International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	DARIDOREXANT IN THE TREATMENT OF INSOMNIA IN ELDERLY PATIENTS WITH COMORBIDITIES
DOI	https://doi.org/10.31435/ijitss.1(49).2026.4790
RECEIVED	08 December 2025
ACCEPTED	05 January 2026
PUBLISHED	14 January 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

DARIDOREXANT IN THE TREATMENT OF INSOMNIA IN ELDERLY PATIENTS WITH COMORBIDITIES

Zofia Hałabuda *(Corresponding Author, Email: zofia.halabuda@outlook.com)*
The Floriana Ceynowy Specialist Hospital in Wejherowo, Wejherowo, Poland
ORCID ID: 0009-0005-0976-5602

Kornelia Rynkiewicz
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-0686-3618

ABSTRACT

Introduction and objective: Insomnia is one of the most prevalent sleep disorders in the adult population, thereby new methods of pharmacological treatment ought to be analyzed. Current novelty in insomnia treatment is daridorexant, a representative of the dual orexin receptor antagonist (DORA). Given that, the orexin system becomes overactive with age, explaining sleep of lower quality and quantity observed in older population, it is worth analysing the effect of the dual receptor antagonist (DORA) on the insomnia issue in older adults, and whether it proposes a safer choice among the existing pharmacological possibilities.
Review methods: A comprehensive literature review was conducted, analyzing studies from the PubMed database of articles published between 2020 and 2025.
Brief description of the state of knowledge: Insomnia treatment is based on both non-pharmacological and pharmacological methods. While among non-pharmacological methods cognitive-behavioral therapy is the one recommended, the choice of proper pharmacotherapy can impose more difficulties. The most commonly used medications, nonbenzodiazepine sedative hypnotics, lead to serious adverse effects and impose a risk of dependency. Daridorexant, a medication of proven efficacy, may propose a safer alternative, and furthermore, a more effective one.
Summary: In this review, we decided to analyse the existing literature to present the current state of knowledge on the above-mentioned issue with a perspective of the future of this branch of medicine.

KEYWORDS

Daridorexant, Insomnia, Elderly, Comorbidities

CITATION

Zofia Hałabuda, Kornelia Rynkiewicz (2026) Daridorexant in the Treatment of Insomnia in Elderly Patients With Comorbidities. *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.4790

Introduction

Insomnia is nowadays considered as one of the “civilization diseases" (Wichniak et al., 2023), next to cardiovascular disease (Baglioni et al., 2011), type 2 diabetes, obesity, hypertension, stroke, COPD, and depression (Khalchitsky, 2021). Not only is insomnia a disease in itself, but it is also a cause of other somatic disorders, such as cardiovascular diseases (Sofi et al., 2014) or mental disorders such as depression (Baglioni et al., 2011). In the last decade, the prevalence of insomnia rose drastically. Recent research indicates that insomnia affects up to 16.2 % of the global population (Benjafield et al., 2025). The world’s older population continues to grow exponentially. At present, according to the United *Nations Departament of Economics on Social Affairs Population Division*, over 700 million people are 65 years old or older, and by 2050, the number will double. Taking that into consideration, it is crucial to focus research efforts on insomnia in this demographic and to develop age-appropriate interventions.

Although Cognitive-Behavioral Therapy for Insomnia (CBT-I) is the gold standard for all adults, the conduct of this treatment is often rejected by both patients and physicians. As a result, pharmacological treatment remains widely used (Table 1), with nonbenzodiazepine sedative hypnotics (zolpidem, zopiclone, eszopiclone, zaleplon) being the most commonly prescribed agents (León-Barriera et al., 2025; Wichniak et al., 2023). These nonbenzodiazepine sedative hypnotics can present adverse effects such as headaches, dizziness, morning sleepiness, and memory disorders (Wichniak et al., 2023). Furthermore, zolpidem was proven to be a risk factor for hip fracture and TBI, resulting in hospitalization (Tom et al., 2016). This encourages research for a safer and at the same time possibly more effective insomnia treatment, especially for patients over 65 years.

Table 1. Pharmacological treatment of insomnia based on *The European Insomnia Guideline 2023* (Riemann et al., 2023)

Group	Medications
Benzodiazepines	Diazepam, flunitrazepam, flurazepam, lormetazepam, nitrazepam, oxazepam, temazepam, triazolam
Benzodiazepine receptor agonists	Zaleplone, zolpidem, zopiclone, eszopiclone
Sedating antidepressants	Agomelatine, amitriptyline, doxepin, mianserin, mirtazapine, trazodone, trimipramine
Antipsychotics	Chlorprothixene, levomepromazine, melperone, olanzapine, pipamperone, prothipendyl, quetiapine
Antihistamines	Diphenhydramine, doxylamine, hydroxyzine, promethazine
Phytotherapeutics	Hops, kava-kava, melissa, passiflora, valerian, lavender
Melatonin receptor agonists	Fast-release melatonin, ramelteon, prolonged-release melatonin
Orexin receptor antagonist	Daridorexant

Methods

This narrative review was based on a non-systematic literature search of PubMed articles published between 2020 and 2025. The following keywords were used in the search for scientific papers: “daridorexant”, “insomnia”, “elderly patients”, “comorbidities”, “chronic pulmonary obstructive disease”. We included peer-reviewed clinical trials, meta-analyses, the latest guidelines, systematic reviews, regulatory agency reports, and statistics from international organizations, in both English and Polish. The selection process included the evaluation of titles, abstracts, and full texts for relevance and methodological quality. No formal inclusion or exclusion criteria were applied.

Epidemiology, Definition, Signs & Symptoms

Insomnia is the most common sleep disorder among adults aged 65 or older (Fietze et al., 2022). The prevalence of insomnia symptoms rises with age, affecting nearly 50% of this population. While intermittent symptoms affect approximately 50% of older adults, 12% to 20% of those over age 65 meet the formal diagnostic criteria of chronic insomnia disorder (CID) (Janto et al., 2018). However, when including broader subjective complaints, some studies suggest that it can be as high as 40 to 70% (Wichniak et al., 2023; Żełabowski et al., 2025). Females have a 1.4 times greater risk of experiencing insomnia compared to males, and this is also observed in later life (Żełabowski et al., 2025).

Insomnia disorder is characterized by subjective reports of difficulty initiating or maintaining sleep, early-morning awakenings, or non-restorative sleep despite adequate opportunity for rest (Cyrkler et al., 2025; León-Barriera et al., 2025; Rosenberg et al., 2021; Skalski, 2012). We can diagnose chronic insomnia disorder (CID) when sleep disturbances occur at least three times per week for a duration of 3 months or longer, and short-term if it persists for less than 3 months. What is crucial for a proper diagnosis is to determine whether the patient's significant areas of life, such as social interactions, work, school, or other critical functions, are impaired, or if these nighttime issues are leading to significant distress (Riemann et al., 2023; Rosenberg et al., 2021).

Common patient complaints include difficulty initiating and/or maintaining sleep, frequent or prolonged nighttime awakenings, and early-morning awakenings with an inability to resume sleep (Riemann et al., 2023; Rosenberg et al., 2021). In addition to nocturnal symptoms, daytime complaints include fatigue, malaise, daytime sleepiness, and irritability. Patients frequently report cognitive deficits, including impaired attention, concentration, and memory, as well as a tendency to errors or accidents in workplace or driving environments (Riemann et al., 2023; Skalski, 2012).

The presentation of insomnia in individuals aged 65 and older differs in terms of quality from that in younger populations. Common complaints among older adults include frequent nocturnal awakenings and difficulty maintaining sleep. In contrast, younger individuals are more likely to have trouble falling asleep (León-Barriera et al., 2025; Wichniak et al., 2023; Żełabowski et al., 2025). Aging is also associated with changes in circadian rhythms, leading older adults to feel sleepy earlier in the evening and wake up earlier in the morning (León-Barriera et al., 2025). Most age-related changes stabilize around age 60, while sleep efficiency continues to decline after age 90, which is linked to increased morbidity (León-Barriera et al., 2025).

Pathophysiology of insomnia and the orexin system

Current understanding of the origin of insomnia, or its pathophysiology, largely centers on hyperarousal, in which there's an imbalance or overactivity in the body's sleep-wake regulation. This condition is characterized by increased cognitive, somatic, and cortical activation. Unlike healthy individuals, patients with insomnia experience a failure of the wake-promoting system to deactivate at habitual bedtime (Karol Grabowski, 2011; Muehlan et al., 2023; Rosenberg et al., 2021).

The orexin system (Figure 1), also known as the hypocretin system, is recognized as a key central player in maintaining alertness and regulating wakefulness stability, and is highly implicated in the mechanism underlying chronic insomnia (Cyrkler et al., 2025; Muehlan et al., 2023; Rosenberg et al., 2021). The system uses two neuropeptides, orexin-A (OX-A) and orexin-B (OX-B), derived from a common precursor. These peptides bind to two G-protein-coupled receptors, Orexin Receptor type 1 (OX1R) and Orexin Receptor type 2 (OX2R). OX-A binds strongly to both, while OX-B primarily targets OX2R (Muehlan et al., 2023; Rosenberg et al., 2021; Sarathi Chakraborty et al., 2023).

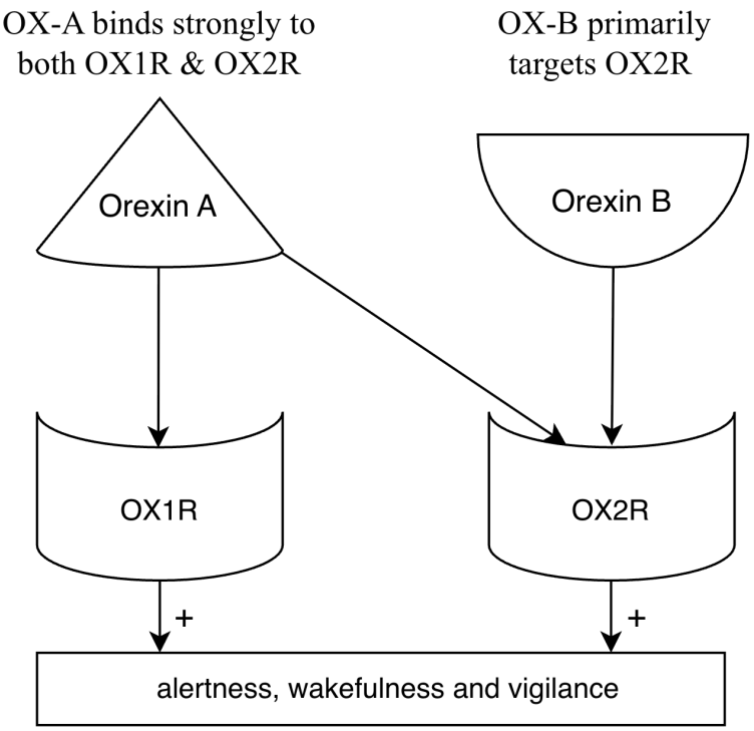

Fig. 1. *Schematic presentation of the orexin system; OX-A - orexin A, OX-B - orexin B, OX1R - Orexin Receptor type 1, OX2R - Orexin Receptor type 2*

Orexin peptides are exclusively produced by a small group of neurons in the hypothalamus. These neurons have extensive excitatory projections throughout the brain, targeting major wake-promoting regions. They integrate both external and internal information, such as light/dark cycles, emotional states, and energy balance, to appropriately adjust arousal levels (Muehlan et al., 2023). Orexin neurons are very active during wakefulness, decrease firing during calm waking, and become mostly silent during sleep. This cycle helps to stabilize wakefulness by allowing the body to cope with growing sleep pressure that accumulates during prolonged wakefulness (Muehlan et al., 2023).

The core mechanism of insomnia is proposed to be a disruption of the natural "flip-flop switch" between wake and sleep states, driven by inappropriate orexin signaling. In individuals with insomnia, it is hypothesized that inappropriately high orexin levels contribute to the hyperarousal state by continuing to stimulate wake-promoting systems and inhibiting sleep-active centers (Muehlan et al., 2023). Aging is associated with increased activity in the orexin/hypocretin system, which may contribute to difficulties in sleep consolidation and the increased sleep fragmentation commonly observed in older adults (Fietze et al., 2022).

Since orexin promotes wakefulness, drugs that act as Dual Orexin Receptor Antagonists (DORAs), such as daridorexant, block orexin's binding to its receptors, thereby reducing excessive wake signaling (Boof et al., 2022; Muehlan et al., 2023; Rosenberg et al., 2021). This approach promotes sleep without inducing the widespread central nervous system inhibition associated with traditional GABA receptor agonists (Muehlan et al., 2023).

Dual orexin receptor antagonists (DORA)

Dual orexin receptor antagonists (DORA) is the most recent development in insomnia treatment. This class of medication reacts with the orexin receptors that most commonly are localized in the hypothalamic region (Vraka et al., 2023). Through activating corresponding receptors orexin A and B, they reduce the onset of REM sleep and suppress non-REM sleep (Fietze et al., 2022). DORA interacts with the previously mentioned orexin receptors, enabling orexin A and B activity, and promoting wakefulness and alertness through blockage of the wake promotion associated with the orexin signaling pathway (Beuckmann et al., 2017; Janto et al., 2018), and resulting in anti-insomnia properties, though preserving the normal sleep architecture (i.e., non-REM/total sleep and REM/total sleep ratios) (Clark et al., 2020; Snyder et al., 2016) The DORA's representatives that are currently in the spotlight are daridorexant, lemborexant, and suvorexant (Table 2). In a recent meta- analysis, all active treatments, considering

those medications outperformed placebo in terms of all efficacy outcomes (Kishi et al., 2025). All three of them are approved in the USA by the FDA (Food and Drug Administration). However, only daridorexant has been approved by the EMA (European Medicines Agency) in 2022 to be used in the European Union (*Quviviq | European Medicines Agency (EMA)*, 2022).

Table 2. Properties of Daridorexant, Lemborexant, Suvorexant

Properties of Daridorexant, Lemborexant, Suvorexant			
Name of the drug	**Daridorexant**	**Lemborexant**	**Suvorexant**
Trade Name	Quviviq	Dayvigo	Belsomra
Tmax	1-2 h	1-3 h	2 h
Half- life	8 h	17- 19 h	15 h
Approved doses	25 mg, 50 mg	5 mg, 10 mg	5 mg, 10 mg, 15 mg, 20mg
Adverse effects	Headache, somnolence/fatigue, dizziness, nausea	Somnolence, headache, nightmares, parasomnias	Somnolence, abnormal dreams, headache, potential narcolepsy-like symptoms
Date of FDA approval	2022	2019	2014
Date of EMA approval	2022	-	-

Daridorexant

Daridorexant – the only representative of DORA accepted both in the USA and in Europe, is a highly potent molecule, equally affecting both the OX1 and OX2 receptors (Treiber et al., 2017). Compared to lemborexant and suvorexant, it provides a more favorable pharmacokinetic profile, shorter time needed to achieve the maximum plasma concentration (Tmax 1-2h) that enables fast sleep onset and a short half-life of 8 hours, compared to other DORAs' half-life duration (Żełabowski et al., 2025), enabling sleep maintenance without next-morning sleepiness and no accumulation upon repeated nightly dosing (Treiber et al., 2017).

Daridorexant is extensively metabolized by CYP3A4. Considering that, according to a cross-sectional analysis of 34,232 participants (aged 65 years or more) in Europe and Israel, the overall prevalence of polypharmacy, defined as the simultaneous use of five or more medications, ranges to around 30 % (Pazan & Wehling, 2021), the issue of pharmacological interaction must be considered. For patients using strong CYP3A4 inhibitors, daridorexant is contraindicated, and in case of moderate inhibitors, dose adjustment is required (Muehlan et al., 2023; Sarathi Chakraborty et al., 2023; Żełabowski et al., 2025). Both CYP3A4 activators and inhibitors (Table 3) can affect its efficacy. CYP3A4 activators can cause faster daridorexant metabolism, which can weaken the effect of insomnia treatment. While, CYP3A4 inhibitors lengthen the drug metabolism, which can worsen adverse effects such as nasopharyngitis, headache, drug overdose, fatigue, dizziness, nausea, or somnolence (Sarathi Chakraborty et al., 2023).

Table 3. Most commonly used drugs that are cytochrome P450 3A (including 3A4) inhibitors and inducers (bold font indicates strong inhibitors/inducers)
(*Cytochrome P450 3A inhibitors and inducers - UpToDate*, b.d.)

Cytochrome P450 3A (including 3A4) inhibitors and inducers	
Inhibitors	**Inducers**
Amiodarone Ciprofloxacin **Clarithromycin** Diltiazem Erythromycin Fluconazole Grapefruit juice Verapamil **Itraconazole** **Ketoconazole** **Levoketoconazole** **Posaconazole** Voriconazole	Barbiturates (phenobarbital) Dexamethasone Apalutamide **Carbamazepine** Encorafenib Enzalutamide Fosphenytoin **Mitotane** **Phenytoin** **Rifampin (rifampicin)**

The predominantly used medications in insomnia treatment, benzodiazepines (BZDs) and non-BZDs ("Z-drugs"), are associated with a relevant menace of addiction. In contrast to that, daridorexant exhibits a comparatively low risk of dependency. In a human abuse potential study conducted in 63 recreational sedative drug users, the dosage of daridorexant of 50 mg (next to 25 mg, the only approved dosage in insomnia treatment) showed a significantly lower "drug liking" ratings than zolpidem (30mg) and Suvorexant (150mg). Solely, daridorexant dosage of 100 mg and 150 mg – a dose neither used nor recommended, showed similar "drug liking" ratings to zolpidem (30mg) and suvorexant (150mg) (Ufer et al., 2022).

Daridorexant for the elderly population

One in two adults confesses to symptoms that can be associated with insomnia (Wichniak et al., 2023). Treating elderly patients can be a challenge due to polypharmacology or comorbidities. More than 80% of older adults who have insomnia have at least one chronic medical condition, and for those with multiple underlying health issues, managing polypharmacy is crucial. The new class of drugs in insomnia treatment, the dual receptor antagonist (DORA), may be a valid alternative. Several studies have shown the efficacy of dual orexin antagonists on sleep endpoints such as WASO (wake after sleep onset), LPS (latency to persistent sleep), and TST (total sleep time) (Kishi et al., 2025; Williams & Rodriguez-Cué, 2023; Zammit et al., 2020).

Published in 2022, two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials showed daridorexant efficacy of 50 mg and 25 mg dosage when compared to 10 mg and placebo (Mignot et al., 2022). The aim of the study was to measure both objective endpoints, such as change in WASO and LPS measured by PSG, and two subjective endpoints, such as change in sTST -self-reported total sleep time and in self-reported daytime functioning, recorded respectively, in a sleep diary, and using the IDSIQ -Insomnia Daytime Symptoms and Impacts Questionnaire. A reduction in WASO and LPS, and an increase in sTST, were observed, with numerically greater effects with daridorexant 50 mg than 25 mg. Interestingly, the same year, a secondary analysis of this phase III study was published (Fietze et al., 2022) in order to analyse if there are any differences in the outcome when the age of participants is considered. They analyzed changes in the IDSIQ scoring, reports provided using a Visual Analog Scale (VAS) to assess depth, quality of sleep, ability to function, and daytime alertness, and an ISI score, when comparing younger and older adults.

In the group of elderly adults, depth and quality of sleep assessed by VAS were improved, and daridorexant outperformed placebo, both 25 and 50 mg dosages showed similar efficacy. When assessing daytime alertness and ability to function, 50 mg of daridorexant outperformed the dosage of 25 mg, whose effectiveness was comparable to placebo. In all categories of IDSIQ (total score, sleepiness domain score, mood domain score, and alert/ cognition domain score), the dosage of 50 mg showed relevant effectiveness, while the efficacy of 25 mg was similar to placebo. In comparison, in younger adults, the dosage of 25 mg of

daridorexant presented better results than placebo, when analyzing IDSIQ scoring and VAS scores, although the effectiveness was not as potent as the dosage of 50 mg.

That suggests that the dosage of daridorexant in elderly adults in order to achieve all of the benefits, including improvement in daytime functioning, must be the highest registered of 50 mg. Research suggests that this is due to overactivity of the orexin system that comes with age (Li et al., 2022). It also has not been linked to the increased risks of falls, cognitive impairment, or motor coordination issues that are commonly associated with benzodiazepines (Fietze et al., 2022; Kunz et al., 2022; Żełabowski et al., 2025).

However, in recent years, daridorexant has been a subject in numerous studies, and its efficacy in insomnia treatment has been proven, the use of it in patients with coexisting comorbidities is a field for further examination. An example of that are cardiovascular diseases. Considering that one in two adults suffers from cardiovascular disease, a lack of studies might be surprising. However, a double-blind, randomized, placebo-controlled study by Schilling et al. might present a clue. The researchers sought to examine the effect of daridorexant on QTc duration, based on ECGs from a Holter monitor. The 36 healthy patients received 50 or 200 mg of daridorexant, 400 mg of moxifloxacin (used as a positive control to detect a relevant QT prolongation), or a placebo. In both doses of daridorexant (50 mg or 200 mg), the mean values of delta QTcF ranged from 1.92 ms to 3.77 ms. Thus, no relevant correlation between the use of daridorexant and cardiac repolarization was shown.

In the case of other comorbidities, the existing research is much more promising. The usage of daridorexant in patients with pulmonary disease, such as OSA, has been studied. Additionally compelling research of daridorexant use in patients with Alzheimer's disease and substance use disorders has been published. However, the selected studies analyzed in this paper present certain limitations: potential conflicts of interest due to funding from pharmaceutical companies that employed many researchers, small participant sample sizes, and short duration of the study. Taking all of that into consideration, further research on this topic is required.

Obstructive sleep apnea

More than 80% of older adults who have insomnia have at least one chronic medical condition. Obstructive sleep apnea coexists with insomnia in approximately 30-35% of patients (Boof et al., 2022; Lettieri et al., 2025). Individuals who suffer from both insomnia and sleep apnea, referred to as COMISA, might face more significant daytime difficulties, a lower quality of life, and an increased likelihood of developing cardiovascular issues compared to those affected by just one of these conditions (Lettieri et al., 2025). It is unclear whether treatment for insomnia is safe and effective in patients with COMISA, as many sleep medications can impair nighttime respiration or exacerbate common symptoms of insomnia and OSA (e.g., daytime somnolence) (Lettieri et al., 2025).

In the assessment of daridorexant in participants with insomnia and untreated mild OSA, post hoc subgroup analysis showed that daridorexant 50 mg was well tolerated and improved sleep parameters in these patients. The efficacy of daridorexant in treating insomnia was assessed using nighttime endpoints, including WASO, LPS and TST. Use of the medication resulted in improvements in these areas. Additionally, the results for participants with mild obstructive sleep apnea (OSA) did not differ significantly from those observed in the overall study population (Lettieri et al., 2025). It is worth mentioning that in this clinical trial, patients aged> 65 years accounted for 56.6% of the study group; however, the overall sample was small, comprising only 30 participants. Moreover, participants were diagnosed with mild obstructive sleep apnea while participating in the study, and those with existing OBA were excluded.

In another clinical trial of 28 participants, daridorexant (50mg) in patients with mild-to-moderate OSA indicates no clinically meaningful effects on the Apnea-Hypopnea Index (AHI) or nocturnal oxygen saturation (SpO2) (Boof et al., 2022). While an increase in total respiratory events may be observed, this is primarily attributed to a prolongation of total sleep time (TST) rather than impaired ventilatory control. However, the mentioned study has some limitations, e.g., a small sample size and a relatively short treatment duration of 4-8 days. In addition, none of the participants had a diagnosis of insomnia, and their age is unknown, so the applicability to our study group is limited. Nevertheless, given that daridorexant did not worsen AHI or nocturnal oxygen saturation, this data support further investigation in this population.

Chronic Obstructive Pulmonary Disease (COPD)

Daridorexant is an important pharmacological option for the treatment of insomnia in elderly patients (aged ≥ 65 years) with Chronic Obstructive Pulmonary Disease (COPD), in which traditional hypnotics have significant respiratory safety concerns (Muehlan et al., 2023; Sarathi Chakraborty et al., 2023). Unlike benzodiazepines and Z-drugs, which can cause global central nervous system depression and potential respiratory impairment, daridorexant specifically targets the orexin system to reduce excessive wake signaling (Kunz et al., 2022; Rosenberg et al., 2021). Nighttime administration of the highest approved dose (50 mg) did not have a clinically meaningful effect on respiratory function, as evidenced by no significant change in the apnea-hypopnea index (AHI) or peripheral oxygen saturation (SpO2) (Muehlan et al., 2023; Sarathi Chakraborty et al., 2023). Moreover, no respiratory adverse events were reported when daridorexant was administered to this population (Muehlan et al., 2023).

Alzheimer's Disease (AD)

Interestingly, there is a linkage between sleep disruption and the progression of Alzheimer's Disease (AD). The glymphatic system is the brain's unique waste-removal network, which uses cerebrospinal fluid to excrete waste, and it's most effective during the NREM phase of sleep. During sleep, toxic metabolic waste, such as amyloid-beta and tau proteins, is cleared by the glymphatic system. DORAs may alleviate symptoms of Alzheimer's Disease by facilitating restorative sleep, thereby increasing glymphatic flux and decreasing protein aggregation (Ragsdale et al., 2025). Daridorexant has been successfully used to treat disturbances in elderly patients with AD, showing potential to reduce nocturnal delirium and agitation in comparison to traditional sedating agents (Ragsdale et al., 2025; Sarathi Chakraborty et al., 2023).

Substance use disorders

Insomnia is a significant predictor of relapse in patients with SUDs, yet traditional hypnotics are often contraindicated due to risk of misuse and cross-tolerance (Nicola et al., 2025). Research indicates that a three-month treatment with daridorexant (50mg) in outpatients with comorbid SUDs significantly improved sleep outcomes, enhanced quality of life, and was associated with a 65,8% abstinence rate and reduced cravings. Human abuse potential studies demonstrate that daridorexant has a lower "drug-liking" rating than zolpidem or suvorexant, supporting its use in this vulnerable population, especially older people addicted to benzodiazepines for hypnotic purposes.

Conclusions

As the elderly population grows, more targeted therapy aimed at them, must be developed. Daridorexant as a highly studied novelty may present an alternative to the existing pharmacological methods. Daridorexant efficacy has been proven, both in younger and older adults. In elderly patients with mentioned above comorbidities, dosage 50 mg of daridorexant was effective and safe, it neither exacerbated chronic illnesses nor imposed additional toxicity. Regardless, both the effectiveness of daridorexant in insomnia treatment with coexisting comorbidities and its safety in those circumstances warrant further exploration. Nevertheless, daridorexant, based on the current knowledge, can be considered as a viable alternative to the existing methods in insomnia treatment in the elderly population.

REFERENCES

1. Baglioni, C., Battagliese, G., Feige, B., Spiegelhalder, K., Nissen, C., Voderholzer, U., Lombardo, C., & Riemann, D. (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies. *Journal of Affective Disorders*, *135*(1–3), 10–19. https://doi.org/10.1016/j.jad.2011.01.011
2. Benjafield, A. V., Sert Kuniyoshi, F. H., Malhotra, A., Martin, J. L., Morin, C. M., Maurer, L. F., Cistulli, P. A., Pépin, J.-L., & Wickwire, E. M. (2025). Estimation of the global prevalence and burden of insomnia: A systematic literature review-based analysis. *Sleep Medicine Reviews*, *82*, 102121. https://doi.org/10.1016/j.smrv.2025.102121
3. Beuckmann, C. T., Suzuki, M., Ueno, T., Nagaoka, K., Arai, T., & Higashiyama, H. (2017). In Vitro and In Silico Characterization of Lemborexant (E2006), a Novel Dual Orexin Receptor Antagonist. *The Journal of Pharmacology and Experimental Therapeutics*, *362*(2), 287–295. https://doi.org/10.1124/jpet.117.241422
4. Boof, M.-L., Ufer, M., Fietze, I., Pépin, J., Guern, A., Lemoine, V., & Dingemanse, J. (2022). Assessment of the effect of the dual orexin receptor antagonist daridorexant on various indices of disease severity in patients with mild to moderate obstructive sleep apnea. *Sleep medicine*, *92*, 4–11.

5. Clark, J. W., Brian, M. L., Drummond, S. P. A., Hoyer, D., & Jacobson, L. H. (2020). Effects of orexin receptor antagonism on human sleep architecture: A systematic review. *Sleep Medicine Reviews*, *53*, 101332. https://doi.org/10.1016/j.smrv.2020.101332
6. Cyrkler, M., Drabik, A., Śledziewska, A. M., Sieradocha, K., Zagajewska, A., Słupik, D., Reda, A., Giba, A., Krygowska, A., & Wąsik, M. (2025). Daridorexant: A new horizon in the treatment of insomnia - characteristics, safety and use in geriatric therapy. *Archiv Euromedica*, *15*(3). https://doi.org/10.35630/2025/15/3.315
7. *Cytochrome P450 3A inhibitors and inducers—UpToDate*. (b.d.). Pobrano 31 grudnia 2025, z https://www.uptodate.com/contents/image?imageKey=CARD%2F76992
8. Fietze, I., Bassetti, C. L. A., Mayleben, D. W., Pain, S., Seboek Kinter, D., & McCall, W. V. (2022). Efficacy and Safety of Daridorexant in Older and Younger Adults with Insomnia Disorder: A Secondary Analysis of a Randomised Placebo-Controlled Trial. *Drugs & Aging*, *39*(10), 795–810. https://doi.org/10.1007/s40266-022-00977-4
9. Janto, K., Prichard, J. R., & Pusalavidyasagar, S. (2018). An Update on Dual Orexin Receptor Antagonists and Their Potential Role in Insomnia Therapeutics. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*, *14*(8), 1399–1408. https://doi.org/10.5664/jcsm.7282
10. Karol Grabowski. (2011). *Terapia poznawczo-behawioralna bezsenności*. Psychiatria.
11. Khalchitsky, S. (2021, grudnia 14). *DISEASES OF CIVILIZATION: HISTORY, ECOLOGY, GENETICS*. https://doi.org/10.34660/INF.2021.66.97.026
12. Kishi, T., Ikuta, T., Citrome, L., Sakuma, K., Hatano, M., Hamanaka, S., Nishii, Y., & Iwata, N. (2025). Comparative efficacy and safety of daridorexant, lemborexant, and suvorexant for insomnia: A systematic review and network meta-analysis. *Translational Psychiatry*, *15*. https://api.semanticscholar.org/CorpusId:279592745
13. Kunz, D., Dauvilliers, Y., Beneš, H., Garcia-Borreguero, D., Plazzi, G., Kinter, D. S., Coloma, P., Rausch, M., Sassi-Sayadi, M., & Thein, S. (2022). Long-Term Safety and Tolerability of Daridorexant in Patients with Insomnia Disorder. *CNS Drugs*, *37*, 93–106.
14. León-Barriera, R., Chaplin, M., Kaur, J., & Modesto-Lowe, V. (2025). Insomnia in older adults: A review of treatment options. *Cleveland Clinic Journal of Medicine*, *92*, 43–50.
15. Lettieri, C. J., Briasoulis, O., Léger, D., Luyet, P., Pépin, J., Quan, S. F., Raphelson, J., Saskin, P., & Malhotra, A. (2025). The Effects of Daridorexant on Patients With Comorbid Insomnia Disorder and Untreated Mild Obstructive Sleep Apnoea: A Post Hoc Subgroup Analysis of a Phase 3, Randomised Clinical Trial. *Journal of Sleep Research*, e70135. https://doi.org/10.1111/jsr.70135
16. Li, S.-B., Damonte, V. M., Chen, C., Wang, G. X., Kebschull, J. M., Yamaguchi, H., Bian, W.-J., Purmann, C., Pattni, R., Urban, A. E., Mourrain, P., Kauer, J. A., Scherrer, G., & de Lecea, L. (2022). Hyperexcitable arousal circuits drive sleep instability during aging. *Science*, *375*(6583), eabh3021. https://doi.org/10.1126/science.abh3021
17. Mignot, E., Mayleben, D., Fietze, I., Leger, D., Zammit, G., Bassetti, C. L. A., Pain, S., Kinter, D. S., & Roth, T. (2022). Safety and efficacy of daridorexant in patients with insomnia disorder: Results from two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials. *The Lancet Neurology*, *21*(2), 125–139. https://doi.org/10.1016/S1474-4422(21)00436-1
18. Morin, C. M., Jarrin, D. C., Ivers, H., Mérette, C., LeBlanc, M., & Savard, J. (2020). Incidence, Persistence, and Remission Rates of Insomnia Over 5 Years. *JAMA Network Open*, *3*(11), e2018782. https://doi.org/10.1001/jamanetworkopen.2020.18782
19. Muehlan, C., Roch, C., Vaillant, C., & Dingemanse, J. (2023). The orexin story and orexin receptor antagonists for the treatment of insomnia. *Journal of Sleep Research*, *32*. https://doi.org/10.1111/jsr.13902
20. Nicola, M. D., Pepe, M., Bonomo, L., Milintenda, M., Panaccione, I., Brugnoli, R., & Sani, G. (2025). A Preliminary Report on the Effects of Daridorexant in Patients with Comorbid Insomnia and Substance Use Disorders. *Pharmaceuticals*, *18*. https://api.semanticscholar.org/CorpusId:276858913
21. Pazan, F., & Wehling, M. (2021). Polypharmacy in older adults: A narrative review of definitions, epidemiology and consequences. *European Geriatric Medicine*, *12*(3), 443–452. https://doi.org/10.1007/s41999-021-00479-3
22. *Quviviq | European Medicines Agency (EMA)*. (2022, maja 3). https://www.ema.europa.eu/en/medicines/human/EPAR/quviviq
23. Riemann, D., Espie, C. A., Altena, E., Arnardottir, E. S., Baglioni, C., Bassetti, C. L. A., Bastien, C., Berzina, N., Bjorvatn, B., Dikeos, D., Dolenc Groselj, L., Ellis, J. G., Garcia-Borreguero, D., Geoffroy, P. A., Gjerstad, M., Gonçalves, M., Hertenstein, E., Hoedlmoser, K., Hion, T., … Spiegelhalder, K. (2023). The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023. *Journal of Sleep Research*, *32*(6), e14035. https://doi.org/10.1111/jsr.14035
24. Rosenberg, R., Citrome, L., & Drake, C. (2021). Advances in the Treatment of Chronic Insomnia: A Narrative Review of New Nonpharmacologic and Pharmacologic Therapies. *Neuropsychiatric Disease and Treatment*, *17*, 2549–2566.
25. Sarathi Chakraborty, D., Choudhury, S., & Lahiry, S. (2023). Daridorexant, a Recently Approved Dual Orexin Receptor Antagonists (DORA) in Treatment of Insomnia. *Sleep Science*, *16*(02), 256–264. https://doi.org/10.1055/s-0043-1770805

26. Skalski, M. (2012). The Diagnosis and Treatment of Insomnia. W S. Sahoo (Red.), *Can't Sleep? Issues of Being an Insomniac*. InTech. https://doi.org/10.5772/31056
27. Snyder, E., Ma, J., Svetnik, V., Connor, K. M., Lines, C., Michelson, D., & Herring, W. J. (2016). Effects of suvorexant on sleep architecture and power spectral profile in patients with insomnia: Analysis of pooled phase 3 data. *Sleep Medicine*, *19*, 93–100. https://doi.org/10.1016/j.sleep.2015.10.007
28. Sofi, F., Cesari, F., Casini, A., Macchi, C., Abbate, R., & Gensini, G. F. (2014). Insomnia and risk of cardiovascular disease: A meta-analysis. *European Journal of Preventive Cardiology*, *21*(1), 57–64. https://doi.org/10.1177/2047487312460020
29. Tom, S. E., Wickwire, E. M., Park, Y., & Albrecht, J. S. (2016). Nonbenzodiazepine Sedative Hypnotics and Risk of Fall-Related Injury. *Sleep*, *39*(5), 1009–1014. https://doi.org/10.5665/sleep.5742
30. Treiber, A., de Kanter, R., Roch, C., Gatfield, J., Boss, C., von Raumer, M., Schindelholz, B., Muehlan, C., van Gerven, J., & Jenck, F. (2017). The Use of Physiology-Based Pharmacokinetic and Pharmacodynamic Modeling in the Discovery of the Dual Orexin Receptor Antagonist ACT-541468. *The Journal of Pharmacology and Experimental Therapeutics*, *362*(3), 489–503. https://doi.org/10.1124/jpet.117.241596
31. Ufer, M., Kelsh, D., Schoedel, K. A., & Dingemanse, J. (2022). Abuse potential assessment of the new dual orexin receptor antagonist daridorexant in recreational sedative drug users as compared to suvorexant and zolpidem. *Sleep*, *45*(3), zsab224. https://doi.org/10.1093/sleep/zsab224
32. Vraka, K., Mytilinaios, D., Katsenos, A. P., Serbis, A., Baloyiannis, S., Bellos, S., Simos, Y. V., Tzavellas, N. P., Konitsiotis, S., Vezyraki, P., Peschos, D., & Tsamis, K. I. (2023). Cellular Localization of Orexin 1 Receptor in Human Hypothalamus and Morphological Analysis of Neurons Expressing the Receptor. *Biomolecules*, *13*(4), 592. https://doi.org/10.3390/biom13040592
33. Wichniak, A., Bieńkowski, P., Dąbrowski, R., Mastalerz-Migas, A., & Rymaszewska, J. (2023). Treatment of insomnia in older adults. Recommendations of the Polish Sleep Research Society, Polish Society of Family Medicine and the Polish Psychiatric Association. *Psychiatria Polska*, *57*(3), 495–516. https://doi.org/10.12740/PP/OnlineFirst/161597
34. Williams, S. G., & Rodriguez-Cué, D. (2023). Use of Daridorexant among Patients with Chronic Insomnia: A Retrospective Observational Analysis. *Journal of Clinical Medicine*, *12*(9), 3240. https://doi.org/10.3390/jcm12093240
35. Zammit, G., Dauvilliers, Y., Pain, S., Kinter, D. S., Mansour, Y., & Kunz, D. (2020). Daridorexant, a new dual orexin receptor antagonist, in elderly subjects with insomnia disorder. *Neurology*, *94*, e2222–e2232.
36. Żełabowski, K., Petrov, W., Wojtysiak, K., Ratka, Z., Biedka, K., Wesołowski, M., Fus, K., Ślebioda, D., Rusinek, M., Sterkowicz, M., Radzka, I., & Chłopaś-Konowałek, A. (2025). Targeting the Orexin System in the Pharmacological Management of Insomnia and Other Diseases: Suvorexant, Lemborexant, Daridorexant, and Novel Experimental Agents. *International Journal of Molecular Sciences*, *26*(17), 8700. https://doi.org/10.3390/ijms26178700