Media Release
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Swissmedic approves QUVIVIQ (daridorexant) – a first-in-class treatment for chronic insomnia disorder to improve both nighttime symptoms and daytime functioning

- QUVIVIQ™ is indicated for the treatment of adult patients with insomnia characterized by symptoms present for at least three months and considerable impact on daytime functioning
- QUVIVIQ, Switzerland's first approved dual orexin receptor antagonist, offers a new targeted mechanism of action that decreases nighttime overactive wakefulness in insomnia
- Idorsia Switzerland – led by General Manager Alice Huisman – aims to make QUVIVIQ available to patients with chronic insomnia disorder in Switzerland around mid-2023

Allschwil, Switzerland – December 5, 2022
Idorsia Ltd (SIX: IDIA) today announced that Swissmedic has granted marketing authorization for QUVIVIQ™ (daridorexant) for the treatment of adult patients with insomnia characterized by symptoms present for at least three months and considerable impact on daytime functioning.[1] Chronic insomnia disorder is one of the most prevalent sleep disorders in Europe, affecting between 6%-12% of the adult population,[2] and impacting both physical and mental health.[3,4]

QUVIVIQ will be the first dual orexin receptor antagonist (DORA) available in Switzerland for the treatment of chronic insomnia disorder. Rather than inducing sleep through broad inhibition of brain activity (sedation), QUVIVIQ blocks the activation of orexin receptors[1] known for their key role in wakefulness. Consequently, QUVIVIQ decreases the 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.[1] In certain circumstances, such as patients with moderate hepatic impairment or who are taking moderate CYP3A4 inhibitors, the recommended dose is 25 mg once per night.[1]

Jean-Paul Clozel, MD and Chief Executive Officer, commented:
"I am very proud that a little more than five years after Idorsia's creation, we are so close to bringing our first product to patients in our home market. The discovery of daridorexant is the result of more than 20 years of research in our laboratories here in Allschwil. With QUVIVIQ, we are bringing the first and only approved dual orexin receptor antagonist to the Swiss market, offering patients with chronic insomnia disorder not only a better night sleep, both in terms of sleep onset and duration, but also an improvement in daytime functioning at the recommended dose. We have a great product paired with a great team in Switzerland, led by Alice, to get QUVIVIQ to patients as quickly as possible."

Alice Huisman, General Manager of Idorsia Switzerland and Austria, commented:
"The approval of QUVIVIQ by Swissmedic is great news for patients suffering from chronic insomnia disorder in Switzerland. The Idorsia Switzerland team, based at Idorsia's headquarters in Allschwil, is now preparing to make QUVIVIQ available to patients in Switzerland around mid-2023. I am confident that with QUVIVIQ we can revolutionize the way insomnia is treated in Switzerland."

The Swissmedic decision 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 chronic insomnia disorder.[5] The effects of QUVIVIQ on sleep variables were observed early in treatment and were maintained over time.[1] A major focus of the trials was to evaluate the impact of QUVIVIQ on daytime functioning in patients with insomnia disorder, as assessed by IDSIQ, a patient-reported outcomes instrument. The recommended dose of QUVIVIQ demonstrated statistically significant improvement from baseline compared to placebo in the daytime sleepiness domain of IDSIQ, which means patients reported feeling less mentally and physically tired, less sleepy and more energetic during the day, at months one and three.[1]

In clinical trials, the most frequently reported adverse reactions were headache and somnolence.[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] Somnolence was reported in 3% and 2% of patients treated with QUVIVIQ 25 mg and 50 mg, respectively, compared to 2% of subjects on placebo.[1] Furthermore, no rebound insomnia or withdrawal symptoms indicative of physical dependence upon treatment discontinuation were observed in clinical studies, nor was there an indication of any drug abuse potential.[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 Switzerland, please review the Patient Information and Information for Healthcare Professionals.

About QUVIVIQ (daridorexant) in insomnia disorder
Studies over the past decades have shown that hyperarousal processes in the brain play a key role in the pathology of insomnia.[6] Chronic insomnia disorder is the result of continued brain hyperarousal that requires sustained management with therapy suitable for daily use over months.[7] Orexin is a neuropeptide, a small protein-like molecule, produced by the brain that promotes wakefulness.[1,6] QUVIVIQ reduces nocturnal hyperarousal to improve sleep (onset and maintenance) without next-morning residual effects in insomnia patients, and thus improve daytime functioning.[5]

Regulatory status of daridorexant
In addition to this approval of QUVIVIQ (daridorexant) in Switzerland, QUVIVIQ was approved by the US Food and Drug Administration (FDA) in January 2022, and subsequently made commercially available in May 2022. For more information about QUVIVIQ in the US, see the Full Prescribing Information (PI and Medication Guide). 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. Daridorexant is currently under review with Health Canada.

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] It is a common problem with an estimated prevalence in Europe of 6-12% of the adult population.[2]

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.[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.[5] Current recommended treatment of insomnia includes sleep hygiene therapy, cognitive behavioral therapy, and pharmacotherapy.[6]

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.[5,7,10] 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.[7] Orexin promotes wakefulness through its receptors OX1R and OX2R.[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.[5,9]

The daridorexant Phase 3 registration program

The Phase 3 registration program comprised two three-month studies, together with a long-term double-blind extension study.[1] The program enrolled a total of 1,854 patients with insomnia disorder.[1] 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.[5]

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.[5] The impact of insomnia on patients' daytime functioning was measured daily using the sleepiness domain score from the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ©) – a patient-reported outcome (PRO) instrument developed and validated according to the FDA Guidance for Industry.[5]

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.[14]

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.[5] 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.[5] In all treatment groups the proportions of sleep stages were preserved, in contrast to findings reported with benzodiazepine receptor agonists.[5]

A major focus of the trials was to evaluate the impact of daridorexant on daytime functioning in patients with insomnia disorder, as assessed by the IDSIQ.[5] IDSIQ is a patient-reported outcomes instrument specifically developed and validated according to FDA guidelines, to measure daytime functioning in patients with insomnia.[15] The sleepiness domain score of the IDSIQ was evaluated as a key secondary endpoint in both pivotal studies and comparisons to placebo included type I error control for multiplicity.[5] Daridorexant 50 mg demonstrated highly statistically significant improvement in daytime sleepiness at month one and month three.[5] The sleepiness domain score was not significantly improved on 25 mg in either study at either timepoint.[5]

The overall incidence of adverse events was comparable between treatment groups.[1] The most frequently reported adverse reactions were headache and somnolence and, overall, 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]

Contraindications

- Hypersensitivity to daridorexant or any of the excipients
- Narcolepsy
- Concomitant use with strong CYP3A4 inhibitors

Warnings and precautions for use
Use with caution in elderly patients because of the general risk of falls. Efficacy and safety data in patients >75 are limited.

Patients should be advised not to consume alcohol during treatment.

Sleep paralysis and hypnagogic/hypnopompic hallucinations can occur. Symptoms similar to mild cataplexy have been reported with dual orexin receptor antagonists. Prescribers should explain this to patients and should consider discontinuing in case events occur.

Use with caution in patients exhibiting symptoms of depression.

Use with caution in patients with unstable psychiatric and neurological co-morbidities due to limited efficacy and safety data.

Daridorexant did not have significant respiratory effects in patients with mild or moderate OSA or moderate COPD. In the absence of data, use with caution in patients with severe OSA and severe COPD.

There was no evidence of abuse or withdrawal symptoms indicative of physical dependence upon treatment discontinuation in clinical studies with daridorexant in subjects with insomnia. Because individuals with a history of abuse or addiction to alcohol or other substances may be at increased risk for abuse of QUVIVIQ, these patients should be followed carefully.

Use is not recommended in patients with severe hepatic impairment.

Effects on availability to drive and use machines
Patients should be cautioned about engaging in potentially hazardous activities, driving, or operating heavy machinery unless they feel fully alert, especially in the first few days of treatment. In order to minimize this risk, a period of approximately 9 hours is recommended between taking QUVIVIQ and driving or using machines.

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 broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, state-of-the-art facilities, and a strong balance sheet – the ideal constellation to translate R&D efforts into business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 1,200 highly qualified specialists dedicated to realizing our ambitious targets.

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