Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Seltorexant

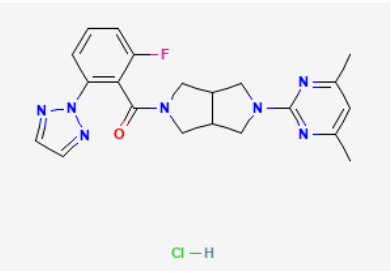
Evidence Summary

Seltorexant improves total sleep time, latency to persistent sleep, sleep efficiency, and wake after sleep onset. A phase 3 trial is ongoing in elderly people with depression and insomnia.

Neuroprotective Benefit: Early clinical evidence suggests that seltorexant treatment ameliorates depression, particularly in those who also suffer from severe insomnia. A phase 3 trial is testing seltorexant in elderly people with depression and insomnia.

Aging and related health concerns: . Seltorexant treatment appears to increase total sleep time, decrease latency to persistent sleep, improves sleep efficiency, and decrease wake after sleep onset.

Safety: In general, adverse event rates with seltorexant are numerically lower than with placebo or other sleep medications. Common adverse events with seltorexant include somnolence and headache.

Availability: not approved, in clinical trials	**Dose**: not established. The most common dose tested is 20 mg, nightly, orally.	**Chemical formula:** $C_{21}H_{23}ClFN_7O$ **MW**: 443.9  Source: PubChem
Half-life: 2-3 hours	**BBB**: penetrant	
Clinical trials: The largest clinical trial completed to date enrolled 364 participants with insomnia disorder.	**Observational studies**: N/A	

What is it?

Seltorexant is a selective antagonist of the human orexin-2 receptor under development as an adjunctive treatment for adults with major depressive disorder with insomnia symptoms.

Orexin is a wake-promoting neuropeptide produced in the hypothalamus. Orexin neurons originating in the lateral hypothalamic area and posterior hypothalamus regulate sleep and wakefulness by sending excitatory projections to monoaminergic and cholinergic nuclei in the brain stem and hypothalamic regions, including the locus coeruleus (containing noradrenaline), tuberomammilary nucleus (containing histamine), raphe nuclei (containing serotonin), and laterodorsal/pedunclopontine tegmental nuclei (containing acetylcholine)(reviewed in Sakurai 2007). The binding of orexin A and orexin B at orexin receptors OX1R and OX2R activates these neurons and promotes alertness (Mieda et al., 2013). These neurons remain dormant in sleep.

Several dual orexin receptor antagonists, such as daridorexant, suvorexant, and lemborexant, are already approved for the treatment of insomnia. Seltorexant is a selective orexin-2 receptor antagonist. Some studies suggest that selective blockade of orexin-2 receptors is sufficient to initiate and prolong sleep (Dugovic et al., 2014).

Neuroprotective Benefit: Early clinical evidence suggests that seltorexant treatment ameliorates depression, particularly in those who also suffer from severe insomnia. A phase 3 trial is testing seltorexant in elderly people with depression and insomnia.

Types of evidence:

- 2 systematic reviews or meta-analyses
- 4 randomized controlled clinical trials
- Numerous laboratory studies
- Numerous review articles

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

In a phase 2 randomized controlled crossover trial of 27 people with insomnia without psychiatric comorbidity, seltorexant treatment (40 mg, nightly) for 5 days slightly increased alertness (measured by the Bond and Lader Visual Analogue Scale) compared to placebo (De Boer et al., 2018). Speed of performance and attention were evaluated using the Cogstate detection and identification tasks and seltorexant treatment did not affect these endpoints on day 2 or day 6.

Human research to suggest benefits to patients with dementia:

No studies have tested the effects of seltorexant in people with dementia.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Having depression in midlife is a risk factor for dementia (Livingston et al., 2024). A major subgroup of people with major depressive disorder (~80%) exhibit hyperarousal, which contributes to difficulty falling and staying asleep (Xie et al., 2024).

In a systematic review of 5 randomized controlled trials testing orexin antagonists in a total of 498 participants with major depressive disorder, seltorexant (20 mg nightly dose, orally) significantly decreased depression scores when compared to placebo, including in people with inadequate responses to antidepressants (Meshkat et al., 2025). Because outcome measures differed across studies, a meta-analysis could not be performed. The authors noted that the results remained mixed with varying dosages yielding different outcomes, and future studies should explore the effects of orexin antagonists

on other clinical symptoms associated with depression, including cognitive impairment, fatigue, and anhedonia.

In a phase 2b double-blind randomized placebo-controlled dose-finding study in 283 patients with major depressive disorder who had inadequate responses to SSRIs/SNRIs, adjunctive treatment with seltorexant at the 20 mg daily dose for 6 weeks resulted in greater improvement in the primary endpoint of Montgomery-Åsberg Depression Rating Scale (MADRS) total score at week 3 (p=0.003) and 6 (p=0.083) compared to placebo; however, one-sided statistical tests were used with no control for multiplicity (Savitz et al., 2021). Improvement in MADRS total score was numerically less with the seltorexant 40 mg dose. The 10 mg seltorexant dose did not significantly affect MADRS total score compared to placebo at any timepoint. The improvement in MADRS score at week 6 for the 20 mg seltorexant dose was greater in patients with baseline Insomnia Severity Index (ISI) ≥ 15 compared to those with ISI < 15. At week 6, response rates (≥50% reduction from baseline in MADRS total score) for the seltorexant 10 mg, 20 mg, and 40 mg doses were 24.2%, 41.0%, and 38.5%, respectively, compared to 28.5% for the placebo group. Remission rates (based on MADRS total score at study endpoint) for the seltorexant 10 mg, 20 mg, and 40 mg doses were 15.2%, 29.5%, and 26.9%, respectively, compared to 19.0% for the placebo group. There was no apparent difference in improvement in anxiety symptoms based on the HAM-A total score change from baseline to week 6 between any seltorexant doses compared with placebo. The authors of this study speculated that the 20 mg daily dose may be the most effective dose for augmenting antidepressant effects of SSRI/SNRI treatments in major depressive disorder.

In a phase 1b double-blind randomized controlled trial of 128 people with major depressive disorder, seltorexant monotherapy (20 or 40 mg daily) for 5 weeks significantly improved depression symptoms, as measured by the Hamilton Rating Scale for Depression-17 item (HDRS17) (Mesens et al., 2025). The mean changes from baseline in the HDRS17 score at week 5 differed significantly across arms: -7.0 (5.04) for 20 mg seltorexant, -5.5 (4.34) for 40 mg seltorexant, and -4.4 (3.67) for placebo (p=0.0456), which was attributable to the difference between the 20 mg seltorexant and placebo arms (p=0.0049). Improvement in depression severity at week 5 for 20 mg seltorexant was numerically greater in patients with higher baseline insomnia severity (nominal p=0.0059). Efficacy (mean change in HDRS17) was numerically larger with the 20 mg dose compared to the 40 mg dose. In secondary analyses, the waking cortisol response was significantly decreased with 20 mg seltorexant (by -52.0 nmol/L) compared to placebo (+0.9 nmol/L), but not with 40 mg seltorexant (-15.6 nmol/L). Although total sleep increased more in the 40 mg seltorexant arm, this arm also showed reduced REM onset latency and increased stage N1 sleep, which were not observed with 20 mg seltorexant.

In a double-blind randomized controlled trial of 47 patients with major depressive disorder, seltorexant treatment (20 mg, nightly, orally) for 28 days resulted in a significant improvement of core depressive symptoms (measured by Hamilton Depression Rating 17-item) compared to placebo, though benefits were seen only in patients who received it as adjunctive therapy to a monoaminergic antidepressant drug and not in those who received seltorexant monotherapy (Recourt et al., 2019).

In a meta-analysis of treatments for depression and sleep disorders in the elderly population, all types of interventions (e.g., sertraline, fluoxetine, escitalopram, paroxetine, zolpidem, melatonin, seltorexant, etc.) were effective in decreasing Insomnia Severity Index and depression score, with sertraline having the highest probability of being the most effective intervention in decreasing the Insomnia Severity Index and Hamilton Depression Scale (Wang et al., 2025). Seltorexant (along with escitalopram and zuranolone) did not show material benefits in reducing the Insomnia Severity Index.

APOE4 interactions: Unknown

Aging and related health concerns: Seltorexant treatment appears to increase total sleep time, decrease latency to persistent sleep, improves sleep efficiency, and decrease wake after sleep onset.

Types of evidence:

- 2 meta-analyses
- 3 randomized controlled clinical trials
- Numerous laboratory studies

Insomnia: INCREASES TOTAL SLEEP, LATENCY TO SLEEP, SLEEP EFFICIENCY

In a double-blind randomized placebo-controlled trial of 364 patients with insomnia disorder, seltorexant treatment (10 or 20 mg, nightly, orally) for 14 days improved sleep initiation and maintenance (Mesens et al., 2025). Seltorexant treatment was compared with placebo as well as zolpidem (marketed as Ambien; 5 or 10 mg, nightly, orally). Seltorexant treatment significantly improved latency to persistent sleep (LPS) on night 1, with 36% and 49% greater improvements with the 10 mg and 20 mg doses, respectively, compared to placebo, and 29% greater improvement with the 20 mg dose compared to zolpidem. Seltorexant treatment also significantly improved night 1 wake after sleep onset over the first 6 hours (WASO-6). Improvements in LPS and WASO-6 were maintained on night 13

for seltorexant at 10 and 20 mg doses but diminished for zolpidem. On night 13, compared with zolpidem, seltorexant at 10 and 20 mg doses improved LPS by 30% and 28%, respectively, and seltorexant at the 20 mg dose improved WASO-6 by 31%. All 3 doses of seltorexant (5, 10, and 20 mg, nightly) significantly improved sleep efficiency (SE) and total sleep time (TST) during the first 6 hours, and wake during the total sleep period compared to placebo; these improvements were also maintained on night 13 in the seltorexant 10 mg and 20 mg dose groups. With regards to subjective measures, all 3 seltorexant doses showed improvements in subjective sleep diary assessments, including subjective sleep onset latency, subjective WASO, subjective refreshed feeling on waking, and subjective quality of sleep (5 mg and 10 mg only), compared with placebo. On day 14, compared with zolpidem, seltorexant at the 10 mg and 20 mg doses showed greater improvements in subjective sleep onset latency and subjective refreshed feeling on waking, while seltorexant, 5 mg and 10 mg, showed improvements in subjective quality of sleep. With regards to sleep architecture, seltorexant (at 10 and 20 mg doses) showed similar improvements in both REM and non-REM sleep, which were maintained over time.

In a phase 2b double-blind randomized placebo-controlled dose-finding study in 283 patients with major depressive disorder who had inadequate responses to SSRIs/SNRIs, seltorexant treatment (10, 20, or 40 mg daily dose) for 6 weeks significantly improved the Insomnia Severity Index for the 20 and 40 mg dose groups compared with placebo (Savitz et al., 2021). Improvement in sleep disturbance (as measured using the change in PROMIS-SD T-score from baseline) was greater for patients in the seltorexant 40 mg dose group compared to placebo at week 3 and 6; similar improvement was seen with the 20 mg dose group.

In a phase 1b double-blind randomized controlled trial of 128 people with major depressive disorder, seltorexant monotherapy (20 or 40 mg daily) for 5 weeks significantly improved polysomnographic parameters, including LPS, WASO, TST, and SE at week 3/4 compared to placebo (Mesens et al., 2025). For both seltorexant doses, the reductions in LPS and the increases in TST and SE showed effect sizes over 0.5. For TST, LPS, WASO, and SE, the mean changes from baseline and mean changes versus placebo were numerically larger with 40 mg seltorexant than with 20 mg seltorexant. Patients treated with 40 mg seltorexant spent significantly more time in stage N1 sleep post-treatment, suggesting increased time spent in light sleep stage. Also, the time from sleep onset to REM onset (REM latency) decreased significantly in the 40 mg seltorexant group but did not change significantly in the 20 mg seltorexant or placebo groups.

In a phase 2 randomized controlled crossover trial of 27 people with insomnia without psychiatric comorbidity, seltorexant treatment (40 mg, nightly) for 5 days significantly improved sleep efficiency

compared to placebo on day 1/2 and day 5/6 (p<0.001)(De Boer et al., 2018). Seltorexant treatment resulted in longer total sleep time (p<0.0001), shorter latency to persistent sleep (p<0.001), and wake after sleep onset (p=0.0212). Mean total sleep time with seltorexant versus placebo were 427 min and 400 min, respectively, on day 1/2, and 410 min and 371 min, respectively, on day 5/6. Mean latency to sleep were 27.6 min for placebo and 11.2 min for seltorexant on day 1/2 and 33.8 min for placebo and 10.6 min for seltorexant for day 5/6. The mean wake after sleep onset was 43.3 min for placebo and 31.2 min for seltorexant on day 1/2 and 54.7 min for placebo and 43.7 min for seltorexant on day 5/6. A significant and persistent reduction in the time to REM onset and increase in the total duration of REM sleep was detected for 40 mg seltorexant versus placebo (p = 0.0001 and p = 0.0004, respectively). Total duration of REM sleep was 86.4 min for placebo and 101.2 min for 40 mg seltorexant for day 1/2, and 83.6 min for placebo and 98.4 min for 40 mg seltorexant on day 5/6. The study authors speculated that the reduction in REM onset and the increase in total REM observed with 40 mg seltorexant are at least partly related to the reduction in latency to persistent sleep and the increase in total sleep time, reflecting correction of baseline abnormalities in these parameters. Time spent in deep sleep (Stage N3) were comparable between seltorexant and placebo (86.6 min vs. 88.5 min, respectively, on day 1/2 and 87.0 min vs. 85.8 min, respectively, on day 5/6).

In a double-blind randomized controlled crossover trial of 18 people with antidepressant-treated major depressive disorder patients with persistent insomnia, a single oral dose of seltorexant (10, 20, or 40 mg) significantly reduced the latency to persistent sleep, increased total sleep time, and improved sleep efficiency (Brooks et al., 2019). Mean latency to persistent sleep in the placebo group was 84.1 min and was reduced to 38.8, 13.4, and 24 min with seltorexant 10 mg, 20 mg, and 40 mg, respectively (p<0.001 for all). Mean total sleep time was 351.3 min after placebo, and was increased to 380.3, 397.8, and 400.5 min after treatment with 10 mg, 20 mg, and 40 mg seltorexant, respectively (p<0.05 for all). Wake time after sleep onset was not significantly affected by seltorexant treatment. Seltorexant also did not change overall sleep architecture (measured by a lack of effect on % time spent in REM, N2, and N3). There was also no significant effect of seltorexant treatment on the saliva concentrations of cortisol compared to placebo.

In a network meta-analysis of randomized controlled trials assessing the acute effects of various pharmacological interventions for insomnia disorder, benzodiazepines, doxylamine, eszopiclone, lemborexant, seltorexant, zolpidem, and zopiclone were more efficacious than placebo (de Crescenzo et al., 2022). For long-term effects of various pharmacological interventions for insomnia disorder, eszopiclone and lemborexant were more effective than placebo. Efficacy data on seltorexant, doxepin, and zaleplon were scarce at the time of analysis and did not allow firm conclusions.

Safety: In general, adverse event rates with seltorexant are numerically lower than with placebo or other sleep medications. Common adverse events with seltorexant include somnolence and headache.

Types of evidence:

- 3 meta-analyses
- 7 randomized controlled clinical trials

In a double-blind randomized placebo-controlled trial of 364 patients with insomnia disorder, seltorexant treatment (5, 10, or 20 mg, nightly, orally) for 14 days resulted in treatment-emergent adverse events that were lower in incidence (33.8%) compared to placebo (49.3%) and zolpidem (42.5%)(Mesens et al., 2025). Two participants experienced serious treatment-emergent adverse events during the double-blind phase: 1 patient in the seltorexant 20 mg dose group experienced cerebral hemorrhage and hematoma, leading to treatment discontinuation and 1 patient in the zolpidem group exhibited a cognitive disorder followed by seizure in the days following treatment discontinuation. Three participants in the seltorexant 5 mg dose group, and 1 in the seltorexant 20 mg dose group experienced asymptomatic electrocardiogram-related treatment-emergent adverse events leading to discontinuation. However, overall, there were no clinically significant changes in electrocardiogram parameters, including heart rate, PR interval, and QT interval. All study drug discontinuations were reported in older adult patients based on electrocardiogram monitoring performed onsite and none of these patients showed clinical symptoms.

The most common treatment-emergent adverse events in participants receiving seltorexant was headache (7.9%) versus 10.7% in the placebo group and 11.0% in the zolpidem group (Mesens et al., 2025). The incidence of somnolence was slightly higher in the combined seltorexant dose group (5/216 [2.3%]) compared to the placebo group (1/75 [1.3%]). A higher percentage of participants in the seltorexant 20 mg dose group (4/271 [5.6%]) and zolpidem (4/73 [5.5%]) group reported somnolence compared with the seltorexant at the 5 mg (1/72 [1.4%]) and 10 mg (0/73) doses. Most treatment-emergent adverse events were mild or moderate in severity.

With regards to treatment-emergent adverse events leading to discontinuation of study medication, incidences were comparable in the combined seltorexant (5/216 [2.3%]), placebo (2/75 [2.7%]), and zolpidem (2/73 [2.7%]) groups (Mesens et al., 2025). Three participants receiving 5 mg seltorexant experienced adverse events leading to discontinuation: atrial fibrillation in 2 participants and

electrocardiogram PR prolongation in 1 participant. Two participants in the 20 mg seltorexant group experienced adverse events leading to discontinuation: 1 participant had arrythmia and 1 had cerebral hemorrhage/hematoma. There were no cases of cataplexy or sleep paralysis. One fall was reported in the 20 mg seltorexant group.

With regards to safety across age groups, the incidence of treatment-emergent adverse events was higher in people aged 65 to 85 years old in all treatment groups compared to people aged 18 to 64 years old. For seltorexant (combined across doses), the incidence of treatment-emergent adverse events was 39.5% in 65-85 year-olds versus 30.7% in 18-64 year-olds (Mesens et al., 2025). However, in older participants, the treatment-emergent adverse events was lower for seltorexant (39.5%) compared to zolpidem (48.0%).

Seltorexant showed favorable tolerability relative to zolpidem, including lower incidences of disturbance in attention and somnolence (Mesens et al., 2025).

In a phase 2b double-blind randomized placebo-controlled dose-finding study in 283 patients with major depressive disorder who had inadequate responses to SSRIs/SNRIs, adjunctive treatment with seltorexant (10, 20, or 40 mg daily dose) for 6 weeks resulted in discontinuation rates (14%) that were similar to that of placebo (11%)(Savitz et al., 2021). The most common reason for discontinuation was withdrawal of consent (3.5%), followed by adverse events (2.8%), including insomnia (2.1%), sleep paralysis (1.4%), irritability (0.7%), nausea (0.7%), vomiting (0.7%), and increased liver enzymes (0.7%). Overall, 37.7% patients in seltorexant groups (33.3% with 10 mg dose, 41.0% with 20 mg dose: 36.5% with 40 mg dose) and 40.9% patients in the placebo group experienced at least 1 treatment emergent adverse event. The most common treatment emergent adverse events (occurring in ≥5% of patients in the seltorexant groups versus placebo) were headache (9 [6.2%] vs 9 [6.6%]), somnolence (9 [6.2%] vs 7 [5.1%]), and nausea (8 [5.5%] vs 4 [2.9%]). Somnolence-related adverse events were reported in 7 (5.1%) patients in the placebo group and 12 (8.2%) patients in seltorexant treatment arms, of whom 7 (11.5%) were patients from the seltorexant 20 mg dose arm. Treatment-emergent adverse events of special interest reported in seltorexant treatment groups versus placebo group were abnormal dreams (2.7% vs 0.7%), sleep paralysis (1.4% vs 0.7%), and nightmare (1.4% vs 0), but there was no clear evidence of a dose effect. No serious treatment emergent adverse events were reported in any of the seltorexant treatment groups. One patient in the placebo group reported a serious treatment emergent adverse event of polycythemia vera. There was no clinically relevant increase in suicidal ideation across treatment groups and there were no cases of suicidal behavior during the study.

In a phase 1b double-blind randomized controlled trial of 128 people with major depressive disorder, seltorexant monotherapy (20 or 40 mg daily) for 5 weeks resulted in treatment-emergent adverse event incidences (≥1) of 45.2% for 20 mg seltorexant, 61.0% for 40 mg seltorexant, and 47.7% for placebo (Mesens et al., 2025). The most common treatment-emergent adverse events were headache (7.1% [3/42] in the 20 mg seltorexant, 14.6% [6/41] in the 40 mg seltorexant, and 22.7% [10/44] in the placebo group) and nasopharyngitis (9.5% [4/42] in the 20 mg seltorexant, 12.2% [5/41] in the 40 mg seltorexant, and 6.8% [3/44] in the placebo group). Treatment-emergent adverse events leading to study discontinuation were reported in 2 (4.8%) patients in the 20 mg seltorexant group: 1 patient with elevated hepatic enzymes and 1 patient with elevated hepatic enzymes, blood creatinine, and rhabdomyolysis. No patient in the placebo or 40 mg seltorexant groups discontinued due to an adverse event. The most common adverse events of special interest during the treatment period were sleep paralysis (7.1% [3/42] with 20 mg seltorexant, 7.3% [3/41] with 40 mg seltorexant), abnormal dreams (4.8% [2/42] with 20 mg seltorexant, 9.8% [4/41] with 40 mg seltorexant, 4.5% [2/44] with placebo), and nightmare (9.8% [4/41] with 40 mg seltorexant). There were no significant changes across groups on vital signs, laboratory measures, or electrocardiogram parameters. No patient reported suicidal behavior during the study.

In a double-blind randomized controlled trial of 47 patients with major depressive disorder, seltorexant treatment (20 mg, nightly, orally) for 28 days was associated with mild, self-limiting adverse events (Recourt et al., 2019). Suicidal ideation scores either improved or were maintained to the end of the study. There were no serious adverse events with seltorexant treatment.

In a phase 2 randomized controlled crossover trial of 27 people with insomnia without psychiatric comorbidity, seltorexant treatment (40 mg, nightly) for 5 days led to 46.4% of subjects experiencing at least 1 treatment emergent adverse event (De Boer et al., 2018). There were no serious treatment emergent adverse events or adverse events that led to death or discontinuation of the study. There were no treatment emergent abnormalities in vital signs or laboratory values. The most common adverse events were headache and somnolence. Headache occurred with seltorexant in 14.8% (4/27) of participants compared with 10.7% (3/28) of participants under placebo. Somnolence was experienced by 11.1% (3/27) of subjects after seltorexant treatment and by 7.1% (2/28) of subjects after placebo. There was one incidence of sleep paralysis in the seltorexant treatment arm. A 54-year-old man received 40 mg seltorexant at night on day 1 and reported a feeling of sleep paralysis for 105 min. He felt exhausted the following day and had difficulty concentrating, but he continued to receive 40 mg seltorexant and the event did not occur again. This event was considered by the investigator to be moderate in intensity, non-serious, and very likely related to seltorexant.

In a double-blind randomized controlled crossover trial of 18 people with antidepressant-treated major depressive disorder patients with persistent insomnia, a single oral dose of seltorexant (10, 20, or 40 mg) did not result in any serious adverse events, but all subjects reported at least one treatment-emergent adverse event (Brooks et al., 2019). The most frequent occurring adverse events which were possibly related to study medication were headache (40%), dizziness (25%), and somnolence (25%) across all conditions. Somnolence appeared dose-dependent. Adverse events were mild and they all disappeared within a few hours to days. Next-day central nervous system effects (measured by VAS-BL, VAS sleepiness, body sway, and eye movement) were negligible and not significantly different from placebo in the morning after dosing.

In a double-blind randomized controlled multiple ascending dose study in 30 healthy people, daytime administration of seltorexant (5-60 mg, once daily, orally) for 10 days was well tolerated (van der Ark et al., 2018). One subject receiving 60 mg seltorexant had insomnia at night and somnolence on day 3 and day 4 and withdrew consent, so was discontinued from the study on day 5. There were no consistent dose-related changes from baseline in mean vital signs or mean electrocardiogram parameters (PR, QRS, QT, QTcB, and QTcF intervals). The mean half-life was 2-3 hours. At doses at or over 20 mg, seltorexant consistently induced somnolence on all study days, typically reported shortly after dose administration (within 1 hour). At 4 hours post-dose, dose levels over 5 mg were sedating, measured by the Addiction Research Center Inventory-49. There were no clinically relevant changes in other central measures and residual effects on attention and reaction time were minimal or absent.

In a network meta-analysis of randomized controlled trials assessing the side effects of various pharmacological interventions for insomnia disorder, seltorexant had fewer side effects than benzodiazepines, eszopiclone, zolpidem, and zopiclone (de Crescenzo et al., 2022).

Drug interactions: Drug interactions have not been well documented to date. Based on its mechanism of action, seltorexant likely will interact with other medications that are used to promote sleep, particularly other orexin receptor antagonists, but also other classes of sleep medications.

Sources and dosing:

Seltorexant is under development by Janssen Pharmaceutica as an adjunctive treatment for adults with major depressive disorder with insomnia symptoms. In a phase 2b double-blind randomized placebo-

controlled dose-finding study in 283 patients with major depressive disorder who had inadequate responses to SSRIs/SNRIs, adjunctive treatment with seltorexant at the 20 mg nightly dose for 6 weeks resulted in greater improvement in depression symptoms compared to placebo (Savitz et al., 2021). In a double-blind randomized placebo-controlled trial of 364 patients with insomnia disorder, seltorexant treatment at a 10 mg or 20 mg nightly dose improved sleep initiation and maintenance (Mesens et al., 2025).

Research underway:

A phase 3 trial is testing the adjunctive treatment of seltorexant in 752 adult and elderly people with major depressive disorder and insomnia symptoms (NCT06559306). Participants will be those who have had an inadequate response to current antidepressant therapy with SSRI or SNRI. This study is scheduled to be completed in November 2027.

Search terms:

Pubmed, Google: seltorexant, JNJ-42847922

Websites visited for seltorexant:

- Clinicaltrials.gov
- NIH RePORTER (0)
- DrugAge (0)
- Geroprotectors (0)
- Drugs.com (0)
- WebMD.com (0)
- PubChem
- DrugBank.ca
- Cafepharma
- Pharmapro.com (0)

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