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Eisai Co., Ltd.

ARICEPT® APPROVED FOR ADDITIONAL INDICATION OF SEVERE ALZHEIMER'S DISEASE IN CHINA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that Aricept® (donepezil hydrochloride, brand name in China: 安理申®) has been approved for the additional indication of severe Alzheimer's disease in China. Aricept is the first Alzheimer's disease treatment with a broad indication that covers mild to severe Alzheimer's disease in China.

The approval of the additional indication was based on the results of a Phase III clinical study (Study 339¹) in China. Study 339 was a multi-center, randomized, double-blind, placebo controlled, parallel-group study to evaluate the efficacy and safety of Aricept 10 mg per day in 313 Chinese patients with severe Alzheimer's disease. In this study, Aricept demonstrated a statistically significant improvement in total Severe Impairment Battery scores after 24 weeks compared to placebo, which was the primary endpoint of the study. In the study, the four most commonly observed adverse events in the Aricept arm were bradycardia, anorexia, QT interval prolongation, and dizziness.

In China, it has been estimated that approximately 6 million people suffer from Alzheimer's disease.¹ Furthermore, with the progressive aging of the population, the number of patients with dementia is expected to greatly increase in the future. Eisai launched Aricept in China in September 1999, and in collaboration with various stakeholders including government, hospitals and non-government organizations, is actively promoting dementia disease awareness initiatives for civilians as well as support for establishing memory clinics and other initiatives.

With the approval of this indication covering severe Alzheimer's disease, Eisai strives to further contribute to increasing the quality of life of patients with Alzheimer's disease in China, and as the originator of Aricept, continues to make comprehensive contributions in dementia such as improving treatment and care, increasing public awareness of the disease and discovering new treatment methods.

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[Notes to editors]

1. About Aricept in China

Eisai launched Aricept in China in September 1999. The indication for Aricept in China covers mild to moderate Alzheimer's disease, and can be used in either 5 mg or 10 mg dosages. By obtaining approval for severe Alzheimer's disease, Aricept is the first Alzheimer's disease treatment with a broad indication that covers mild to severe Alzheimer's disease in China.

2. About the Phase III Clinical Study Conducted in China (Study 339)¹

Study 339 was a multi-center, randomized, double-blind, placebo controlled, parallel-group study to evaluate the efficacy and safety of Aricept 10 mg per day in 313 Chinese patients with severe Alzheimer's disease. Patients were in the Aricept arm received 5 mg for 6 weeks and 10 mg for the remaining 18 weeks (24 weeks in total).

From the results of this study, the change in Severe Impairment Battery scores* from baseline at week 24, the study's primary endpoint, was 2.9 for Aricept compared to -2.0 for placebo, suggesting a statistically significant improvement for Aricept (difference: 4.8, 95% confidence interval [CI] 1.56 to 8.08, p=0.004).

In the study's secondary endpoint of change in CIBIC-plus scores**, Aricept demonstrated a statistically significant difference compared to placebo (difference: -0.4, 95%CI -0.66 to 0.03, p=0.04), suggesting that treatment with Aricept is clinically meaningful compared to placebo. However, in change in MMSE scores*** from baseline, another secondary endpoint of the study, a statistically significant difference was not observed between the Aricept and placebo arms.

In the study, adverse events were observed in 26.7% of patients in the Aricept arm, and the four most commonly observed adverse events in the Aricept arm were bradycardia (5.7%), anorexia (4.5%), QT interval prolongation (3.8%), and dizziness (3.2%).

- * Severe Impairment Battery: A validated clinical instrument used to measure severely impaired cognitive function. Patients are evaluated in an interview that assesses cognitive function in nine domains: Social Interaction, Memory, Orientation, Attention, Praxis, Visuospatial, Language, Construction, and Name Orientation. Test scores range from 100 (normal) to 0 (severely impaired).
- ** CIBIC-plus (the Clinician's Interview-Based Impression of Change plus caregiver input): a validated clinical instrument used to measure change in global function through an interview with patients and their caregivers. Patients are evaluated by an assessor who is independent from the attending physician on a 7-point scale (very much improved, much improved, minimally improved, no change, minimally worse, much worse and very much worse) in four major categories: General, Mental/Cognitive State, Behavior, and Activities of Daily Living.
- *** MMSE (Mini-Mental State Examination): A method for assessing cognitive function. Comprised of the categories orientation, memorization, attention, calculation, recent and distant memory, comprehension, reading and writing, as well as design. Test scores range from 30 (normal) to 0 (severely impaired).

¹ Jia J, Wei C, Jia L, et al. Efficacy and safety of donepezil in Chinese patients with severe Alzheimer's disease: A randomized controlled trial. *J. Alzheimers Dis* 2017; 56: 1495-1504.