Aduhelm®
(aducanumab-avwa)
100 mg/mL injection, for intravenous use

PATH Patient Access to Therapy

ADUHELM Educational Module

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Biogen

Table of Contents

Aduhelm®
(aducanumab-avwa)
100 mg/mL injection, for intravenous use

Aduhelm®
(aducanumab-avwa)
100 mg/mL injection, for intravenous use

INDICATION AND IMPORTANT SAFETY INFORMATION

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

INDICATION

Aduhelm®
(aducanumab-avwa)
100 mg/mL injection, for intravenous use

ADUHELM is indicated for the treatment of Alzheimer's disease. Treatment with ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. 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).

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IMPORTANT SAFETY INFORMATION

Aduhelm®
(aducanumab-avwa)
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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. The safety of ADUHELM in patients with 10 or more brain microhemorrhages, any pre-treatment localized superficial siderosis, and/or with a brain hemorrhage greater than 1 cm within one year of treatment initiation has not been established

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm® (aducanumab-avwa)
100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- 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
- 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)

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm®
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100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- ARIA-E was observed in 35% of patients treated with ADUHELM 10 mg/kg, compared to 3% of patients on placebo
- In Studies 1 and 2, 16% of patients in the ADUHELM 10 mg/kg group were apolipoprotein E ε4 (ApoE ε4) homozygotes, 51% were heterozygotes, and 32% were noncarriers. In these studies, randomization was stratified by ApoE ε4 carrier status (i.e., carrier or noncarrier); therefore, interpretation of analyses by ApoE ε4 homozygous and heterozygous carrier status should consider the limitations of the unbalanced subgroups and the small number of homozygotes enrolled in the study. The incidence of ARIA-E was higher in ApoE ε4 carriers than in ApoE ε4 noncarriers (64% in homozygotes, 35% in heterozygotes, and 20% in noncarriers). Severe radiographic ARIA-E occurred in 11% of homozygotes, 4% of heterozygotes, and 2% of noncarriers. However, the incidence of serious adverse reactions with ARIA-E, including risk of death, persistent or significant disability or incapacity, hospitalization, or other medically important event that may require intervention to prevent serious outcomes, was similar for ApoE ε4 carriers and noncarriers (2% in homozygotes, 1% in heterozygotes, 2% in noncarriers). The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers. Testing for ApoE ε4 carrier status may be considered when initiating treatment with ADUHELM to inform the risk of developing ARIA

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm®
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100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- 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, and 1% had three or more episodes 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. Intracerebral hemorrhage greater than 1 cm in diameter was reported in 0.5% of patients after treatment with ADUHELM 10 mg/kg compared to 0.4% of patients on placebo

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm®
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100 mg/mL injection, for intravenous use

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. Overall, recurrent episodes of ARIA-E were less frequently symptomatic (12%) compared with initial episodes of ARIA-E (25%). Clinical symptoms associated with ARIA resolved in the majority of patients (88%) during the period of observation
- Seizure, including status epilepticus, which can be serious and life-threatening, has been associated with ARIA. The overall incidence of seizure, independent of ARIA, was 0.5% in the 10 mg/kg ADUHELM group and 0.8% in the placebo group in Studies 1 and 2. In patients with ARIA in the 10 mg/kg ADUHELM group, the incidence of seizure was 0.7%. Status epilepticus was reported in the placebo-controlled and long-term extension studies in patients treated with ADUHELM

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm® (aducanumab-avwa)
100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

Monitoring and Management

- *Monitoring for ARIA-E and ARIA-H*
  - Obtain recent (within one year) baseline brain magnetic resonance imaging (MRI) prior to initiating treatment
  - 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 suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment
  - Obtain brain MRIs prior to the 5th infusion (first dose of 6 mg/kg), 7th infusion (first dose of 10 mg/kg), 9th infusion (third 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

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm® (aducanumab-avwa)
100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- *ARIA-E Management*
  - In Studies 1 and 2, dosing was suspended for symptomatic patients with ARIA-E of any severity and for asymptomatic patients with moderate or severe ARIA-E. There is limited experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic moderate or severe ARIA-E
  - Recommendations for dosing in patients with ARIA-E are dependent on clinical symptoms and radiographic severity. There is limited data in dosing patients who experienced three or more episodes of ARIA-E. Use clinical judgment in considering whether to continue dosing in patients with recurrent ARIA-E (more than two episodes)

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm® (aducanumab-avwa)
100 mg/mL injection, for intravenous use

WARNINGS AND PRECAUTIONS (cont'd)

Amyloid Related Imaging Abnormalities (cont'd)

- *ARIA-H Management*
  - In Studies 1 and 2, dosing was suspended for symptomatic patients with ARIA-H of any severity and for asymptomatic patients with moderate or severe ARIA-H. Dosing was permanently discontinued for any severe ARIA-H
  - Recommendations for dosing in patients with ARIA-H are dependent on the type of ARIA-H and radiographic severity

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm®
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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

IMPORTANT SAFETY INFORMATION (cont'd)

Aduhelm® (aducanumab-avwa)
100 mg/mL injection, for intravenous use

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, headache, ARIA-H microhemorrhage, ARIA-H superficial siderosis, fall, diarrhea, and confusion/delirium/altered mental status/disorientation
- 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 Important Safety Information on pages 5-14 and full Prescribing Information.

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Objectives

Objectives

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- Increase confidence around identifying patients for ADUHELM
- Ensure understanding about safety, dosing, monitoring, and management of patients being treated with ADUHELM per the FDA-approved Prescribing Information
- Complete educational attestation requirements for becoming enrolled in the PATH program

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

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PATH Patient Access to Therapy

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PATH Patient Access to Therapy

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Enroll in the PATH program, and you could help your eligible patients access ADUHELM at a lower cost.* Enrollment for a provider or treatment site only needs to be completed once.

- ✓ **Complete Educational Module**
- ✓ **Complete the PATH program enrollment form by contacting Biogen Support Services for Patients (*including attestation fields verifying completion of educational module*)**
- ✓ **Help patients enroll in the PATH program to determine eligibility**

To learn more about the PATH program, please reach out to your Biogen account manager or Biogen Support Services for Patients.

*Patient out-of-pocket cost may vary based on financial and other income considerations. This program only covers the cost of ADUHELM. Other services or fees associated with treatment are not included and patient may have out-of-pocket costs associated with the same. Other restrictions apply. Biogen reserves the right to modify or discontinue this program with respect to any patient, or in its entirety, at any time. New enrollment ends 9/1/2023; program ends 12/31/2023. Contact Biogen Support Services for Patients for full program details and Terms and Conditions.

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

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100 mg/mL injection, for intravenous use

Patient Criteria for PATH Program

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Patient Criteria for PATH Program

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Stage of Alzheimer's disease[1]

ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, consistent with the population treated with ADUHELM in clinical trials.

Before starting a patient on ADUHELM[1]

- Confirm the presence of amyloid beta pathology prior to initiating treatment
- Obtain recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment

Only patients that align with the criteria above may be considered for the PATH program.

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Safety, Dosing, Monitoring, and Management

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Warnings and Precautions: Amyloid-related imaging abnormalities

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ADUHELM can cause amyloid-related imaging abnormalities (ARIA)[1]

- Amyloid-related imaging abnormalities (ARIA) is a term used to describe a spectrum of imaging abnormalities detected via magnetic resonance imaging (MRI). They can present as[1]:
  - Brain edema or sulcal effusions (ARIA-E)
  - Hemosiderin deposition, which includes microhemorrhage and superficial siderosis (ARIA-H)
- In the phase 3 studies, ARIA was detected through protocol-defined routine MRI monitoring[2]
- The safety of ADUHELM in patients with 10 or more brain microhemorrhages, any pretreatment localized superficial siderosis, and/or with a brain hemorrhage greater than 1 cm within one year of treatment initiation has not been established[1]
- ARIA (-E and/or -H) occurred in 41% of patients treated with ADUHELM 10 mg/kg (454/1105) compared to 10% of patients on placebo (111/1087)[1]

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Warnings and Precautions: Amyloid-related imaging abnormalities

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In the Phase 3 trials of ADUHELM, the severity of ARIA was classified under the following criteria[1]

ARIA TYPE	Radiographic Severity		
	MILD	MODERATE	SEVERE
ARIA-E	FLAIR hyperintensity confined to sulcus and/or cortex/subcortical white matter in one location <5 cm	FLAIR hyperintensity 5 to 10 cm, or more than 1 site of involvement, each measuring <10 cm	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.
ARIA-H microhemorrhage	≤4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	>2 focal areas of superficial siderosis

FLAIR=fluid-attenuated inversion recovery.

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Warnings and Precautions: Amyloid-related imaging abnormalities

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100 mg/mL injection, for intravenous use

ARIA-E occurred in 35% of patients treated with ADUHELM (10 mg/kg) vs 3% with placebo[1]

- The majority of events occurred early in treatment (within the first 8 doses), although ARIA can occur at any time
- 10% of patients who received ADUHELM (10 mg/kg) had >1 episode of ARIA-E and 1% had ≥3 episodes of ARIA-E

ARIA-E: Maximum radiographic severity[1]

Mild	30%
Moderate	58%
Severe	13%

ARIA-E: Resolution after detection[1]

12 weeks	68%
20 weeks	91%
Overall	98%

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Warnings and Precautions: Amyloid-related imaging abnormalities

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In Studies 1 and 2, the incidence of ARIA-E was higher in ApoE ε4 carriers than noncarriers in the ADUHELM (10 mg/kg) group[1]

ApoE ε4 Status	Homozygotes (16%)	Heterozygotes (51%)	Noncarriers (32%)
ARIA-E	64%	35%	20%
Severe Radiographic ARIA-E	11%	4%	2%
Severe Adverse Reactions with ARIA-E	2%	1%	2%

- Randomization was stratified by ApoE ε4 carrier status (ie, carrier or noncarrier). Therefore, interpretation of analysis by ApoE ε4 homozygous and heterozygous carrier status should consider the limitations of the unbalanced subgroups and the small number of homozygotes enrolled in the study

Warnings and Precautions: Amyloid-related imaging abnormalities

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In Studies 1 and 2, the incidence of ARIA-E was higher in ApoE ε4 carriers than noncarriers in the ADUHELM (10 mg/kg) group (cont'd)[1]

- The incidence of serious adverse reactions with ARIA-E, including risk of death, persistent or significant disability or incapacity, hospitalization, or other medically important event that may require intervention to prevent serious outcomes, was similar for ApoE ε4 carriers and noncarriers
- The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers
- Testing for ApoE ε4 carrier status may be considered when initiating treatment with ADUHELM to inform the risk of developing ARIA

Warnings and Precautions: Amyloid-related imaging abnormalities

Aduhelm® (aducanumab-avwa) 100 mg/mL injection, for intravenous use

In the setting of ARIA-E, ARIA-H occurred in 21% of patients treated with ADUHELM (10 mg/kg) vs 1% for placebo[1]

- There was no imbalance in isolated ARIA-H (eg, ARIA-H in patients who did not also experience ARIA-E) between ADUHELM and placebo
- Intracerebral hemorrhage >1 cm in diameter was reported in 0.5% of patients after treatment with ADUHELM (10 mg/kg) vs 0.4% for placebo

Warnings and Precautions: Amyloid-related imaging abnormalities

Aduhelm® (aducanumab-avwa)
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Patients were excluded from enrollment in Studies 1 and 2 for the following criteria[1]:

- Prior intracerebral hemorrhage >1 cm in diameter
- >4 microhemorrhages
- Superficial siderosis
- History of diffuse white matter disease
- Use of antiplatelet/anticoagulant medications, other than ≤325 mg of daily aspirin

Although patients were allowed to receive aspirin in daily doses of 325 mg or less, some patients, because of intercurrent medical events that occurred after enrollment and required treatment, received aspirin in doses greater than 325 mg, other antiplatelet drugs, or anticoagulants during Studies 1 and 2

Warnings and Precautions: Amyloid-related imaging abnormalities

Aduhelm® (aducanumab-avwa) 100 mg/mL injection, for intravenous use

Patients were excluded from enrollment in Studies 1 and 2 for the following criteria (cont'd)[1]:

- In patients treated with ADUHELM (10 mg/kg) during the placebo-controlled period of the studies, those who received any antithrombotic medication* (n=435) did not have an increased risk for ARIA or intracerebral hemorrhage vs those who did not receive any antithrombotic medication (n=670)

- The majority of exposures to antithrombotic medications were to aspirin; 77 patients were exposed to other antiplatelet drugs or anticoagulants, limiting any definitive conclusions about the risk of ARIA or intracerebral hemorrhage in patients taking other antiplatelet drugs or anticoagulants

*Aspirin at any dose, other antiplatelet drugs, or anticoagulants.

Warnings and Precautions: Amyloid-related imaging abnormalities

Aduhelm® (aducanumab-avwa)
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Clinical symptoms were present in 24% of patients treated with ADUHELM (10 mg/kg) who had an observation of ARIA (-E and/or -H) vs 5% with placebo[1]

- The most common symptom 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
- Overall, recurrent episodes of ARIA-E were less frequently symptomatic (12%) compared with initial episodes of ARIA-E (25%)
- Clinical symptoms associated with ARIA-E resolved in the majority of patients (88%) during the period of observation

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Warnings and Precautions: Amyloid-related imaging abnormalities

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Seizure, including status epilepticus, which can be serious and life-threatening, has been associated with ARIA[1]

- The overall incidence of seizure, independent of ARIA, was 0.5% in the ADUHELM (10 mg/kg) group and 0.8% in the placebo group in Studies 1 and 2
- In patients with ARIA in ADUHELM (10 mg/kg) group, the incidence of seizure was 0.7%
- Status epilepticus was reported in the placebo-controlled and long-term extension studies in patients treated with ADUHELM

Warnings and Precautions: Amyloid-related imaging abnormalities

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Monitoring and Management for ARIA-E and ARIA-H[1]

- Obtain recent (within one year) baseline brain magnetic resonance imaging (MRI) prior to initiating treatment
- 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 suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment
- Obtain brain MRIs prior to the 5th infusion (first dose of 6 mg/kg), 7th infusion (first dose of 10mg/kg), 9th infusion (third 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

Warnings and Precautions: Amyloid-related imaging abnormalities

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ARIA-E Management[1]

- In Studies 1 and 2, dosing was suspended for symptomatic patients with ARIA-E of any severity and for asymptomatic patients with moderate or severe ARIA-E. There is limited experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic moderate or severe ARIA-E

- Recommendations for dosing in patients with ARIA-E are dependent on clinical symptoms and radiographic severity. There is limited data in dosing patients who experienced three or more episodes of ARIA-E. Use clinical judgment in considering whether to continue dosing in patients with recurrent ARIA-E (>2 episodes)

Warnings and Precautions: Amyloid-related imaging abnormalities

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ARIA-H Management[1]

- In Studies 1 and 2, dosing was suspended for symptomatic patients with ARIA-H of any severity and for asymptomatic patients with moderate or severe ARIA-H. Dosing was permanently discontinued for any severe ARIA-H
- Recommendations for dosing in patients with ARIA-H are dependent on the type of ARIA-H and radiographic severity

Adverse Reactions

Aduhelm® (aducanumab-avwa)
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Adverse reactions reported in ≥2% of patients treated with at least one dose of ADUHELM 10 mg/kg and ≥2% higher than placebo in Studies 1 and 2[1]

	ADUHELM 10 mg/kg	Placebo
ADVERSE REACTION	**N=1105**	**N=1087**
ARIA-E	35%	3%
Headache	21%	16%
ARIA-H microhemorrhage	19%	7%
ARIA-H superficial siderosis	15%	2%
Fall	15%	12%
Diarrhea	9%	7%
Confusion/delirium/altered mental status/disorientation	8%	4%

- 5% (66/1386) of patients in the ADUHELM 10 mg/kg group withdrew from the study due to an adverse reaction in the combined placebo-controlled and LTE periods
- ARIA-H superficial siderosis was the most common adverse reaction resulting in study withdrawal

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Adverse Reactions

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Immunogenicity[1]

- 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

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

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Before treatment initiation with ADUHELM[1]

- Confirm the presence of Aβ pathology prior to initiating treatment
- Obtain recent (within 1 year) brain MRI prior to initiating treatment

After initial titration, the recommended dose is 10 mg/kg, administered as an intravenous (IV) infusion over ~1 hour every 4 weeks[1]

Dosing schedule[1]

IV Infusion (every 4 weeks)	ADUHELM Dosage (administered over approximately one hour)
Infusion 1 and 2	1 mg/kg
Infusion 3 and 4	3 mg/kg
Infusion 5 and 6	6 mg/kg
Infusion 7 and beyond	10 mg/kg

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

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After initial titration, the recommended dose is 10 mg/kg, administered as an intravenous (IV) infusion over ~1 hour every 4 weeks (cont'd)[1]

- ADUHELM is titrated over the course of 7 doses to achieve the recommended dose of 10 mg/kg
- Infusions are to be administered over ~1 hour every 4 weeks and at least 21 days apart
- If an infusion is missed, resume the schedule at the same dose as soon as possible

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

Aduhelm®
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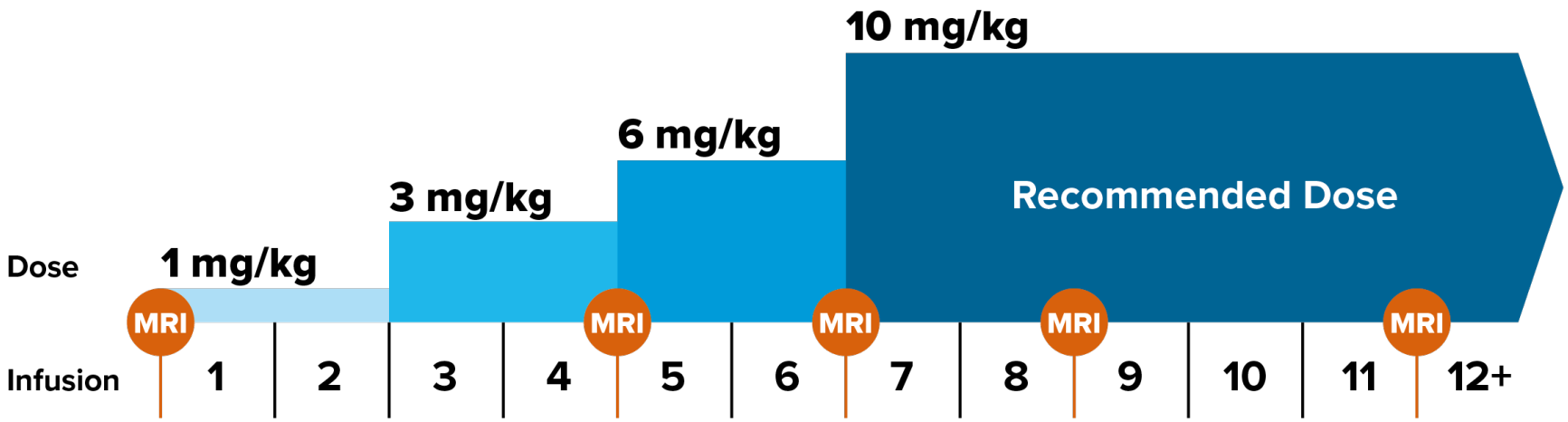
Obtain brain MRIs prior to infusions 1, 5, 7, 9, and 12 of ADUHELM to evaluate for the presence of ARIA[1]



Please see Important Safety Information on pages 5-14 and full Prescribing Information.

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

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Enhanced vigilance for ARIA is recommended for the first 8 doses of treatment[1]

- If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI testing if indicated
- If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment
- For patients with radiographic findings of ARIA, enhanced clinical vigilance is recommended. Additional MRIs may be considered if clinically indicated

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

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Recommendations for dosing interruptions in patients with ARIA[1]

- If dosing is resumed following a temporary suspension, dosing may resume at that same dose and titration schedule prior to the dosing suspension
- The benefits of reaching and maintaining the 10 mg/kg dose should be considered when evaluating a potential dose suspension

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

Aduhelm® (aducanumab-avwa) 100 mg/mL injection, for intravenous use

Recommendations for dosing interruptions in patients with ARIA (cont'd)[1]

The dosing interruptions for patients with ARIA-E are provided in the table below.

Dosing Recommendations for Patients with ARIA-E

Clinical Symptom Severity	ARIA-E Severity on MRI		
	MILD	MODERATE	SEVERE
ASYMPTOMATIC	May continue dosing at current dose and schedule	Suspend dosing*	Suspend dosing*
MILD	May continue dosing based on clinical judgement	Suspend dosing*	
MODERATE OR SEVERE	Suspend dosing*		

*Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment.

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Recommendations for dosing interruptions in patients with ARIA (cont'd)[1]

The dosing interruptions for patients with ARIA-H are provided in table below.

Dosing Recommendations for Patients with ARIA-H

Clinical Symptom Severity	ARIA-H Severity on MRI		
	MILD	MODERATE	SEVERE
ASYMPTOMATIC	May continue dosing at current dose and schedule	Suspend dosing*	Suspend dosing†
SYMPTOMATIC	Suspend dosing*	Suspend dosing*	

*Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment.
†Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; use clinical judgment in considering whether to continue treatment or permanently discontinue ADUHELM.

Initiating ADUHELM, monitoring for ARIA, and dosing interruptions

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Recommendations for dosing interruptions in patients with ARIA (cont'd)[1]

- In patients who develop intracerebral hemorrhage >1 cm in diameter during treatment with ADUHELM, suspend dosing until MRI demonstrates radiographic stabilization and symptoms, if present, resolve
  - In Studies 1 and 2, dosing was permanently discontinued for patients who developed intracerebral hemorrhage >1 cm in diameter
  - Use clinical judgment in considering whether to continue treatment or permanently discontinue

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Patient Counseling

Patient Counseling

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Advise the patient or their caregiver to read the FDA-approved patient labeling (Medication Guide) and inform them to:

Watch for symptoms of ARIA. ARIA most commonly presents as temporary swelling in areas of the brain that usually resolves over time. Some people may also have small spots of bleeding in or on the surface of the brain. Inform patients that most people with swelling in areas of the brain do not experience symptoms, however, some people may experience symptoms such as headache, confusion, dizziness, vision changes, nausea, or seizure.[1]

Contact the patient's physician immediately if the patient experiences any of these symptoms or any other symptoms.

Talk to the patient's doctor about the need for MRI to monitor for ARIA.

Patient Counseling

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Advise the patient or their caregiver to read the FDA-approved patient labeling (Medication Guide) and inform them to (cont'd):

Be aware of **hypersensitivity reactions**, which may include angioedema or urticaria and to contact their healthcare provider if hypersensitivity reactions occur.[1]

Schedule the **next infusion appointment**. Schedule an **MRI** prior to the next infusion if clinically indicated.

Module Complete

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You have completed the ADUHELM Educational Module. Educational requirements for the PATH program have now been fulfilled. Please reach out to your Biogen account manager or call the number below to access your enrollment form.

READY TO ENROLL?

Contact Biogen Support Services for Patients at **1-833-425-9360**

Please see Important Safety Information on pages 5-14 and full Prescribing Information.

References: 1. ADUHELM [Prescribing Information]. Cambridge, MA: Biogen; April 2022. **2**. Data on file ARIA 2021. Biogen.

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