LEQEMBI® 100mg/mL Concentrate for Solution for Infusion
Lecanemab 200mg & 500mg

1. PRODUCT NAME

Leqembi® 100mg/mL concentrate for solution for infusion (2mL)
Leqembi® 100mg/mL concentrate for solution for infusion (5mL)

2.WARNINGS

2.1 This drug should be administered only to patients who are considered appropriate to receive this drug, under the supervision of the physician with sufficient knowledge and experience in the Alzheimer's disease pathophysiology, diagnosis and the treatment and with capability to explain and manage the risk of this drug at a medical institution capable of performing tests and management necessary for the administration of this drug such as amyloid PET and MRI or at a medical institution capable of communicating with such a medical institution.

2.2 Prior to initiating administration of this drug, sufficient information should be provided to patients and their families/caregivers about the occurrence rate of ARIA due to this drug, the risk of ARIA, tests necessary for risk management, and measures to be taken when ARIA occurs. This drug should be administered after being informed and obtaining their consent. Also, patients should be instructed to immediately contact their attending physician if any abnormalities are observed.
（see section 8.1, 9.1, 12.1.2）

3.CONTRAINDICATIONS

（This drug is contraindicated to the following patients.）

3.1 Patients with a history of serious hypersensitivity to the ingredients of this drug.

3.2 Patients with cerebral vasogenic edema confirmed before the start of administration of this drug.
[Due to the possible increased risk of ARIA］
（See Section 8.1, 9.1.1）

3.3 Patients with 5 or more cerebral microbleeds, focal cerebral surface hemosiderosis or cerebral hemorrhage >1 cm in size confirmed before the start of administration of this drug.
[Due to the possible increased risk of ARIA］
（see section 8.1, 9.1.1）

4. COMPOSITION AND PRODUCT DESCRIPTION

4.1 Composition

Trade name		Leqembi for IV Infusion 200mg	Leqembi for IV Infusion 500mg
		Weight/volume in a vial	
		2mL	5mL
Active ingredient	Lecanemab (Genetical Recombination)	200mg	500mg
Excipient	L-histidine	0.36mg	0.90mg
	L-histidine hydrochloride monohydrate	9.98mg	24.95mg
	L-arginine hydrochloride	84.26mg	210.65mg
	Polysorbate 80	1.00mg	2.50mg
	water for injection	q.s.	q.s.

Lecanemab is manufactured using Chinese hamster ovary cell.

4.2 Product Description

Trade name	Leqembi for IV Infusion 200mg	Leqembi for IV Infusion 500mg
Appearance	Clear to very opalescent, colorless to pale yellow liquid	
pH	4.5～5.5	
Ratio of Osmolarity	approximately 1.4	

5. INDICATIONS

Slowing of progression in mild cognitive impairment or mild dementia due to Alzheimer’s disease

6. PRECAUTIONS CONCERNING INDICATIONS

6.1 This drug does not completely halt the progression or cure the disease.

6.2 Can be used only for patients who are diagnosed with Alzheimer’s disease by confirming the finding which suggests the presence of amyloid beta pathology using approved methods such as amyloid PET, CSF, or equivalent methods.

6.3 This drug should not be initiated in persons who have amyloid β pathology but are asymptomatic, or patients with moderate/severe AD-D.

6.4 This drug therapy should be initiated based on the full understanding of not only the description in the section of Clinical study (section 16.1) but also the diagnostic criteria used in the global phase 3 study, the range of clinical symptom scores of the patients enrolled, and the study results, etc. (see section 16.1.2)

7. DOSAGE AND ADMINISTRATION

The recommended dosage is 10 mg/kg that must be administered as an intravenous infusion over approximately one hour, once every two weeks.

8. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION

8.1 LEQEMBI, can cause amyloid related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E), which can be observed on MRI as brain edema or sulcal effusions, and ARIA with hemosiderin deposition (ARIA-H), which includes microhemorrhage, superficial siderosis and macrohemorrahage.
(see section 2.2, 3.2, 3.3, 9.1, 12.1.2)

(1) Patients with ARIA-E and/or ARIA-H of radiographically mild and asymptomatic may continue dosing based on careful clinical judgement. The patients should be carefully monitored after continuation.

(2) If radiographically moderate or severe ARIA-E is observed, administration should be temporarily suspended until MRI

demonstrates radiographic resolution. If intracerebral hemorrhage greater than 1 cm, or moderate or severe ARIA-H (microhemorrhages, superficial siderosis) is observed on MRI, administration of this drug should be suspended until MRI demonstrates radiographic stabilization. In any case, patients should be carefully monitored, and resumption of dosing should be guided by careful clinical judgment.

(3) When symptomatic ARIA is observed, administration of this drug should be suspended until resolution of the symptoms and radiographic resolution (ARIA-E)/stabilization (ARIA-H). Patients should be carefully monitored, and resumption of dosing should be guided by careful clinical judgment.

[Reference]

〈ARIA Classification criteria； Radiographic Severity〉

ARIA-E

Severity on MRI	Brain MRI findings
Mild	Fluid-attenuated inversion recovery (FLAIR) hyperintensity confined to the sulcus or cortex/subcortical white matter in one location measuring < 5 cm
Moderate	FLAIR hyperintensity 5 to 10 cm in single greatest dimension, or more than 1 site of involvement, each measuring < 10 cm
Severe	FLAIR hyperintensity >10 cm with associated gyral swelling and sulcal effacement. One or more separate / independent sites of involvement may be noted.

ARIA-H

Severity on MRI	Brain MRI findings	
	ARIA-H microhemorrhage	ARIA-H superficial siderosis
Mild	≤ 4 new incident microhemorrhages	1 focal area of superficial siderosis
Moderate	5 to 9 new incident microhemorrhages	2 focal areas of superficial siderosis
Severe	10 or more new incident microhemorrhages	> 2 focal areas of superficial sideros

〈Dosing Recommendations for Patients with ARIA〉

ARIA-E

Severity on MRI	Presence/abcence of clinical symptoms	
	asymptomatic	symptomatic
Mild	May continue dosing[1]	Suspend dosing until MRI demonstrates radiographic resolution and symptoms resolve[2]
Moderate	Suspend dosing until MRI demonstrates radiographic resolution[2]	
Severe		

1: Consider whether to continue dosing based on careful clinical judgement. In the case of continuing dosing, the patients should be carefully monitored after continuation.

2: Patients should be carefully monitored, and resumption of dosing should be guided by careful clinical judgment.

ARIA-H

Severity on MRI	Presence/abcence of clinical symptoms	
	asymptomatic	symptomatic
Mild	May continue dosing[1]	Suspend dosing until MRI demonstrates radiographic stabilization and symptoms resolve[2]
Moderate	Suspend dosing until MRI demonstrates radiographic stabilization[2]	Suspend dosing until MRI demonstrates radiographic stabilization and symptoms resolve[2]
Severe	Suspend dosing until MRI demonstrates radiographic stabilization[3]	Suspend dosing until MRI demonstrates radiographic stabilization and symptoms resolve[3]

1: Consider whether to continue dosing based on careful clinical judgement. In the case of continuing dosing, the patients should be carefully monitored after continuation.

2: Patients should be carefully monitored, and resumption of dosing should be guided by careful clinical judgment.

3: Patients should be carefully monitored. Use clinical judgment in considering whether to continue treatment or permanently discontinue this drug. Resumption of dosing should be guided by careful clinical judgment.

〈Brain MRI monitoring after ARIA occurrence〉

ARIA-E

Severity on MRI	Brain MRI Monitoring
Mild	In asymptomatic case of continued dosing, to confirm the presence or absence of aggravation of ARIA, follow-up MRI 1-2 months after occurrence should be considerd. In asymptomatic case of suspended dosing or symptomatic case, follow MRI monitoring procedures for moderate or severe ARIA-E.
Moderate	Perform follow-up MRIs approximately 2 to 4 months after the event identification. If ARIA-E is not resolved, perform additional MRIs.
Severe	

ARIA-H

Severity on MRI	Brain MRI Monitoring
Mild	In case of symptomatic ARIA-H, perform follow-up MRIs approximately 2 to 4 months after the event identification. If ARIA-H is not stabilized radiographically, perform additional MRIs.
Moderate	Perform follow-up MRIs approximately 2 to 4 months after the event identification. If ARIA-H is not stabilized radiographically, perform additional MRIs (including the case of intracerebral hemorrhages greater than 1 cm).
Severe	

8.2 During the administration of this drug, clinical symptoms should be evaluated by cognitive tests and interviews of the patient, family members and caregivers about subjective and objective symptoms, etc., approximately every 6 months. If the efficacy of this drug is not expected based on the course of clinical symptoms and severity of dementia, administration of drug should be discontinued. Besides, the efficacy of continued administration in patients with progression to moderate/severe AD-D during administration of this drug has not been established.

9. IMPORTANT PRECAUTIONS

9.1 This drug should be used under the supervision of physicians with adequate knowledge in the management of ARIA. In addition, attention should be given to the following points before and during administration of this drug [see section 2.2, 8.1, 12.1.2].

9.1.1 Obtain a recent (within one year) brain MRI prior to initiating treatment to evaluate abnormal findings containing pre-existing Amyloid Related Imaging Abnormalities (ARIA). (see section 3.2, 3.3, 16.1.2)

9.1.2 Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment as this is when ARIAs are frequently observed. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI scanning, if indicated.

9.1.3 Obtain an MRI prior to the 5th, 7th and 14th infusions (by 2 months, 3 months and 6 months after the start of administration as guideline) and periodically after that regardless of the presence or absence of symptoms suggestive of ARIA. If ARIA is detected on MRI, be alert for emergence of symptoms and perform additional MRI tests as needed. (see table in section 8.1)

9.1.4 Although a higher incidence and radiographic severity of ARIA and higher incidence of symptomatic ARIA in ApoEε4 homozygotes compared to heterozygotes and non-carriers has been reported, ARIA should be managed regardless of ApoEε4 status by reference to the same recommendations defined in section 9.1.1, 9.1.2, 9.1.3, 12.1.2.
Approximately 15% of Alzheimer's disease patient are ApoEε4 homozygotes.

The incidence of ARIA by ApoEε4 genotype in Study 301 Core

	Non-carriers		Heterozygotes		Homozygotes	
	Placebo	lecanemab	Placebo	lecanemab	Placebo	lecanemab
ARIA-E	0.3	5.4	1.9	10.9	3.8	32.6
ARIA-H	4.2	11.9	8.6	14.0	21.1	39.0

(%)

9.2 There is no experience with initiation of this drug in patients with a history of transient ischemic attack, stroke, or seizure within 1 year. If patients have a history of these conditions, carefully consider the risks and benefits of administering this drug before deciding whether to administer it.

9.3 Presence of hypertension should be confirmed before administration of this drug, and administration to patients with persistent hypertension should be performed with caution. Appropriate blood pressure control should be performed during administration of this drug.

10. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

10.1 Pregnant Women

Pregnant or possibly pregnant women should receive only when the benefit of treatment is considered to outweigh the risks. Reproductive and development toxicity studies has not been conducted. It is known that human IgG is passed through the placenta.

10.2 Breast-feeding Women

Continuation or discontinuation of breast-feeding should be considered in view of the therapeutic benefits and the benefits of breast-feeding. Although the transfer of this drug into human milk is unknown, it is known that human IgG is transferred into human milk.

10.3 Pediatric Use

The safety and effectiveness have not been established in pediatric patients.

11. Interactions

11.1 Precautions for Co-administration

(This drug should be administered with caution when co-administered with the following.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Anticoagulants Warfarin Potassium Heparin Sodium, Apixaban, etc	If cerebral hemorrhage occurs during administration of this drug, bleeding may be exacerbated. Attention should be given to the side effect of cerebral hemorrhage when used concomitantly.	Cerebral hemorrhage has been reported as a side effect of this drug. Concomitant use of these drugs listed on the left may promote bleeding.
Antiplatelets Aspirin Clopidogrel Sulfate etc		
Thrombolytic agents Alteplase, etc		

12. ADVERSE REACTIONS

Since the following adverse reactions may occur, patients should be carefully monitored. If any abnormalities are observed, appropriate measures such as discontinuation of administration should be taken.

12.1 Clinically Significant Adverse Reactions

12.1.1 Infusion-Related Reactions (26.1%)

Symptoms of infusion-related reactions include fever and flu-like symptoms (headache, chills), nausea, vomiting, etc. In the event of an infusion-related reaction, the infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated. Prophylactic treatment with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids prior to future infusions may be considered.

12.1.2 ARIA

ARIA-edema/ sulcal effusions (12.6%) as ARIA-E, and ARIA-H including ARIA-microhemorrhage and haemosiderin deposits (13.6%), superficial hemosiderinosis (5.2%), and intracerebral hemorrhage (0.4%) may occur. (see section 8.1, 9.1)

(1) Although ARIA is usually asymptomatic, serious and life-threatening events, including seizure and status epilepticus, can occur. When symptomatic, reported symptoms associated with ARIA include headache, confusion, visual changes, dizziness, nausea, and gait difficulty.

(2) ARIA can recur. When resuming administration of this drug, the patient's condition should be carefully monitored, and periodical follow-up MRI are recommended.

(3) There are limited data in dosing patients who experienced recurrent ARIA.

12.2 Other Adverse Reactions

	≥ 1 %	0.5>, ≥5%	<0.5%
Hypersensitivity	Hypersensitivity	Rash	Erythema
Gastrointestinal			Nausea
Hepatic			Aspartate aminotransferase increased
Psychoneurologic	Headache		Dizziness, Balance disorder, Confusional state, Depressive symptom, Memory impairment, Tension headache
Systemic		Malaise	Orthostatic hypotension
Musculoskeletal			Fall
Others		Injection site reaction	Blood cholesterol increased, Proteinuria, Infusion site extravasation

13. PRECAUTIONS CONCERING USE

13.1 Precausions Concerning the Preparation of the Drug

13.1.1 Use aseptic technique when preparing the LEQEMBI diluted solution for intravenous infusion.

Each vial is for one time-use only. Discard any unused portion.

13.1.2 Prior to administration, LEQEMBI must be diluted in 250 mL of 0.9% Sodium Chloride Injection.

13.1.3 Gently invert the infusion bag containing the LEQEMBI diluted solution to mix completely. Do not shake.

13.1.4 After dilution, immediate use is recommended.

If not administered immediately, store LEQEMBI at 2 to 25°C and use within 4 hours.

13.1.5 Prior to infusion, allow LEQEMBI diluted solution to warm to room temperature.

13.1.6 Do not mix LEQEMBI with other medicinal products.

13.2 Precautions Concerning Administration of the Drug

13.2.1 Visually inspect the LEQEMBI diluted solution for particles or discoloration prior to administration. Do not use if it is discolored, or opaque or foreign particles are seen.

13.2.2 Infuse LEQEMBI diluted solution through an intravenous line containing a low-protein binding 0.2 or 0.22 micron in-line filter.

13.2.3 Flush infusion line to ensure all LEQEMBI is administered.

14. OTHER PRECAUTIONS

14.1 Information Based on Clinical Use

14.1.1 In Study 301, 49/884(5.5%) of patients treated with LEQEMBI 10 mg/kg every two weeks developed anti-lecanemab antibodies with low titers. Of these patients neutralizing anti-lecanemab-irmb antibodies were detected in 2/49 (4.1%) patients with low titers. ADA did not meaningfully affect PK, PD, efficacy and safety of LEQEMBI.

14.1.2 In the OLE phase of study 301, cases of cerebral hemorrhage or severe ARIA-E/H (concurrence) resulting in death during administration of this drug have been reported. However, this study report also includes information that cerebral hemorrhage or severe ARIA-E/H was not the cause of death.

15. PHARMACOKINETICS

15.1 Blood Level

15.1.1 Single and multiple dosing

In patients with MCI due to AD or mild AD, lecanemab was administered as an intravenous infusion followed by a 6-week washout period after the first dose. Then, lecanemab was administered once every 2 weeks for a total of 5 infusions. Mean serum concentration-time profile of lecanemab and PK parameters after the first dose and the fifth repeated dose are shown in Figure 1 and Table 1. The accumulation ratio was 1.59 fold based on AUC. (The dosage and administration of this drug is 10 mg/kg biweekly)

*Approved dosage and administration of this drug is 'The recommended dosage is 10 mg/kg that must be administered as an intravenous infusion over approximately one hour, once every two weeks.'

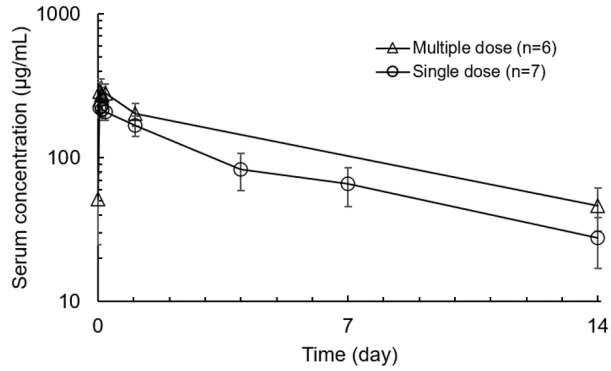

Figure 1: Mean serum concentration-time profile of lecanemab after single and repeated biweekly intravenous administration of 10 mg/kg of LEQEMBI in patients with MCI due to AD or mild AD (means±SD)

Table 1: Serum PK parameters of lecanemab after single and repeated biweekly intravenous administration of 10 mg/kg of LEQEMBI in patients with MCI due to AD or mild AD

	C_{max} (μg/mL)	T_{max} (h)	$AUC_{(0-336h)}$ (μg•h/mL)	$t_{½}$ (h)
1st dose (n=7)	235 (34.1)	2.1 (1.1-2.9)	26800 (6430)	159 (16.0)
Multiple dose 5th dose (n=6)	299 (45.7)	2.0 (1.0-4.9)	39500 (7330)	-

Data are shown as mean (SD) except $t_{max.}$ For t_{max}, median (min, max) is shown.

15.3 Distribution

The estimated value (95% CI) for central volume of distribution at steady-state is 3.24 (3.18 – 3.30) L based on PPK analysis.

15.4 Metabolism

Lecanemab is degraded by catabolism in the same manner as endogenous IgGs.

15.5 Excretion

The terminal half-life is 5 to 7 days.

Lecanemab clearance (95% CI) is 0.0154 (0.0147 – 0.0160) L/h based on PPK analysis.

16. CLINICAL STUDIES

16.1 Clinical studies for Efficacy and Safety

16.1.1 Multi-national Phase 2 study

A double-blind, parallel-group, dose finding study was conducted in 856 patients with mild cognitive impairment and mild dementia stage due to Alzheimer's disease (including 34 Japanese subjects), to whom LEQEMBI or placebo was administered intravenously for 18 months. Enrolled were patients with a Clinical Dementia Rating (CDR) global score of 0.5 or 1.0, a Memory Box score of 0.5 or greater, MMSE score of ≥22 & ≤30 and confirmed presence of amyloid pathology by amyloid PET or CSF. The subjects were randomized to PBO (247), LEQEMBI 2.5 mg/kg bi-weekly (52), 5 mg/kg monthly (51), 5 mg/kg bi-weekly (92), 10 mg/kg monthly (253), or 10 mg/kg bi-weekly (161).

The primary endpoint was change from baseline in ADCOMS at 12 months, however, LEQEMBI 10 mg/kg biweekly had a 64% likelihood of 25% or greater slowing of progression on the primary endpoint relative to placebo, which did not meet the prespecified success criterion of 80%.

LEQEMBI demonstrated a dose-dependent and time-dependent reduction of brain amyloid beta plaque in amyloid PET SUVR versus placebo. There was a dose-dependent slowing of clinical decline as measured by Alzheimer's Disease Composite Score (ADCOMS), Clinical Dementia Rating- Sum of Boxes (CDR-SB) and Alzheimer's Disease Assessment Scale - Cognitive subscale with 14 tasks (ADAS-Cog14) with LEQEMBI compared to placebo over 18 months, and LEQEMBI 10 mg/kg bi-weekly showed 29.7%, 26.5% and 47.2% less decline respectively at 18 month.

The change from baseline in these clinical efficacy assessments are shown in Table 2.

The most common (incidence ≥5% and higher than PBO) TEAEs that occurred in LEQEMBI 10 mg/kg biweekly were infusion-related reactions (19.9%), headache (13.7%), ARIA-E (9.9%), cough (8.7%), diarrhea (8.1%), dizziness (7.5%) and cerebral microhemorrhage (5.6%).

Table 2: Biomarker and Clinical Efficacy Results at 18 months

Endpoints	LEQEMBI 10mg/kg bi-weekly	placebo
Amyloid PET SUVR	44 subjects	98 subjects
Mean baseline	1.37	1.40
Adjusted mean change from baseline*	-0.31	0.00
Difference from PBO*	-0.31	
ADCOMS	152 subjects	238 subjects
Mean baseline	0.37	0.37
Adjusted mean change from baseline*	0.14	0.19
Difference from PBO*	-0.06	
CDR-SB	152 subjects	238 subjects
Mean baseline	2.97	2.89
Adjusted mean change from baseline*	1.10	1.50
Difference from PBO*	-0.40	
ADAS-Cog14	152 subjects	237 subjects
Mean baseline	22.06	22.56
Adjusted mean change from baseline*	2.59	4.90
Difference from PBO*	-2.31	

* Adjusted Mean (MMRM)

16.1.2 Multi-national Phase 3 study

A double-blind, parallel-group study was conducted in 1795 patients with mild cognitive impairment and mild dementia stage due to Alzheimer's disease (including 152 Japanese subjects), to whom LEQEMBI 10 mg/kg bi-weekly or placebo was administered intravenously for 18 months. The subjects were randomized to PBO (897 including 64 Japanese) or 10 mg/kg bi-weekly (898 including 88 Japanese). The main inclusion criteria were as follows:

(1) Have a global CDR score of 0.5-1 and a CDR Memory Box score of 0.5 or greater
(2) Have a MMSE score of 22-30
(3) Confirmed presence of amyloid pathology by amyloid PET or CSF
(4) Do not have a history of transient ischemic attacks (TIA), stroke, or seizures within 12 months of Screening.
(5) Do not have other significant pathological findings on brain MRI at Screening, including but not limited to:
- More than 4 microhemorrhages (defined as 10 mm or less at the greatest diameter)
- A single macrohemorrhage greater than 10 mm at greatest diameter
- An area of superficial siderosis
- Evidence of vasogenic edema
- Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infective lesions
- Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease
- Space occupying lesions; or brain tumors (however, lesions diagnosed as meningiomas or arachnoid cysts and less than 1 cm at their greatest diameter need not be exclusionary)

There was a statistically significant slowing of clinical decline as measured by CDR-SB (primary endpoint)(27.1%) with LEQEMBI compared to placebo over 18 months. LEQEMBI also slowed clinical decline as measured by ADAS-Cog14(25.8%), ADCOMS(23.5%), AD Cooperative Study – Activities of Daily Scale for Mild Cognitive Impairment (ADCS MCI-ADL) (36.6%) compared to placebo. There was a time-dependent reduction of brain amyloid beta plaque level in amyloid PET using Centiloids with LEQEMBI. The change from baseline in these clinical efficacy assessments are shown in Table 3.

The most common (incidence ≥1%) treatment related TEAEs that occurred in LEQEMBI 10 mg/kg biweekly were infusion-related reactions (26.1%), ARIA-H (16.5%), ARIA-E (12.6%), headache (1.8%) and hypersensitivity (1.7%).

The incidence of symptomatic ARIA-E and ARIA-H in LEQEMBI 10 mg/kg biweekly was 2.8% and 1.4%, respectively. [see section 6.4, 9.1.1]

Table 3 Biomarker and Clinical Efficacy Results at 18 months

Endpoints	LEQEMBI 10mg/kg bi-weekly	placebo
CDR-SB	859 subjects	875 subjects
Mean baseline	3.17	3.22
Adjusted mean change from baseline*	1.213	1.663
Difference from PBO*	-0.451	
P-value	<0.0001	
Amyloid PET SUVR	354 subjects	344 subjects
Mean baseline	77.918	75.026
Adjusted mean change from baseline*	-55.481	3.637
Difference from PBO*	-59.118	
ADAS-Cog14	854 subjects	872 subjects
Mean baseline	24.45	24.37
Adjusted mean change from baseline*	4.140	5.581
Difference from PBO*	-1.442	
ADCOMS	857 subjects	875 subjects
Mean baseline	0.398	0.400
Adjusted mean change from baseline*	0.164	0.214
Difference from PBO*	-0.050	
ADACS MCI-ADL	783 subjects	796 subjects
Mean baseline	41.2	40.9
Adjusted mean change from baseline*	-3.484	-5.500
Difference from PBO *	2.016	

* Adjsuted Mean (MMRM)

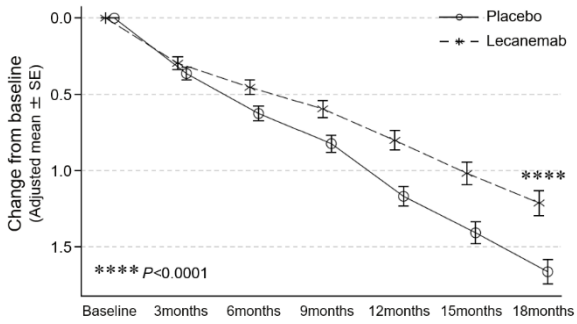

Figure 2: CDR-SB change from baseline (FAS+, MMRM, adjusted mean)

17. PHARMACOLOGY / PHARMACODYNAMICS

17.1 Mechanism of Action

The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. Lecanemab is a humanized IgG1 monoclonal antibody. Lecanemab preferentially binds with highest affinity to large soluble amyloid-beta protein aggregates, known as protofibrils, while maintaining high affinity for fibril that are a major component of amyloid beta plaques. Lecanemab inhibited Aβ protofibril binding to rat hippocampal neurons. Lecanemab promoted Fc-dependent-phagocytosis of amyloid-β by microglial cells contributing to the reduction of amyloid-β in the brain.

17.2 Effect on Aβ level in brain

The murine surrogate antibody of lecanemab reduced brain Aβ-protofibril and amyloid plaque levels in mice expressing human mutant amyloid precursor protein (APP).

18. PHYSICOCHEMICAL PROPERTIES

Nonproprietary name： Lecanemab（Genetical Recombination）

Essential nature：

Lecanemab is recombinant anti-human amyloid beta peptide monoclonal antibody, the complementarity-determining regions of which are derived from mouse antibody and other regions are derived from human IgG1. Lecanemab is produced in Chinese hamster ovary cells. Lecanemab is a glycoprotein (molecular weight: ca. 150,000) composed of 2H-chain (γ1-chains) of 454 amino acid residues each and 2L-chains (κ-chains) consisting of 219 amino acid residues each.

19. PRECAUTIONS FOR HANDLING

19.1 Do not freeze or shake vials

19.2 Store unopened vials of LEQEMBI with protecting from light.

20. PACKAGING

Leqembi for IV Infusion 200mg/2mL [1 vial]

Leqembi for IV Infusion 500mg/5mL [1 vial]

21. STORAGE CONDITIONS

Storage: 2 - 8℃

22. Shelf life

LEQEMBI should be used before the expiration date indicated on the package.

23. MANUFACTURER

Biogen US Corporation
900 Davis Drive, Research Triangle Park,
North Carolina 27709, USA

24. RELEASED BY

Eisai Co., Ltd. Kawashima Plant
1, Kawashimatakehaya-machi, Kakamigahara-shi,
Gifu-ken, Japan

25. PRODUCT REGISTRATION HOLDER

Eisai (Malaysia) Sdn. Bhd.
Unit 701D, Level 7, Tower D, Uptown 5
No.5, Jalan SS21/39, Damansara Uptown
47400 Petaling Jaya
Selangor, Malaysia

26. DATE OF REVISION

October 2025

[Supplemental information for section 8. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION]

<MRI monitoring after the onset of ARIA>