

## Summary of Investigation Results

### Donanemab (genetical recombination)

Non-proprietary name	Non-proprietary name	Brand name (marketing authorization holder)
Brand name	Donanemab (genetical recombination)	Kisunla Intravenous Infusion 350 mg (Eli Lilly Japan K.K.)
Japanese market launch	November 2024	
Indications	Slowing the progression of mild cognitive impairment and mild dementia due to Alzheimer's disease	
Summary of revisions	<p>1. In the 8. IMPORTANT PRECAUTIONS section, the descriptions to the following effect should be added as precautions concerning the occurrence of amyloid related imaging abnormalities (ARIA): Patients and their families/caregivers should be instructed to seek immediate medical attention if a patient experiences symptoms suggestive of ARIA, irrespective of the treatment duration, and in such cases, clinical evaluation should be promptly performed, including MRI scanning if ARIA is suspected.</p> <p>2. The description regarding MRI scanning prior to the 3rd dose in the case where a patient has no symptoms suggestive of ARIA in the 8. IMPORTANT PRECAUTIONS section should be changed from "It is advisable to perform MRI scanning if indicated" to "MRI scanning should be performed to check whether ARIA occurs or not" as with the description for MRI scanning prior to the 2nd, 4th, and 7th doses and thereafter.</p>	
Investigation results and background of the revision	<p>Adverse reaction reports and overseas prescribing information were investigated. As a result of consultation with expert advisors regarding the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary for the following reasons:</p> <ul style="list-style-type: none"> <li>• Some cases of symptomatic ARIA for which it took a long time from the onset of the symptoms to MRI scanning have been reported. Therefore, it is considered important to instruct patients and their families/caregivers to seek immediate medical attention if a patient experiences ARIA-related symptoms, irrespective of the treatment duration, and in such cases, to promptly perform clinical evaluation, including MRI scanning if ARIA is suspected.</li> <li>• Cases of serious ARIA (ARIA-E, ARIA-H) reported in adverse reaction reports include many cases that occurred after the 2nd dose. Therefore, it is considered important to change the description regarding MRI scanning</li> </ul>	

	prior to the 3rd dose to "MRI scanning should be performed to check whether ARIA occurs or not." The Optimal Use Guidelines state that "MRI scanning prior to the 3rd dose should be performed to check whether ARIA occurs or not" as with the description regarding MRI scanning prior to the 2nd, 4th, and 7th doses and thereafter.
Reference: Number of cases* <sup>1</sup> involving ARIA reported in Japan	A total of 58 cases* <sup>2</sup> have been reported to date. No deaths have been reported to date.

\*1: Cases collected in the PMDA's safety database for drugs.

\*2: Cases corresponding to any of MedDRA ver. 28.0 PTs "amyloid related imaging abnormalities," "amyloid related imaging abnormality-oedema/effusion," "brain oedema," "vasogenic cerebral oedema," "amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits," "cerebellar microhaemorrhage," "cerebral haemorrhage," "haemorrhage intracranial," "thalamus haemorrhage," "superficial siderosis of central nervous system," "cerebral microhaemorrhage," and "brain stem haemorrhage." Causality assessment was not performed.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).