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Medication Policy Manual **Policy No:** dru740

Topic: Monoclonal Antibodies for Alzheimer's Disease **Date of Origin:** April 15, 2023

- Aduhelm, aducanumab
- Kisunla, donanemab
- Leqembi, lecanemab
- Leqembi Iqlik, lecanemab

Committee Approval Date: January 22, 2026 **Next Review Date:** 2027

Effective Date: April 1, 2026

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Medications included in this policy are monoclonal antibodies used for Alzheimer's disease (AD). A clinical benefit, such as slowing of disease progression, of these monoclonal antibodies for Alzheimer's disease has yet to be established.

Policy/Criteria

Most contracts require pre-authorization approval of monoclonal antibodies for Alzheimer's disease (as listed in Table 1 or *Table 2*) prior to coverage.

I. Continuation of therapy (COT): Monoclonal antibodies for Alzheimer's disease (as listed in *Table 1*) may be considered medically necessary for COT when full policy criteria below are met, including quantity limit.

Please note: *Medications obtained as samples, coupons, or promotions, paying cash for a prescription ("out-of-pocket") as an eligible patient, or any other method of obtaining medications outside of an established health plan benefit (from your insurance) does NOT necessarily establish medical necessity. Medication policy criteria apply for coverage, per the terms of the member contract with the health plan.*

II. New starts (treatment-naïve patients): Monoclonal antibodies for Alzheimer's disease (as listed in *Table 1* or *Table 2*) are considered investigational for all conditions, including Alzheimer's disease.

III. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services considers Aduhelm (aducanumab), Kisunla (donanemab), and Leqembi (lecanemab) coverable under the medical benefit (as a provider-administered medication).

B. Regence Pharmacy Services considers Leqembi Iqlik (lecanemab) coverable under the pharmacy benefit (as a self-administered medication).

C. Although the use of monoclonal antibodies for Alzheimer's disease (as listed in *Table 1* or *Table 2*) is considered investigational for all conditions, including Alzheimer's disease, if pre-authorization is approved, monoclonal antibodies for Alzheimer's disease (as listed in *Table 1* or *Table 2*) will be authorized as follows:

TABLE 1. Provider Administered Monoclonal Antibodies for Alzheimer's Disease

Product	Quantity Limit
Aduhelm (aducanumab)	Doses up to 10 mg/kg every 4 weeks.
Kisunla (donanemab)	Doses up to 1400 mg every 4 weeks.
Leqembi (lecanemab)	Doses up to 10 mg per kg every 2 weeks.

TABLE 2. Self-administered Monoclonal Antibodies for Alzheimer's Disease

Product	Quantity Limit
Leqembi Iqlik (lecanemab) autoinjector	Doses up to 360 mg every week (after 18 months of Leqembi (lecanemab) intravenous treatment)

D. Authorization **shall** be reviewed at least every six months for documented benefit. Clinical documentation (such as chart notes) must be provided to confirm that current medical necessity criteria are met. Specifically, documentation that the medication is providing clinical benefit, including disease stability or improvement, and lack of disease progression.

Position Statement

Summary

- Aduhelm (aducanumab), Kisunla (donanemab), and Leqembi (lecanemab), are intravenous therapies, while Leqembi Iqlik (lecanemab) is a subcutaneous therapy. All are indicated for the treatment of Alzheimer's disease (AD).
- A clinical benefit (e.g., prolongation of independence, improved quality of life, prevention of disease progression and disability) with monoclonal antibodies for AD has not been established. [1 2]
    * The results of two nearly identical unpublished studies (EMERGE and ENGAGE) [1 3] of Aduhelm (aducanumab) had inconsistent clinical benefit after 18 months of treatment. Of the two trials, one demonstrated cognitive and functional improvements based on clinical scores in a subgroup who received high dose aducanumab while no endpoint was met in a second study regardless of dose.
    * In the TRAILBLAZER-ALZ2 trial, treatment with Kisunla (donanemab) resulted in cognitive and functional improvements after 18 months of treatment. However, the clinical meaningfulness of the improvement is unclear as the changes did not meet the defined minimal clinically important difference. [4]
    * In a phase 2 dose-ranging trial (Study 201), Leqembi (lecanemab) showed improvements in composite scores for cognition and function; however, these improvements did not reach the prespecified threshold for clinical success. In a phase 3 trial (CLARITY AD), treatment with lecanemab demonstrated improvements in cognitive assessment scores although the changes did not meet the defined minimal clinically important difference. As lecanemab has not consistently demonstrated clinically meaningful improvements in prospective trials, its efficacy in AD is inconclusive. [2 5-7]
    * Aduhelm (aducanumab), Kisunla (donanemab) and Leqembi (lecanemab) demonstrated improvements in amyloid beta imaging; however, the reduction of beta-amyloid plaque is a surrogate endpoint whose causal link to clinical benefit for patients with AD has yet to be established. [2]
    * Given the lack of overall clinical benefit and potential for harms, the use of monoclonal antibodies for AD is considered investigational.
- Of note, the manufacturer announced discontinuation of Aduhelm (aducanumab) in late 2024.
- Treatment of AD is largely supportive and may include the avoidance of poly-pharmacy as well as treatment of comorbid conditions. Currently available pharmacological therapy focuses on symptom management but does not modify disease course. [8]

Clinical Efficacy

Aduhelm (aducanumab) for Alzheimer's disease

- The results of two nearly identical studies did not have consistent clinical benefit after 18 months of treatment. The FDA standard is typically two demonstrative clinical trials with positive data on patient reported outcomes/symptoms.

- The evidence regarding the effect of Aduhelm (aducanumab) is based on the change from baseline on the CDR-Sum of Boxes is inconclusive. The (CDR-SB) is an extensive cognitive and functional assessment tool used primarily in clinical trials. Higher scores suggest greater disease severity; a minimal clinically significant difference (MCID) is estimated to be 1-2 points. [9]
- Patients in the pivotal trials had prodromal or mild AD along with confirmed amyloid pathology [positive amyloid positron emission tomography (PET) scan]. All patients in the trials had either mild cognitive impairment associated with AD or mild AD; patients with more severe disease were not studied.
    * EMERGE: A statistically significant improvement in CDR-SB was observed in the high-dose aducanumab arm (difference vs. placebo -0.39 [95% CI -0.69 to -0.09]) but not the low-dose arm. Although the results were statistically significant in the high-dose arm, the change in CDR-SB was less than the 1-2 point change that has been suggested as the MCID.
    * ENGAGE: Neither low dose or high dose had any statistically significant improvement vs placebo in CDR-SB or any secondary efficacy endpoints.
- Both studies demonstrated significant improvements in amyloid plaques based on PET imaging; however, the effect of amyloid beta on clinical outcomes has not yet been established. There have been 16 trials of other drugs in which the treatment arm did worse than placebo despite reduction of amyloid, albeit typically in a population with more severe disease. [2]
- Although the existing evidence is promising, an additional confirmatory trial is needed to establish the safety and efficacy of Aduhelm (aducanumab) in AD. Aduhelm (aducanumab) has not yet proven to improve clinically relevant outcomes such as quality of life, prolongation of independent functioning, or prevention of disease progression and disability, or mortality.
- The FDA advisory committee as well as the Institute for Clinical and Economic Review (ICER) openly advised against approval of Aduhelm (aducanumab). [10 11] Prior to approval, the American Academy of Neurology (AAN) advised against a broad label approval and that further characterization of patients who would benefit most is warranted. [8]
- At this time, there is not enough data available to determine that the benefits of Aduhelm (aducanumab) use would outweigh the risks or provide any meaningful benefit in the AD population. Aduhelm (aducanumab) has uncertain benefit in the face of known harms.

Kisunla (donanemab) for Alzheimer's disease

- The efficacy of Kisunla (donanemab) was evaluated in a single phase 3, double-blind, placebo-controlled trial (TRAILBLAZER-ALZ2, N=1736) in patients with AD with mild cognitive impairment or mild dementia. [4]
    * Results of the trial showed that patients treated with Kisunla (donanemab) achieved greater improvements compared to placebo based on the integrated Alzheimer's Disease Rating Scale (iADRS).

    * The iADRS is a cognitive and functional assessment scale that combines components of two other AD scales commonly used in clinical trials. Scores in the iADRS can range from 0 to 144 with lower scores indicating greater disease severity.
    * The minimal clinically important difference (MCID) for a score is 5 points in AD with mild cognitive impairment and 9 points in AD with mild dementia. After 18 months of treatment, the difference in the iADRS scores between Kisunla (donanemab) and placebo was 2.9, which did not reach the threshold for clinically meaningful change for cognition or function.[4]

- Although the existing evidence is promising, additional confirmatory trials are needed to establish the safety and efficacy of Kisunla (donanemab) in AD. Based on the results of the TRAILBLAZER trial, there is not enough evidence that any potential benefit of treatment with Kisunla (donanemab) outweighs the harms associated with treatment. Kisunla (donanemab has not yet proven to improve clinically relevant outcomes such as prolongation of independent functioning nor has it proven prevention of disease progression and disability, or mortality.

Leqembi (lecanemab) for Alzheimer's disease

- The FDA accelerated approval of Leqembi (lecanemab) was based on a single phase 2b, double-blind, placebo-controlled, dose finding trial (Study 201, N=856). A phase 3, global, multicenter, randomized, double-blind, placebo-controlled confirmatory trial (CLARITY AD, N=1795) was subsequently published and submitted to the FDA, leading to Leqembi (lecanemab) receiving full approval. [6]
- Patients in both pivotal trials had either mild cognitive impairment associated with AD or mild dementia due to AD. Patients with more severe disease were not studied. Confirmation of amyloid pathology [positive amyloid positron emission tomography (PET) scan or via cerebrospinal fluid (CSF)] was also required. [6 12]
    * Study 201: The primary endpoint was the change from baseline on a weighted composite score from selected items from three commonly used scales: Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB), the Mini-Mental State Examination (MMSE), and the AD assessment scale-Cognitive 14 Subscale (ADAS-Cog 14). At week 53, Leqembi (lecanemab) demonstrated a 64% likelihood of a 25% or greater slowing of progression on the primary endpoint compared to placebo. However, the results did NOT meet prespecified success criterion of 80%. [5]
    * CLARITY AD: A statistically significant improvement in the primary endpoint of the change from baseline of CDR-SB at month 18 was observed in the Leqembi (lecanemab) arm (difference vs. placebo -0.45 [95% CI -0.67 to -0.23, p-value of 0.00005], which represents a 27% reduction in progression). Although the results were statistically significant, the change in CDR-SB was less than the 1 to 2-point change that has been suggested as the MCID. [6]
- Both studies demonstrated significant improvements in amyloid plaques based on PET imaging; however, the effect of amyloid beta on clinical outcomes has not yet been established. There have been at least previous 16 trials of other drugs in which the

treatment arm did worse than placebo despite reduction of amyloid, albeit typically in a population with more severe disease. [2]

- Although the existing evidence is promising, additional confirmatory trials are needed to establish the safety and efficacy of Leqembi (lecanemab) in AD. Lecanemab (lecanemab) has not yet proven to improve clinically relevant outcomes such as prolongation of independent functioning nor has it proven prevention of disease progression and disability, or mortality. [13]
- Updated safety results from the open-label extension phase of the CLARITY AD trial were recently published. Although additional safety data for selection and monitoring of patients at higher risk of adverse events were described, the evidence for clinical efficacy (health outcomes) of Leqembi (lecanemab) still remains uncertain. [14]
- Although Leqembi (lecanemab) has been given full FDA approval, the evidence is limited to one trial which failed to meet its primary endpoint, and a second trial which showed a treatment effect which was not clinically meaningful. As such, there is not enough data available to show the benefits of Leqembi (lecanemab) use outweigh the risks or provide any meaningful benefit in the AD population; Leqembi (lecanemab) has uncertain benefit in the face of known harms.
- Additionally, a subcutaneous formulation of Leqembi (lecanemab) was recently approved by the FDA based on sub-studies of the CLARITY AD open-label extension trial. The studies were dose-finding studies for maintenance treatment after 18 months of the IV formulation. There is still no evidence that it improves a clinically meaningful net health outcome.

Safety

- Approximately 40% of patients on the high-dose Aduhelm (aducanumab) had amyloid related imaging abnormalities (ARIA) which may be linked to brain bleeds/swelling. [1]
- 36.8% of patients treated with Kisunla (donanemab) experienced ARIA reactions compared to 14.9% of patients treated with placebo. [15]
- 21.5% of patients on Leqembi (lecanemab) had ARIA reactions compared to only 9.5% in placebo. [7]
- Labeling for monoclonal antibodies for AD carry warnings for ARIA as well as require periodic brain magnetic resonance imaging (MRI) to monitor for ARIA.

Cross References
BlueCross BlueShield Association Medical Policy, 5.01.38 - Aducanumab for Alzheimer Disease [November 2025]

Codes	**Number**	**Description**
HCPCS	J0172	Injection, aducanumab-avwa (Aduhelm), 2 mg
HCPCS	J0175	Injection, donanemab (Kisunla), 17.5 mg
HCPCS	J0174	Injection, lecanemab-irmb (Leqembi), 1 mg

References

1. Aduhelm (aducanumab) [Prescribing Information]. Cambridge, MA: Biogen Inc.; February 2023.
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3. Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting. Combined FDA and Applicant PCNS Drugs Advisory Committee Briefing Document. November 6, 2020. Available at: https://www.fda.gov/media/143502/download.
4. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early sumptomatic Alzheimer disease: The TRAILBLAZER-ALZ2 randomized clinical trial. *JAMA*. 2023;330(6):512-27. PMID: 37459141
5. Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Abeta protofibril antibody. Alzheimers Res Ther. England, 2021:80.
6. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. *N Engl J Med*. 2023;388(1):9-21. PMID: 36449413
7. Leqembi (lecanemab) [Prescribing Information]. Cambridge, MA: Biogen Inc.; January 2023: Eisai, Inc.
8. American Academy of Neurology. Practice Guideline Update Summary: Mild Cognitive Impairment. Available at: https://www.aan.com/Guidelines/home/GuidelineDetail/881.
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11. FDA panel urges rejection of experimental Alzheimer's drug. November 6, 2020. Available at: https://abcnews.go.com/Health/wireStory/fda-panel-reviews-1st-alzheimers-drug-decades-74053911.
12. Center for Drug Evaluation and Research; U.S. Food and Drug Administration Summary Review for NDA 761269; lecanemab (Leqembi™). Secondary Center for Drug Evaluation and Research; U.S. Food and Drug Administration Summary Review for NDA 761269; lecanemab (Leqembi™) [cited 01/30/2023]. 'Available from:' https://www.accessdata.fda.gov/drugsatfda_docs/summary_review/2023/761269Orig1s000SumR.pdf.
13. Doctors for America. Press Release: Doctors for America's FDA Task Force is Deeply Concerned that the FDA Failed to Prioritize Patient Safety in Recent Alzheimer's Drug Approval. January 11,2023. Available at: https://doctorsforamerica.org/press-release-doctors-for-americas-fda-task-force-is-deeply-concerned-that-the-fda-failed-to-prioritize-patient-safety-in-recent-alzheimers-drug-approval/.
14. Honig LS, Sabbagh MN, van Dyck CH, et al. Updated safety results from phase 3 lecanemab study in early Alzheimer's disease. *Alzheimers Res Ther*. 2024;16(1):105. PMID: 38730496
15. Kisunla (donanemab) [Prescribing Information]. Indianopolis, IN: Eli Lilly; July 2024.

Revision History

Revision Date	Revision Summary
1/22/2026	Added Leqembi Iqlik (lecanemab) autoinjector for self-administration to policy. No criteria changes with this annual review.
12/12/2024	No criteria changes with this annual review.
9/19/2024	Added newly FDA-approved Kisunla (donanemab) to policy.
12/7/2023	No criteria changes with this annual review.
9/14/2023	Updated position statement to reflect recent Leqembi (lecanemab) full FDA approval. Leqembi (lecanemab) has now received full approval based upon the results of the CLARITY AD trial. No change to criteria.
3/16/2023	New combination policy (effective 4/15/2023) Combined newly FDA-approved drug Leqembi (lecanemab) with previously medication policy: dru670 Aduhelm (aducanumab), into a new policy, monoclonal antibodies for Alzheimer's disease with no change to intent.

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