

**NEW DRUG APPLICATION FOR IN-HOUSE DEVELOPED
NEW ANTI-INSOMNIA DRUG DAYVIGO® ACCEPTED IN HONG KONG**
FIRST NEW DRUG APPLICATION FOR DAYVIGO IN ASIA OUTSIDE JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today that the new drug application for approval of its in-house-discovered and developed orexin receptor antagonist DAYVIGO® (generic name: lemborexant) for the treatment of adults with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance, has been accepted by the Hong Kong Department of Health. This application is the first application for DAYVIGO in Asia outside of Japan. Eisai plans to continue further applications for approval in respective Asian countries.

DAYVIGO is a dual orexin receptor antagonist that inhibits orexin neurotransmission regulating sleep-wake rhythm by binding competitively to the two subtypes of orexin receptors (OX1R and OX2R). Blocking the binding of wake-promoting neuropeptides orexin to orexin receptors is thought to balance sleep-wake circuitry by suppressing excessive wake drive. DAYVIGO binds to orexin receptors OX1R and OX2R and acts as a competitive antagonist with stronger inhibition effect on OX2R, which suppresses both REM and non-REM sleep drive, such that DAYVIGO can be expected to provide faster sleep onset and better sleep maintenance to patients.

In June 2020, DAYVIGO was launched in the U.S. for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance; and in July 2020, DAYVIGO was launched in Japan for the treatment of insomnia.

Insomnia is characterized by difficulty falling asleep, staying asleep or both, despite an adequate opportunity to sleep, that can lead to daytime consequences, such as fatigue, difficulty concentrating and irritability.^{1,2} Insomnia is one of the most common sleep-wake disorders. Approximately 30% of adults worldwide have symptoms of insomnia.^{3,4} In Hong Kong, over 35% of adults are reported to have symptoms of insomnia.⁵ In particular, older adults tend to have a higher prevalence rate with many experiencing insomnia symptoms for months to years. As a result, insomnia causes various social losses, such as long absences and reduced productivity. It can increase the risk of falling in older adults.⁶

Eisai will continue its efforts to deliver DAYVIGO as a new treatment option to insomnia patients in Asia, contributing to restoration of daytime function and recovery for patients with insomnia by delivering an active daytime life through fast sleep onset and good quality sleep.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. About DAYVIGO (Lemborexant)

DAYVIGO is Eisai's in-house discovered and developed small molecule that binds to orexin receptors, OX1R and OX2R, and acts as a competitive antagonist (IC₅₀ values of 6.1 nM and 2.6 nM, respectively). The mechanism of action of lemborexant in the treatment of insomnia is presumed to be through antagonism of orexin receptors. The orexin neuropeptide signaling system plays a role in wakefulness. DAYVIGO binds to orexin receptors OX1R and OX2R and acts as a competitive antagonist with stronger inhibition effect on OX2R, which suppresses both REM and non-REM sleep drive, such that DAYVIGO can be expected to provide faster sleep onset and better sleep maintenance to patients (K_i values: OX1R 8.1 nM, OX2R 0.48 nM).

In June 2020, DAYVIGO was launched in the U.S. for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance; and in July 2020, DAYVIGO was launched in Japan for the treatment of insomnia. In addition, Eisai has submitted new drug applications seeking approval of DAYVIGO in Canada and Australia.

Based on clinical study results, the effects of lemborexant are suggested not only for primary insomnia, but also for insomnia associated with other diseases, such as depression (SUNRISE 2).

In addition to the indication of insomnia, a Phase II clinical study of lemborexant in patients with Irregular Sleep Wake Rhythm Disorder (ISWRD) associated with mild-to-moderate Alzheimer's dementia is underway.

2. About Sleep-Wake Disorders and Insomnia

Sleep-wake disorders consist of disease categories such as insomnia, ISWRD, hypersomnia and breathing-related sleep disorders. Among the sleep-wake disorders, insomnia is the most common with persistent insomnia symptoms experienced by approximately 30 percent of the adult population worldwide.^{3,4} Insomnia disorder is characterized by difficulty falling asleep, staying asleep or both, despite an adequate opportunity to sleep. It can lead to daytime consequences, such as fatigue, difficulty concentrating and irritability.^{1,2}

Good quality sleep is essential for good health, including brain health.⁷ Studies suggest an optimal sleep duration between seven and eight hours.⁸ Poor sleep is associated with a wide range of health consequences, including an increased risk of hypertension, accidental injury, diabetes, obesity, depression, heart attack, stroke, dementia and adverse effects on mood and behavior.^{1,8}

Women are 1.4 times more likely than men to suffer from insomnia.⁹ Older adults also have higher prevalence of insomnia as aging is often accompanied by changes in sleep patterns, including disrupted sleep, frequent waking, and early waking, that can lead to less sleep time.¹⁰

1. Ferrie JE, et al. Sleep epidemiology – a rapidly growing field. *Int J Epidemiol.* 2011;40(6):1431–1437.
2. Roth T. Insomnia: definition, prevalence, etiology and consequences. *J Clin Sleep Med.* 2007;3(5 Suppl):S7–S10.
3. Institute of Medicine. Sleep disorders and sleep deprivation: An unmet public health problem. Washington, DC: *National Academies Press.* 2006.
4. Ohayon MM, et al. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev.* 2002;6(2):97-111.
5. Wong, et. al. Prevalence of Insomnia among Chinese adults in Hong Kong: a population-based study. *J Sleep Res.* 2011; 20: 117-126
6. National Institute of Public Health. Sleep disorders practice guidelines - for the proper usage of sleeping medications and the withdrawal: insomnia medical manual aiming for breaking through (available in Japanese only)
7. Cappuccio FP, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep.* 2010;33(5):585-592.
8. Pase MP, Himali JJ, Grima NA, et al. Sleep architecture and the risk of incident dementia in the community. *Neurology.* 2017;89(12):1244-1250
9. Roth T, et al. Prevalence and perceived health associated with insomnia based on DSM-IV-TR; International Statistical Classification of Diseases and Related Health Problems, tenth revision; and Research Diagnostic Criteria/International Classification of Sleep Disorders, second edition criteria: results from the America Insomnia Survey. *Biol Psychiatry.* 2011;69:592– 600.
10. Crowley K. Sleep and sleep disorders in older adults. *Neuropsychol Rev.* 2011;21(1):41-53.