PREPARING YOUR EMERGENCY DEPARTMENT FOR PATIENTS ON AMYLOID-TARGETING THERAPY

TIPS FOR ADMINISTRATIVE NEEDS, PROTOCOLS, AND INTRADISCIPLINARY COMMUNICATION

EDUCATION & TRAINING

- ❑ **Work with hospital administration to develop and implement protocols and guidelines** for the assessment, triage, and management of patients on amyloid-targeting therapy or with suspected or confirmed amyloid-related imaging abnormalities (ARIA)
- ❑ Ensure that all emergency department staff, including EMS, physicians, nurses, and support staff, are **educated about ARIA and its potential complications**
- ❑ Ensure that there is a **designated point of contact** for ARIA-related cases. Ideally the ATT prescribing neurologist.

PATIENT SCREENING & ASSESSMENT

BEFORE A PATIENT PRESENTS WITH ARIA

- ❑ Implement a plan for the **accurate medication reconciliation** for patients on amyloid-targeting therapies

WHEN A PATIENT PRESENTS WITH ARIA

- ❑ Ensure they receive timely and appropriate assessments, including **neurology consultations**

IMAGING CONSIDERATIONS

BEFORE A PATIENT PRESENTS WITH ARIA

Discuss with your administrative and radiology team:

- ❑ How to implement appropriate and consistent imaging protocols for patients on amyloid-targeting therapies
- ❑ What to do if MRI is not readily available

WHEN A PATIENT PRESENTS WITH ARIA

When ordering ARIA-related imaging, directly communicate to the radiologist:

- ❑ History of amyloid-targeting therapy use
- ❑ If baseline and monitoring MRI results are readily available

TREATMENT CONSIDERATIONS

BEFORE A PATIENT PRESENTS WITH ARIA

For patients on amyloid-targeting therapies, develop a:

- ❑ P**rotocol** for those who present with **signs of stroke**
- ❑ Discuss the **risk vs benefit of fibrinolytics.** *Thrombolytics likely contraindicated until more data available*

WHEN A PATIENT PRESENTS WITH ARIA

- ❑ **Communicate any ARIA findings immediately with the patient's neurology team**
  - Moderate or severe ARIA may change management.

PLAN

ARIA ADMISSION/DISCHARGE PLAN

- ❑ Develop an **admission/discharge plan** for the management of patients with ARIA, including monitoring for symptoms and complications, as well as follow-up care.

ARIA REPORTING PLAN

- ❑ Discuss a plan for who is responsible to **report any cases** of ARIA to the appropriate regulatory authorities or healthcare agencies

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AMYLOID-TARGETING THERAPY OVERVIEW[1,2]

WHAT: Monoclonal antibodies designed to clear amyloid-beta in the brain

WHY: Slows the cognitive decline associated with AD

WHO: Patients with MCI or mild AD dementia

LECANEMAB (BIWEEKLY INFUSION)

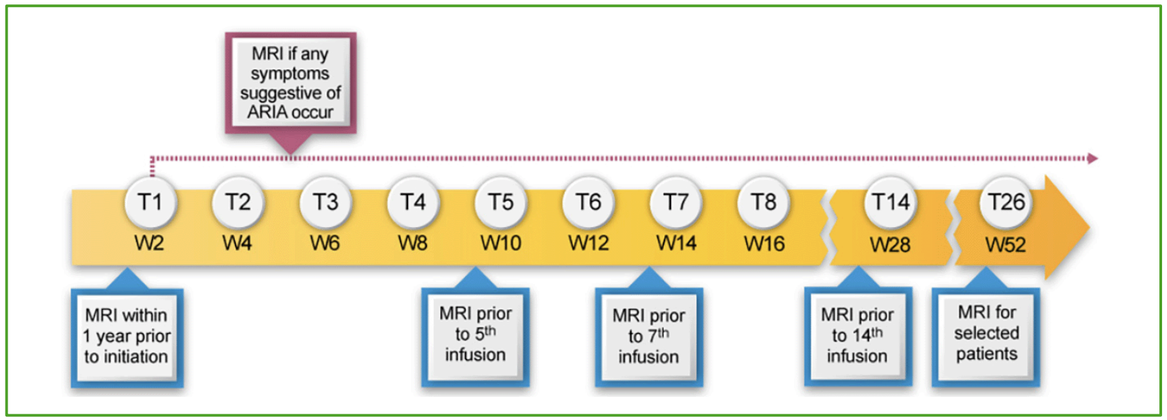
FDA APPROVED

MRI MONITORING SCHEDULE:
Baseline and prior to the
5th, 7th, 14th , 26th infusion

Nonscheduled for ARIA symptoms + ARIA follow-up

DONANEMAB (MONTHLY INFUSION)

UNDER REGULATORY REVIEW



1. Sims JR et al. Donanemab in Early Symptomatic AD: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. *JAMA*. 2023;330(6):512-527. **2.** Eisai Inc. Lecanemab for early ad: long-term outcomes, predictive biomarkers, and novel subcutaneous administration. Late-Breaking Symposium 4; Presented at CTAD 2023, Stockholm, Sweden.

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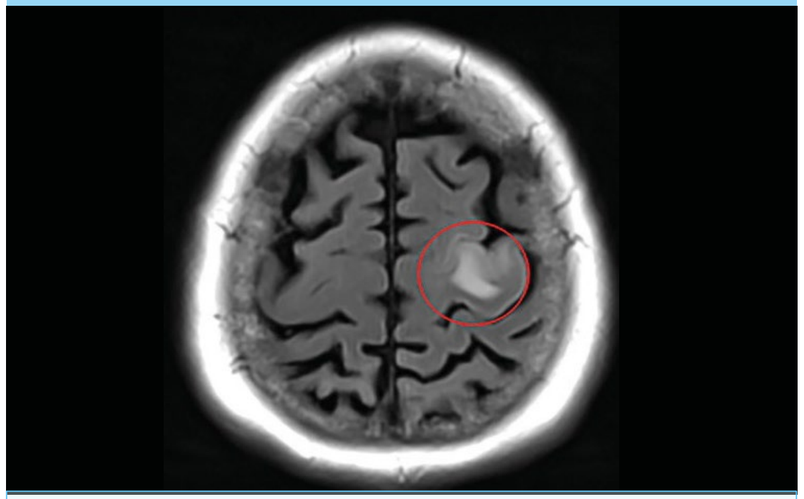
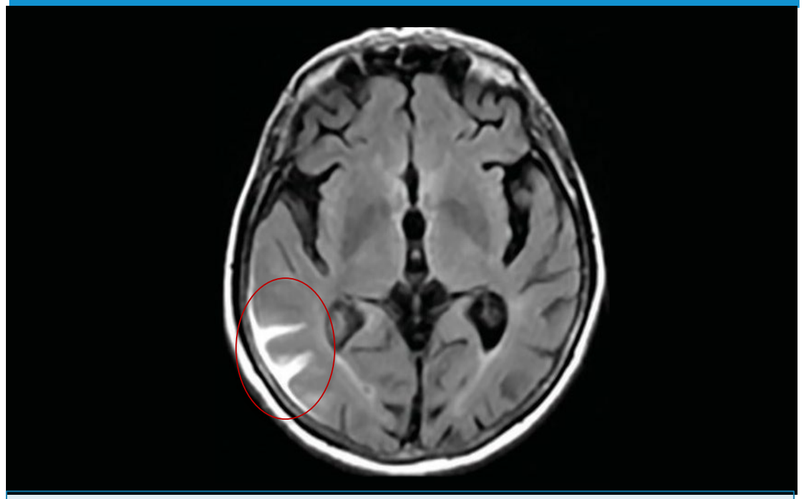
ARIA-E (EDEMA) SEVERITY[1]

MILD
1 location; <5 cm



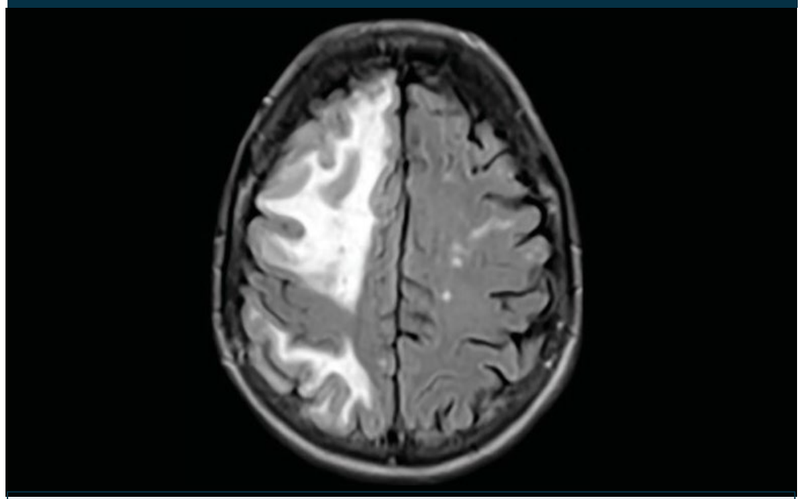
Mild ARIA-E (edema)
Hyperintensity involving the left superior frontal cortex and subcortical white matter

MODERATE
1 location; 5-10 cm **OR**
>1 location; <10 cm



Moderate ARIA-E (effusion)
Hyperintensity involving the right temporal-occipital lobe

SEVERE
≥1 locations; >10 cm

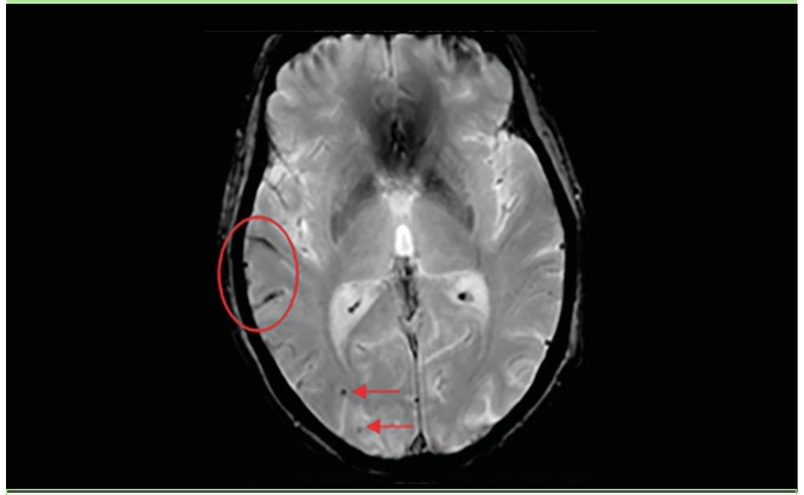


Severe ARIA-E (edema)
Hyperintensity involving the right frontal and parietal lobes

1. Cogswell PM et al. Amyloid-related imaging abnormalities with emerging Alzheimer disease therapeutics: detection and reporting recommendations for clinical practice. *AJNR Am J Neuroradiol.* 2022;43(9):E19-E35.

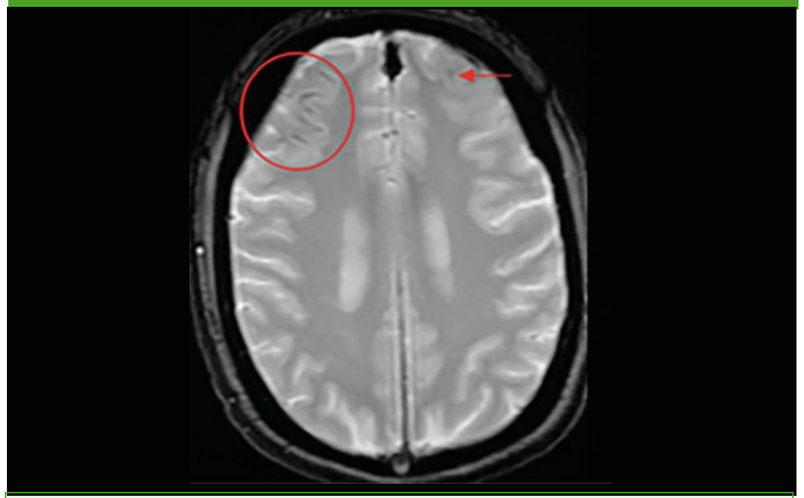
ARIA-H (HEMORRHAGE) SEVERITY[1]

MILD
1 focal area of superficial siderosis
AND/OR ≤4 microhemorrhages



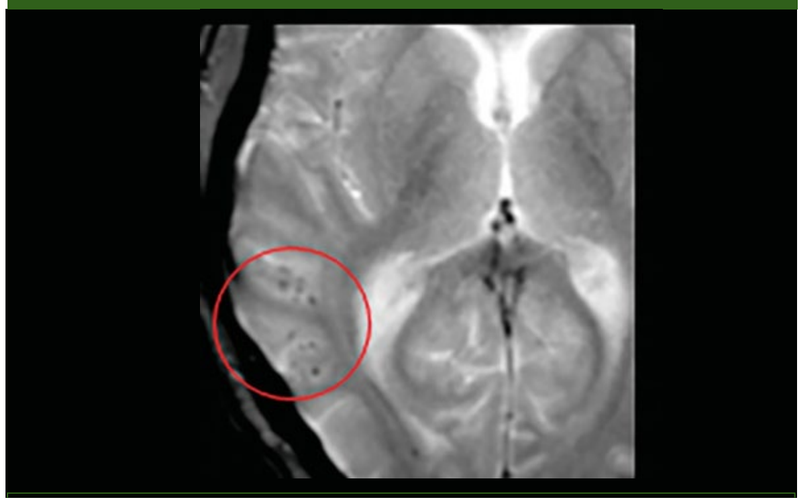
Mild ARIA-H
This image: 1 area of superficial siderosis (circle), 2 microhemorrhages (arrows)

MODERATE
2 focal areas of superficial siderosis
AND/OR 5-9 microhemorrhages



Moderate ARIA-H
This image:
2 areas of superficial siderosis

SEVERE
>2 focal areas of superficial siderosis
AND/OR >10 microhemorrhages



Severe ARIA-H
This image:
>10 microhemorrhages

1. Cogswell PM et al. Amyloid-related imaging abnormalities with emerging Alzheimer disease therapeutics: detection and reporting recommendations for clinical practice. *AJNR Am J Neuroradiol.* 2022;43(9):E19-E35.

RECOGNIZING THE CLINICAL SYMPTOMS OF ARIA

- Headache
- Confusion/altered mental status
- Dizziness
- Nausea/vomiting
- Gait disturbance
- Visual disturbance
- Seizure (rare)

BE AWARE OF CLINICAL AND IMAGING MIMICS[2,3]

ACUTE ISCHEMIC STROKE

PRES

SUBARACHNOID HEMORRHAGE

PRES: posterior reversible encephalopathy syndrome. **1.** Salloway S et al. Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early alzheimer disease. *JAMA Neurol*. 2022;79(1):13-21. **2.** Yew KS, Cheng EM. Diagnosis of acute stroke. *Am Fam Physician*. 2015;91(8):528-536. 3. Zelaya JE, Al-Khoury L. Posterior reversible encephalopathy syndrome. **3.** *StatPearls*. NCBI Bookshelf. StatPearls Publishing; May 1, 2022. Accessed March 14, 2024. https://pubmed.ncbi.nlm.nih.gov/32119379/.

WHAT DOES RADIOLOGY NEED YOU TO COMMUNICATE?

IN ADDITION TO A BASELINE MRI, PATIENTS ON AMYLOID-TARGETING THERAPY REQUIRE SEVERAL MRIS TO MONITOR FOR ARIA THROUGHOUT THE FIRST YEAR OF THERAPY.

It is vital to communicate to radiology:

- ✓ **History of ATT use**
- ✓ **Baseline and monitoring MRI results**

- If available**, provide prior MR images to your radiologist** as the change in microhemorrhages, siderosis, and white matter hyperintensities is important to assess for ARIA-E and ARIA-H.
- **If images are not available**, prior reports that list the number and location of these imaging findings would be helpful.

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SUMMARY OF RECOMMENDED MRI PROTOCOLS

OPTIMAL STRATEGIES TO ENSURE CONSISTENCY AND ACCURACY OF IMAGING[1,2]

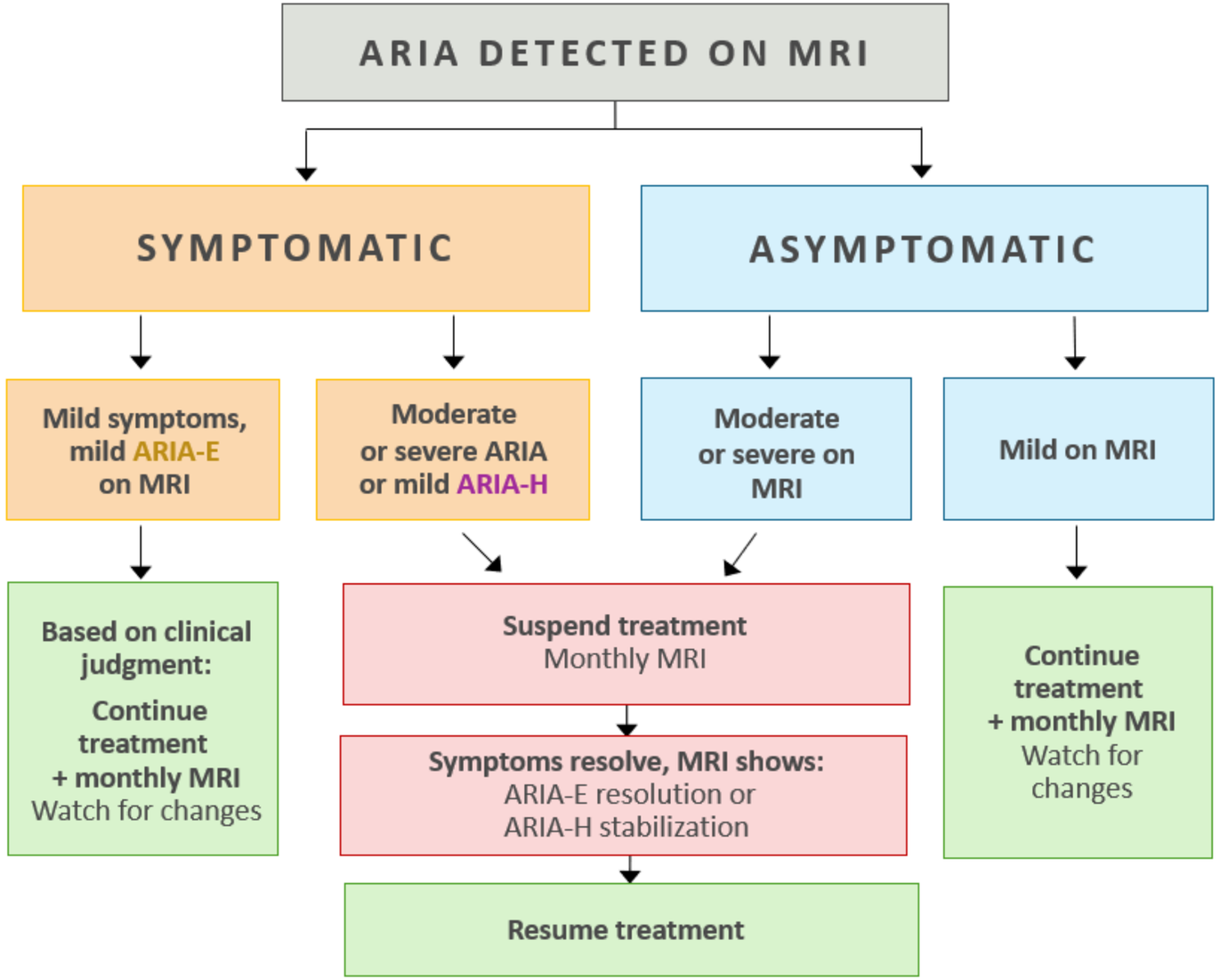
SLICE THICKNESS	**5 mm**	Consistency is key
ARIA-E DETECTION	**T2-FLAIR**	Can be missed by conventional T2 due to CSF hyperintensity
ARIA-H DETECTION	**2D T2 GRE or SWI**	SWI more sensitive
INFARCT ASSESSMENT	**DWI**	Differentiate ARIA-E from infarct

NOTE: A GENERAL BRAIN OR STROKE PROTOCOL MRI WILL HAVE ALL THE APPROPRIATE SEQUENCES.

GRE: gradient-recalled echo; SWI: susceptibility-weighted imaging; T2-FLAIR: T2-weighted-fluid-attenuated inversion recovery.

1. Barakos J et al. *J Prev Alzheimers Dis*. 2022;9(2):211-220. 2. Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35.

MANAGEMENT STRATEGIES FOR ARIA[1]



This chart serves as a recommendation, rather than a predetermined algorithm.

Clinical judgement and discussion with the patient's neurologist is critical for each individual patient presentation

1. LEQEMBI (lecanemab-irmb). Prescribing information. Eisai Inc.; 2023.

CONTRAINDICATED MEDICATIONS FOR PATIENTS ON AMYLOID-TARGETING THERAPY

The NEW ENGLAND JOURNAL of MEDICINE

Multiple Cerebral Hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke

RISK VS BENEFIT OF FIBRINOLYTICS[1,2]

Because of the increased risk of hemorrhage, current recommendations state that **acute thrombolytics (e.g., tPA) should not be administered to individuals on lecanemab** until safety evidence of their combined use is available

CURRENT RECOMMENDATIONS: Patients on anticoagulants (coumadin, dabigatran, edoxaban, rivaroxaban, apixaban, betrixaban, or heparin) should not receive lecanemab.[2]

***NOTE:** Data on concurrent anticoagulant and antiplatelet use is mixed

tPA: tissue plasminogen activator. **1.** Reish NJ et al. Multiple cerebral hemorrhages in a patient receiving lecanemab and treated with T-PA for stroke. *N Engl J Med*. 2023;388(5):478-479. **2.** Cummings J et al. Lecanemab: appropriate use recommendations. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

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TREATING ARIA

DOES ARIA EVER REQUIRE ADDITIONAL TREATMENT BEYOND THERAPY SUSPENSION/DISCONTINUATION?

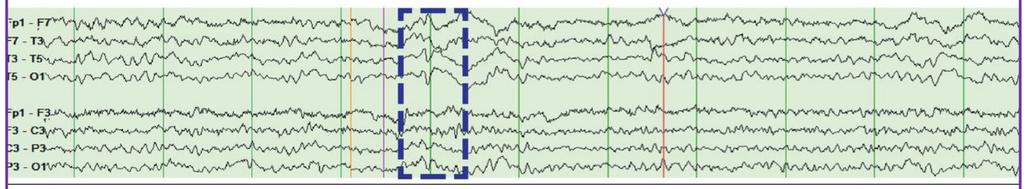
FOR **SEVERE** SYMPTOMATIC CASES OF ARIA[1]

RECOMMENDATION:
High-dose glucocorticoids

IV methylprednisolone followed by oral prednisone tapered over weeks or months

FOR SEIZURES OR EEG EVIDENCE OF EPILEPTIFORM ACTIVITY[1]

RECOMMENDATION:
Anticonvulsants



1. Cummings J et al. Lecanemab: appropriate use recommendations. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

ADMISSION VS DISCHARGE

DISCHARGE PLANNING BASED ON NEUROLOGY RECOMMENDATION

DISCUSS NEUROLOGY OUTPATIENT FOLLOW-UP

- ATT and/or MRI monitoring schedule can be adjusted as needed

ADMISSION PLAN FOR SEVERE ARIA[a]

IN-HOSPITAL NEUROLOGY CONSULTATION

- Preferably a vascular neurologist with experience in ARIA

HOSPITAL ADMISSION

- Admittance to a **hospital ward** for close neurologic monitoring ***or***
- Admittance to a **stroke care or neurological intensive care unit** if warranted

[a] There is no official criteria for ARIA-related hospital admissions at this time.

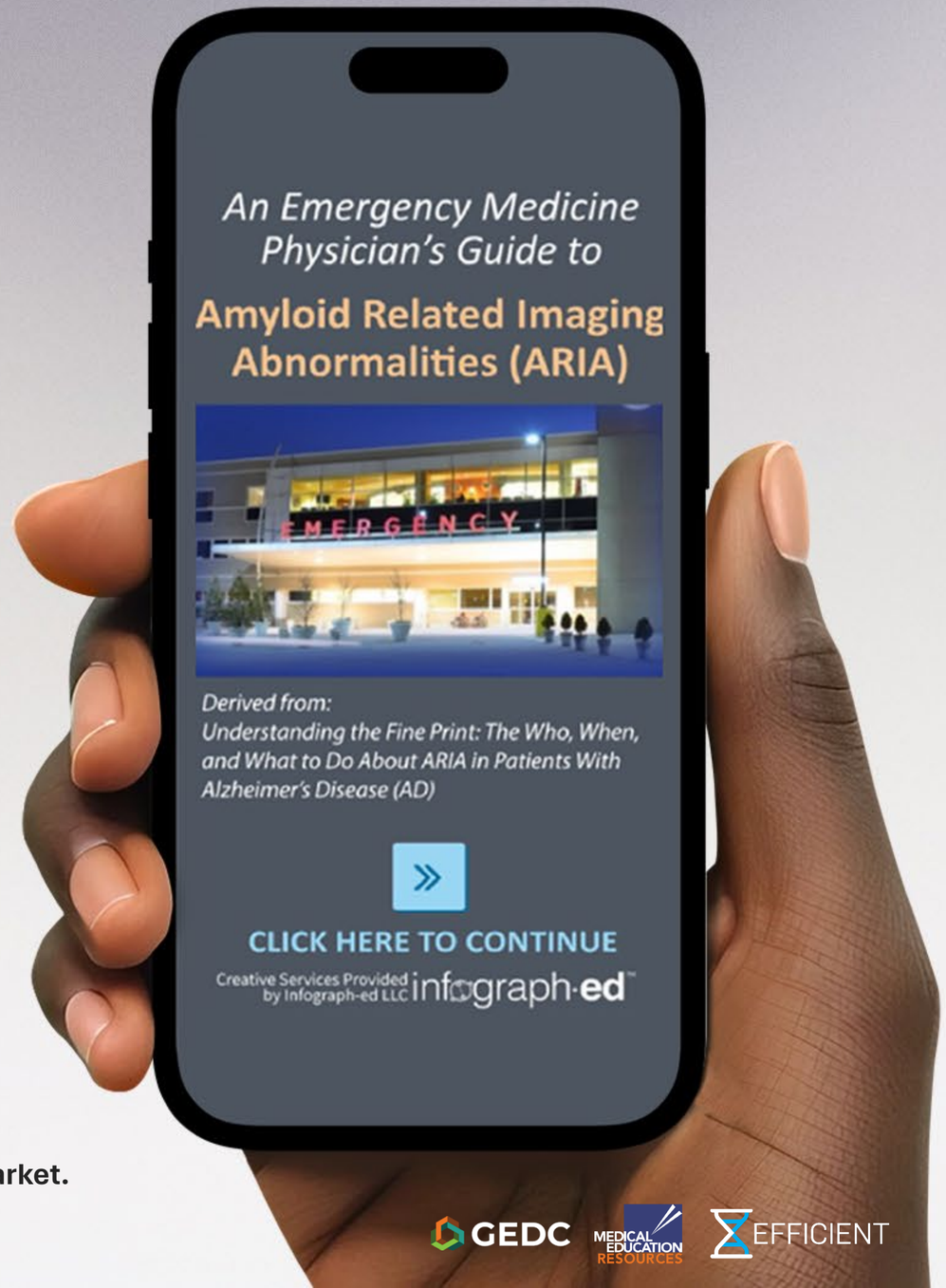
1. Cummings J et al. Aducanumab: appropriate use recommendations update. *J Prev Alzheimers Dis.* 2022;9(2):221-230.

LOOKING TO APPLY INFORMATION TO YOUR CLINICAL PRACTICE

Check Out our Interactive Clinical Summary Designed Specifically for **EMERGENCY MEDICINE** Practitioners

*This mobile-friendly tool allows for convenient access to ARIA guidelines for easy implementation into day-to-day clinical practice**

efficientcme.com/ARIA/EmergencyMedicine



**Please note that this resource was developed prior to the withdrawal of aducanumab from the market.

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