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Lecanemab in Singapore: Appropriate use recommendations for early Alzheimer's disease

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ABSTRACT

Introduction: Lecanemab, a monoclonal antibody targeting β-amyloid oligomers, protofibrils, and insoluble fibrils, has been approved for Alzheimer's disease (AD) treatment in Singapore, based on the phase 3 Clarity AD study. In this paper, the Singapore-adapted Appropriate Use Recommendations (AURs) serve to assist Singapore physicians in identifying patients who will likely benefit from treatment while ensuring effective monitoring.

Methods: The AURs are based on the Singapore-approved prescribing information combined with lecanemab phase 2 and 3 clinical trials and real-world data up to April 2026.

Results: The decision to initiate lecanemab should be based on careful evaluation of individuals, including Singapore-validated cognitive status tests to identify mild cognitive impairment (MCI) due to AD and mild AD dementia. Other important evaluations include baseline brain magnetic resonance imaging (MRI), assessment of the apolipoprotein E ε4 (*APOEε4*) genotype, and amyloid pathology confirmation. Guidance on identifying patients at increased risk of amyloid-related imaging abnormalities (ARIA) during treatment and other patient profiles warranting additional caution is provided. Recommendations for monitoring patients, managing infusion-related reactions, and identifying lecanemab discontinuation scenarios are included.

Conclusion: Lecanemab should only be prescribed for patients with MCI due to AD or mild AD dementia following careful clinical evaluation confirming AD pathology, with caution exercised in patients at increased ARIA risk (e.g. *APOEε4* gene carriers). During treatment, patients should receive regular monitoring for ARIA symptoms including follow-up MRI scans. Future directions include the development of a Singapore-specific registry to monitor patients and gather long-term data to support a consensus-driven framework to inform and optimise the use of lecanemab in Singapore.

Keywords: Alzheimer's disease, amyloid beta-peptides, anti-amyloid, antibodies, cognitive dysfunction, dementia, lecanemab, monoclonal, Singapore

CLINICAL IMPACT

What is New

- These Appropriate Use Recommendations (AURs) for lecanemab provide a structured approach to patient selection using Singapore-validated cognitive assessments, amyloid pathology confirmation, baseline MRI, and APOEε4 genotyping.
- These AURs provide guidance on ARIA risk stratification, treatment monitoring, infusion-reaction management, and criteria for treatment discontinuation.
- The checklist included in this paper details treatment candidate evaluation, comprising guidance for safety monitoring and adverse event management.

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Clinical Implications

- These AURs support Singapore physicians in identifying suitable candidates for lecanemab by individualising risk–benefit assessments and guiding safety monitoring throughout treatment.

INTRODUCTION

Lecanemab is a recombinant humanised immunoglobulin gamma 1 monoclonal antibody (mAB), targeting β-amyloid oligomers, protofibrils, and insoluble fibrils, facilitating their clearance, and thereby reducing amyloid plaques in the brain.[1-4] In January 2023, the US Food and Drug Administration (FDA) approved lecanemab under the accelerated approval pathway for the treatment of mild cognitive impairment (MCI) or mild dementia due to Alzheimer's disease (AD), which was later converted to a traditional approval in July 2023.[5] Subsequently, lecanemab was approved by regulatory authorities in other territories, including the European Union,[6] Japan,[7] and Korea.[8] In Singapore, lecanemab was approved for slowing progression in patients at the MCI or mild dementia stage of AD in May 2025.[9]

To ensure that patients in Singapore who may benefit from lecanemab treatment can be appropriately identified and effectively monitored during treatment, guidance in addition to the prescribing information and guideline publications is needed. International guidance is available—notably, appropriate use recommendations (AURs) published in the US, France, and South Korea.[6,8,10]

Due to differences in healthcare systems and patient-specific factors, such as education, ethnicity, and language influencing cognitive performance tests,[11] guidance tailored to the Singapore clinical landscape and population is needed. Therefore, clinicians with expertise in the diagnosis and management of AD have formulated AURs for lecanemab in Singapore to optimise patient selection and monitoring and minimise risks of adverse events. This AUR does not discuss reimbursement or the monitoring of lecanemab efficacy in clinical practice.

METHODS

The AURs for lecanemab were developed by the author group to ensure its appropriate use in Singapore. The author group comprised 9 clinicians in Singapore with extensive experience in the management of AD. After a series of face-to-face explorations in November 2023, April 2023, and June 2025, involving some of the authors, a collective decision to develop a formal AUR to support Singaporean clinicians was made. The drafting of the AURs commenced through online circulation among the authors from July 2025 onwards. The recommendations described within this AUR are based primarily on the Singapore prescribing information for lecanemab,[9] with reference to important details from the Clarity AD trial and its Asian sub-study.[3] Recommendations based entirely on expert opinions are not described here. Additional publications to guide the discussion were identified through literature review focusing on "lecanemab" and its associated "clinical" and "real-world studies" using PubMed up to April 2026, the US prescribing information (USPI),[12] and the European Summary of Product Characteristics (SmPC).[13] All decisions were reached collaboratively by the author group, who were in full alignment with all the recommendations described.

Efficacy and safety of lecanemab in clinical development and real-world studies

Lecanemab initially received accelerated FDA approval based on a phase 2b placebo-controlled trial that showed a reduction in amyloid plaques as assessed by positron emission tomography (PET) scans of participants.[3,5,14] Confirmatory data for standard FDA approval were from the phase 3 Clarity AD trial, which enrolled early AD patients with MCI or mild dementia and evidence of amyloid pathology.[3] The mean age of participants was 71 years, and 69% were carriers of the apolipoprotein E ε4 allele (*APOEε4*). Patients were randomised to intravenous (IV) lecanemab (10 mg/kg every 2 weeks, n=898) or placebo (n=897).[3] Efficacy analyses were conducted on the modified intention-to-treat population (859 and 874 participants in the lecanemab and placebo groups, respectively).[3]

At 18 months, changes from baseline in the primary endpoint, the Clinical Dementia Rating-Sum of Boxes (CDR-SB) score, were 1.21 with lecanemab and 1.66 with placebo (difference, −0.45; 95% confidence interval [CI] −0.67 to −0.23; $P<0.001$).[3] Changes favouring lecanemab were also noted in several secondary endpoints, including the Alzheimer's Disease Assessment Scale, Alzheimer's Disease Composite Score, and Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment.[3] An imaging sub-study found a greater decrease in brain amyloid burden in the lecanemab group than in controls.[3] Notable adverse events in the lecanemab group were infusion-related reactions (IRRs) (26.4% versus [vs] 7.4% with placebo) and amyloid-related imaging abnormalities with oedema (ARIA-edema [ARIA-E], 12.6% vs 1.7% with placebo) or with haemorrhage (ARIA-hemosiderin [ARIA-H], 17.3% vs 9.0%).[3]

As randomisation in Clarity AD was stratified by geographic region (i.e. North America, Europe, and

Asia), an Asian sub-study of Clarity AD could be conducted to assess the efficacy and safety of lecanemab in the 294 patients from Japan (n=152), South Korea (n=129), and Singapore (n=13) who were enrolled in the study.[15]

In this Asian regional subset, the adjusted mean difference in CDR-SB at 18 months was −0.349 (95% CI −0.773 to +0.076), representing a 24% slowing of decline (compared to placebo) that was directionally consistent with the core trial but not statistically significant at the subgroup level, reflecting limited power in this 294-patient subset.[15] Common adverse event of special interest in Asian participants included IRRs (12.3% vs 1.4%, lecanemab vs placebo) and ARIA-E (6.2% vs 1.4%). Rates of ARIA-H were numerically higher in the placebo group (16.2% vs 14.4% in the lecanemab group); however, this is likely attributable to the effect of a small sample size.[15] Relative to the overall population, the incidence of adverse events leading to lecanemab interruption or withdrawal was lower in Asian patients (7.1% vs 0.7% for withdrawal, and 19.5% vs 10.3% for interruptions).[15] A 36-month open-label extension (OLE) of Clarity AD demonstrated that patients continued to benefit from ongoing lecanemab treatment for up to 36 months.[16] Furthermore, this OLE suggests that early initiation of lecanemab at early-stage AD, based on low-tau status (PET standardised uptake value ratio <1.06), may be associated with clinical stability.[16] The OLE identified no new safety signals, and after the first 6 months, rates of ARIA were low and comparable between treatment and placebo groups.[16]

Observational data on lecanemab in clinical practice are increasing. A retrospective study in a US centre has reported initial data for 71 AD patients treated with up to 14 infusions of lecanemab.[17] Of those with safety monitoring imaging available, 12/50 (24%) had ARIA, and 26/71 (37%) experienced IRRs after their first infusion.[17] A retrospective study in Israel that included 86 patients treated with lecanemab reported that 22.1% of patients experienced IRRs (all mild and transient), and 18.6% of patients developed ARIA.[18]

Other retrospective data on experience with lecanemab therapy are available from the US, including an analysis of 234 patients that reported IRRs in 37% of patients and ARIA in 22%.[19] Another retrospective analysis of the first 70 patients treated with lecanemab at a single centre reported a 20% ARIA rate, and the incidence of ARIAs was significantly associated with APOE genotype.[20]

Emerging real-world data from Japan show rates of ARIA that are approximately half of those seen in the US. In clinical usage so far, approximately 7% of Japanese patients developed ARIA (ARIA-E in 3% and ARIA-H in 5.2%),[21] consistent with reported rates among the Japanese population enrolled in Clarity AD.[22] In contrast to this Japanese real-world finding, another Japanese single-centre real-world study reported higher rates of ARIA (20%), all of which were asymptomatic.[23] The authors suggested that this could be due to a higher prevalence of baseline microhaemorrhage and inclusion of patients with white matter lesions as well as the higher sensitivity for detecting microhaemorrhages (susceptibility weighted imaging [SWI] vs T2-weighted gradient recall echo [T2*GRE] used in Clarity AD).[23]

A Chinese real-world study also showed lower rates of ARIA, with 6.9% of patients developing ARIA-E with or without ARIA-H and 10% developing isolated ARIA-H.[24] Moreover, another ongoing real-world Chinese study reported similar findings, with 3.1% of ARIA-E and 9.4% of ARIA-H among the 64 patients enrolled.[25]

Serious adverse events and mortality

Serious adverse events occurred in 14% (n=126) of participants in the lecanemab arm of the main Clarity AD trial, and no deaths related to lecanemab were reported.[3] However, in the Clarity AD OLE, which had no untreated control arm, there were 9 deaths, 4 of which were deemed due to lecanemab.[26]

From the safety analysis of the combined core Clarity AD study and its OLE, there was a total of 24 deaths, 3 of which were due to intracranial haemorrhage.[26] A case report by Solopova et al. described the index case of fatal iatrogenic cerebral β-amyloid-related arteritis in a patient treated with lecanemab.[27] Reish et al. reported another fatal case of multiple cerebral haemorrhages that developed after treatment with tissue plasminogen activator in a patient receiving lecanemab.[28] It is therefore essential that patients being treated with lecanemab carry a patient alert card, and setting up alerts in electronic medical records should also be considered, as previously suggested.[29]

Which patients should receive lecanemab?

The recommendations for patient evaluations, lecanemab infusion, and monitoring discussed below are summarised in a checklist document included as Supplementary Annex S1.

In Singapore, lecanemab is indicated for slowing progression in patients at the MCI or mild dementia stage of AD.[9] This is aligned with the USPI indication, whereas the European indication specifies that patients should be *APOEε4* non-carriers or heterozygotes.[12,13]

Amyloid-beta pathology should be confirmed using a validated test prior to initiation. These criteria are based on the population included in Clarity AD, which enrolled patients 50–90 years of age with

AD and MCI/mild dementia, with amyloid pathology confirmed by PET scans or cerebrospinal fluid (CSF) testing.[3]

Potential cognitive assessment tools suitable for use in Singapore

Neither Singapore nor international prescribing information specifies which tests should be used to diagnose MCI or mild dementia.[9,12,13] The mild severity of AD used as an enrolment criterion for Clarity AD was based on several evaluations.[3] Specifically, those with MCI due to AD had to meet the National Institute on Aging–Alzheimer's Association's (NIA-AA) core criteria for MCI and have a global CDR score of 0.5 and a CDR Memory Box score ≥0.5 at screening and baseline.[3] Additionally, a history of subjective memory decline with gradual onset and slow progression over the last year prior to screening was required.[3] Those with mild AD dementia had to meet NIA-AA core clinical criteria for probable AD dementia and have a global CDR score of 1.0 and a CDR Memory Box score of ≥0.5 at screening and baseline.[3] Additional inclusion criteria for all participants in Clarity AD were a Mini Mental State Examination (MMSE) score of 22–30, and objective impairment in episodic memory as indicated by at least 1 standard deviation below the age-adjusted mean in the Wechsler Memory Scale IV–Logical Memory II.[3]

In Singapore, several tests are available for screening of cognitive status, such as the MMSE (various languages available),[30] Frontal Assessment Battery,[31] a Singapore-adapted version of the Montreal Cognitive Assessment (MoCA),[32,33] and the Visual Cognitive Assessment Test.[34]

However, physicians should apply these scales cautiously and note that the MMSE alone is not sufficient to identify candidates for treatment. Data from cohorts in Singapore and Korea suggest that conventional MMSE thresholds are inaccurate in these populations for identifying those with early dementia, particularly when testing less educated patients.[11,35] The Quick Dementia Rating System (QDRS) may be a useful adjunct, as it has been validated in a cohort of older Singaporeans, with and without MCI/dementia, and it demonstrated good internal consistency and correlation with other scores, including the CDR.[35]

Emerging digital tools for cognitive evaluation that are less dependent on the patient's literacy levels may be of particular value in multiethnic populations with diverse literacy rates, such as in Singapore. Examples of less literacy-dependent testing approaches that have been investigated in Singapore cohorts include tools based on drawing and on-screen games.[36,37] If validated, digital testing may assist screening, but it would complement, rather than replace, in-person tests such as MMSE, MoCA, or QDRS.

Currently, the diagnosis of MCI or mild dementia in AD varies in Singapore clinical practice, with clinicians often selecting the screening tools they are most familiar with. In line with AURs from South Korea and the Clarity AD study,[3,8] the author group suggests that clinicians select 1 or more tools to identify patients with AD and MCI/mild dementia with clinical staging corresponding to a CDR score of 0.5–1.0 as candidates for treatment. However, in practice, multiple cognitive tests in combination with the physician's clinical judgement may provide a more complete picture of the patient's suitability. Considering the importance of timely lecanemab initiation suggested by the OLE data,[16] clinicians should promptly identify those eligible for treatment.

How should amyloid pathology be evaluated?

Although the prescribing information from Singapore, the US, and Europe notes that amyloid pathology should be confirmed before initiation, a testing method is not specified. In Clarity AD, amyloid pathology was confirmed prior to enrolment by PET scan or CSF testing.[3] In Singapore, amyloid PET scans are available at both public and private institutions, and local testing of AD biomarkers in CSF is also available. Furthermore, assays of plasma tau phosphorylated at threonine 217 (p-tau217) have shown strong performance as a diagnostic and prognostic biomarker in diverse populations, including Asian cohorts.[38-40] Because biomarker levels can be influenced by demographic factors such as ethnicity, body mass index, and kidney function, population-specific cutoffs may need to be established.[41] A simplified approach to determining plasma p-tau217 cutoffs using finite mixture modelling in place of more invasive or costlier approaches has been reported.[41] Plasma p-tau217 assays can reduce the invasiveness and costs of evaluating amyloid pathology and may play an important role in the diagnosis and monitoring of AD in the near future. At the time of writing, 2 plasma assays have been cleared by the FDA to assist the diagnosis of AD,[42] and multiple others are in development.[43]

What is the role of *APOEε4* testing?

The *APOEε4* allele is the strongest genetic risk factor for the onset of AD, with heterozygotes having an approximately 2–3-fold increased lifetime risk of AD, and homozygotes having an approximately 60% lifetime risk of AD dementia by 85 years of age, with near-complete biomarker-defined AD biology by 90 years of age.[44] *APOEε4* homozygosity is increasingly characterised as a genetic risk for AD with implications for cascade counselling. Additionally, *APOEε4* carriers treated with anti-amyloid therapies, including lecanemab, are at increased risk of developing ARIA, with homozygous individuals at greatest risk (see

section below).[45] In accordance with the Singapore prescribing information, the author group recommends that all patients undergo *APOEε4* genotyping prior to treatment to assist in the evaluation of risk–benefit profile for each patient. A notable difference between the Singapore prescribing information and USPI versus the European SmPC is that the latter limits the indication of lecanemab to *APOEε4* non-carriers and heterozygotes only, due to the higher risk of ARIA in homozygous patients.[6,9,12,13]

Currently, only one *APOEε4* test has received FDA clearance,[46] and commercial testing kits with local approval are not available in Singapore. Direct-to-consumer test kits are available, but these vary in accuracy and are not intended for clinical use. Genetic counselling should be available to patients and their carers to ensure they understand the impact of their genotype on disease prognosis and treatment risk. Furthermore, as the patient's *APOEε4* status has implications for the genetic risk of all first-degree relatives,[47] counselling and testing of family members should also be discussed. Specialist memory clinics in Singapore may need to develop resources for counselling, as local availability of genetic counselling services is currently limited and focused on other diseases. Since *APOEε4* homozygotes are not excluded from the approved Singapore lecanemab indication, the author group recommends physicians to take additional precautions, including more risk discussion and informed decision-making when treating this high-risk patient group.

Which patients should be excluded from treatment?

Although the Singapore prescribing information only lists serious hypersensitivity to lecanemab or its excipients as a contraindication,[9] caution should be exercised in several subgroups of patients. Notable exclusion criteria in Clarity AD were psychiatric conditions that could interfere with study procedures in the subject, and cognitive impairment caused by neurological and medical causes other than AD.[3] Patients with contraindications to MRI scanning (e.g. intracranial and cardiac devices not approved for safe use in MRI scanners) were also excluded.[3] Patients were also excluded based on findings of the screening brain MRI suggestive of increased risk of ARIA, or brain lesions that could indicate forms of dementia other than AD.[3] Additionally, those with immunological diseases that were not adequately controlled or those needing treatment with immunoglobulins or systemic mABs were also excluded.[3]

Patients in Clarity AD on approved AD treatments at a stable dose for ≥12 weeks were permitted in the study, as were those on concomitant drugs for other conditions for ≥4 weeks prior to baseline assessment.[3] Due to its mode of action, lecanemab is not expected to interact with small-molecule drugs.[9] Patients with uncontrolled bleeding disorders and those on anticoagulants not at a stable dose for >4 weeks were excluded due to increased risks of haemorrhage. A detailed list of the Clarity AD inclusion/exclusion criteria and the author group recommendations for Singaporean AD patients are included in Table 1. In general, the recommendations are aligned with the inclusion/exclusion criteria of Clarity AD. Physicians who are considering the initiation of lecanemab must be aware that although the only absolute contraindication to lecanemab is hypersensitivity, lecanemab must be prescribed on an individualised basis due to the selected clinical trial population of Clarity AD. The authors propose various criteria for excluding patients from treatment, for example, those with untreated bleeding disorders, and those with neurological or medical conditions other than AD that may be a primary cause of cognitive impairment.

How should candidates for treatment be radiologically evaluated?

Baseline brain MRI is recommended in the prescribing information to assess a patient's eligibility for treatment and to exclude patients with brain lesions that may be associated with dementia independently of AD. International expert groups recommend non-contrast MRI with a minimum of 3 sequences: T2 fluid-attenuated inversion recovery (FLAIR), T2*GRE or equivalent sequences (e.g. SWI and diffusion-weighted imaging [DWI]), preferably using a 3 T scanner, and minimally on a 1.5 T scanner, with ≤5 mm slice thickness.[8,10] Where a GRE sequence is performed, an echo time of ≥25 ms at 1.5T MRI and ≥15 ms at 3T MRI should be ensured. Follow-up MRI scans after treatment initiation should be performed, using the same scanner, with the same field strength and imaging parameters as the baseline scan to facilitate optimal comparison. The authors suggest a standardised MRI protocol be developed to harmonise the imaging and reporting of lecanemab candidates across all centres in Singapore.

Practical considerations for lecanemab use

Lecanemab should be stored at 2–8°C, protected from light and diluted immediately prior to use. It should not be frozen or shaken; the recommended dosage is 10 mg/kg infused intravenously over 1 hour, every 2 weeks. After dilution, immediate use is recommended. If not administered immediately, lecanemab must be stored refrigerated at 2–8°C for up to 4 hours or stored at room temperature up to 30°C for up to 4 hours. It is recommended not to freeze. If a dose is missed, the next infusion should be given as soon as possible. Infusions can be given on an outpatient basis.

Table 1. Inclusion/exclusion criteria in Clarity AD, and recommendations for lecanemab use in Singapore.

	Clarity study inclusion criteria[3]	**Recommendations for Singapore: Initiation of lecanemab treatment**
Diagnosis	• Diagnosis of MCI due to AD (global CDR 0.5) and mild AD dementia • CDR memory score 0.5−1.0 • Wechsler memory scale-IV logical memory test showing objective memory impairment below one standard deviation vs age-adjusted mean • MMSE ≥22 and ≤30 at screening and baseline	• Clinical diagnosis of MCI due to AD and mild AD dementia, based on clinicians' judgement + Singapore-validated cognitive tests, e.g. MMSE, MoCA, QDRS, CDR, others ○ MMSE score alone should not be used for identifying Singaporean patients with early dementia • Care should be taken in the evaluation of patients with lower literacy/education levels
Amyloid pathology	• Positive amyloid PET or CSF test	• Positive amyloid PET or CSF test
Age	• 50–90 years	• Based on the physician's judgement, if outside 50–90 years
BMI	• >17 and <35 kg/m^2 at screening	• Physician judgement if outside >17 and <35 kg/m^2 at screening
Concomitant medications	• If receiving an acetylcholinesterase inhibitor (donepezil, rivastigmine, galantamine) or memantine, or both, participants must be on a stable dose for at least 12 weeks prior to baseline • Unless otherwise stated, participants must have been on stable doses of all other (that is, non-AD-related) permitted concomitant medications for at least 4 weeks prior to baseline	• Other AD treatments approved for use in Singapore may be used concomitantly
Patient support	• Have an identified study partner	• Ensure the patient has a carer or family member to provide support during treatment • Ensure the patients and carer/family members understand the risks and benefits of treatment
	Exclusion criteria in Clarity AD	**Recommendations for Singapore: Considerations for exclusion or additional caution**
Additional causes of cognitive impairment	• Any neurological condition that may be contributing to cognitive impairment beyond that caused by the participant's AD	• Any medical, neurological, or mental health condition that may be a primary cause of cognitive impairment or non-AD MCI or dementia
MRI contra-indications	• Patients with contraindications to MRI scan were excluded from the study	• Patients with contraindications to MRI scan or unable to tolerate repeated MRI (e.g. claustrophobia)
Brain MRI findings	• >4 microhaemorrhages (≤10 mm at the greatest diameter) • A single macrohaemorrhage (>10 mm at greatest diameter) • An area of superficial siderosis • Evidence of vasogenic oedema • Multiple lacunar infarcts or stroke involving a major vascular territory • Severe small vessel disease, or other major intracranial pathology • Other clinically significant lesions on brain MRI indicative of a dementia diagnosis other than AD	• >4 microhaemorrhages (≤10 mm at the greatest diameter) • A single macrohaemorrhage (>10 mm at greatest diameter) • An area of superficial siderosis; evidence of vasogenic oedema • >2 lacunar infarcts or stroke involving a major vascular territory. Severe small vessel disease consistent with a Fazekas score of 3, or other major intracranial pathology • Brain MRI evidence of ABRA or CAA-ri • Other major intracranial pathology that may cause cognitive impairment, including contusions or gliosis due to past traumatic injuries, aneurysms, vascular malformations, infective lesions or brain tumours • Severe enlarged perivascular spaces in the centrum semiovale are not an absolute exclusion criterion but may be a pointer to underlying cerebral a myloid angiopathy and require heightened clinical vigilance

Table 1. Inclusion/exclusion criteria in Clarity AD, and recommendations for lecanemab use in Singapore. (Cont'd)

	Clarity study inclusion criteria[3]	Recommendations for Singapore: Initiation of lecanemab treatment
CV history	• History of TIA, stroke, seizures within 12 months of screening	• History of TIA, stroke, or seizures within 12 months of treatment initiation
Other psychiatric diagnoses	• Any psychiatric diagnosis or symptoms (e.g. hallucinations, major depression, or delusions) that could interfere with study procedures in the participant • Geriatric Depression Scale-15 score ≥8 at screening	• Any mental illness that interferes with comprehension of the requirements, potential benefits, and potential harms of treatment, and is considered by the physician to render the patient unable to comply with management requirements • Major depression that will interfere with comprehension of the requirements, potential benefit, and potential harms of treatment; patients for whom disclosure of a positive biomarker may trigger suicidal ideation. • Patients with less severe depression or whose depression resolves may be treatment candidates
Immunological diseases	• Any immunological disease that is not adequately controlled, or that requires treatment with immunoglobulins, systemic monoclonal antibodies (or derivatives of monoclonal antibodies), systemic immunosuppressants, or plasmapheresis during the study	• Any immunological disease that is not adequately controlled • Patients treated with other monoclonal antibodies can be considered for lecanemab treatment, based on the treating clinician's individualised risk assessment • For patients treated with other monoclonal antibodies, consultation with the treating physician is required
Bleeding disorders	• Participants with a bleeding disorder that is not under adequate control (including a platelet count <50,000 or INR >1.5 for participants who are not on anticoagulant treatment, for example, warfarin)	• Untreated bleeding disorder, platelet count <50,000 x 10^9/L, or INR >1.5 but not on anticoagulant
Anticoagulants	• Participants on anticoagulants should have their anticoagulant status optimised and have a stable dose for 4 weeks before screening	• Patients taking anticoagulants must be evaluated with additional caution • Consider consultation with neurologists/stroke specialists/cardiologists/ anticoagulant prescribing physicians to discuss suitability and risks of lecanemab treatment
Other medical conditions	• Any other medical conditions (e.g. cardiac, respiratory, gastrointestinal, renal disease) that are not stably and adequately controlled, or which could affect the participant's safety or interfere with the study assessments	• Any other medical condition with the potential to affect lecanemab treatment

ABRA: amyloid beta-related angiitis; AD: Alzheimer's disease; BMI: body mass index; CAA-ri: cerebral amyloid angiopathy-related inflammation; CDR: Clinical Dementia Rating; CSF: cerebrospinal fluid; CV: cardiovascular; INR: international normalised ratio; MCI: mild cognitive impairment; MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive Assessment; MRI: magnetic resonance imaging; PET: positron emission tomography; QDRS: Quick Dementia Rating System; TIA: transient ischaemic attack; vs: versus

Adapted from van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med 2023;388:9-21.[3] Changes were made: inclusion and exclusion criteria were reorganised into a single table, and a column of recommendations for Singapore was added.

Superscript number: refer to REFERENCES

How should infusion-related adverse events be monitored and managed?

In Clarity AD, IRRs were reported in 26.4% of patients in the lecanemab group (vs 7.4% in placebo); these were predominantly mild to moderate in severity (96% grade 1 or 2), and 75% occurred with the first dose.[3] In the Asian sub-study of Clarity AD, IRR rates were lower than in the overall study population, at 12.3% of patients in the lecanemab group and 1.4% in the placebo group; all were grade 1 or 2.[15] IRRs may manifest through a range of symptoms, including fever and systemic flu-like effects such as chills, muscle aches, and joint pain.[9] Other notable symptoms may encompass gastrointestinal distress (such as nausea and vomiting), blood pressure fluctuations (hypertension or hypotension), or oxygen desaturation.[9] In Clarity AD, IRRs typically resolved within 24 hours without the need for hospitalisation. Furthermore, 63% of the study participants taking prophylactic medications did not experience subsequent IRRs.[3]

In agreement with the US Alzheimer's Disease and Related Disorders Therapeutics Work Group, the authors suggest that milder cases of IRRs can be treated with diphenhydramine and paracetamol.[10] For IRRs of grade 2 or higher severity, the infusion should be stopped, and patients should be treated with oral dexamethasone or oral prednisolone. Patients who have experienced a grade 2 or higher IRR should be prophylactically treated with oral diphenhydramine and oral paracetamol 30 minutes prior to the next infusion. Low-dose oral dexamethasone or oral prednisolone (6 hours prior to infusion) can be used for prophylaxis or treatment if diphenhydramine and paracetamol are ineffective.[10] Prophylaxis against IRRs should continue for the next 2 to 4 infusions. A summary of these recommendations is included in Table 2. For patients who experience grade 3 or higher IRRs, the infusion should be stopped immediately and lecanemab discontinued.

Monitoring and management of ARIA

ARIA are abnormal radiographic findings indicative of cerebral amyloid angiopathy-related inflammation and have been associated with various anti-amyloid

Table 2. Pharmacological recommendations for treatment and prophylaxis of IRRs of lecanemab.

Agent	Dosing recommendations	Author group's remarks
Treatment of mild IRR		
Paracetamol (oral)	500 mg to 1 g	For milder cases; dosing can be repeated every 4–6 hours until symptoms resolve.
Diphenhydramine or other antihistamines (oral)	Diphenhydramine 25–50 mg	For milder cases; dosing can be repeated every 4–6 hours until symptoms resolve. Antihistamine choice and dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs.
Dexamethasone or other corticosteroids (oral) when significant symptoms are present	Daily for 2–3 days	Corticosteroid choice and dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs.
Prophylactic treatment in patients with previous IRR		
Paracetamol (oral)	500–1000 mg	To be given 30 minutes prior to infusion. Antihistamine choice and dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs.
Diphenhydramine or other antihistamines (oral)	Diphenhydramine 25–50 mg	
Dexamethasone or other corticosteroids (oral)	Individualised	May be given as a single prophylactic dose in patients where paracetamol/ diphenhydramine is not effective. Corticosteroid choice and dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs.

IRR: infusion-related reaction

For more detailed information, refer to the Lecanemab infusion guide in Supplementary Annex S2.

Adapted from Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: Appropriate Use Recommendations. J Prev Alzheimers Dis 2023;10:362-77.[10] Licensed under CC BY 4.0 (https://creativecommons.org/licenses/by/4.0/). Changes were made: recommendations on treatment and prophylaxis of IRRs were reorganised into tabular format; the dose recommendation of corticosteroids for the treatment of mild IRR was excluded; the dosage recommendation for corticosteroids for prophylactic treatment in patients with previous IRR was modified to "individualised"; and a remarks column reflecting the views of the author group was added.

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therapies, including lecanemab.[48] Although they are most commonly reported in AD patients receiving anti-amyloid-β mABs, they are also observed in untreated AD patients.[49] In the main Clarity AD study ,[3] ARIA-E events were mostly mild-to-moderate (96%) and 78% were asymptomatic.[3] In the Asian sub-study of Clarity AD, the incidence of ARIA-E and ARIA-H was lower than in the overall study population,[15] and this difference is also reflected in emerging real-world data from Japan and China.[21,24]

All ARIA-E events in the Asian subpopulation were asymptomatic and mild-to-moderate in radiographic severity, as were almost all ARIA-H events.[15] The exact pathogenesis of ARIA is unclear, but it appears to share overlapping features with cerebral amyloid angiopathy (CAA), the deposition of amyloid-β in the vascular wall, a phenomenon observed in the majority of AD patients, with moderate-to-severe CAA in 25–50%.[50] ARIA are thought to be caused by increased blood vessel permeability and leakage induced by clearance of amyloid deposits from and alongside cerebral arteries.[50] In clinical trials, ARIA-E and ARIA-H events are usually asymptomatic, but in some cases, ARIA-E are associated with headaches, blurred vision, confusion, vomiting, or gait disturbance.[49] In rare instances, ARIA can be serious and life-threatening or fatal.[9]

The main risk factors for ARIA development are treatment with anti-amyloid-β antibodies, the presence of pre-existing microhaemorrhages, and *APOEε4* status.[48,49] The risk of ARIA development increases with drug dose and treatment duration, and patients are at the highest risk in the first few months of treatment when amyloid-β deposits are mobilised.[48] *APOEε4* status also has a dose-dependent effect, with homozygous patients at higher risk than heterozygous patients.[48,49]

Beyond established haemorrhagic markers, severe centrum semiovale enlarged perivascular spaces (CSO-ePVS) are incorporated into the Boston 2.0 criteria as a validated non-haemorrhagic marker of advanced CAA.[51] While recent data suggest a plausible link to ARIA risk, these studies rely heavily on automated quantitative techniques that are not widely available in everyday clinical practice.[52] The visual semi-quantitative scoring systems remain difficult to standardise in routine clinical practice. Consequently, ePVS is currently not utilised as an exclusion criterion in existing consensus guidelines. To ensure Singapore recommendations remain practical and easily adoptable, severe CSO-ePVS has been acknowledged in the authors' checklist not as a contraindication, but as a marker warranting heightened clinical vigilance.

In studies of various anti-amyloid treatments, including lecanemab, concomitant use of anticoagulants, antithrombotics, or antiplatelets has also been associated with increased risk of ARIA.[49] The Clarity AD trial included patients with concomitant antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) at baseline if the patient was on a stable dose, and the majority of the antithrombotic exposures were to aspirin.[9,26] Among patients receiving lecanemab alongside anticoagulants (either alone or with antiplatelet drugs or aspirin), intracerebral haemorrhage occurred in 2.5%, whereas no such cases were reported in the placebo group.[26]

The European SmPC for lecanemab recommends that it not be used in patients needing ongoing anticoagulation, and that concomitant use of thrombolytics be avoided except for life-threatening situations.[13] However, the Singapore prescribing information and USPI take a less restrictive approach, noting that lecanemab may be used in such patients, but physicians must exercise additional caution.[9,12] Additional guidance was provided by the UK guideline, which suggested that additional caution should be observed in patients receiving dual antiplatelet therapy, with such cases discussed in a multidisciplinary team to assess individual risk.[29]

Although there was no known pharmacological or immunological risk associated with lecanemab, patients undergoing treatment with other mABs were excluded from Clarity AD as a precautionary measure and to maintain scientific validity. In clinical practice, however, such an approach may be excessively restrictive and risk denying treatment to patients with clear clinical need without a corresponding safety rationale. Therefore, patients treated with other mABs can be considered for lecanemab treatment, based on individualised risk assessment, in consultation with their treating clinician.

Patients treated with lecanemab should undergo monitoring for ARIA with brain MRI scans prior to the fifth, seventh, and fourteenth infusions.[9] If a patient experiences symptoms, a clinical evaluation should be performed, including an MRI, if indicated.[9] The MRI protocol should include at least 3 sequences (T2 FLAIR, T2*GRE or SWI, and DWI) and should be done on a 1.5 T scanner at the minimum with ≤5 mm slice thickness,[53] using the same technical parameters and scanner as the baseline scan to aid the detection of ARIA. ARIA protocols for several models of MRI scanner are available from the American Society of Neuroradiology website (https://www.asnr.org/education-resources/alzheimers-webinar-series/).[54] Use of a DWI sequence is important for the identification of an acute infarct, which may be a clinical differential in a patient presenting with acute neurological symptoms. Use of T2 FLAIR and T2*GRE/SWI sequences can identify ARIA-E and ARIA-H, respectively. Both ARIA-E and ARIA-H should be graded in severity based on their clinical and MRI features to guide management

(Supplementary Annex S3, Table S1). Additionally, patients and caregivers should be informed about ARIA, their symptoms, and when to seek care, because if such patients are misdiagnosed with stroke, treatment with thrombolytics is potentially fatal (Table 3).[48]

Table 3. Critical safety point.

Critical safety point: Anticoagulants or thrombolytic agents in lecanemab recipients[9]
Intracerebral haemorrhages of 1 cm or larger have been documented in patients receiving lecanemab. Follow your institutional guidelines on the use of mechanical thrombectomy versus anticoagulants or thrombolytic agents. When evaluating whether to administer anticoagulants or thrombolytic agents (e.g. tissue plasminogen activator) to a patient already on lecanemab, additional caution should be exercised.

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Based on the approach taken in Clarity AD, the authors suggest that for patients with moderate to severe ARIA-E and ARIA-H and symptomatic ARIA of any severity, lecanemab should be suspended (Supplemental Annex S3, Tables S2 and S3) until signs or symptoms resolve.[9] A follow-up MRI 2–4 months after initial identification of ARIA should be considered. Continuation of treatment after suspension and the suspension of lecanemab in patients with mild asymptomatic ARIA should be based on the clinician's judgement after resolution of ARIA-E and stabilisation of ARIA-H. The initiation of high-dose steroids (e.g. IV methylprednisolone 1 g daily for 3–5 days, and subsequent oral steroid taper over several weeks) may be considered in patients with symptomatic or severe ARIA.[55]

When should lecanemab be discontinued?

Currently, there are no long-term data to guide the discontinuation of lecanemab. In the 18-month Clarity AD study, adverse events leading to discontinuation of lecanemab were reported in 6.9% of participants (vs 2.9% in the placebo group).[3] The authors recommend lecanemab be discontinued if patients experience severe symptomatic or radiologic ARIA, and in patients who experience grade 3 or higher IRRs. Guidance from the French Federation of Memory Clinics suggests treatment discontinuation at 18 months if a detailed cognitive examination suggests progression to moderate stages of dementia.[6] The Singapore prescribing information specifically recommends discontinuing lecanemab if the treatment is no longer expected to be effective, if patients develop intracerebral haemorrhage greater than 1 cm in diameter during treatment, or in the event of IRR, where the infusion rate may be reduced or the infusion discontinued.[9] Overall, the decision to stop lecanemab should be individualised based on the clinician's judgement and be made after consideration of the preferences of patients and caregivers, imaging evidence of amyloid clearance, and the costs and logistics of treatment.

DISCUSSION

Although their long-term impact is unclear, the introduction of lecanemab and other anti-amyloid-β antibodies marks the start of a new era for AD treatment. Because the indication for these agents is limited to early stages of AD, efforts should be made to streamline and standardise the diagnostic pathway to ensure such patients are diagnosed in a timely manner.[56,57] Patient registries will be important to provide longer-term data on the safety and efficacy of these drugs.

Shields et al. provide some practical insights into lessons learned during the introduction of lecanemab into regular clinical practice.[17] These include the establishment of a multidisciplinary team approach to lecanemab use, a standardised approach to radiology reporting, and a protocol for the identification and management of lecanemab patients in the emergency department.[17] This study also reported the use of a standardised prophylactic treatment for IRRs.[17] These approaches are consistent with the recommendations of a regional expert group promoting best practices and readiness for the introduction of anti-amyloid therapy in Asia.[57]

Early data suggest that dosing may be modified for long-term treatment. In early 2025, the US FDA approved the option of monthly IV maintenance dosing in patients who completed 18 months of bi-weekly treatment.[12] Additionally, in August 2025, the US FDA approved a subcutaneous form of lecanemab, administered using an autoinjector with a dosage of 360 mg once a week, for maintenance dosing after 18 months.[12,57] This development may reduce treatment barriers and associated costs.[59] The optimal forms of monitoring for longer-term treatment, for example, the need for repeated amyloid PET imaging for follow-up, are unclear. However, given the inconvenience and expense of imaging-based methods, plasma biomarkers may play a role in long-term monitoring.[60,61]

CONCLUSION

Lecanemab is recommended for the treatment of patients with MCI due to AD and mild AD dementia. The diagnosis of these patients should be established by CSF or PET confirmation of amyloid pathology, as well as cognitive testing using tools validated in the Singapore population. It should not be used in patients

with hypersensitivity to the drug and should be used with caution in patients at increased risk of ARIA (e.g. those who carry *APOEε4*, or MRI findings associated with increased risk). During treatment, patients should receive regular follow-up, including MRI scans and evaluation for ARIA symptoms.

To optimise the use of lecanemab in Singapore, several key priorities must be addressed. First, the development of a Singapore-specific registry will provide critical long-term data on the safety and efficacy of anti-amyloid-β antibodies and the role of plasma biomarker testing in the diagnosis and management of patients. A formal consensus process—informed by registry findings—will help resolve outstanding uncertainties and provide Singapore guidance, including concerns regarding cognitive screening protocols, co-prescription of antiplatelet agents, and discontinuation criteria (which should be anchored to objective, measurable thresholds). Localisation efforts must also extend beyond registries to include Singapore-adapted cognitive screening algorithms, explicit management strategies for discordant or borderline amyloid pathology readings, including centiloid thresholds for confirmation and plasma p-tau217 integration; clear operationalised discon-tinuation criteria to ensure standardised clinical practice; and a defined approach to *APOEε4* homozygosity, given their pivotal role in patient selection. Finally, ongoing policy discussions should integrate these clinical refinements with considerations of cost, equity, and reimbursement to facilitate access to lecanemab in Singapore.

Supplementary materials

Annex S1. A checklist summarising the recommendations for the use of lecanemab for early Alzheimer's disease in Singapore.

A. Lecanemab patient selection checklist.

B. Lecanemab diagnostic checklist.

C. Lecanemab safety monitoring checklist.

Annex S2. Lecanemab infusion guide.

Annex S3. ARIA MRI classification and dosing recommendations.

Table S1. MRI classification of radiographic severity of ARIA-E and ARIA-H.

Table S2. Dosing recommendations for patients with ARIA-E.

Table S3. Dosing recommendations for patients with ARIA-H.

Ethics statement

Not applicable, as this review did not involve the recruitment of participants or the collection of new data from human participants.

Declaration

CLC has received research funding paid to the National University Hospital, Singapore from Eisai, and has participated in advisory board meetings for Actinogen, Cerecin, Eisai, and Lilly. NK has received honoraria from Eisai for continuing medical education events. SK has received honoraria for lectures and workshops from Eisai and from DKSH. TML has provided consultation to Eisai and Lundbeck and is listed as co-inventor for the provisional patent of PENSIEVE-AI (referenced in the manuscript). KEL, ASLN, KPN, and SKST have received honorarium from Eisai. LBGT has no conflict to declare.

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