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

A. Lecanemab patient selection checklist.

Inclusion Criteria

Inclusion Criteria (ALL the following must be fulfilled to meet criteria)		Yes	No
1	Patient meets criteria for mild cognitive impairment (MCI) or mild Alzheimer's disease (AD) dementia based on clinicians' judgement and locally validated cognitive tests	☐	☐
2	Patient has had a recent (within last 12 months) brain magnetic resonance imaging (MRI) scan	☐	☐
3	Amyloid positron emission tomography (PET) imaging and/or cerebrospinal fluid (CSF) analysis consistent with Alzheimer's disease	☐	☐
4	Neuroradiologist or qualified radiologist trained in detection of amyloid-related imaging abnormalities (ARIA) is available to review serial brain MRI scans	☐	☐
5	Have a care partner or family member(s) who can ensure that the patient has support needed to be treated with lecanemab	☐	☐
6	Patients, care partners, and appropriate family members understand requirements for lecanemab therapy and the potential benefit and potential risk of treatment	☐	☐
Patient has met all inclusion criteria for lecanemab		☐	☐

Exclusion Criteria

Contraindications (If the answer to below is met, the patient should NOT receive lecanemab)		Yes	No
1	Prior serious hypersensitivity to lecanemab or to any of the excipients. Hypersensitivity reactions may include angioedema and anaphylaxis	☐	☐

Treatment should be considered in a case-by-case risk/benefit discussion. Any "yes" checked box below indicates a precaution that should be discussed with the primary treating physician.

Potential exclusion criteria (If the answer to ANY item below is met, the treatment should be considered in a case-by-case risk/benefit discussion)		Yes	No
1	Any medical, neurological, or mental health condition that may be a contributing/primary cause of cognitive impairment or non-AD MCI or dementia	☐	☐
2	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	☐	☐

3	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.		☐	☐
4	Contraindication or inability to tolerate brain MRI (e.g., claustrophobia)		☐	☐
5	Transient ischaemic attack, stroke, and any history of seizures within the past 12 months		☐	☐
6	Evidence on screening brain MRI that would exclude treatment		☐	☐
	a.	More than 4 microhaemorrhages (defined as 10 mm or less at the greatest diameter)	☐	☐
	b.	A single macrohaemorrhage >10 mm at greatest diameter;	☐	☐
	c.	An area of superficial siderosis; evidence of vasogenic oedema;	☐	☐
	d.	More than 2 lacunar infarcts or stroke involving a major vascular territory.	☐	☐
	e.	Severe subcortical white matter hyperintensities consistent with a Fazekas score of 3;	☐	☐
	f.	Brain MRI evidence of amyloid beta-related angiitis (ABRA) or cerebral amyloid angiopathy-related inflammation (CAA-ri);	☐	☐
	g.	Other major intracranial pathology	☐	☐
7	Any immunological disease which is not controlled, or which requires treatment with biologic drugs		☐	☐
8	Untreated bleeding disorder, platelet count <50,000 x 10^9/L, or international normalised ratio (INR) greater than 1.5 but not on anticoagulant (to be considered where correction of INR would enable eligibility)		☐	☐
9	Patients on anticoagulants (coumadin, dabigatran, edoxaban, rivaroxaban, apixaban, betrixaban, or heparin) must be monitored with additional caution and risks discussed with caregivers; tissue plasminogen activators (tPAs) should not be administered to individuals on lecanemab. Consider consultation with neurologists/stroke specialists/ cardiologist/anticoagulant prescribing physician to discuss suitability and risks of lecanemab treatment		☐	☐
Patient has met one or more potential exclusion criteria for lecanemab			☐	☐

Genetic Testing and Counselling		Yes	No
Apolipoprotein ε4 (*APOEε4*) status must be tested prior to initiation of treatment. Prior to testing, prescribers should discuss the risk of ARIA with patients, who should be appropriately counselled. Consider the benefit of lecanemab for the treatment of Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with lecanemab.			
1	*APOEε4* genetic testing performed, and patient has been counselled on the implications	☐	☐
2	Date of pre-test counselling		

	Yes	**No**
IS THE PATIENT ELIGIBLE FOR LECANEMAB TREATMENT?		

B. Lecanemab diagnostic checklist.

This document is intended to help health care providers determine the appropriateness of lecanemab therapy and document clinical decision making. For complete information, refer to the full Prescribing Information. This content is intended for health care providers only for informational purposes and does not substitute for sound medical judgment or clinical decision making in the context of medical treatment.

Diagnosis							
☐	Mild cognitive impairment due to Alzheimer's Disease						
☐	Mild dementia stage of Alzheimer's Disease						
Triage and Confirmation of Amyloid Beta (Aβ) Pathology							
Date performed:							
☐	Amyloid PET		Result:				
			PET centiloid value				
☐	CSF analysis		Results:				
			☐	Aβ42:			
			☐	p-tau181:			
			☐	t-tau:			
			☐	p-tau/Aβ42 ratio:			
			☐	Others:			
☐	Plasma analysis		Results:				
			☐	p-tau217:			
			☐	Others:			
Recommended *APOEε4* Test							
☐	Performed		Date performed:				
	☐	Homozygous	☐	Heterozygous	☐	Non-carrier	
☐	Not Performed						
Baseline Brain MRI							
☐	Within past 1 year		Date performed:				
	☐	Microhaemorrhages	☐	Yes	Severity:	☐	No
	☐	Superficial siderosis	☐	Yes	Severity:	☐	No
	☐	Macrohaemorrhages	☐	Yes	Severity:	☐	No
	☐	Other findings: e.g., white matter lesions (Fazekas score)	☐	Yes	Notes:	☐	No
	☐	Contraindications on brain MRI	☐	Yes		☐	No
	Notes:						
Patient has met all inclusion criteria for lecanemab							
☐	Yes						
Patient has not met any exclusion criteria for lecanemab							
☐	Yes						

C. Lecanemab safety monitoring checklist.

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Monitoring for ARIA

Obtain a recent baseline brain MRI prior to initiating treatment with lecanemab. Obtain a brain MRI prior to the 5th, 7th, and 14th infusions. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including a brain MRI if indicated.

Minimal recommendations: It is recommended to standardise the use of MRI scanners, protocols and sequences to ensure consistency across follow-up scans and minimise variability from different scanners and sequences. If the scan is not performed on the same MRI scanner, the reporting radiologist should be mindful of the potential variability when interpreting and reporting the images. The brain MRI ARIA protocol should include T2 fluid-attenuated inversion recovery (FLAIR), T2-weighted gradient recall echo (GRE) or susceptibility weighted imaging (SWI) and diffusion-weighted imaging (DWI) sequences done on a minimum 1.5T scanner with ≤5 mm slice thickness. For GRE sequence, the echo time (TE) ≥25 ms on 1.5T MRI and ≥15 ms on 3T MRI. 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/)

<table>
<tr><th colspan="6">ARIA Brain MRI Monitoring</th></tr>
<tr><td colspan="3">Number of lecanemab infusions completed:</td><td colspan="3"></td></tr>
<tr><td colspan="3">Date performed:</td><td colspan="3"></td></tr>
<tr><td colspan="2">Previous ARIA Event</td><td>☐ Yes</td><td colspan="2">Date of last event:</td><td>☐ No</td></tr>
<tr><td colspan="2" rowspan="3">MRI sequence level confirmation</td><td colspan="4">☐ T2 FLAIR</td></tr>
<tr><td colspan="4">☐ T2*GRE/SWI</td></tr>
<tr><td colspan="4">☐ T2 DWI</td></tr>
<tr><td colspan="2">Same scanner as baseline</td><td colspan="2">☐ Yes</td><td>☐ No</td></tr>
<tr><td colspan="2">Same parameters as baseline</td><td colspan="2">☐ Yes</td><td>☐ No</td></tr>
<tr><td colspan="6">ARIA type and Radiographic Severity</td></tr>
<tr><td rowspan="4">☐</td><td rowspan="4">ARIA-E (oedema)</td><td colspan="4">☐ No</td></tr>
<tr><td colspan="4">☐ Yes Size and location:</td></tr>
<tr><td colspan="4">Severity[a]:</td></tr>
<tr><td>☐Mild</td><td colspan="2">☐Moderate</td><td>☐Severe</td></tr>
<tr><td rowspan="4">☐</td><td rowspan="4">ARIA- H (Microhaemorrhages)</td><td colspan="4">☐ No</td></tr>
<tr><td colspan="4">☐ Yes Number:</td></tr>
<tr><td colspan="4">Severity[a]:</td></tr>
<tr><td>☐Mild</td><td colspan="2">☐Moderate</td><td>☐Severe</td></tr>
<tr><td rowspan="4">☐</td><td rowspan="4">Superficial siderosis</td><td colspan="4">☐ No</td></tr>
<tr><td colspan="4">☐ Yes Number:</td></tr>
<tr><td colspan="4">Severity[a]:</td></tr>
<tr><td>☐Mild</td><td colspan="2">☐Moderate</td><td>☐Severe</td></tr>
</table>

☐	Intracerebral haemorrhage (>1 cm)	☐ Yes	☐ No
Notes:			
Is the patient symptomatic?		☐Yes	☐No
Continue lecanemab treatment[b]?		☐Yes	☐No

[a]*Refer to Table S1 in Annex S3 on radiographic severity of ARIA-E and ARIA-H*

[b]*Refer to Tables S2 and S3 in Annex S3 on dosing recommendations for patients with ARIA-E and ARIA-H*

Annex S2. Lecanemab infusion guide.

Indication of lecanemab

Lecanemab is indicated for slowing the progression of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage of disease.

The safety and efficacy of lecanemab have not been established in patients with moderate or severe Alzheimer's disease.

Drug regimen and dosing instructions

The recommended dosage of lecanemab is 10 mg/kg, which must be diluted and then administered as an intravenous infusion over approximately one hour, once every two weeks.

Pre-assessment

Ensure pre-administration vital signs, laboratory tests, brain MRI, and amyloid PET or CSF are completed and reviewed

Assess patient for any prior symptoms of ARIA from previous infusion (headache, confusion, dizziness, vision changes, nausea, difficulty walking, seizures). Consult primary treating physician if present and not informed.

Anticoagulants or thrombolytic agents in lecanemab recipients

Exercise additional caution when considering the administration of anticoagulants or a thrombolytic agent (e.g., tissue plasminogen activator [tPA]).

Perform medication reconciliation to ensure any newly started medication has been reviewed

- Antiplatelets/anticoagulants
- Thrombolytic agents
- NSAIDs
- Immunomodulatory drugs
- Monoclonal antibodies
- Others

Assess whether the patient has any significant changes to health status since the last lecanemab infusion

- Body weight
- New diagnosis
- Clinically significant worsening of pre-existing condition
- ER visit and/or hospital admission
- Other

Prophylactic medications

The use of prophylactic medications should be tailored based on the patient's prior infusion-related events and the physician's clinical judgment.

Prophylactic medications are usually not required, but following an infusion reaction, patients should be pretreated with oral diphenhydramine 25–50 mg and oral paracetamol 500–1,000 mg 30 minutes prior to the next infusion. Consider use of low dose oral corticosteroids (6 hours prior to infusion; refer to **Table 2**) or intravenous (IV) hydrocortisone (30–60 minutes prior to infusion) for prophylaxis or treatment if diphenhydramine and paracetamol are ineffective. Antihypertensive treatment may be needed for management of elevated blood pressure. Continue this prophylactic regimen until the patient remains asymptomatic in clinic and at home following 2–4 infusions.

Dilution instructions

- Prior to administration, lecanemab must be diluted in 250 mL of 0.9% Sodium Chloride Injection.
- Use aseptic technique when preparing the lecanemab diluted solution for intravenous infusion.
- Calculate the dose (mg), the total volume (mL) of lecanemab solution required, and the number of vials needed based on the patient's actual body weight and the recommended dose of 10 mg/kg. Each vial contains a lecanemab concentration of 100 mg/mL.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Check that the lecanemab solution is clear to opalescent and colourless to pale yellow. Do not use if opaque particles, discoloration, or other foreign particles are present.
- Remove the flip-off cap from the vial. Insert the sterile syringe needle into the vial through the centre of the rubber stopper.
- Withdraw the required volume of lecanemab from the vial(s) and add to an infusion bag containing 250 mL of 0.9% Sodium Chloride Injection.
- Each vial is for one-time use only. Discard any unused portion.
- Gently invert the infusion bag containing the lecanemab diluted solution to mix completely. Do not shake.

- After dilution, immediate use is recommended. If not administered immediately, store lecanemab refrigerated at 2°C to 8°C for up to 4 hours, or at room temperature up to 30°C for up to 4 hours. Do not freeze.

Administration instructions

- Visually inspect the lecanemab diluted solution for particles or discoloration prior to administration. Do not use if it is discoloured, or opaque or foreign particles are seen.
- Prior to infusion, allow the lecanemab diluted solution to warm to room temperature.
- Infuse the entire volume of the lecanemab diluted solution intravenously over approximately one hour through an intravenous line containing a terminal low-protein binding 0.2 micron in-line filter. Flush infusion line to ensure all lecanemab is administered.

Monitoring

Monitor for any signs or symptoms of an infusion-related reaction (IRR). The infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy administered as clinically indicated. Consider pre-medication at subsequent dosing with antihistamines, non-steroidal anti-inflammatory drugs, or corticosteroids

Post infusion observation

Patients should be observed for 3 hours after the first infusion with a follow-up telephone call later that day, as delayed infusion reactions are occasionally observed. The post-infusion observation period may be reduced to 2 hours for the second and third infusions and to 30 minutes for subsequent infusions if no infusion reactions have occurred.

Adverse events

IRRs can present as fever, flu-like symptoms (chills, generalised aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.

Grading and management of IRRs		
Grade 1	Mild reaction	Infusion interruption not indicated; may be treated with oral (PO) diphenhydramine (25–50 mg) or PO paracetamol (500 mg to 1 g) every 4–6 hours until symptoms resolve.
Grade 2	Infusion interruption or treatment indicated but responds promptly to symptomatic treatment (e.g. antihistamines, paracetamol, NSAIDs, narcotics, IV fluids); prophylactic medications indicated for <24h	Stop the infusion. Administer IV diphenhydramine 25–50 mg and PO paracetamol 500–1000 mg in milder cases and with PO corticosteroids (2–3 days) when significant symptoms are present. Corticosteroid dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs. If the infusion reaction improves or resolves, infusion may be resumed as per clinical judgment, at 50% of the previous

		rate. The infusion duration should not exceed 2 hours. Diphenhydramine or paracetamol may be given every 4–6 hours until symptoms fully resolve. The patient or caregiver should be called later that day to assess symptom resolution. For subsequent infusions, the physician should consider giving prophylactic medications such as IV diphenhydramine 25–50 mg and PO paracetamol 500–1000 mg, 30 minutes prior to infusion. Corticosteroids (6 hours prior to infusion) can be used for prophylaxis or treatment if diphenhydramine and paracetamol are ineffective. Corticosteroid dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs.
Grade 3	Prolonged; recurrence of symptoms following initial improvement; hospitalisation required for clinical sequelae (e.g. poorly controlled hypertension)	Stop the infusion and disconnect the infusion tubing from the patient. Administer IV diphenhydramine 25–50 mg and PO paracetamol 500–1000 mg, bronchodilators for bronchospasms, and IV fluids for hypotension. Low dose PO corticosteroids (for 2–3 days) can be used for treatment if diphenhydramine and paracetamol are ineffective. Corticosteroid dosage should be based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs. The physician may administer other medications as clinically indicated. Hospital admission for observation may be required. Discontinue the lecanemab infusion. An immediate assessment and follow-up visit 3 months after the last dose of the drug should be done.
Grade 4	Life-threatening consequences: urgent treatment needed (may require pressor or ventilatory support)	Stop the infusion and disconnect the infusion tubing from the patient. Administer IV diphenhydramine 25–50 mg, IV dexamethasone 10 mg (or equivalent), PO paracetamol 500–1000 mg, bronchodilators for bronchospasm, IV fluids, IV epinephrine for hypotension, and oxygen. Administer other medications as clinically indicated. Hospital admission for treatment is highly indicated. Discontinue the lecanemab infusion. An immediate assessment and follow-up visit 3 months after the last dose of the drug should be performed.

In the event of an IRR, the infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated. Prophylactic treatment with antihistamines (e.g. IV diphenhydramine 25–50 mg), paracetamol (500–1000 mg), nonsteroidal anti-inflammatory drugs, or corticosteroids (PO; 2–3 days); dosage based on the treating physician's clinical judgement and/or hospital protocols for managing IRRs) prior to future infusions may be considered. Management of

specific reactions (e.g. hypotension, desaturation) should be performed according to standard protocols.

Post infusion

Educate patient/caregivers on post discharge advice:

- Inform patient to contact their healthcare provider or go to the nearest hospital emergency department if they have signs of a serious allergic reaction including:
    - Swelling of the face, lips, mouth, or tongue, hives, or difficulty breathing
- Inform patient to tell their healthcare provider right away if they encounter infusion-related symptoms during an infusion of lecanemab including:
    - Fever
    - flu-like symptoms (chills, body aches, feeling shaky and joint pain)
    - nausea
    - vomiting
    - dizziness or light-headedness
    - changes in heart rate or a feeling that the chest is pounding
    - difficulty breathing or shortness of breath
- Inform patients to call their healthcare provider or go to the nearest hospital emergency department immediately if they have symptoms associated with ARIA including:
    - Headache
    - Confusion
    - Dizziness
    - Vision changes
    - Nausea
    - Difficulty walking
    - Seizures
- Provide patients and caregivers with a summary sheet of ARIA symptoms with emergency contact details (lecanemab patient alert card)

References

LEQEMBI (lecanemab). Singapore approved Prescribing Information; October 2025; Eisai (Singapore) Pte. Ltd.

Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: Appropriate Use Recommendations. J Prev Alzheimers Dis 2023;10(3):362-77. PMID: 37357276. doi: 10.14283/jpad.2023.30.

Joint Formulary Committee. British National Formulary, 80th ed. London: BMJ and Pharmaceutical Press; 2020.

Annex S3. ARIA MRI classification and dosing recommendations.

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

ARIA Type	**Radiographic Severity**		
	Mild	**Moderate**	**Severe**
ARIA-E	FLAIR hyperintensity confined to sulcus and/or cortex/subcortex white matter in one location <5 cm	FLAIR hyperintensity 5 to 10 cm in single greatest dimension, or more than 1 site of involvement, each measuring <10 cm	FLAIR hyperintensity >10 cm. One or more separate/ independent sites of involvement may be noted.
ARIA-H microhaemorrhage	≤4 new incident microhaemorrhages	5 to 9 new incident microhaemorrhages	10 or more new incident microhaemorrhages
ARIA-H superficial siderosis	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	>2 areas of superficial siderosis

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

Clinical Symptom Severity[1]	**ARIA-E Severity on MRI**[2]		
	Mild	**Moderate**	**Severe**
Asymptomatic	Consider suspending dosing	Suspend dosing[3]	Suspend dosing[3]
Mild	Suspend dosing[3]		
Moderate or Severe	Suspend dosing[3]		

[1] Clinical Symptom Severity Categories:
Mild: discomfort noticed, but no disruption of normal daily activity.
Moderate: discomfort sufficient to reduce or affect normal daily activity.
Severe: incapacitating, with inability to work or to perform normal daily activity.
[2] See Table S1 for MRI severity.
[3] Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; consider a follow-up MRI to assess for resolution 2 to 4 months after initial identification. Resumption of dosing should be guided by clinical judgment. Evaluation of risk factors again prior to restarting is recommended. Supportive treatment, including corticosteroids, may be considered in case of ARIA-E. In the Clarity AD trial, ARIA-E events with lecanemab were mostly mild to moderate (91%). These events mostly resolved within 4 months after detection (81%).

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

<table>
<tr><th rowspan="2">Clinical Symptom Severity</th><th colspan="3">ARIA-H Severity on MRI[1]</th></tr>
<tr><th>Mild</th><th>Moderate</th><th>Severe</th></tr>
<tr><td>Asymptomatic</td><td>Consider suspending dosing</td><td rowspan="2">Suspend dosing[2]</td><td rowspan="2">Suspend dosing[3]</td></tr>
<tr><td>Symptomatic</td><td>Suspend dosing[2]</td></tr>
</table>

[1] See Table S1 for MRI severity
[2] Suspend until MRI demonstrates radiographic stabilisation and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgement; consider a follow-up MRI to assess for stabilisation 2 to 4 months after initial identification. Evaluation of risk factors again prior to restarting is recommended. In the Clarity AD trial, ARIA-E events with lecanemab were mostly mild to moderate (91%). These events mostly resolved within 4 months after detection (81%).
[3] Suspend until MRI demonstrates radiographic stabilisation and symptoms, if present, resolve; use clinical judgement in considering whether to continue treatment or permanently discontinue lecanemab.

Following an initial event of ARIA, recurrence can occur in non-carriers and in heterozygous and homozygous carriers, with the highest risk in homozygous carriers

Intracerebral haemorrhage
In patients who develop intracerebral haemorrhages greater than 1 cm in diameter during treatment with lecanemab, discontinue treatment.

References

LEQEMBI (lecanemab). Singapore approved Prescribing Information; October 2025; Eisai (Singapore) Pte. Ltd.

van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med 2023;388(1):9-21. PMID: 36449413. doi: 10.1056/NEJMoa2212948.