Media Release
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Health Canada approves QUVIVIQ (daridorexant) for the management of adult patients with insomnia

- QUVIVIQ is indicated for the management of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.
- Idorsia Canada – led by General Manager Ron Morcos – aims to make QUVIVIQ available in Canada by the end of the year.

Allschwil, Switzerland – May 3, 2023
Idorsia Ltd (SIX: IDIA) today announced that Health Canada has granted marketing authorization for QUVIVIQ™ (daridorexant) for the management of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance, on April 28, 2023.[1] Insomnia is one of the most prevalent sleep disorders in Canada, affecting over 2.2 million working age Canadians with an estimated annual GDP lost in Canada due to reduced productivity associated with chronic insomnia of USD 19.6 billion[15], and impacting both physical and mental health.[2,3]

QUVIVIQ is a dual orexin receptor antagonist (DORA) acting on both orexin 1 and orexin 2 receptors equipotently. Rather than inducing sleep through broad inhibition of brain activity (sedation), QUVIVIQ blocks only the activation of orexin receptors which promote wakefulness.[1] Consequently, for patients with insomnia, QUVIVIQ decreases the over-active wake drive, allowing sleep to occur, without altering the proportion of sleep stages.[1]

The recommended dose of QUVIVIQ is one tablet of 50 mg once per night, taken orally in the evening within 30 minutes before going to bed, with at least 7 hours remaining prior to planned awakening.[1] Some patients may be treated with 25 mg once per night.[1]

Jean-Paul Clozel, MD and Chief Executive Officer, commented:
"I'm very pleased with the positive decision from Health Canada, particularly seeing the recommended dose of 50 mg, which we know works best. It is estimated that 8.8% of adults in Canada suffer from chronic insomnia, which we know takes its toll on their physical and mental health. Sleep is one of the key pillars of health, so for these patients, regular, nightly use of QUVIVIQ can have a big impact on both their night's sleep and their daily life. I am very proud of the entire Idorsia team for achieving another regulatory approval and I'm confident that Ron and his expert team in Canada will be successful in transforming the Canadian sleep market."

The decision by Health Canada is supported by robust Phase 3 results – published in The Lancet Neurology – which demonstrated that at the recommended dose, QUVIVIQ improved sleep onset, sleep maintenance and self-reported total sleep time in adults with insomnia disorder.[1] The effects of QUVIVIQ on sleep variables were observed early in treatment and were maintained over time.[1]

The most frequently reported adverse reaction during the double-blind treatment period in Phase 3 clinical trials with QUVIVIQ (reported in at least 2% of patients and with a ≥ 1% difference vs placebo) was headache.[1] The majority of adverse reactions were mild to moderate in intensity.[1] No evidence of a dose-relationship for the frequency or severity of adverse reactions was observed.[1] The adverse reaction profile in elderly patients was consistent with younger patients.[1] There was no indication of non-medicinal use, and no evidence of withdrawal symptoms upon drug discontinuation.[1] This

suggests that QUVIVIQ does not produce physical dependence.[1] No sign of rebound insomnia was observed upon treatment discontinuation.[1]

The marketing authorization was also supported by a long-term follow-up extension study, which together with the pivotal trials, provides clinical data for up to 12 months of cumulative treatment.[1]

For more information on the marketing authorization of QUVIVIQ in Canada and important safety information, please review the Product Monograph.

Notes to the editor

About insomnia disorder

Insomnia disorder is defined as difficulty initiating or maintaining sleep, causing clinically significant distress or impairment in important areas of daytime functioning.[3] This impact on sleep quantity or quality should be present for at least three nights per week, lasts for at least three months, and occurs despite an adequate opportunity to sleep.[3]

Insomnia is a condition of overactive wake signaling and studies have shown that areas of the brain associated with wakefulness remain more active during sleep in patients with insomnia.[8,9] Chronic insomnia is a common problem with an estimated prevalence in Canada of 8.8% of the adult population.[15]

Insomnia as a disorder is quite different from a brief period of poor sleep, and it can take its toll on both physical and mental health.[3,4] It is a persistent condition with a negative impact on daytime functioning.[3] Idorsia's research has shown that poor quality sleep can affect many aspects of daily life, including the ability to concentrate, mood, and energy levels.

The goal of treatments for insomnia is to improve sleep quality and quantity, as well as daytime functioning, while avoiding adverse events and next-morning residual effects. Current recommended treatment of insomnia includes sleep hygiene therapy, cognitive behavioral therapy, and pharmacotherapy.

About the orexin system

Wake and sleep signaling is regulated by intricate neural circuitry in the brain. One key component of this process is the orexin system, which helps promote wakefulness.[7,10] There are two forms of orexin neuropeptides – small protein-like molecules used by nerve cells (neurons) to communicate with each other in the brain – orexin A and orexin B.[6,7] Orexin promotes wakefulness through its receptors OX1R and OX2R.[6,7] Together, these neuropeptides and receptors make up the orexin system. The orexin system stimulates targeted neurons in the wake system – leading to the release of several chemicals (serotonin, histamine, acetylcholine, norepinephrine) – to promote wakefulness.[11] Under normal circumstances, orexin levels rise throughout the day as wakefulness is promoted and then fall at night.[12] Overactivity of the wake system is an important driver of insomnia.[5,10]

Idorsia's research team has been working on the science of orexin and orexin receptors since they were first described in 1998. The team's initial work led to the conclusion that antagonism of the orexin system was the key to preserving a natural sleep architecture for patients with insomnia. With this as the target, the team designed dual antagonists with the goal of rapid onset of effect and duration of action sufficient to cover the night but short enough to minimize any negative next-morning residual activity at optimally effective doses.

About daridorexant

Daridorexant is a dual orexin receptor antagonist, acting on both orexin 1 and orexin 2 receptors and equipotent on both.[1] The orexin neuropeptides (orexin A and orexin B) act on orexin receptors to promote wakefulness.[1] Daridorexant antagonizes the activation of orexin receptors by the orexin neuropeptides and consequently decreases the wake drive, allowing sleep to occur.[1] In patients with insomnia, daridorexant increases both non-REM and REM sleep without altering proportion of sleep stages, as assessed by polysomnography.[1]

Global regulatory status of QUVIVIQ

In January 2022, QUVIVIQ was approved by the US Food and Drug Administration (FDA) and subsequently made commercially available in May 2022. For more information about QUVIVIQ in the US, see the Full Prescribing Information. In April 2022, marketing authorization of QUVIVIQ was granted by the European Commission and subsequently by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain via the European Commission Decision Reliance Procedure. For more information about QUVIVIQ in the EU, see the Summary of Product Characteristics. Launch preparations are underway in the major European markets and QUVIVIQ was made available in both Italy and Germany in November 2022. Marketing authorization of QUVIVIQ was granted by Swissmedic in December 2022, the company aims to make QUVIVIQ available to patients in Switzerland in June 2023. For more information about QUVIVIQ in Switzerland, see the Patient Information and Information for Healthcare Professionals.

The daridorexant Phase 3 registration program[5]

The Phase 3 registration program comprised two three-month studies, together with a long-term double-blind extension study. The program enrolled a total of 1,854 patients with insomnia disorder. As insomnia often presents later in life, and older adults are more susceptible to experience fragmented sleep, early awakening and daytime sleepiness,[13] around 40% of the recruited population was at least 65 years of age.[16]

The placebo-controlled studies investigated the effects of three doses of daridorexant (10 mg, 25 mg, and 50 mg) on sleep and daytime functioning parameters, objectively in a sleep lab by polysomnography and subjectively with a daily patient diary at home.

More than 800 patients continued treatment in the 40-week extension study, which measured the effect of all three doses vs. placebo, generating data for long-term treatment of insomnia disorder.[17]

Phase 3 data has been reported in The Lancet Neurology: The pivotal studies demonstrated that daridorexant 50 mg significantly improved sleep onset, sleep maintenance and self-reported total sleep time at months one and three compared to placebo. The largest effect was observed with the highest dose (50 mg), followed by 25 mg, while the 10 mg dose did not have a significant effect. In all treatment groups the proportions of sleep stages were preserved, in contrast to findings reported with benzodiazepine receptor agonists.

The most frequently reported adverse reaction during the double-blind treatment period in Phase 3 clinical trials with daridorexant (reported in at least 2% of patients and with a ≥ 1% difference vs placebo) was headache. The majority of adverse reactions were mild to moderate in intensity.

References

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About Idorsia

Idorsia Ltd is reaching out for more – We have more ideas, we see more opportunities and we want to help more patients. In order to achieve this, we will develop Idorsia into a leading biopharmaceutical company, with a strong scientific core.

Headquartered near Basel, Switzerland – a European biotech-hub – Idorsia is specialized in the discovery, development and commercialization of small molecules to transform the horizon of therapeutic options. Idorsia has a 20-year heritage of drug discovery, a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, and commercial operations in Europe, Japan, and the US – the ideal constellation for bringing innovative medicines to patients.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 1,300 highly qualified specialists dedicated to realizing our ambitious targets.

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