC-DS)**. This is a longitudinal study funded by the National Institute on Aging (NIA), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the National Institutes of Health (NIH) INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome) [Alzheimer's Biomarkers Consortium — Down Syndrome \(ABC-DS\) | National Institute on Aging \(nih.gov\)](https://www.nia.nih.gov/health/Alzheimer's-Biomarkers-Consortium-Down-Syndrome-ABC-DS)

¹⁰ [Aducanumab / Aduhelm: Benefits, Side-Effects, Costs & Medicare Coverage \(dementiacarecentral.com\)](https://www.dementiacarecentral.com/Aducanumab-Aduhelm-Benefits-Side-Effects-Costs-Medicare-Coverage)

- ii. **The LIFE-DSR (Longitudinal Investigation for Enhancing Down Syndrome Research) study.** LIFE-DSR is a natural history study led by the LuMind IDSC Foundation. Natural history studies of disease focus on understanding the natural course of a disease from the time before disease initiation, through its pre-symptomatic phase and various clinical stages, until an outcome occurs without treatment intervention. [LuMind IDSC Foundation - LIFE-DSR Study – Why Natural History Studies Are Important on the Path to New Treatments](#)
- iii. **Horizon 21.** This is a European consortium project with research teams linked among 10 different sites. The consortium is working to employ clinical trials designed to examine the prevention or delay of Alzheimer’s disease in adults with Down syndrome. The group’s aims include identifying the factors that influence the development of Alzheimer’s disease in persons with Down syndrome and to develop cognitive assessment tools and biomarkers which could be relevant for clinical trials. [Horizon 21 \(horizon-21.org\)](#)

Q: As the accumulation of beta amyloid in the brains of people with Down syndrome begins decades before dementia is seen, will future therapies to prevent or to mitigate dementia also begin long before any cognitive decline starts?

- A. Theoretically, starting disease modifying drugs early on would make sense, especially before irreversible damage occurs. There are no current research studies that have been done or are being undertaken to validate this. It would take more than a decade or so for someone to be on medication to really know if this intervention would be viable, proving that it is safe and effective. Also, given ethical considerations, random controlled trials (RCTs) pairing adults with Down syndrome in their 20s and giving one group the medication and the other a placebo over a lengthy period would be problematic.

Q: What are the other treatments for Alzheimer’s disease?

- A. There are other FDA approved drugs for Alzheimer’s disease (i.e., Aricept®, Exelon®, Razadyne®, Namenda®). These drugs help with memory symptoms but do not stop or slow the progression of Alzheimer’s disease. As Alzheimer’s progresses, brain cells die and connections among cells are lost, causing cognitive symptoms to worsen. While these medications do not stop the damage Alzheimer’s causes to brain cells, they may help lessen or stabilize symptoms for a limited time by affecting certain chemicals involved in carrying messages among and between the brain's nerve cells.

There are also non-cognitive symptoms (behavioral and psychological symptoms) that are common in Alzheimer’s disease. At this time, the FDA has approved one drug to address insomnia in people living with dementia, but trials into drugs that address other non-cognitive symptoms are underway. Belsomra® is FDA approved to treat insomnia for individuals living with dementia.

Besides medications, there are several evidence-based non-pharmacological interventions (NPIs) in play that can be used to mitigate behavioral and psychological symptoms of dementia (BPSDs). Many of these BPSDs are symptoms of the effects of Alzheimer's disease. While these interventions are not pharmacological treatments, they are still treatments that are effective in ameliorating these symptoms; thus, can help ease caregiving and help the person living with dementia with respect to their daily activities, relationships, and quality of life.

Q: *Would drugs like Aduhelm work in people with Down syndrome who have 'regression syndrome'?*

- A. Down syndrome disintegrative disorder (DSDD), a [developmental regression](#) in children and adolescents with Down syndrome (which is sometimes misidentified as early dementia), is a clinical entity that is characterized by a loss of previously acquired adaptive, cognitive, and social functioning in persons with Down syndrome -- usually in adolescence to early adulthood. This rare and very complex problem, which mimics severe dementia, is not caused by the same brain condition and therefore, amyloid targeted therapies would not be effective.

Q: *Has the NTG, along with other organizations, issued a policy statement relative to the aducanumab and its use with adults with intellectual disability?*

- A. The NTG and a collective of organizations issued a [public statement](#) on August 2, 2021, which raised several concerns related to the use of Aduhelm with adults with Down syndrome. The statement recommended (a) including participants with Down syndrome in ongoing and further clinical trials and research, (b) assuring research-informed appropriate oversight over its usage, (c) developing protocols that guide assessment and decision-making for the use of the drug with this group, (d) screening systematically for early symptoms of AD, (e) determining optimal age for prophylactic use of drug, (f) involving families and caregivers in the prescribing and decision making process, and (g) providing orientation and education to healthcare providers and ancillary staff involved with use and aftercare.

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This FAQ was developed by the NTG's Medical Advisory Group, led by Seth M. Keller, MD. [Comments or queries should be directed to the MAG.](#)