This document is an English-translated version of an attachment of a notification for Revision of PRECAUTIONS issued by the Ministry of Health, Labour and Welfare.

Attachment 1

August 17, 2026

【Therapeutic category】Other agents affecting central nervous system

【Non-proprietary name】Donanemab (genetical recombination)

【Safety measure】PRECAUTIONS should be revised.

A revised description is underlined.

Current	Revision
1. WARNINGS Prior to the start of treatment with this drug, the incidence and risks of ARIA associated with the administration of this drug, tests required for management of the risks of ARIA, and measures to be taken when ARIA occurs should be explained to patients and their families/caregivers by providing sufficient information to them and their consent should be obtained. <u>In addition,</u> patients should be instructed to immediately contact their physician if any abnormalities are observed.	1. WARNINGS <u>The incidence of ARIA was higher in apolipoprotein E allele 4 (APOEε4) homozygote carriers. Implementation of APOE genetic testing should be considered before starting treatment with this drug.</u> Prior to the start of treatment with this drug, the incidence and risks of ARIA associated with the administration of this drug, tests required for management of the risks of ARIA, and measures to be taken when ARIA occurs should be explained to patients and their families/caregivers by providing sufficient information to them and their consent should be obtained. Patients should be instructed to immediately contact their physician if any abnormalities are observed.
8. IMPORTANT PRECAUTIONS The frequencies of ARIA-E, ARIA-H, and the serious ARIA-E and ARIA-H are higher in patients who are <u>apolipoprotein E allele 4 (</u>APOEε4<u>)</u> (homozygote or heterozygote) carriers. Of note, the frequencies were	8. IMPORTANT PRECAUTIONS The frequencies of ARIA-E, ARIA-H, and the serious ARIA-E and ARIA-H are higher in patients who are APOEε4 (homozygote or heterozygote) carriers. Of note, the frequencies were highest in APOEε4 (homozygote)

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highest in APOEε4 (homozygote) carriers, followed by APOEε4 (heterozygote) carriers and APOEε4 non-carriers. Management of ARIA including MRI scanning specified in the 8.2.1 to 8.2.3 sections and the 11.1.2 section should be performed regardless of ApoEε4 carrier status. The percentage of APOEε4 homozygote carriers in a global phase III study (AACI Study) and an overseas phase III study (AACQ Study) of this drug involving patients with mild cognitive impairment or mild dementia due to Alzheimer's disease was 16.7% and 10.1%, respectively.	carriers, followed by APOEε4 (heterozygote) carriers and APOEε4 non-carriers. Implementation of APOE genetic testing should be considered before starting treatment with this drug in principle for management of risks of ARIA. Even if the testing was not performed prior to the start of the treatment as a result of the consideration, implementation of the testing should be considered if it is deemed necessary during treatment with this drug. When performing the genetic testing, approved in vitro diagnostics should be used, and the significance of APOE genetic testing should be fully explained to patients and their families/caregivers with reference to the latest guidelines, etc., and their consent should be obtained. In addition, management of ARIA including MRI scanning specified in the 8.2.1 to 8.2.3 sections and the 11.1.2 section should be performed regardless of ApoEε4 carrier status. The percentage of APOEε4 homozygote carriers in a global phase III study (AACI Study) and an overseas phase III study (AACQ Study) of this drug involving patients with mild cognitive impairment or mild dementia due to Alzheimer's disease was 16.7% and 10.1%, respectively.

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