

No.22-40

May 27, 2022
Eisai Co., Ltd.

**MINISTRY OF HEALTH, LABOUR AND WELFARE GRANTS ORPHAN DRUG
DESIGNATION IN JAPAN TO MECOBALAMIN ULTRAHIGH-DOSE FORMULATION WITH
PROSPECTIVE INDICATION FOR DELAYING THE PROGRESSION OF DISEASE AND
FUNCTIONAL IMPAIRMENT OF AMYOTROPHIC LATERAL SCLEROSIS**

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has received orphan drug designation for ultrahigh-dose mecobalamin, with a prospective indication for delaying the progression of disease and functional impairment of amyotrophic lateral sclerosis (ALS), by the Ministry of Health, Labour and Welfare (MHLW).

ALS is an intractable, progressive, neurodegenerative disease with significant unmet medical needs. In Japan, the estimated number of ALS patients is approximately 10,000.

Based on a favorable clinical results of the JETALS (The Japan Early-Stage Trial of Ultrahigh-Dose Methylcobalamin for ALS), an investigator-initiated Phase III trial to evaluate efficacy and safety of ultrahigh-dose methylcobalamin (mecobalamin) in early onset ALS patients, led by a research team with Extraordinary Professor Ryuji Kaji (Principal Investigator), Tokushima University and Professor Yuishin Izumi (Coordinating Investigator), the Department of Neurology, Tokushima University Graduate School of Biomedical Sciences, Eisai has initiated preparation on a new drug application (NDA) of ultrahigh-dose mecobalamin for ALS, and plans to submit a NDA during the fiscal year 2023 in Japan.

Eisai considers neurology a therapeutic area of focus and is committed to new drug development in this field in order to fulfill unmet medical needs, and ultimately further its contribution to improving the benefit of patients and their families.

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[Notes to editors]

1. About Amyotrophic Lateral Sclerosis (ALS)

ALS is an intractable, progressive, neurodegenerative disease that results in severe muscle atrophy and weakness in the muscles due to motor neuron dysfunction. As the main cause of death is respiratory failure due to paralysis of the respiratory muscles, without the use of an artificial respirator, death occurs within approximately 3 to 6 years from the onset of the disease. According to the number of patients issued a Certificate of the Recipient of Specified Disease Treatment, there were 10,514 patients with ALS in Japan in 2020. Currently, there is no curative treatment established for ALS, and since there are only limited number of medicines approved in Japan and abroad, this is a disease with significant unmet medical needs.

2. About Mecobalamin

Mecobalamin (generic name, development code: E0302) is approved and marketed as Methycobal®, a 500 µg injection of mecobalamin indicated for the treatment of peripheral neuropathies and megaloblastic anemia caused by vitamin B12 deficiency. Methycobal is also approved as a tablet formulation (250µg and 500 µg) as well as a fine granule formulation (0.1%) indicated for the treatment of peripheral neuropathies. While the mechanism of action of mecobalamin in ALS is not known, it has been suggested in non-clinical research that mecobalamin may have efficacy through a neuroprotective effect and regeneration of nerve axons. Since the 1990s, clinical research has been carried out on ultrahigh-dose mecobalamin in ALS by a study group on neurodegenerative disease, funded through the Ministry of Health, Labour and Welfare's Specified Disease Treatment Research Program. Short- and long-term trials of intramuscular injection of mecobalamin at 25 mg and 50 mg per day, which is respectively 50 and 100 times the approved dosage of Methycobal, suggested that ultrahigh-dose mecobalamin could have a clinical effect in ALS. Therefore, Eisai had conducted the Phase II/III clinical trial (Study 761) since 2006 and submitted a new drug application for ultrahigh-dose mecobalamin as treatment for ALS in May 2015 but withdrew the application in March 2016 after the Pharmaceuticals and Medical Devices Agency (PMDA) indicated that additional clinical trials were necessary.