Aduhelm™ (aducanumab-avwa)

100 mg/mL solution for infusion

Not actual size.

MANUFACTURER: Biogen

PRODUCT TRADE NAME: ADUHELM

GENERIC NAME: aducanumab-avwa

INDICATION

ADUHELM is indicated for the treatment of Alzheimer's disease. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Amyloid Related Imaging Abnormalities

- ADUHELM can cause amyloid related imaging abnormalities-edema (ARIA-E), which can be observed on MRI as brain edema or sulcal effusions, and amyloid related imaging abnormalities-hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis
- Obtain recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment. The safety of ADUHELM in patients with any pre-treatment localized superficial siderosis, 10 or more brain microhemorrhages, and/or with a brain hemorrhage greater than 1 cm within one year of treatment initiation has not been established
- In clinical studies of ADUHELM, the severity of ARIA was classified by radiographic criteria. **Mild ARIA-E:** FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location < 5 cm. **Moderate ARIA-E:** FLAIR hyperintensity 5 to 10 cm, or more than 1 site of involvement, each measuring < 10 cm. **Severe ARIA-E:** FLAIR hyperintensity measuring > 10 cm, often with significant subcortical white matter and/or sulcal involvement. One or more separate sites of involvement may be noted. **Mild ARIA-H microhemorrhage:** ≤ 4 new incident microhemorrhages. **Moderate ARIA-H microhemorrhage:** 5 to 9 new incident microhemorrhages. **Severe ARIA-H microhemorrhage:** 10 or more new incident microhemorrhages. **Mild ARIA-H superficial siderosis:** 1 focal area of superficial siderosis. **Moderate ARIA-H superficial siderosis:** 2 focal areas of superficial siderosis. **Severe ARIA-H superficial siderosis:** > 2 focal areas of superficial siderosis

Please see additional Important Safety Information throughout and full Prescribing Information.

PRODUCT INFORMATION

How supplied[1]	ADUHELM injection is a preservative-free, sterile, clear to opalescent, and colorless to yellow solution
Storage requirements[1]	Store ADUHELM in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze or shake. If no refrigeration is available, ADUHELM may be stored unopened in its original carton, protected from light, at or below 25°C (77°F) for up to 3 days. Prior to dilution, unopened vials of ADUHELM can be removed from and returned to the refrigerator if necessary. Total combined time out of refrigeration and exposure to light should not exceed 24 hours at room temperature. After dilution, immediate use is recommended. If not administered immediately, store the prepared solution of ADUHELM in 0.9% sodium chloride injection, USP for up to 3 days at 2°C to 8°C (36°F-46°F), or at room temperature up to 30°C (86°F) for up to 12 hours
Packaging[1]	Single-dose vial
Individual carton information	Dimensions (inches): 2.4769 w x 3.2396 h x 2.3195 d Weight: 0.09 lbs Volume: 18.612051 mL
Shipping case information (36 units per case)	Dimensions (inches): 7.9375 w x 7.25 h x 14.6255 d Weight: 3.7 lbs Volume: 841.65182 mL

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- In Studies 1 and 2, ARIA (-E and/or -H) was observed in 41% of patients treated with ADUHELM with a planned dose of 10 mg/kg (454 out of 1105), compared to 10% of patients on placebo (111 out of 1087)
- ARIA-E was observed in 35% of patients treated with ADUHELM 10 mg/kg, compared to 3% of patients on placebo. The incidence of ARIA-E was higher in apolipoprotein E ε4 (ApoE ε4) carriers than in ApoE ε4 non-carriers (42% and 20%, respectively). The majority of ARIA-E radiographic events occurred early in treatment (within the first 8 doses), although ARIA can occur at any time. Among patients treated with a planned dose of ADUHELM 10 mg/kg who had ARIA-E, the maximum radiographic severity was mild in 30%, moderate in 58%, and severe in 13% of patients. Resolution occurred in 68% of ARIA-E patients by 12 weeks, 91% by 20 weeks, and 98% overall after detection. 10% of all patients who received ADUHELM 10 mg/kg had more than one episode of ARIA-E
- ARIA-H in the setting of ARIA-E associated with the use of ADUHELM 10 mg/kg was observed in 21% of patients treated with ADUHELM 10 mg/kg, compared to 1% of patients on placebo. There was no imbalance in isolated ARIA-H (i.e., ARIA-H in patients who did not also experience ARIA-E) between ADUHELM and placebo. There was no imbalance in hemorrhage greater than 1 cm between ADUHELM and placebo

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PRODUCT INFORMATION *(cont'd)*

WAC[2]	$952.00 per 170 mg/1.7 mL (100 mg/mL) single-dose vial $1680.00 per 300 mg/3 mL (100 mg/mL) single-dose vial	
NDC numbers[1]	**NDC 64406-101-01**	170 mg/1.7 mL (100 mg/mL) single-dose vial
	NDC 64406-102-02	300 mg/3 mL (100 mg/mL) single-dose vial
HCPCS codes[3,4]	**J-code**	**J3590:** Unclassified biologics
	C-code	**C9399:** Unclassified drugs or biologicals
Potential ICD-10-CM codes for Alzheimer's disease diagnosis[5,6]	**G30.0:** Alzheimer's disease with early onset	
	G30.1: Alzheimer's disease with late onset	
	G30.8: Other Alzheimer's disease	
	G31.84: Mild cognitive impairment, so stated	

HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=*International Classification of Diseases, Tenth Revision, Clinical Modification*; NDC=National Drug Code; WAC=wholesale acquisition cost.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- Clinical symptoms were present in 24% of patients treated with ADUHELM 10 mg/kg who had an observation of ARIA (-E and/or -H), compared to 5% of patients on placebo. The most common symptom in patients treated with ADUHELM 10 mg/kg with ARIA was headache (13%). Other frequent symptoms were confusion/delirium/altered mental status/disorientation (5%), dizziness/vertigo (4%), visual disturbance (2%), and nausea (2%). Serious symptoms associated with ARIA were reported in 0.3% of patients treated with ADUHELM 10 mg/kg. Clinical symptoms resolved in the majority of patients (88%) during the period of observation
- Enhanced clinical vigilance for ARIA is recommended during the first 8 doses of treatment with ADUHELM, particularly during titration, as this is the time the majority of ARIA was observed in Studies 1 and 2. If a patient experiences symptoms which could be suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated. If ARIA is observed on MRI in the presence of clinical symptoms, careful clinical evaluation should be performed prior to continuing treatment
- Obtain brain MRIs prior to the 7th infusion (first dose of 10 mg/kg) and 12th infusion (sixth dose of 10 mg/kg) of ADUHELM to evaluate for the presence of asymptomatic ARIA. For patients with radiographic findings of ARIA, enhanced clinical vigilance is recommended. Additional MRIs may be considered if clinically indicated. If radiographically severe ARIA-H is observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrates radiographic stabilization (i.e., no increase in size or number of ARIA-H). For ARIA-E or mild/moderate ARIA-H, treatment may continue with caution. If dosing is temporarily suspended, dosing may resume at that same dose and titration schedule. There are no systematic data on continued dosing with ADUHELM following detection of radiographically moderate or severe ARIA. In Studies 1 and 2, temporary dose suspension was required for radiographically moderate or severe ARIA-E and radiographically moderate ARIA-H. In Studies 1 and 2, permanent discontinuation of dosing was required for radiographically severe ARIA-H. The benefits of reaching and maintaining the 10 mg/kg dose should be considered when evaluating a potential dose suspension

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PRODUCT INFORMATION *(cont'd)*

CPT® codes for administration[7]	**Injection and intravenous infusion chemotherapy and other highly complex drug or highly complex biologic agent administration** **96413:** Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
	Therapeutic, prophylactic, and diagnostic injections and infusions (excludes chemotherapy and other highly complex drug or highly complex biologic agent administration) **96365:** Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour

CPT=*Current Procedural Terminology*.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity Reactions

- Angioedema and urticaria were reported in one patient in the placebo-controlled period of Studies 1 and 2, and occurred during the ADUHELM infusion. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction, and initiate appropriate therapy

ADVERSE REACTIONS

- In the combined placebo-controlled and long-term extension periods, 5% (66 out of 1386) of patients in the 10 mg/kg dose group withdrew from the study because of an adverse reaction. The most common adverse reaction resulting in study withdrawal in the combined placebo-controlled and long-term extension periods was ARIA-H superficial siderosis
- The most common adverse reactions reported in at least 2% of patients treated with ADUHELM 10 mg/kg and at least 2% more frequently than in patients on placebo in Studies 1 and 2 were ARIA-E (35% ADUHELM vs. 3% placebo), headache (21% ADUHELM vs. 16% placebo), ARIA-H microhemorrhage (19% ADUHELM vs. 7% placebo), ARIA-H superficial siderosis (15% ADUHELM vs. 2% placebo), fall (15% ADUHELM vs. 12% placebo), diarrhea (9% ADUHELM vs. 7% placebo), and confusion/delirium/altered mental status/disorientation (8% ADUHELM vs. 4% placebo)
- Immunogenicity: The immunogenicity of ADUHELM has been evaluated using an in vitro assay for the detection of binding anti-aducanumab-avwa antibodies. In up to 41 months of treatment in the combined placebo-controlled and long-term extension periods of Studies 1 and 2, up to 0.6% (15/2689) of patients receiving ADUHELM once monthly developed anti-aducanumab-avwa antibodies. Based on the limited number of patients who tested positive for anti-aducanumab-avwa antibodies, no observations were made concerning a potential effect of neutralizing activity of anti-aducanumab-avwa antibodies on exposure or efficacy; however, the available data are too limited to make definitive conclusions regarding an effect on pharmacokinetics, safety, or efficacy of ADUHELM. Quantification of neutralizing anti-aducanumab-avwa antibodies has not been assessed

Please see additional Important Safety Information throughout and full Prescribing Information.

References: 1. ADUHELM [Prescribing Information]. Cambridge, MA: Biogen; June 2021. **2.** Biogen. Data on file. **3.** HCPCS code J3590. HCPCS Codes website. https://hcpcs.codes/j-codes/J3590/. Accessed April 30, 2021. **4.** HCPCS code C9399. HCPCS Codes website. https://hcpcs.codes/c-codes/C9399/. Accessed April 30, 2021. **5.** Alzheimer's disease G30. ICD10Data website. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G30-G32/G30-. Accessed April 30, 2021. **6.** American Medical Association. *CPT® 2020 Professional Edition*. Chicago, IL: American Medical Association; 2019. **7.** Alzheimer's disease G31. ICD10Data website. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G30-G32/G31-. Accessed April 30, 2021.

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