



NEWS RELEASE

## Merck Receives Approval for BELSOMRA® (suvorexant) C-IV Label Update to Include Findings from Study of Insomnia in Patients with Mild-to-Moderate Alzheimer's Disease

2/3/2020

KENILWORTH, N.J. -- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the company has received approval from the U.S. Food and Drug Administration (FDA) for an update to the prescribing information for BELSOMRA® (suvorexant) C-IV to include findings on its use for the treatment of insomnia in patients with mild-to-moderate Alzheimer's disease. BELSOMRA is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

"Alzheimer's disease is often accompanied by disruptions to an individual's sleep-wake patterns and overall difficulty sleeping," said Dr. W. Joseph Herring, associate vice president, Global Clinical Research, Neuroscience, Merck Research Laboratories. "We're pleased that the prescribing information for BELSOMRA now includes findings from Merck's first dedicated study of an insomnia medication in patients with mild-to-moderate Alzheimer's disease."

This update includes findings of a randomized, double-blind, placebo-controlled, parallel-group, multi-site 4-week polysomnography trial of BELSOMRA in patients with mild-to-moderate Alzheimer's disease, which were recently published online in *Alzheimer's & Dementia: Journal of the Alzheimer's Association*. In this study, BELSOMRA exhibited a statistically significant improvement for both Total Sleep Time (TST) and Wake After Sleep Onset (WASO) measures, compared to those treated with placebo, as assessed objectively by polysomnography.

Adverse reactions occurring  $\geq 2\%$  and greater than placebo were somnolence (4% compared to 1% for placebo), dry

mouth (2% compared to 1% for placebo), and falls (2% compared to 0% for placebo). Results were originally presented at the 2019 American Academy of Neurology Annual Meeting.

## About the Study

The Phase 3 randomized, double-blind, placebo-controlled, parallel-group, multi-site 4-week trial of BELSOMRA was conducted in patients with mild-to-moderate Alzheimer's disease (n=285) for the treatment of insomnia. Male and female subjects aged 50-90 years (inclusive) were treated with BELSOMRA (n=142) or placebo (n=143). Patients treated with BELSOMRA received 10 mg for approximately 14 days, of whom 77% were increased to 20 mg for approximately 14 additional days.

## Insomnia and Alzheimer's Disease

Insomnia is a sleep disorder that can make it difficult to fall asleep and/or stay asleep, or it can cause people to wake up too early. Many factors contribute to insomnia, including evidence suggesting that wake-promoting signaling overrides sleep-promoting signaling in the brain. Insomnia is more common in people with Alzheimer's disease than in individuals who do not have Alzheimer's disease.

## About BELSOMRA (suvorexant)

BELSOMRA (suvorexant) is a first-in-class oral orexin receptor antagonist. Orexin is a neurotransmitter found in a specific part of the brain that can help keep a person awake. The mechanism by which BELSOMRA exerts its therapeutic effect is presumed to be through antagonism of orexin receptors.

## Indication for BELSOMRA (suvorexant)

BELSOMRA® (suvorexant) is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

## Selected Safety Information for BELSOMRA

BELSOMRA is contraindicated in patients with narcolepsy.

BELSOMRA contains suvorexant, a Schedule IV controlled substance.

BELSOMRA can impair daytime wakefulness. Central nervous system (CNS) depressant effects can last for up to several days after discontinuation.

BELSOMRA can impair driving skills and may increase the risk of falling asleep while driving. Caution patients taking BELSOMRA 20 mg against next-day driving and other activities requiring full mental alertness.

Coadministration with other CNS depressants increases the risk of CNS depression. Patients should be advised not to consume alcohol in combination with BELSOMRA due to additive effects. Dosage adjustments of BELSOMRA and of other concomitant CNS depressants may be necessary when administered together because of potentially additive effects. The use of BELSOMRA with other drugs to treat insomnia is not recommended.

The risk of next-day impairment, including impaired driving, is increased if BELSOMRA is taken with less than a full night of sleep remaining, if a higher than recommended dose is taken, if coadministered with other CNS depressants, or if coadministered with other drugs that increase blood levels of BELSOMRA. Patients should be cautioned against driving and other activities requiring complete mental alertness if taken in these circumstances.

In clinical studies, a dose-dependent increase in suicidal ideation was observed in patients taking BELSOMRA, as assessed by questionnaire. Immediately evaluate patients with suicidal ideation or any new onset behavioral changes. Suicidal tendencies may be present and intentional overdose is more common in this group of patients. Intentional overdose is more common in this group of patients; therefore, the lowest number of tablets that is feasible should be prescribed for the patient at any one time.

Complex sleep behaviors, including sleep-walking, sleep-driving, and engaging in other activities while not fully awake (eg, preparing and eating food, making phone calls, having sex), have been reported to occur with the use of hypnotics such as BELSOMRA. These events can occur in hypnotic-naïve as well as hypnotic-experienced persons. Patients usually do not remember these events. Complex sleep behaviors may occur following the first or any subsequent use of BELSOMRA, with or without the concomitant use of alcohol and other CNS depressants. Discontinue BELSOMRA immediately if a patient experiences a complex sleep behavior.

Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms can occur. The risk of cataplexy-like symptoms increases with the dose of BELSOMRA.

The effect of BELSOMRA on respiratory function should be considered.

Reevaluate patients for comorbid conditions if insomnia persists after 7 to 10 days of treatment.

BELSOMRA is not recommended for patients with severe hepatic impairment or those taking a strong CYP3A inhibitor.

In pivotal clinical studies, the most common adverse reaction (reported in 5% or more of patients treated with 15

mg or 20 mg of BELSOMRA and at least twice the placebo rate) was somnolence (BELSOMRA 7%, placebo 3%).

In the insomnia study in patients with mild to moderate Alzheimer's disease receiving BELSOMRA, the adverse reaction occurring  $\geq 2\%$  and greater than placebo were somnolence (4% compared to 1% placebo), dry mouth (2% compared to 1% placebo), and falls (2% compared to 0% placebo).

Because BELSOMRA can increase drowsiness, patients, particularly the elderly, are at a higher risk of falls.

The recommended dose of BELSOMRA is 5 mg in patients receiving moderate CYP3A inhibitors.

Digoxin levels should be monitored, as slight increases were seen with coadministration of BELSOMRA.

## About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

## Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health

care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2018 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

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Please see Prescribing Information for BELSOMRA (suvorexant) at [https://www.merck.com/product/usa/pi\\_circulars/b/belsomra/belsomra\\_pi.pdf](https://www.merck.com/product/usa/pi_circulars/b/belsomra/belsomra_pi.pdf) and Patient Information/Medication Guide for BELSOMRA (suvorexant) at [https://www.merck.com/product/usa/pi\\_circulars/b/belsomra/belsomra\\_mg.pdf](https://www.merck.com/product/usa/pi_circulars/b/belsomra/belsomra_mg.pdf)

Contact:

Media:

Pam Eisele

[\(267\) 305-3558](tel:(267)305-3558)

Sienna Choi

[\(908\) 873-4311](tel:(908)873-4311)

Investors:

Peter Dannenbaum

[\(908\) 740-1037](tel:(908)740-1037)

Michael DeCarbo

[\(908\) 740-1807](tel:(908)740-1807)