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Practical Guide of the Korean Association for Geriatric Psychiatry to Anti-Amyloid Monoclonal Antibody Therapy for Alzheimer's Disease: Focused on Lecanemab

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ABSTRACT

The advent of anti-amyloid monoclonal antibody (mAb) therapies represents a paradigm shift in the treatment of Alzheimer's disease (AD), from symptomatic relief to disease modification. Lecanemab, a humanized mAb targeting soluble Aβ protofibrils and plaque, received regulatory approval in Korea in July 2024, following global randomized controlled trial data demonstrating its efficacy to reduce amyloid burden and slow cognitive decline. However, the introduction of such therapies into routine clinical realm presents several practical and systemic challenges, particularly in the context of Korea's unique healthcare infrastructure and reimbursement environment. In response, the Korean Association for Geriatric Psychiatry has developed the first comprehensive domestic guidance to facilitate the safe, evidence-based, and patient-centered use of anti-amyloid mAb therapies, first focused on lecanemab. This practical guide goes beyond simple eligibility criteria. It provides detailed recommendations on clinical and imaging-based candidate selection, amyloid-related imaging abnormalities (ARIA) risk stratification and monitoring protocols, infusion workflows, adverse event management strategies, and multidisciplinary coordination within hospital systems. It also emphasizes shared decision-making and outlines how to navigate situations where treatment is not appropriate, such as in patients with advanced dementia, high-risk magnetic resonance imaging findings, or poor treatment adherence, reinforcing that non-treatment can also represent a legitimate, evidence-based clinical decision.
The guidance further highlights the urgent need to generate real-world data that reflect the treatment experiences of Korean patients. Multicenter collaboration will be essential for collecting data on adherence rates, ARIA incidence, cognitive outcomes, and functional trajectories, which in turn can inform policy decisions, insurance reimbursement models, and future updates to clinical guidelines. This publication represents the first nationwide

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roadmap in Korea to support clinicians in the appropriate integration of monoclonal antibody therapies for AD. By combining scientific rigor, operational feasibility, and ethical sensitivity, it aims to promote safe and responsible adoption of disease-modifying treatment across various clinical settings.

Keywords: Lecanemab; Donanemab; Practical Guide; Appropriate Use; Antiamyloid Monoclonal Antibodies; Alzheimer's Disease

INTRODUCTION

The advent of anti-amyloid monoclonal antibody therapies targeting cerebral amyloid-beta (Aβ) has ushered in a transformative shift in Alzheimer's disease (AD) treatment. The CLARITY AD phase 3 clinical trial demonstrated that lecanemab (Leqembi) significantly slowed cognitive decline in patients with mild cognitive impairment (MCI) and early-stage of AD,[1] prompting the U.S. Food and Drug Administration (FDA) to grant full approval in July 2023.[2] In May 2024, Korea Ministry of Food and Drug Safety (KMFDS) also approved lecanemab,[3] making the therapy newly available to patients within Korea and reinforcing its potential impact on clinical practice. Momentum continued in July 2024, when the US FDA approved another anti-amyloid antibody therapy, donanemab (Kisunla),[4] further heightening expectations for more effective treatments.

Nonetheless, safely and effectively integrating anti-amyloid antibody therapies into real-world clinical practice demands a comprehensive, multifaceted approach. Critical components include rigorous patient selection, vigilant monitoring of adverse events, readiness of hospital systems, and robust multidisciplinary collaboration. To facilitate this transition, the Alzheimer's Disease and Related Disorders Therapeutics Work Group (ADRD-TWG) in the US published Appropriate Use Recommendations (AUR) for lecanemab.[5] The Korean Dementia Association has also provided an AUR that aims to reflect the specific circumstances of Korea.[6] However, most existing AURs heavily draw upon the inclusion criteria of phase 3 clinical trials and primarily address the administration of lecanemab, limiting their applicability in the diverse, complex realities of everyday clinical practice. Moreover, clinicians are increasingly expected to manage a growing number of patients seeking antibody therapies who fail to meet eligibility criteria, outnumbering those who are eligible.

To bridge these gaps, the Korean Association for Geriatric Psychiatry (KAGP) developed a practical guide to anti-amyloid monoclonal antibody therapy for AD, first focused on lecanemab, tailored to the domestic healthcare landscape. This guide offers strategies for integrating novel treatment mechanisms into established paradigms, preparing clinical sites for implementation, approaching and communicating with patients who may not be eligible for therapy, and envisioning the future trajectory of antibody treatments.

In September 2024, the KAGP Special Committee on Therapeutics convened a task force composed of researchers who have been involved in early clinical trials for lecanemab or other dementia therapeutics, alongside leading experts in AD research and patient care. After establishing a detailed agenda and inviting a specialist panel, we developed this guide through a series of consensus-building meetings. We reviewed a comprehensive array of published and unpublished resources, including USFDA Prescribing Information,[7] KMFDS approval documents,[3] AURs from the ADRD-TWG[5] and the Korean Dementia Association,[6]

and guidelines from Japan's Ministry of Health, Labour and Welfare.[8] Drawing on these materials, we produced a practical guide carefully adapted to the Korean healthcare context. Following review and formal approval by the KAGP Board of Directors in April 2025, the guidelines were finalized.

This review article systematically synthesizes the core components of the Practical Guide of the KAGP to Anti-amyloid Monoclonal Antibody Therapy for AD[9] and aims to provide a pragmatic framework to support the clinical application of anti-amyloid antibody therapies in real-world clinical settings.

KAGP PRACTICAL GUIDE: CORE CRITERIA FOR THE USE OF ANTI-AMYLOID ANTIBODY THERAPIES

Core criteria to consider before initiating therapy

The Korean Association for Geriatric Psychiatry's Practical Guide to Anti-amyloid Monoclonal Antibody Therapy for AD (hereafter referred to as the KAGP Practical Guide) recommends selecting appropriate patient candidates for anti-amyloid antibody therapy by integrating three key evaluation factors: clinical diagnosis and severity of cognitive impairment, confirmation of amyloid pathology, and neuroimaging findings. Based on these factors, clinicians should conduct a thorough risk-benefit analysis and engage in shared decision-making with patients and caregivers to determine the final treatment plan (**Fig. 1**).

Clinical diagnosis and severity of cognitive impairment

The KAGP Practical Guide recommend the use of lecanemab for individuals with early-stage cognitive decline due to AD, specifically those diagnosed with MCI or early-stage dementia. The primary diagnostic framework is based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) criteria for MCI or AD.[10] The following clinical staging systems may be utilized to assess severity: Clinical Dementia Rating (CDR)[11] scores of 0.5–1, Global Deterioration Scale (GDS)[12] stages 3–5, or National Institute on Aging–Alzheimer's Association (NIA-AA) revised clinical stages 3–4,[13] all of which correspond to early-stage disease.

While some AURs have suggested using Mini-Mental State Examination (MMSE) scores between 22–30 to determine candidacy,[5,8] the present guide elected not to specify MMSE cutoffs considering that raw scores may vary depending on age, sex, and educational level, and that test–retest reliability may be somewhat limited due to potential fluctuations in repeated administrations (**Table 1**).[14,15] Using neuropsychological batteries such as the Consortium to Establish a Registry for Alzheimer's Disease (CERAD),[16-19] Seoul Neuropsychological Screening Battery (SNSB),[20] or Literacy Independent Cognitive Assessment (LICA),[21] comprehensive evaluation across cognitive domains is recommended to assess overall cognitive function and determine eligibility for anti-amyloid antibody therapy. If a patient demonstrates below-average performance, with scores below –1 standard deviations from the norm on one or more cognitive domains tests, and this finding is consistent with relevant clinical impressions, the patient may be in an early stage of cognitive decline.[22,23] This may represent an appropriate point at which to consider initiating lecanemab treatment.

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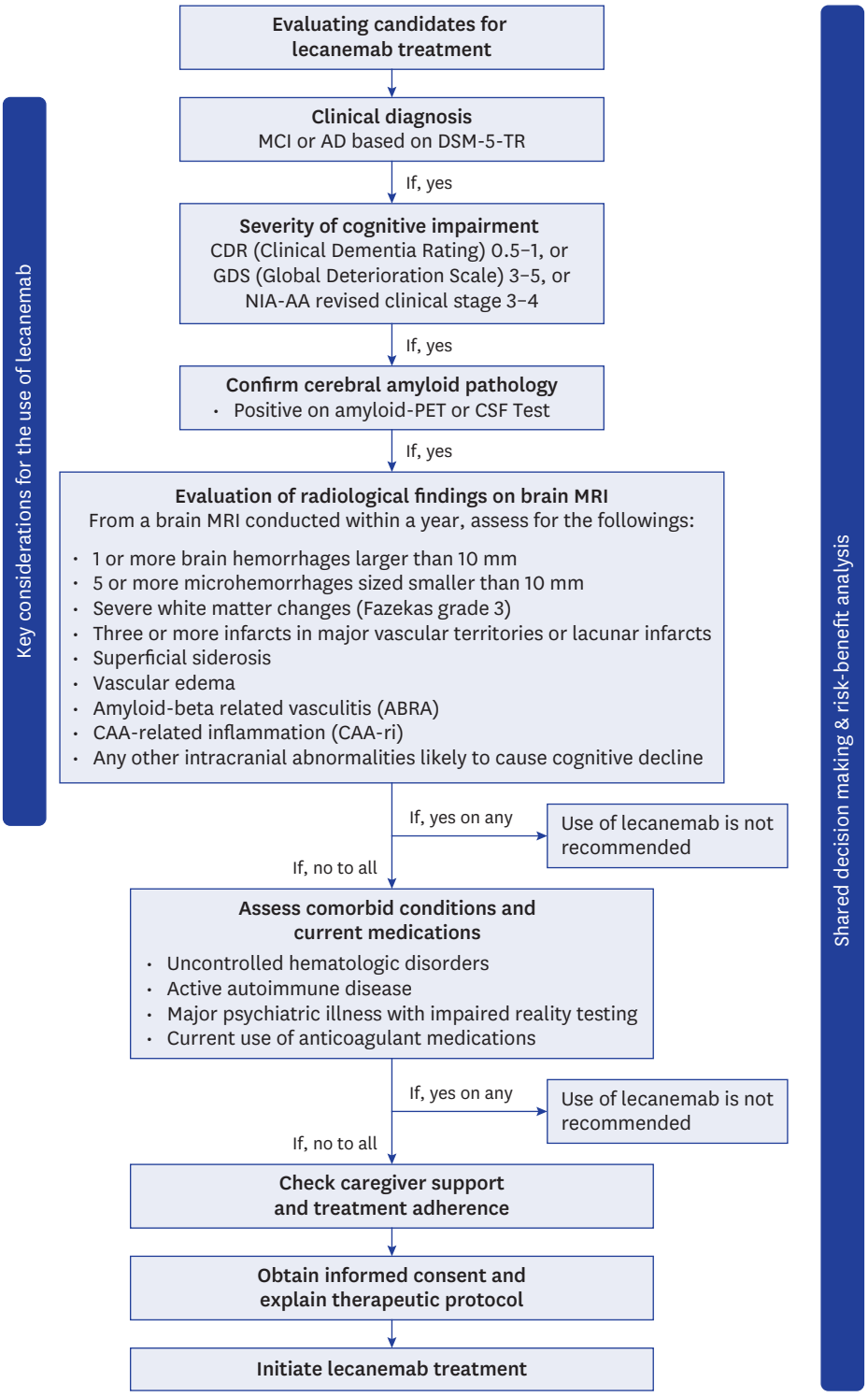

Fig. 1. Eligibility assessment algorithm for lecanemab treatment. The flowchart is designed to guide clinicians in identifying patients who are appropriate candidates for lecanemab treatment. This algorithm outlines a stepwise approach to evaluating treatment candidacy. It integrates three core evaluation domains: 1) clinical diagnosis and assessment of cognitive impairment severity, 2) confirmation of amyloid pathology via PET or CSF biomarkers, and 3) neuroimaging findings that may raise concerns regarding the use of lecanemab. Additional considerations include comorbid medical conditions, concurrent medications, caregiver support, and treatment adherence. Clinicians are advised to perform a comprehensive risk-benefit analysis and engage in shared decision-making with patients and caregivers to determine the final treatment plan.
MCI = mild cognitive impairment, AD = Alzheimer's disease, DSM-5-TR = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision, CDR = Clinical Dementia Rating Scale, GDS = Global Deterioration Scale, NIA-AA = National Institute on Aging–Alzheimer's Association, PET = positron emission tomography, CSF = cerebrospinal fluid.

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Table 1. KAGP practical guide: key considerations for the use of anti-amyloid monoclonal antibody therapies

Category	Criteria
Conditions eligible to use lecanemab	• MCI or early-stage dementia due to AD based DSM-5-TR criteria • Positive amyloid PET imaging or positive CSF biomarker findings • CDR score of 0.5–1, GDS stage 3–5, or NIA-AA clinical stage 3–4 • Presence of a reliable caregiver capable of supporting treatment monitoring and side effect management
Absolute contraindication	• History of hypersensitivity to lecanemab or its component • Inability to undergo MRI scanning
Conditions under which the use of lecanemab is not recommended or conditions necessitating careful consideration when using lecanemab	• Presence of significant mixed pathology that primarily contributes to cognitive impairment beyond AD • Brain MRI findings - One or more brain hemorrhages larger than 10 mm - Five or more microhemorrhages sized smaller than 10 mm - Severe white matter changes (Fazekas grade 3) - Three or more infarcts in major vascular territories or lacunar infarcts - Superficial siderosis - Vascular edema - Amyloid-beta related vasculitis - CAA-related inflammation - Any other intracranial abnormalities likely to cause cognitive decline • Bleeding disorder that is not under adequate control (including a platelet count < 50,000 or international normalized ratio > 1.5 for participants who are not on anticoagulant treatment, example, warfarin) • Current use of anticoagulants (e.g., coumadin, dabigatran, edoxaban, rivaroxaban, apixaban, betrixaban, heparin) • Use of thrombolytic agents (e.g., tPA) requires careful risk-benefit evaluation • Active or high-risk autoimmune conditions requiring immunosuppressants, immunoglobulins, monoclonal antibodies, or derivatives (e.g., lupus, Crohn's disease) • Significant impairment in reality testing, making understanding or cooperation with treatment, outcomes, and side effects difficult (e.g., active delusions or hallucinations) • Elevated suicide risk anticipated upon disclosure of AD-related biomarker results and diagnosis information to the patient • Oldest old age (≥ 90 years) or severe obesity (BMI ≥ 35) — requires careful risk-benefit evaluation

KAGP = Korean Association for Geriatric Psychiatry, MCI = mild cognitive impairment, AD = Alzheimer's disease, DSM-5-TR = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision, PET = positron emission tomography, CSF = cerebrospinal fluid, CDR = Clinical Dementia Rating Scale, GDS = Global Deterioration Scale, NIA-AA = National Institute on Aging–Alzheimer's Association, MRI = magnetic resonance imaging, tPA = tissue plasminogen activator, BMI = body mass index.

Confirmation of cerebral amyloid pathology

Anti-amyloid antibody therapy should be initiated only after confirming cerebral amyloid positivity through amyloid positron emission tomography (PET) imaging or cerebrospinal fluid (CSF) biomarker analysis. Clinical suspicion alone is insufficient to confirm amyloid pathology. In Korea, currently approved PET radioligands for amyloid imaging include flutemetamol (Vizamyl®),[24] florbetaben (Neuraceq®),[25] and florapronol (Alzaview®),[26] all of which enable either visual or quantitative assessment of cerebral Aβ burden. Visual interpretation by experienced readers remains the standard method for evaluating PET scans.[27] Quantitative approaches, such as the centiloid scale,[28] can supplement visual reads and help standardize interpretation across tracers and imaging protocols. Standardized uptake value ratios (SUVr) were the most common method for quantifying cerebral Aβ deposition,[29] but thresholds varied depending on the radioligands.[30] The centiloid system was developed to address this variability, providing a universal scale that calibrates SUVr measurements into a tracer-independent and method-independent unit.[28] This allows consistent comparison of amyloid burden across different PET tracers and facilitates the definition of thresholds for staging AD pathology. In general, centiloid values below 10 are considered negative, while values above 30 strongly suggest amyloid positivity. Intermediate values (10–30) require careful clinical correlation.[31]

In CSF biomarker analysis, amyloid positivity is confirmed by either decreased amyloid-beta 42/amyloid-beta 40 ratio (Aβ42/40)[32,33] or elevated phosphorylated tau (pTau)

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levels.[34,35] Among CSF biomarkers, p-tau181/Aβ42 ratio, t-tau/Aβ 42 ratio, and Aβ 42/40 have been approved by the US FDA and received European CE mark.[13] Although blood-based biomarkers are not yet widely implemented in clinical practice, growing evidence supports the potential utility of plasma markers such as reduced Aβ42/40 ratios and elevated levels of pTau217, pTau181, or MTBR-Tau243 for the diagnosis and monitoring of AD.[36,37] Recently, in May 2025, the US FDA has cleared the Lumipulse G pTau217/Aβ42 Plasma Ratio test, which becomes the first blood-based biomarker test approved for diagnosing AD.[38]

When asymptomatic individuals request amyloid testing or treatment, clinicians should carefully assess true cognitive status through structured interviews and neuropsychological evaluations, incorporating information from caregivers when appropriate. Currently, there is insufficient evidence to support the initiation of anti-amyloid antibody therapy in asymptomatic individuals. Ongoing prevention trials, including AHEAD 3-45(ClinicalTrials.gov ID: NCT04468659) (for lecanemab)[39] and TRAILBLAZER-ALZ3(ClinicalTrials.gov ID: NCT05026866) (for donanemab),[40] aim to determine whether early intervention during the preclinical stage can prevent or delay cognitive decline.

Neuroimaging evaluation

The use of anti-amyloid antibody therapies is not recommended if baseline magnetic resonance imaging (MRI) obtained prior to treatment reveals any of the following findings[3,5,6,8,41]: A single brain hemorrhage larger than 10 mm; five or more microhemorrhages smaller than 10 mm; severe subcortical white matter changes corresponding to Fazekas grade 3; three or more infarcts in major vascular territories or lacunar infarcts; superficial siderosis; vascular edema; Aβ-related vasculitis (ABRA); CAA-related inflammation (CAA-ri); any other significant intracranial abnormalities that may contribute to cognitive decline.

Baseline MRI should be performed within one year prior to the initiation of treatment. The American Society of Neuroradiology (ASNR)[42] and Korean Society of Neuroradiology (KSNR)[43] recommend obtaining a baseline MRI within 3–6 months before starting therapy. If the most recent MRI was performed 7–12 months prior and demonstrates four or fewer microhemorrhages, a repeat scan is recommended to ensure an accurate and up-to-date baseline assessment. Without a recent MRI, it becomes difficult to distinguish whether microhemorrhages detected on follow-up imaging are newly developed due to treatment or were already present beforehand. As a result, pre-existing microhemorrhages could be mistakenly classified as treatment-emergent amyloid-related imaging abnormalities–hemorrhage (ARIA-H), potentially leading to unnecessary clinical concern or inappropriate management decisions.

The three key elements discussed above—clinical diagnosis and severity of cognitive function, confirmation of cerebral amyloid pathology, and neuroimaging findings — constitute essential criteria for determining patient eligibility for anti-amyloid antibody therapy. Clinicians must also incorporate contraindications and additional considerations, as outlined below, into a thorough risk-benefit analysis, culminating in shared decision-making with patients and caregivers before treatment initiation.

Contraindications

We identify two absolute contraindications, in accordance with international and domestic standards: 1) a history of severe hypersensitivity to lecanemab or its components, and 2) inability to undergo MRI scanning. In addition to these absolute contraindications, certain

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conditions associated with a significantly elevated risk of adverse effects from anti-amyloid antibody therapies are categorized not as strict exclusions but as situations where use is discouraged or requires heightened caution. Instead of using the term "exclusion criteria," we refer to these conditions as "Conditions under which the use of lecanemab is not recommended or conditions necessitating careful consideration when using lecanemab." These are not absolute contraindications but represent clinical situations with high-risk profiles requiring thorough risk-benefit assessment and prudent judgment (**Table 1**).

Comorbidities and concomitant medications

Bleeding disorders

Uncontrolled bleeding disorders (e.g., platelet count < 50,000/mm^3 or INR > 1.5) are listed as exclusion criteria in clinical trials[1] and the ADRD-TWG guidelines.[5] A fatal case of multiple brain hemorrhages following tissue plasminogen activator (tPA) administration in a patient treated with lecanemab has been reported.[44] Consequently, both the KMFDS[3] and the US FDA[7] recommend caution when combining anti-amyloid antibody therapies with anticoagulants or thrombolytic agents. Anticoagulants (e.g., warfarin, dabigatran, edoxaban, rivaroxaban, apixaban, heparin) substantially increase the risk of intracranial hemorrhage and require extremely careful consideration if used concurrently with anti-amyloid therapies.[45,46] By contrast, antiplatelet agents (e.g., aspirin, clopidogrel, cilostazol) were allowed in clinical trials and are generally considered safe when used at standard dosages (e.g., aspirin up to 325 mg/day).[5,45] However, in patients carrying the APOE ε4 homozygous genotype, where the risk of ARIA is heightened, combination therapy should be approached with greater caution.[5,47] While current data have not confirmed a statistically significant increase in bleeding risk with antiplatelet use, further studies are warranted.

Autoimmune diseases

Patients with active autoimmune diseases (e.g., lupus, rheumatoid arthritis, Crohn's disease) require special consideration when initiating anti-amyloid antibody therapies.[3,7] Immunosuppressive, immunoglobulin, or monoclonal antibody treatments may attenuate immune responses,[5] potentially reducing therapeutic efficacy and increasing safety concerns. In these cases, cautious clinical judgment is essential to carefully weigh the potential benefits against the heightened risks before proceeding with therapy.

Major psychiatric disorders

A history of major psychiatric disorders—such as schizophrenia, bipolar disorder, or major depressive disorder—does not automatically exclude patients from receiving anti-amyloid antibody therapy. However, in cases involving acute psychiatric symptoms, impaired reality testing, absence of an appropriate caregiver, uncontrolled depression, or elevated suicide risk, the patient's ability to engage in informed consent and adhere to the treatment plan may be compromised. In such situations, clinicians should reassess eligibility after stabilization of psychiatric symptoms.

When amyloid biomarker positivity is likely to cause significant psychological distress, clinicians should perform depression screening prior to initiating treatment. If prominent depressive symptoms are present, they should address these symptoms before proceeding with antibody therapy. Patients with a history of poor treatment adherence also warrant special caution, as maintaining stable therapy may be difficult. Antipsychotic medications are not contraindicated for concurrent use with anti-amyloid antibody therapies; in fact, clinicians are encouraged to maintain a stable antipsychotic regimen during early antibody

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therapy to minimize symptom fluctuations that could be mistaken for ARIA. Although selective serotonin reuptake inhibitors (SSRIs) exhibit antiplatelet effects,[48] they are not formally contraindicated. However, when starting a new SSRI, clinicians should delay the initiation of antibody therapy for approximately 30 days to ensure initial tolerability.[49,50]

Down syndrome

Adults with Down syndrome who develop AD may be considered for anti-amyloid antibody therapy, even if they are younger than 40 years old.[51] The Working Group on Criteria for Access to Alzheimer's Therapeutics for Adults with Down Syndrome has proposed treatment guidelines specifically tailored to this population.[52] Unlike previous recommendations, which set a minimum treatment age of 50 years, the Working Group removed the lower age limit, thereby allowing younger patients with Down syndrome to receive antibody therapy. However, clinicians must recognize that individuals with Down syndrome often exhibit a higher burden of CAA, which may consequently elevate their risk of developing ARIA.[53,54]

Given the current evidence, treatment decisions for the above patient populations, including those with bleeding disorders, autoimmune diseases, major psychiatric disorders, and Down syndrome, must rely heavily on individualized clinical judgment. As additional international and domestic clinical data accumulate, more precise eligibility criteria and safety profiles are expected to emerge. Until then, the most practical approach is to conduct thorough case-by-case evaluations and apply treatment with careful consideration.

Caregiver support and treatment adherence

Anti-amyloid antibody therapies require repeated outpatient visits and regular MRI monitoring. Therefore, it is essential to confirm the presence of a cooperative caregiver and to ensure the patient's basic treatment adherence before initiating therapy.

Overview of eligibility and exclusion criteria across guidelines

In accordance with the KAGP Practical Guide, several existing guidelines advocate the use of lecanemab in patients with MCI or early-stage AD who demonstrate confirmed amyloid pathology through amyloid PET imaging or CSF biomarker analysis.[5,6,8] Although the core eligibility criteria are broadly similar, important differences emerge in how clinical diagnosis and cognitive severity are defined.

We recommend identifying early-stage patients based on a global CDR score of 0.5–1, a GDS stage of 3–5, or a NIA-AA clinical stage of 3–4, without relying on MMSE scores. This reflects the limitations of MMSE, given its variability across education levels, age groups, and daily fluctuations,[14,15] which can undermine reliability in clinical decision-making. In contrast, the ADRD-TWG[5] and Japan's Ministry of Health, Labor and Welfare[8] recommend using MMSE scores between 22 and 30 to determine eligibility. Similarly, the Korean Dementia Association proposes adjusting MMSE scores according to age- and education-based norms, particularly when scores fall below 22, allowing for clinical discretion.[6] For severity assessment, both the Japanese guidelines and the Korean Dementia Association endorse a CDR score of 0.5–1.[6,8] Meanwhile, the ADRD-TWG places greater emphasis on clinical judgment regarding diagnosis and cognitive decline, without strict numerical thresholds.[5]

Regarding absolute contraindications, both the KMFDS[3] and the US FDA[7] restrict exclusions to two conditions: a history of serious hypersensitivity to lecanemab and an inability to undergo MRI scanning. The Japanese Ministry of Health, Labor and Welfare[8] offers

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slightly stricter guidance, advising against use when baseline MRI detects five or more microhemorrhages, a hemorrhage exceeding 1 cm, vasogenic edema, or superficial siderosis. The ADRD-TWG guidelines[5] adopt an even more conservative stance, recommending exclusion in cases where cognitive impairment is attributable to non-AD causes, even if such conditions were not formal exclusion criteria in the lecanemab phase 3 trials.[1] Their imaging criteria also exclude patients with three or more lacunar infarcts, ABRA, or cerebral CAA-ri. These more restrictive criteria reflect evolving safety concerns identified during phase 3 clinical trials, such as fatal cerebral hemorrhage following the concurrent use of lecanemab with anticoagulants or tissue plasminogen activators tPA.[44] In response, the US FDA and Korean regulatory agencies now advise exercising heightened caution when considering the combined use of anti-amyloid antibody therapies and anticoagulant or thrombolytic agents.[3,7] The ADRD-TWG guidelines go further, explicitly prohibiting these combinations, using strong language such as "should not receive" (for donanemab AUR)[46] and "recommend excluding" (for lecanemab AUR).[5] In contrast, we at the KAGP, along with the Korean Dementia Association, have adopted a more practical and flexible approach. Rather than applying rigid exclusion criteria, we emphasize the importance of individualized clinical judgment. We use terms such as "conditions NOT recommended to use lecanemab or necessitating careful consideration" (**Table 1**), allowing clinicians to weigh risks and benefits on a case-by-case basis and to tailor decisions according to patient-specific contexts. **Fig. 1** presents a summary of the eligibility assessment for lecanemab treatment in AD in the form of an algorithm.

OBTAINING INFORMED CONSENT AND EXPLAINING THERAPEUTIC PROTOCOL

Once appropriate patients have been identified, clinicians must engage in detailed discussions with patients and caregivers to explain the purpose of treatment, the expected benefits, the overall course, and potential adverse effects before initiating therapy. It is strongly recommended to use a pre-consent checklist (**Table 2**) to confirm patient eligibility before obtaining informed consent. To facilitate real-world clinical application, we provide a structured framework for counseling and a sample informed consent form. Before starting anti-amyloid antibody therapy, clinicians should thoroughly cover the following key points: 1) mechanism of action and expected benefits; 2) overview of the treatment course; 3) potential adverse effects (infusion-related reactions (IRRs) and ARIAs); 4) patient responsibilities and estimated treatment costs.

Explaining mechanism of action and expected benefits

When introducing anti-amyloid antibody therapy, clinicians should first provide a clear explanation of the drug's mechanism of action and its anticipated clinical impact. Lecanemab specifically targets protofibrillar forms Aβ and Aβ plaques,[1] whereas donanemab is a humanized IgG1 monoclonal antibody that selectively binds to Aβ plaques.[46] As of April 2025, we at the KAGP Practical Guide primarily references lecanemab, which has been approved for clinical use in Korea based on results from the CLARITY-AD Phase 3 trial.[1] In this large-scale study, 1,795 patients with early-stage AD and confirmed amyloid positivity randomized to receive either lecanemab (10 mg/kg biweekly) or placebo for 18 months. Patients treated with lecanemab demonstrated a 0.45-point slower decline on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) compared to placebo, corresponding to approximately a 27% reduction in cognitive deterioration over the study period.

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Table 2. Pre-consent checklist for assessing patient eligibility

Demographics	Age: Sex: ☐ F/ ☐ M BWt: (kg) Height: (cm) BMI: (kg/m²) Available care-taker: ☐ **Absent** ☐ Present (*specify:*)
Clinical diagnosis (most recent)	☐ MCI due to AD ☐ mild AD dementia ☐ **Etc** (Date:) ☐ MMSE score: (Date:) ☐ Global CDR/memory domain/Sum of Box: (Date:) ☐ GDS: **1** / 2 / 3 / 4 / **5** / **6** (Date:)
Amyloid status	☐ Positive ☐ **Negative** ☐ **Unknown** Confirmed by ☐ Amyloid PET imaging ☐ Lumber puncture (Date:)
Brain MRI [FLAIR/SWI(or GRE)/DWI] suggesting exclusion?	**(Date:)** ☐ No ☐ **Yes:** *specify below* ☐ Unable to undergo MRI or has contraindications to MRI ☐ One more macrohemorrhage > 10 mm at greatest diameter ☐ Five or more microhemorrhages smaller than 10 mm ☐ Severe subcortical white matter hyperintensity (Fazekas grade 3) ☐ Stroke involving major vascular territories ☐ Three or more lacunar infarcts ☐ One or more areas of superficial siderosis ☐ Presence of vascular edema ☐ Amyloid-beta related vasculitis (ABRA) ☐ CAA-related inflammation (CAA-ri) ☐ Other intracranial abnormalities suspected to cause cognitive impairment _____ ☐ Other concerning findings _____
APOE genotyping	☐ E3/E3 ☐ E3/E4 ☐ E4/E4 ☐ E2/E3 ☐ E2/E4 ☐ E2/E2
Cardiovascular	☐ Uncontrolled BP ☐ Arrythmia (*specify*:) ☐ Angina history (or potential of future use of anticoagulants or tPA)
Anticoagulants	☐ No ☐ **Yes** (drug: _____)
Antiplatelets	☐ No ☐ Yes (drug: _____)
Immunology	**Any rheumatic or autoimmune disease or any drugs for this condition?** ☐ No ☐ **Yes** (*specify*: _____)
Psychiatric symptom	☐ None ☐ Mild ☐ **Severe** (*specify*: _____)
Recent lab testing (Especially check…) - Platelet < 50K - PT(INR) > 1.5	(Date: _____) **Any results suggesting exclusion?** ☐ No ☐ **Yes** (*specify all*: _____)

Items highlighted in bold within the table indicate factors that require particular caution when considering anti-amyloid antibody therapy. These items warrant careful clinical judgment, and if identified, may necessitate re-evaluation of treatment eligibility, deferral of therapy, or consideration of alternative options based on a thorough risk-benefit analysis.
F = female, M = male, BMI = body mass index, MCI = mild cognitive impairment, AD = Alzheimer's disease, MMSE = Mini-Mental State Examination, CDR = Clinical Dementia Rating, GDS = Global Deterioration Scale, MRI = magnetic resonance imaging, FLAIR = fluid-attenuated inversion recovery, SWI = susceptibility-weighted imaging, GRE = gradient echo, DWI = diffusion-weighted imaging, APOE = apolipoprotein E, BP =blood pressure, tPA = tissue plasminogen activator, PT = prothrombin time, INR = international normalized ratio.

It is essential to differentiate anti-amyloid therapies from conventional symptomatic treatments such as cholinesterase inhibitors. Unlike symptomatic agents, lecanemab is designed to target and remove the underlying pathological protein burden, aiming to modify disease progression rather than simply alleviate symptoms.[1] When discussing benefits with patients and caregivers, clinicians should frame the expected effects along two dimensions: pathological and clinical outcomes. From a pathological standpoint, significant Aβ plaque reduction was observed as early as 3 months into treatment, with an average decrease of approximately 60 centiloids by 18 months (−59.12 centiloids; 95% confidence interval, −62.64 to −55.60; $P < 0.001$).[1] Clinically, the principal benefit is the deceleration of cognitive decline, rather than improvement or restoration of previous cognitive abilities. It is crucial to set realistic expectations, emphasizing that the primary goal of therapy is to slow disease progression—not to cure the disease or reverse existing deficits. Although long-term outcomes beyond three years remain under investigation, early evidence suggests

that substantial early plaque clearance may contribute to more favorable long-term cognitive trajectories.[55] Consequently, early intervention with anti-amyloid therapy may offer potential advantages in altering the course of AD.

Special considerations when discussing expected benefits

Clinicians should recognize that, in some patients, cognitive impairment may remain relatively mild despite the presence of significant underlying pathological changes, such as advanced cerebral Aβ deposition. These patients may argue that treatment can be postponed, as their perceived difficulties are not yet tangible. Therefore, it is important to help them understand that the earlier anti-amyloid antibody therapy is initiated, the greater the likelihood of preserving their current cognitive function. However, this explanation should be delivered with caution, as it may inadvertently convey a sense of coercion or hopelessness in the absence of treatment. Conversely, if a patient presents with significant cognitive decline but only minimal amyloid pathology, clinicians should broaden the diagnostic perspective, carefully evaluating potential contributions from medication side effects, systemic comorbidities, environmental factors, or the presence of mixed pathologies (**Table 3**). A comprehensive and multidisciplinary approach is critical to accurately assess these complex cases.

When mixed pathology is suspected, clinicians should engage in open and transparent discussions with patients and caregivers, emphasizing that therapeutic response could be attenuated and the cost-effectiveness of treatment potentially diminished compared to cases with pure AD pathology. Nevertheless, it should be noted that cases with purely isolated AD pathology are relatively rare in real-world clinical settings.[56,57] Consequently, early intervention aimed at reducing cerebral Aβ burden may still confer meaningful benefits by slowing the trajectory of cognitive decline, even in patients with mixed etiologies.

Providing overview of treatment process

At the outset of lecanemab therapy, clinicians should provide patients and caregivers with a clear and comprehensive explanation of the treatment process. Setting transparent

Table 3. Potential causes of cognitive impairment when clinical severity exceeds biological stage

Category	Examples
Medications	· Antihistamines (H1 and H2 blockers) · Analgesics (e.g., tramadol combinations, opioids, GABAergic agents, anticonvulsants for neuropathic pain) · Benzodiazepines (including Z-drugs) · Anticholinergics or drugs with cumulative anticholinergic effects · Certain chemotherapeutic agents (“chemo brain”) · Combination cold medications (e.g., those with antihistamines, anticholinergics, opioids)
Nutritional, metabolic, endocrine	· Vitamin B12, B1, or folate deficiency · Hypothyroidism · Hyperammonemia (including drug-induced) · Severe anemia · Cerebral hypoperfusion (e.g., heart failure, hypotension, dehydration, alpha-blocker use) · Syndrome of inappropriate antidiuretic hormone secretion
Sleep disorders	· Sleep deprivation · chronic obstructive sleep disorders
Sensory impairment	· Hearing loss · Visual impairment
Environmental factors	· Sensory deprivation (e.g., social isolation) · Chronic exposure to organic solvents
Other	· Alcohol or substance abuse · Low premorbid intellectual function · Depression (pseudodementia, chronic depression) · Chronic medical conditions (e.g., renal dysfunction)

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Table 4. Treatment schedule of lecanemab

Week	Screening	Obtain informed consent	0	2	4	6	8	10	12–24	26–48	50–70	72
Infusion number			1	2	3	4	5	6	7–13	14–25	26–36	
Clinical assessment[a]	v										v	v
Blood tests[b]	v					v		v	v	v		v
Brain MRI[c]	v					v		v	v	v		
Outpatient visits[d]	v	v				v MRI for ARIA assessment and determination of treatment continuation		v MRI for ARIA assessment and determination of treatment continuation	v MRI for ARIA assessment and determination of treatment continuation	v MRI for ARIA assessment and determination of treatment continuation		v
Check body weight & V/S			v	v	v	v	v	v	v	v	v	
Visit infusion room[e]			Day admission	Day admission	Day admission or infusion room	v	v	v	v	v	v	

MRI = magnetic resonance imaging, ARIA = amyloid-related imaging abnormalities.
[a]Clinical evaluation: Annual cognitive assessments are recommended. During treatment, regular evaluation of treatment adherence is also advised.
[b]Blood tests: During screening, conduct standard laboratory tests to rule out secondary causes of cognitive decline. APOE genotyping is also needed. CBC and coagulation studies are recommended after treatment initiation.
[c]Brain MRI: The ADRD-TWG and the Korean Ministry of Food and Drug Safety recommend ARIA monitoring MRIs be performed at the 5th, 7th, and 14th infusions. For patients who carry the APOE4 allele or have previously shown ARIA findings, an additional brain MRI is recommended prior to the 26th infusion.
[d]Adjustments may be made based on current medications and treatment status. After ARIA monitoring MRI, patients should visit the outpatient clinic for ARIA assessment and to determine whether to continue treatment. During the visit, clinicians should place orders for the next brain MRI and the upcoming infusion to ensure continuity of care.
[e]Whether to admit patient to hospital can be decided based on clinical and patient situation.

expectations from the beginning promotes better treatment adherence and helps patients and families develop a well-informed understanding of the therapy. After obtaining informed consent, patients typically initiate treatment with intravenous infusions administered every two weeks over an 18-month period. Each infusion session lasts approximately one hour. Throughout the treatment course, scheduled MRI scans are essential for the early detection and management of potential adverse effects, particularly ARIA (**Table 4**).

Dosing and administration

Lecanemab is administered as a weight-based intravenous infusion at a dose of 10 mg/kg.[3,7] For example, a patient with a body weight of 50 kg would receive a 500 mg dose. The drug is available in vials containing either 500 mg/5 mL or 200 mg/2 mL. Clinicians should reassess and adjust the dosing regimen if the patient's body weight changes by more than 10% from the baseline measurement at the time of treatment initiation.[5]

Treatment schedule and post-infusion monitoring

Patients undergo 36 total infusions over the 18-month course, ideally maintaining two-week intervals (with a permissible variation of ± 1 week), ensuring at least 8 days between doses. Each infusion is administered over one hour. Post-infusion monitoring varies based on the infusion number. Following the first infusion, a three-hour observation period is recommended to monitor for hypersensitivity reactions. After the second and third infusions, a two-hour observation period is advised. If no hypersensitivity has been noted in prior infusions, subsequent monitoring may be shortened to 30 minutes.

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MRI monitoring for ARIA

ARIA represents one of the most critical risks during treatment, necessitating vigilant MRI surveillance. A baseline MRI—conducted within 6 to 12 months prior to treatment initiation—is required. According to KMFDS prescribing information, MRI scans are recommended performed before the 5th, 7th, and 14th infusions.[3] Additionally, The KAGP practical guide recommends considering earlier or additional MRI surveillance depending on the patient's baseline ARIA risk (**Fig. 2A**). At treatment initiation, an individual ARIA risk assessment (using such as the provisional KAGP's ARIA Prediction scale [KAGP ARIA scale], **Supplementary Table 1**) can guide the monitoring strategy. While the 5th infusion is generally recommended as the first time point for ARIA-monitoring MRI, patients with intermediate or high risk (e.g., those with one or more core risk factors of KAGP ARIA scale) may require earlier imaging, such as prior to the 3rd infusion. This risk-adapted approach allows for more proactive detection and management of ARIA, ensuring safety in patients at elevated risk. We along with the ADRD-TWG recommend an extra MRI before the 26th infusion for patients who are APOE ε4 carriers or those with prior ARIA findings.[5] After the first year, subsequent MRI follow-ups are advised every 6 to 12 months based on clinical status and individual risk factors. MRI imaging should also be expedited if patients develop symptoms suggestive of ARIA or if clinically indicated at any point during treatment.[42,58]

Maintenance therapy (post-18 months)

After completing the initial 18-month treatment phase, patients may transition to a 'maintenance treatment' consisting of monthly (every four weeks) infusions. The US FDA formally approved this extended dosing schedule for lecanemab in January 2025.[59] This recommendation stems from data showing that discontinuation of therapy results in re-accumulation of amyloid plaques and a subsequent return to the rate of cognitive decline observed in placebo group.[55] Consequently, clinicians should engage patients and caregivers in detailed discussions when evaluating the continuation of maintenance therapy. Unlike lecanemab, donanemab was administered as monthly infusions from the beginning of therapy. In the donanemab clinical trials, participants also underwent amyloid PET imaging every six months, and those who achieved sufficient amyloid clearance were switched to placebo.[46] Reflecting this strategy, the US FDA now recommends discontinuing donanemab once PET imaging confirms minimal residual cerebral amyloid burden.[41,60]

Providing information on adverse events

During anti-amyloid antibody therapy, close monitoring is particularly warranted for two key categories of adverse events: IRRs and ARIA. IRRs are defined as physiological responses that may occur during or shortly after infusion,[61] typically mild and self-limiting; however, symptomatic management with adjunctive medications may occasionally be required. ARIA refers to radiographic abnormalities detectable on MRI, arising because of amyloid clearance.[62] Although frequently asymptomatic, ARIA may present with clinical manifestations such as headache, dizziness, confusion, or seizures. Given that the incidence of ARIA is highest within the first 14 weeks of therapy,[45] intensified MRI surveillance during the early treatment phase is strongly recommended. Patients should be thoroughly educated regarding the importance of promptly reporting any new neurological symptoms. Early detection of ARIA may necessitate treatment modifications, including dose interruption or discontinuation, to mitigate potential complications.

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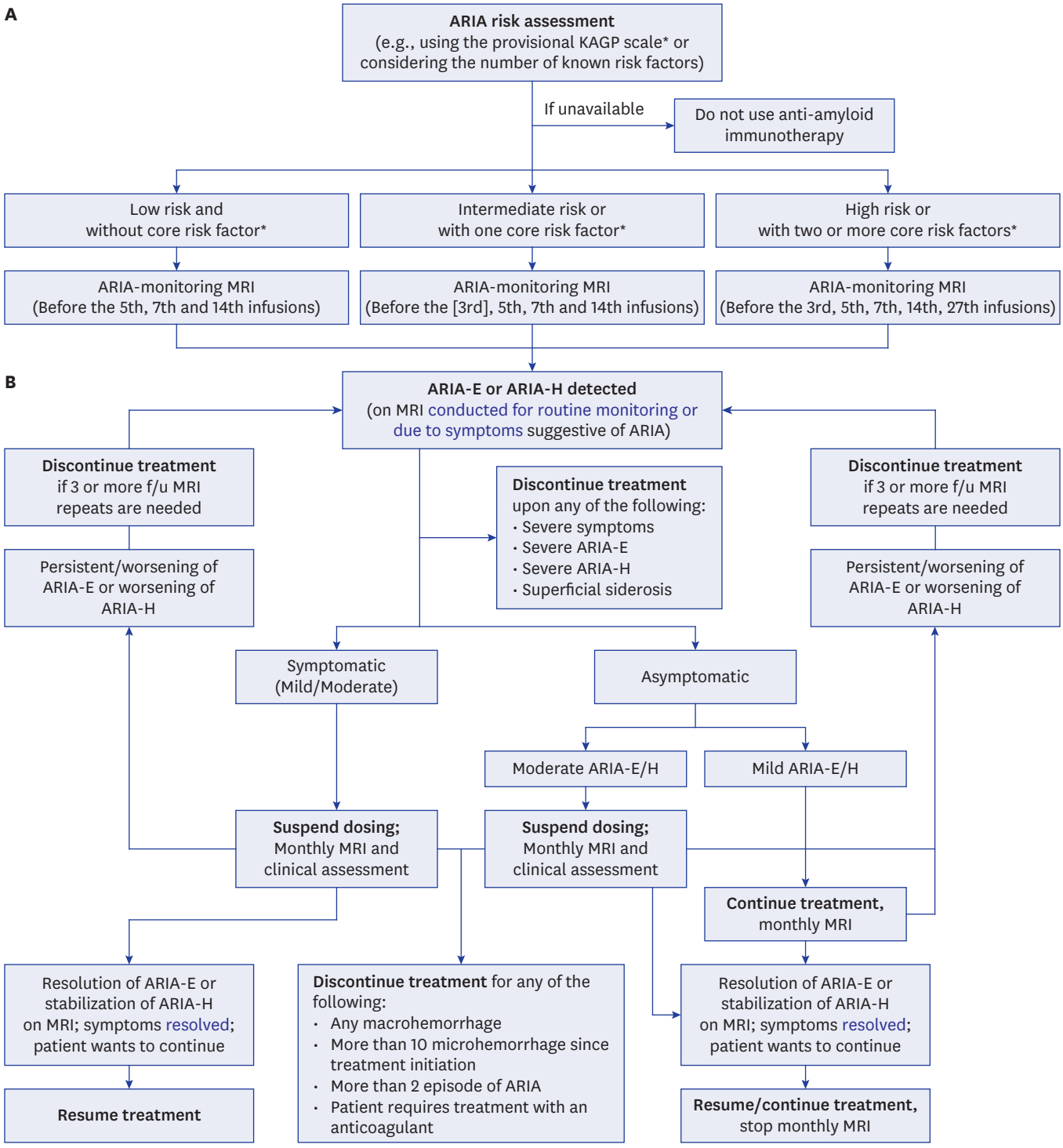

Fig. 2. Clinical algorithm for monitoring and management of ARIA. This algorithm outlines the recommended clinical decision-making process for monitoring and managing ARIA (Amyloid-Related Imaging Abnormalities) during lecanemab treatment. (**A**) Illustrates an ARIA monitoring protocol guided by individual risk stratification using the provisional KAGP risk scale. Patients are categorized into low, intermediate, or high ARIA risk groups. And, the timing of ARIA-monitoring MRI varies accordingly, with earlier imaging (e.g., before the 3rd infusion) recommended for higher-risk individuals. (**B**) Upon identification of suspected ARIA symptoms, an additional MRI is performed to confirm ARIA-E (edema/effusion) or ARIA-H (microhemorrhage/siderosis). Treatment decisions are guided by the presence or absence of symptoms, as well as the severity of ARIA findings.
ARIA = amyloid-related imaging abnormalities, KAGP = Korean Association for Geriatric Psychiatry, MRI = magnetic resonance imaging.

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Patient instructions and safety precautions during lecanemab therapy

Patients already receiving conventional cognitive enhancers—such as donepezil, rivastigmine, galantamine, or memantine—may continue these therapies concurrently with lecanemab without requiring dose adjustments.[5] Nevertheless, it remains critical that patients fully disclose all medications they are currently taking to their healthcare providers, as certain drug interactions necessitate careful monitoring. Particular caution is warranted regarding anticoagulants and antiplatelet agents due to their potential to increase the risk of ARIA.[45] Antiplatelet agents (e.g., aspirin, clopidogrel) administered at stable maintenance doses can generally be continued safely with lecanemab, with clinical trial data showing no meaningful increase in ARIA risk under these conditions.[5,45,63] However, among individuals with homozygous for the APOE ε4 allele, even stable-dose antiplatelet use may elevate risk, and additional counseling is advisable.[3,5,7] The concurrent use of anticoagulants (e.g., warfarin, rivaroxaban, dabigatran) or thrombolytic agents (e.g., tPA) markedly elevates the risk ARIA-H.[44] In such cases, clinicians should conduct a meticulous risk-benefit assessment before initiating lecanemab or other anti-amyloid antibody therapies. For individuals with a history of stroke, cardiovascular disease, or concurrent anticoagulant or antihypertensive use, a comprehensive medication review must precede treatment initiation. Clinicians should withhold lecanemab administration until they have thoroughly evaluated the patient's full medication profile and determined bleeding risks. Furthermore, they should reassess medication regimens at each follow-up visit to promptly detect emerging contraindications or evolving risks.

Patients must inform emergency medical personnel about their ongoing lecanemab therapy if they present to an emergency department. Given that thrombolytic agents such as tPA can precipitate catastrophic intracerebral hemorrhage during anti-amyloid treatment, patients should be strongly encouraged to carry a medical alert bracelet or identification card specifying their treatment status. This precaution ensures that emergency responders have immediate access to critical therapeutic information, even if the patient cannot self-report. If a scheduled infusion is missed, patients should present for rescheduled administration at the earliest opportunity, thereafter, maintaining standard two-week dosing intervals.

Providing clear financial information before treatment initiation

Clinicians must incorporate a discussion of treatment costs into the decision-making process when considering the initiation of anti-amyloid antibody therapy. Before commencing treatment, they should clearly inform patients and their families about the anticipated financial burden, ensuring they are adequately prepared for both initial and ongoing expenses. Providing transparent information regarding the total cost of care helps prevent unexpected financial strain over the course of therapy. At present, lecanemab is prescribed on a self-pay basis, without any governmental subsidy or financial support in Korea, and its price may vary slightly between medical institutions. Delivering a thorough explanation of the entire treatment process—including financial obligations—enables patients and caregivers to better anticipate the therapeutic course and promotes active, informed participation in their care.

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MONITORING AND MANAGING ADVERSE REACTIONS

Infusion-related reactions

IRRs represent a relatively common adverse event associated with administration of anti-amyloid monoclonal antibody therapeutics such as lecanemab and donanemab. In the CLARITY-AD Phase 3 trial with lecanemab, approximately 26.4% of patients in the treatment group experienced IRRs, compared to 7.4% in the placebo group.[1] Notably, most IRRs (96%) were classified as mild to moderate in severity.[1,64] Frequently reported symptoms included low-grade fever, chills, nausea, and fluctuations in blood pressure. Approximately 75% of IRRs occurred during the first infusion, underscoring the importance of extended post-infusion monitoring—typically for 2 to 3 hours—during the initial dosing sessions.[1,64] Although rare, severe hypersensitivity reactions such as anaphylaxis (manifesting as facial or lip swelling and respiratory distress) were reported in about 0.6% of patients, predominantly during the first infusion.[45] Clinicians must proactively counsel patients regarding the potential for IRRs prior to initiating therapy and emphasize the importance of promptly reporting any abnormal symptoms during or after infusion. Clinicians must immediately evaluate suspected cases to initiate timely intervention and protect patient safety.

Management of infusion-related reactions

When IRRs occur during lecanemab administration, clinicians must tailor management strategies according to the severity of the reaction. For Grade 1 (mild and transient) reactions,[65] no specific intervention is typically required. However, if the patient reports significant subjective discomfort, pre-medication prior to the next infusion may be considered. Standard pre-medication options include chlorpheniramine 4 mg intravenously and acetaminophen 650 mg orally, administered approximately 30 minutes before infusion.[1,5] Nonetheless, findings from the CLARITY-AD core and open-label extension studies indicate no significant difference in IRR recurrence rates between patients who received pre-medication and those who did not (39.3% vs. 32.7%, respectively).[45] For Grade 2 reactions (moderate discomfort requiring temporary interruption of infusion), clinicians should pause the infusion and provide symptomatic treatments such as oral or intravenous antihistamines, acetaminophen, or oral prednisolone as appropriate. Following symptom resolution, the clinical team should carefully assess whether it is safe to resume the infusion. In cases of Grade 3 or higher severity—such as anaphylaxis—the infusion must be discontinued immediately, and emergency interventions should be initiated as needed. Further decisions regarding whether to continue future infusions must involve a careful, expert-led evaluation of the patient's overall safety and benefit profile.

Amyloid-related imaging abnormality

ARIA refers to abnormal MRI findings that emerge in patients with AD receiving anti-amyloid antibody therapy.[62] These imaging abnormalities are thought to represent inflammatory changes secondary to CAA triggered by amyloid clearance and are collectively termed ARIA.[66,67] Two major subtypes of ARIA have been identified, which can present either independently or simultaneously. ARIA-E (edema/effusion) involves vasogenic edema within the brain parenchyma or the accumulation of effusion in the cortical sulci, reflecting increased vascular permeability associated with amyloid removal.[68] ARIA-H (microhemorrhage/superficial siderosis) is characterized by hemosiderin deposition, manifesting as either microhemorrhages (≤ 10 mm) within the brain tissue or superficial siderosis along the subarachnoid space.[69] Both forms constitute hallmark radiological findings in patients

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undergoing anti-amyloid therapy and underscore the necessity of vigilant MRI surveillance to enable early detection and management of treatment-related complications.

Clinical symptoms of ARIA

In most cases—approximately 97%—ARIA remains asymptomatic. Even when clinical symptoms occur, they are typically mild, transient, and tend to resolve spontaneously over the course of several months.[45,70] Common symptoms suggestive of ARIA include headache, confusion, dizziness, blurred vision, nausea, vomiting, and seizures.[5] However, it should be noted that, although rare, more severe complications such as significant cerebral edema, seizures, and even mortality have been reported in association with ARIA.[5,70]

Risk factors for ARIA

The risk of developing ARIA is closely associated with APOE ε4 carrier status, higher drug dosages, old age, and pre-existing cerebral microhemorrhages identified on baseline MRI.[45,71,72] The risk of ARIA-E increases in a dose-dependent manner with the number of APOE ε4 alleles carried, higher administered drug doses, and the presence of microhemorrhages prior to treatment. Similarly, ARIA-H is often associated with ARIA-E, as patients who develop ARIA-E exhibit a higher likelihood of concomitant ARIA-H.[58,72] Notably, 48.4% of patients who experienced ARIA-H also demonstrated simultaneous ARIA-E.[63]

While the association between ARIA-H and drug dosage remains unclear, several studies implicate APOE ε4 positivity, preexisting cerebral microhemorrhages, and concomitant anticoagulant use as contributing risk factors.[73] Furthermore, baseline MRI findings of five or more cerebral microhemorrhages, superficial siderosis involving one or more sulcal regions, or evidence of ABRA or CAA-ri constitute formal exclusion criteria for lecanemab initiation.[1] These imaging abnormalities significantly elevate the risk of ARIA during treatment. Clinical trial data also indicate that concomitant use of aspirin or antiplatelet agents did not significantly increase the incidence of ARIA-H compared to patients who did not receive these medications.[45]

Differences in ARIA incidence according to APOE genotype

Numerous studies have consistently demonstrated that carriers of the APOE ε4 allele—particularly homozygotes—exhibit a higher incidence of ARIA compared to non-carriers.[5,45,46,63] Consequently, clinicians must conduct APOE genotyping prior to initiating anti-amyloid antibody treatment and clearly communicate to patients that ARIA risk varies depending on genetic background. In the CLARITY-AD trial,[1] the overall incidence of ARIA-E was reported as 12.6% and ARIA-H as 17.3% among lecanemab-treated participants. Stratifying by APOE genotype revealed substantial differences: patients without an ε4 allele exhibited a 5.4% incidence of ARIA-E, compared to 10.9% among heterozygous carriers and 32.6% among homozygous carriers.[1,45]A similar trend was observed for ARIA-H, with incidences of 11.9%, 14.0%, and 39.9%, respectively. A subgroup analysis focusing on Asian participants, including cohorts from Korea and Japan, further highlighted population-specific patterns.[74] Among the 141 Asian participants, the incidence of ARIA-H was 14.4% overall, with 14.8% in the Japanese cohort and 11.1% in the Korean cohort. Meanwhile, ARIA-E occurred in 6.5% of Asian participants, 4.5% of Japanese participants, and 5.6% of Korean participants—rates notably lower than those observed in non-Asian populations. Importantly, no symptomatic ARIA-E cases were reported among Asian participants. These findings might suggest that racial and ethnic factors may modulate ARIA risk and presentation. Further studies are warranted to elucidate the underlying biological mechanisms and the clinical implications of these observed disparities.

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Temporal patterns of ARIA

ARIA-E typically occurs within the first 14 weeks of treatment, underscoring the need for heightened vigilance during the early therapeutic phase.[45] In contrast, isolated ARIA-H events occur sporadically throughout the treatment course, at a frequency comparable to that observed in placebo group. However, when ARIA-H coincides with ARIA-E, these events tend to cluster within the initial weeks of therapy. Notably, cases of intracerebral hemorrhage have not demonstrated a clear temporal association with treatment initiation.[45,71]

ARIA monitoring protocol

According to guidelines from the ASNR[42] and the KSNR,[43] a minimum MRI protocol for ARIA surveillance should include the following sequences: T2-weighted fluid-attenuated inversion recovery (FLAIR), T2*-weighted gradient echo (GRE), and diffusion-weighted imaging (DWI). T2-FLAIR is essential for detecting ARIA-E (edema/effusion). While 3D FLAIR is preferred for its enhanced spatial resolution, hospitals or medical institutions may opt for 2D FLAIR based on equipment availability. For ARIA-H detection, imaging should include 2D T2*GRE sequences rather than echo planar imaging. When available, susceptibility-weighted imaging (SWI) is recommended, as it offers superior sensitivity and diagnostic precision compared to GRE.[75] DWI is critical for distinguishing ARIA-E from acute or subacute infarctions that may arise during treatment. To ensure reliable comparisons over time, healthcare providers should maintain consistency across serial MRI scans. Both baseline and follow-up ARIA-monitoring MRIs should be obtained using the same imaging sequences, field strength, and MRI system model.

Radiologic severity grading and classification of ARIA

The US FDA classifies ARIA-E and ARIA-H into three severity categories: mild, moderate, and severe.[7] The severity of ARIA-E is determined by the size and distribution of FLAIR hyperintensities.[5] Specifically, a single hyperintense lesion under 5 cm is considered mild; hyperintensities measuring between 5–10 cm or involving multiple discrete regions qualify as moderate; and any lesion exceeding 10 cm is categorized as severe. For ARIA-H, severity is based on the number of cerebral microhemorrhages and the extent of superficial siderosis. Mild ARIA-H includes fewer than four microhemorrhages or one region of superficial siderosis. Moderate cases involve 5–9 microhemorrhages or two siderotic foci, while severe ARIA-H includes ten or more microhemorrhages and more than two foci of siderosis. This stratification plays a critical role in monitoring and therapeutic decision-making during anti-amyloid antibody therapy.

Dose adjustment strategies based on ARIA risk

Unlike donanemab, lecanemab underwent clinical trials without a dose titration protocol.[1] In contrast, donanemab trials demonstrated that a modified titration approach—gradually escalating the dose from 350 mg to 700 mg and then to 1,050 mg—significantly reduced the incidence of ARIA-E compared to a fixed-dose regimen (700 mg from the first to third dose).[76] Notably, in APOE ε4 homozygous individuals, ARIA-E occurred in 57% of participants receiving the standard dose of donanemab, whereas the incidence dropped to 19% in those receiving the modified titration regimen. Furthermore, symptomatic ARIA-E was observed in 5% of the standard-dose group and 0% in the modified group.[76] Although similar modified titration strategies have not yet been formally evaluated for lecanemab, these findings suggest that a lower initial dosing schedule may be worth considering—particularly for patients at elevated genetic risk for ARIA, such as APOE ε4 homozygotes.

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Management of ARIA

The ARIA management strategy recommended in the KAGP practical guide is detailed in **Fig. 2B**. When ARIA develops during lecanemab therapy, clinicians must make subsequent treatment decisions based on the ARIA subtype, severity, and presence of symptoms.[5] Most ARIA cases are asymptomatic and mild, allowing for continuation of treatment with close monitoring.[1,5,45] In such cases, monthly MRI follow-ups are recommended to track lesion progression. If imaging shows resolution or stabilization of ARIA, monthly MRI scans may no longer be necessary. However, symptomatic ARIA warrants a more cautious approach. Clinicians should reassess the risk-benefit balance, consider temporary treatment suspension, and individualize decisions based on symptom severity, radiologic findings, and patient-specific risk factors (**Fig. 2B**).

Although most ARIA cases remain mild and self-limiting, rare but severe complications—including cerebral edema, seizures, encephalopathy, and even death—have been reported. In the CLARITY-AD trial,[1] 22.1% of patients with ARIA-E and 0.4% of those with ARIA-H exhibited clinical symptoms. Severe ARIA often mimics the presentation of CAA-ri, with extensive T2 FLAIR hyperintensities, parenchymal swelling, and accompanying microhemorrhages. Critically, severe ARIA remains unpredictable. While some patients present with no or only mild symptoms, others may rapidly progress into encephalopathy, status epilepticus, or focal neurological deficits.[1,44,46,77] In such cases, irreversible neurological impairment or death cannot be excluded. Clinicians must act swiftly when patients develop significant neurological symptoms. Immediate MRI evaluation using an ARIA-focused protocol, including DWI, is essential to rule out ischemic stroke. Depending on clinical severity, inpatient care—either in a general ward or intensive care unit—may also be warranted.

The KAGP recommendations are largely aligned with those listed in the ADRD-TWG AUR[5] and are also compatible with the KMFDS[3] and U.S. FDA[2] prescribing information. While the latter allow clinicians to continue treatment in cases of radiographically mild ARIA-E with mild symptoms, the KAGP recommends a slightly more conservative approach. Both the KAGP and ADRD-TWG advise monthly MRI monitoring following ARIA detection, whereas the KMFDS[3] and U.S. FDA[2] suggest follow-up imaging within 2 to 4 months. Importantly, the KAGP guideline explicitly states that if ARIA does not resolve and more than three monthly MRI scans are required, treatment discontinuation should be considered. This provision reflects an effort to balance safety with real-world feasibility in clinical practice.

ESTABLISHING INSTITUTIONAL INFRASTRUCTURE FOR SAFE AND EFFECTIVE ANTI-AMYLOID ANTIBODY THERAPY

Administering anti-amyloid antibody therapy is a multifaceted process that extends far beyond a single prescription procedure. It encompasses medication preparation, intravenous infusion, adverse event monitoring, scheduled neuroimaging assessment, and coordination for emergency management. Therefore, hospitals must proactively establish comprehensive infrastructure, streamline workflow protocols, and strengthen interdisciplinary collaboration before initiating therapy. A multidisciplinary system—centered around the prescribing physician responsible for lecanemab administration, with active collaboration from departments of radiology, nuclear medicine, emergency medicine, neurology, and internal

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medicine, as well as nursing and pharmacy—is critical to ensure safe and effective treatment delivery.[5,41,78,79]

Interdepartmental collaboration

Effective lecanemab administration demands seamless collaboration across multiple departments. Physicians should engage early with radiologists to develop standardized MRI protocols for baseline assessments and ongoing ARIA surveillance. Before starting treatment, they need to review baseline brain MRIs with radiology specialists to rule out any contraindications. Continuous coordination with the radiology team ensures timely scheduling and accurate interpretation of follow-up imaging. Because MRI evaluation plays a pivotal role in detecting ARIA, maintaining an open and ongoing dialogue with radiologists remains essential.

Close coordination with the nuclear medicine department is equally critical, as amyloid pathology serves as a key determinant of treatment eligibility. If available, quantitative imaging can help track changes in amyloid burden before and after therapy, and collaboration should be established to support these assessments. Engagement with the emergency medicine team is also essential.[5] Because patients on lecanemab may present with stroke-like symptoms, emergency staff must be fully aware that using thrombolytic agents, such as tPA, in practice, are considered contraindicated in these patients due to the augmented risk of macrohemorrhage in the brain. In addition, strong collaboration with other clinical specialties is vital for managing IRRs and symptomatic ARIA events. Severe IRRs (grade 3 or higher)[65] may require prompt consultation with internal medicine, while cases of symptomatic ARIA-E or ARIA-H often call for coordinated care with neurology or neurosurgery teams. Clinicians should also work proactively with the nursing team to ensure they are well-informed about lecanemab preparation, infusion procedures, and monitoring protocols, allowing for seamless treatment delivery (**Table 5**). Collaborate with the pharmacy to confirm proper storage and handling—lecanemab must be kept in a sealed, light-protected container at 2°C to 8°C,[3] and vials should never be shaken or frozen, as this may affect the drug's stability.[5] Given that infusion spaces may be shared with other services, such as oncology department, it would be required to coordinate infusion schedules in advance to secure availability. The hospital should also ensure that essential resources are in place, including designated IV infusion areas, temperature-controlled storage, emergency carts, and sufficient waiting areas for patients.

Table 5. Interdepartmental Coordination for anti-amyloid monoclonal antibody administration

Departments/Units	Contents Needing Discussion
Radiology	· Establish MRI protocols for both baseline evaluation and ongoing ARIA monitoring to ensure accurate and consistent imaging. · Coordinate MRI scheduling to align with patient treatment timelines and minimize delays in monitoring.
Nuclear Medicine	· Recognize amyloid burden as a critical determinant for treatment eligibility and ensure proper assessment through imaging. · Utilize quantitative analysis and centiloid-based interpretation for precise evaluation of amyloid deposition before and after treatment.
Infusion Unit or Same-Day Admission Room	· Confirm availability of outpatient infusion appointments and assess the daily patient capacity to support smooth scheduling. · Implement standardized procedures for medication preparation and conduct pre-infusion safety checks to minimize risk. · Provide nurses with comprehensive education on patient monitoring before and after infusion, including management of infusion-related reactions.
Pharmacy	· Verify the shelf life and proper storage conditions for the drug to maintain stability and efficacy.
Emergency Medicine, Neurology, and Neurosurgery	· Develop and share diagnostic and treatment protocols for managing symptomatic ARIA cases that may present in the emergency department.
Administration Office	· Ensure appropriate documentation of informed consent and patient rights in the process of inpatient admission for treatment.

MRI = magnetic resonance imaging, ARIA = amyloid-related imaging abnormalities.

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Outpatient and inpatient infusion protocols

Lecanemab can be administered either in an inpatient setting or through an outpatient infusion center, depending on the patient's clinical condition and the resources available at the hospital. Because IRRs are more likely to occur early in treatment and require longer monitoring (typically 2–3 hours for the first few infusions),[45] patients often benefit from hospital admission—either as one-day hospitalization or overnight stay—for the first to the third dose. Once monitoring time is reduced to about 30 minutes, outpatient administration becomes a practical option. The infusion process typically involves three continuous stages. Prior to the infusion, medical or nursing staff should check the patient's temperature, blood pressure, and weight, and prepare the medication. During the infusion, the patient should be monitored for any signs of IRRs or other adverse events.[5] After the infusion, staff should monitor patients for any delayed reactions. Before discharge, they should clearly explain ARIA-related symptoms—such as headache, dizziness, confusion, or changes in speech—and provide written materials for reference. Providing an emergency contact card with clear guidance on when and how to seek medical attention enhances patient safety. By establishing a well-structured, multidisciplinary infusion protocol, healthcare teams can improve the safety of anti-amyloid therapy, foster trust with patients and caregivers, and help ensure long-term treatment adherence.

CLINICAL CONSIDERATIONS AND COMMUNICATION STRATEGIES WHEN ANTIBODY THERAPY IS NOT AN OPTION

Paradoxically, in the era of anti-amyloid antibody therapy, embracing non-eligible patients and providing them with appropriate empathetic concern may emerge as a primary task for clinicians. This imperative is underscored by a recent study indicating that only approximately 10% of clinic visitors meet the eligibility criteria for anti-amyloid antibody therapy.[80,81]

Treatment decisions should consider a range of factors, including not only disease stage, neuroimaging findings, comorbid conditions but also likelihood of treatment adherence, availability of caretakers, and the patient's social and financial circumstances. In some cases, treatment may not be recommended—or patients and their families may choose to decline it. In these situations, clinicians should continue to offer patient-centered care by fostering trust and maintaining open, honest communication with the patients and caregivers.

The KAGP outlines several scenarios in which antibody therapy is not recommended. These include moderate to severe dementia (CDR ≥ 2), marked functional decline, or imaging findings associated with high ARIA risk—such as multiple cerebral microbleeds or severe white matter disease (e.g., Fazekas grade 3).[5,63,72] Other not recommended conditions may include the inability to stop anticoagulants or thrombolytics, psychiatric conditions that impair treatment cooperation (e.g., severe delusions or depression), lack of caregiver support, or limited access to consistent medical care.

Rather than framing the decision as a simple denial of treatment, clinicians should explain that the choice not to proceed with therapy is itself a medically informed, evidence-based decision as a way of ongoing care and protecting patients. They should also guide patients and families toward alternative, individualized care plans—such as established medications

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(e.g., cholinesterase inhibitors, NMDA receptor antagonists) or non-pharmacologic strategies like cognitive rehabilitation, functional support, and psychological interventions. Acknowledging and validating the emotional impact of treatment ineligibility is essential to preserving the therapeutic alliance.

Financial constraints can also prevent access to treatment, leading to additional frustration. This represents one of the most tangible and immediate challenges posed by antibody therapies. Clinicians should address these issues proactively, managing unrealistic expectations and avoiding overstatement of the therapy's benefits. When patients or caregivers express skepticism or distrust toward antibody therapies, the clinical approach should focus on education rather than persuasion. Overly assertive recommendations can undermine trust and make families feel pressured. Rather than trying to convince them, clinicians should offer accessible clinical trial data and objective information to support shared decision-making and help patients make informed choices.

Ultimately, deciding not to start antibody therapy still demands careful clinical judgment, clear communication, and a patient-centered approach. In today's evolving treatment landscape, knowing when and how to withhold therapy is just as important as knowing when to initiate it—and remains a core competency for both psychiatrists and dementia specialists.

DISCUSSION

The arrival of anti-amyloid antibody therapies marks a major shift in AD treatment—not just in clinical practice, but in how we think about care and how healthcare systems are organized. To deliver treatments like lecanemab safely and effectively in Korea, success must extend beyond individual prescribing decisions. It requires coordinated support across the healthcare system, including insurance coverage, research infrastructure, and professional training.

The KAGP's goal goes beyond simply recommending how to use these therapies. Through this practical guide, we offer forward-looking strategies to support their responsible and sustainable use. One of the top priorities is building a strong base of real-world data that reflects the characteristics and treatment responses of Korean patients with AD. Key metrics—like treatment adherence, ARIA rates, cognitive changes, and functional outcomes—should be collected systematically through multicenter collaboration. This could include expanding existing registries or creating new cohorts dedicated to antibody therapies. These data will provide essential evidence to guide policy decisions, shape reimbursement criteria, and refine future clinical guidelines.

Given the high cost of antibody therapies, insurance coverage will play a critical role in determining access to treatment for eligible patients with AD. Reimbursement should be introduced in a stepwise manner, grounded in clinical benefit, cost-effectiveness, and the absence of viable alternatives. Coverage policies must clearly outline eligibility criteria for high-risk patients, MRI requirements, and ARIA management protocols. Open and ongoing communications between healthcare professionals and insurers would be essential, with psychiatric perspectives integrated from the outset of policy development.

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To integrate antibody therapies into routine dementia care, clinical training and guideline development must advance in parallel. Psychiatrists and neurologists should be well-versed in the fundamentals of these treatments and confident in applying them appropriately. The KAGP would lead this effort by providing practical training—through case-based workshops, ARIA-focused conference sessions, and informed consent simulations designed for real-world settings. Clinical guidelines should also be treated as living documents, updated regularly to reflect new evidence and feedback from frontline practice.

This KAGP guide represents the first comprehensive roadmap for integrating anti-amyloid antibody therapy into dementia care—from diagnostic considerations and treatment decisions to monitoring strategies, non-treatment alternatives, and future policy directions. As experience grows and converges, these recommendations will continue to evolve, laying the foundation for a safe, responsible, and patient-centered approach to AD in Korea.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1

Provisional Scale for KAGP's ARIA Generation Prediction scale (KAGP scale)

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