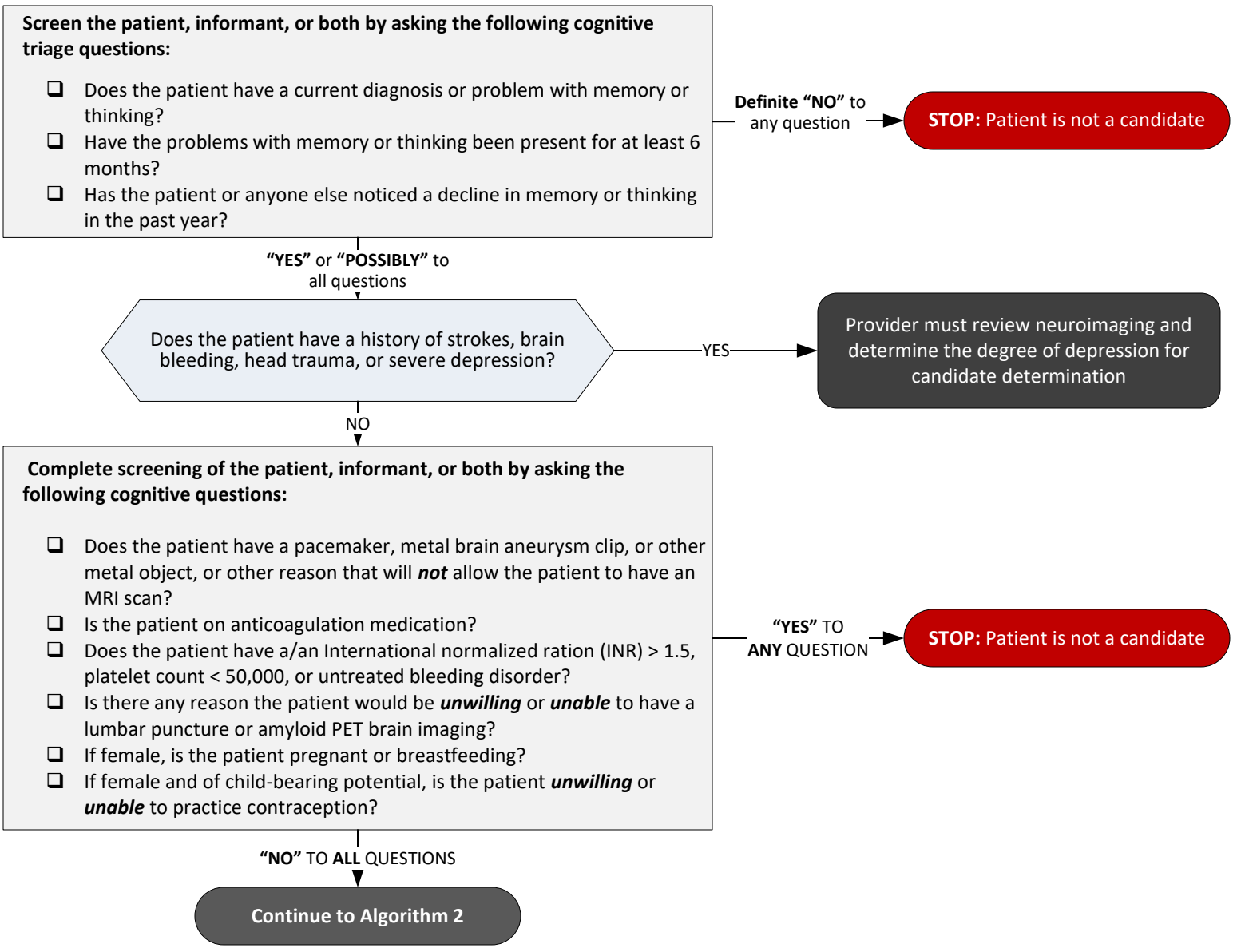
Anti-Amyloid Monoclonal Antibody Prescribing in Patients with Alzheimer's

What You Need to Know

- Aducanumab and Lecanemab are amyloid beta-directed human immunoglobulin G1 (IgG1) monoclonal antibody indicated for the treatment of Alzheimer's disease (AD).
- They work by binding to both aggregated soluble and insoluble forms of Aβ, which includes oligomers, protofibrils, and fibrils.
- Treatment with anti-amyloid monoclonal antibodies should be initiated in patients with Mild Cognitive Impairment (MCI) due to AD or mild AD 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.
- It should be noted continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials (see references 1-5 for drug trial information).
- The full process of evaluation, selection and treatment should be managed by the Memory Disorders Clinic in Neurology; the general practitioner/PCP should make a referral to Neurology (614-293-4969) as soon as cognitive decline/memory disorder is suspected.

Algorithm 1: Anti-Amyloid Monoclonal Antibodies Patient Selection

Completed by Memory Disorders Clinic Staff



THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Algorithm 2: Required Initial Assessments

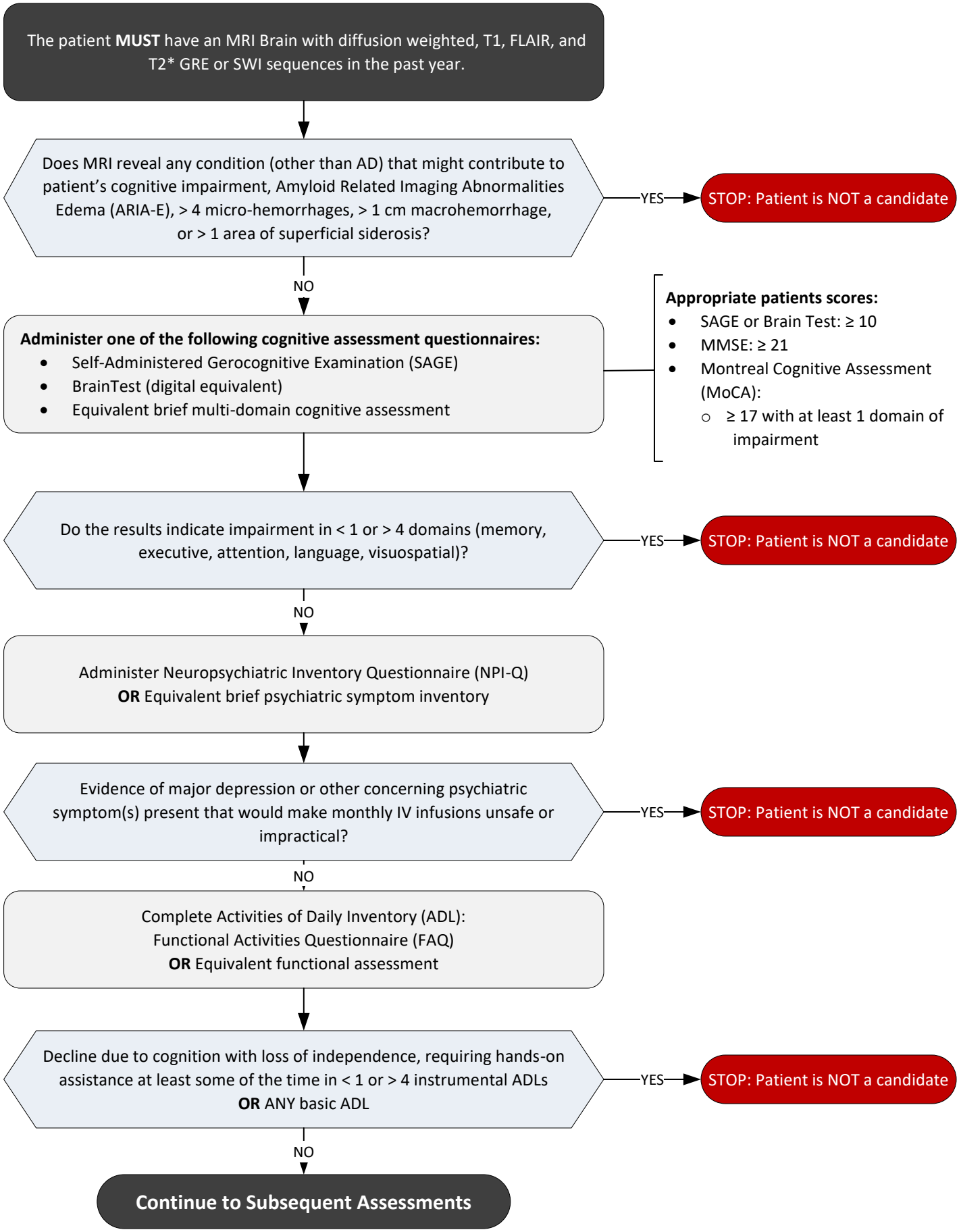


Table 1. Subsequent Assessments

NOTE: Include patient and care partner in decision-making. Discussion should include requirements for therapy, potential adverse events, required safety monitoring, and potential benefits.

Cognitive	Laboratory Workup Considerations	Ongoing Monitoring

Provider evaluation MUST include detailed neurological and physical examination to discern presence of Mild Cognitive Impairment (MCI) due to AD or mild AD dementia stage of disease.
 	
• Cognition decline cannot be explained by any condition other than AD, including:
  ○ Behavioral symptoms, medications, reversible causes, substantial concomitant cerebrovascular disease, core features of dementia with Lewy bodies (DLB), prominent features of behavioral variant frontotemporal dementia (FTD) or prominent features of semantic or non-fluent/agrammatic variants of primary progressive aphasia (PPA)
• Additional laboratory assessment may be required to rule out other causes of cognition impairment.
• Diagnosis may require more detailed neuropsychological evaluation(s) to determine the pattern of cognitive decline and severity level consistent with MCI due to AD or mild AD dementia.
	Patient MUST have positive amyloid testing either by:
	1. Amyloid PET neuroimaging **– OR –**
	2. Lumbar puncture for CSF amyloid beta 42, tau, and p-tau (ensure normal platelets, INR, PT and PTT labs)
	  ▪ **Patient preparation:** 12 hours prior to procedure, the patient should not take multivitamins or dietary supplements containing biotin.
	  ▪ **Specimen volume:** 2 mL
	  ▪ **Specimen collection:** Perform lumbar puncture and discard the first 1 to 2 mL of cerebrospinal fluid (CSF). Collect 2 mL of CSF directly into a **low bind polypropylene tube** using drip method (Polystyrene collection tubes are **NOT** acceptable and may result in falsely low Abeta42 concentrations).
	  ▪ **Send CSF in tube to OSU lab** (in IHIS, order: Alzheimer's Disease Eval, CSF)
	• Provider to determine if optional genotyping for ApoE with or without genetic counseling is desired, as ApoE €4 genotype increases the risks of anti-amyloid monoclonal antibodies.
		• **Monitor cognition and function every 6 months**
		  ○ If patient progresses to moderate AD stages either by cognitive impairment or functional decline, anti-amyloid monoclonal antibody therapy should be discontinued **OR**
		  ○ Provider to enter statement in IHIS that cognitive or functional declines was unrelated to AD progression and that anti-amyloid monoclonal antibody is still appropriate.
		• **Repeat amyloid PET or CSF amyloid levels after 78 weeks, then every 6 months if on treatment.**
		• Discontinue anti-amyloid monoclonal antibody if amyloid levels are lowered to normal range.

Table 2. Anti-Amyloid Monoclonal Antibodies

- Order in IHIS: **Ambulatory Referral Infusion: Infusion Morehouse**
  - In the comments add: **Aducanumab or Lecanemab**
- **Note: Prior authorization (PA) is required for some insurance plans.**
  - Infusion staff will obtain the PA if required and notify patients of approval and co-pay status. CMS will pay as per labeling.

Aducanumab Infusion and Titration Schedule: Titrate to the highest dose

Infusion (every 4 weeks)	Dose (administer over 1 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

Lecanemab Infusion Schedule:

Infusion (every 2 weeks)	Dose (administer over 1 hour)
All infusions	10 mg/kg each dose

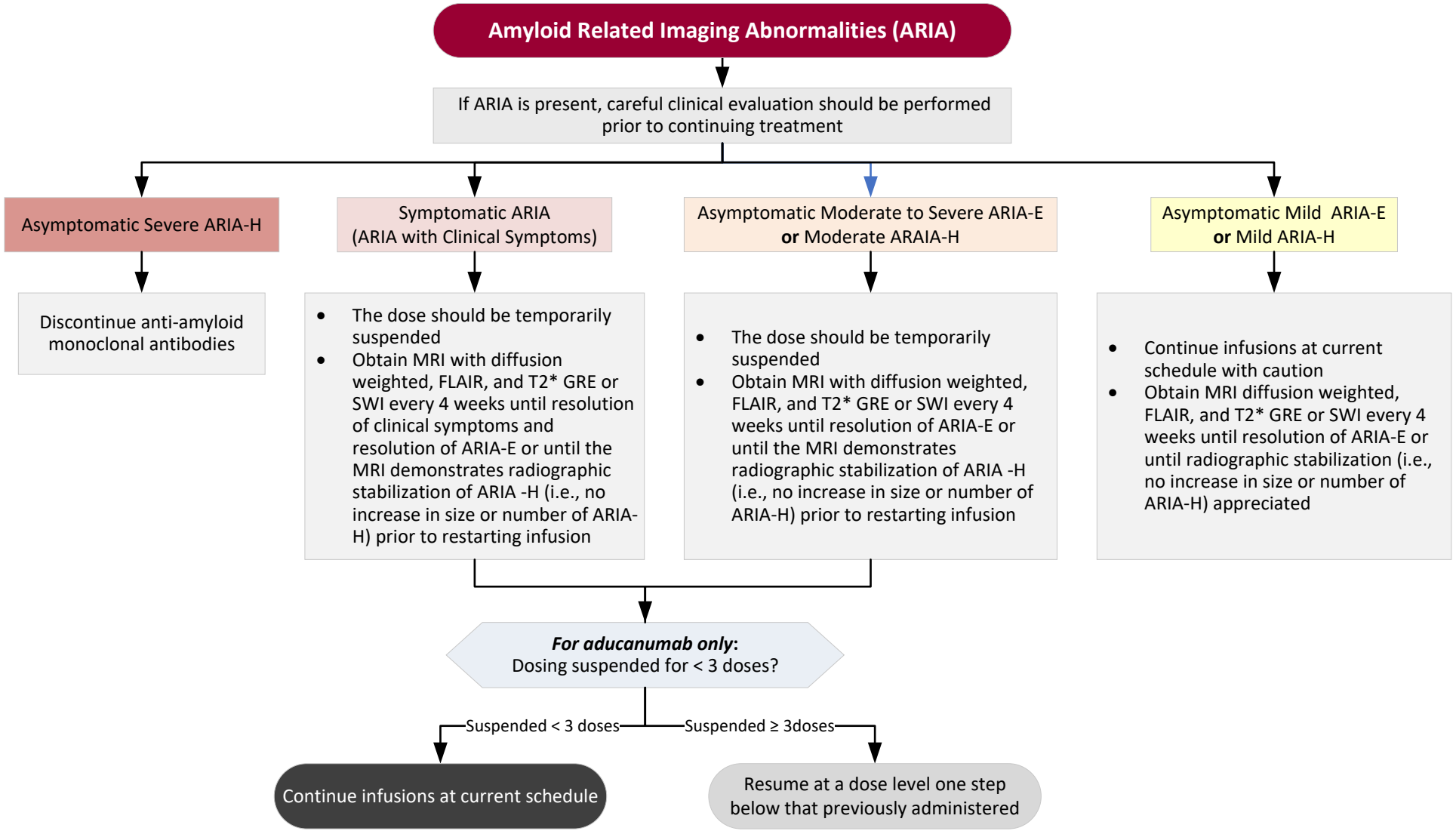
- Patients should be asked about the following symptoms prior to each infusion:
  - Confusion, dizziness, visual disturbances, nausea, headache, vomiting, gait or coordination disturbance, tremor, or seizure.
- If a patient experiences any of the symptoms above, a clinical evaluation and MRI brain should be performed.
- MRI brain (must include diffusion weighted, FLAIR, and T2* GRE or SWI sequences) prior to 5th, 7th, 9th and 12th infusions[5] for aducanumab and prior to 5th, 7th and 14th infusion for lecanemab to evaluate for asymptomatic ARIA.
- Provider to review scans prior to next infusion to determine if infusion should take place.

Adverse event reporting line: 1-833-425-9360

Table 3. Amyloid Related Imaging Abnormalities: Types and Severity Grading

ARIA Type	Radiographic Severity		
	Mild	**Moderate**	**Severe**
ARIA-E	FLAIR hyper-intensity confined to sulcus and/or cortex/ subcortical white matter in one location < 5 cm	FLAIR hyper-intensity 5-10 cm, or > 1 site of involvement, each measures < 10 cm	FLAIR hyper-intensity > 10 cm, often with significant subcortical white matter and/or sulcal involvement. One or more separate sites of involvement may be noted.
ARIA-H Micro-hemorrhage	≤ 4 new incidents micro-hemorrhages	5-9 new incidents micro-hemorrhages	≥ 10 new incidents micro-hemorrhages
ARIA-H Superficial Siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	> 2 focal areas of superficial siderosis

Algorithm 3: ARIA Findings and Infusion Holding or Discontinuation



References

1. Budd et al, J Prev Alzheimers Dis. 2017;4:255-263
2. Aducanumab FDA Prescribing Information sheet, 2021: https://www.globenewswire.com/Tracker?data=mxvcDL0oCxrMP-VF0YLQ8s2shFA6R7RL9Iikuo-ainfOhWJ0-mXgiPcMCmbf45VbVeK4h9wlOZK9OYoVggkWPgJl0VDj8XDQKlQRSqMpwa5wNBpEJsj9geEUvPTTLafa
3. Lecanemab FD prescribing Information sheet, 2023: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761269s000lbl.pdf
4. Haeberlein et al. Alzheimer's Dement. 2020;16(Suppl. 9):e047259; https://investors.biogen.com/static-files/8e58afa4-ba37-4250-9a78-2ecfb63b1dcb
5. van Dyck CH, et al. N Engl J Med. 2023 Jan 5;388(1):9-21. Doi: 10.1056/NEJMoa2212948. Epub 2022 Nov 29. PMID: 36449413
6. Scharre et al. Alzheimer Dis Assoc Disord 2010; 24:64-71
7. Scharre et al. Alzheimers Res Ther. 2017 Jun 27;9:44.
8. Cummings et al. J Prev Alz Dis 2021; Published online July 20, 2021, http://dx.doi.org/10.14283/jpad.2021.41
9. Kaufer et al. Journal of Neuropsychiatry and Clinical Neuroscience 2000; 12:233-239
10. Pfeffer et al. J Gerontol 1982; 37(3):323-329
11. Jack et al. Alzheimers Dement. 2018;14:535-562
12. Albert et al. Alzheimers Dement. 2011;7:270-9
13. McKhann et al. Alzheimers Dement. 2011;7:263-9

Quality Measures

- Evidence of ambulatory referral to the infusion clinic with the specific anti-amyloid monoclonal antibody in the order comments
- Number of infusion visits per patient since ambulatory referral
- Number of brain MRIs completed since ambulatory referral
- Evidence of qualifying diagnosis for treatment
- Evidence of amyloid positive results to support diagnosis
- Evidence of MRIs obtained PRIOR to the 5th, 7th, 9th and 12th aducanumab infusions and evidence of MRIs obtained PRIOR to the 5th, 7th, and 14th lecanemab infusions

Guideline Authors

- Douglas Scharre, MD
- Soumya Bouchachi, MD
- Joseph Castle, RN
- Maria Kataki, MD, PhD
- Renee Kovesci, APRN-CNP
- Arun Ramamurthy, MD
- Jessica Truelove, APRN-CNP

Guideline Approved

June 7, 2023 Second Edition

Disclaimer: *Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC's guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.*