

## Drug Review: Daridorexant

**Registrations:** It had been registered in the following countries United States of America (USA), United Kingdom (U.K.), Canada, and Saudi Arabia (SA).

**Trade name (USA.):\*\*** QUVIVIQ®

**Registration number (S.A.):\*\*** Not Available.

**Insurance Drug Formulary (S.A.):\*\*** Not covered (28.1.2023).

### General Information:

**Registered Company:** Idorsia Pharmaceuticals, Ltd.

**Regulatory Status:** R.X.

**Mechanism of Action:**

The treatment of insomnia is presumed to be through the antagonism of orexin receptors. In addition, the orexin neuropeptide signaling system plays a role in wakefulness.

Blocking the binding of wake-promoting neuropeptides orexin A and orexin B to receptors OX1R and OX2R is thought to suppress wake drive.

### Indication

Insomnia, Difficulties with sleep onset, and sleep maintenance.

**Approved (Labeled) indication:**

**Route of Administration:** Oral.

**Dosage Forms:** Oral *tablet*.

**Dosing/Administration:**

- Take only in the evening, 30 min before going to bed.
- Take only with at least 7 hr remaining prior to planned awakening.
- Time to sleep onset might be delayed if taken with or soon after a meal.

25 to 50 mg orally no more than once at night within 30 min of going to bed, within at least 7 hr remaining prior to awakening.

**Dose in Renal/Hepatic failure:**

- Renal impairment: No specific recommendations are available.
- Hepatic impairment (moderate, Child-Pugh score 7 to 9): 25 mg orally no more than once per night.

**Geriatric Dose:** No dosage adjustment is needed.

**Adjustment required in Specific population**

- Renal impairment: No specific recommendations are available.
- Hepatic impairment (mild): No specific recommendations are available.
- Hepatic impairment (moderate, Child-Pugh score 7 to 9): 25 mg orally no more than once per night.
- Hepatic impairment (severe, Child-Pugh score 10 or greater): Use not recommended.
- Geriatric (older than 65 years): No dosage adjustment is needed.
- Complex sleep behaviors: Discontinue use immediately if it occurs.
- Concomitant potent CYP3A4 inhibitors: Avoid the use.
- Concomitant moderate CYP3A4 inhibitors: 25 mg orally no more than once per night.

- Concomitant moderate or strong CYP3A4 inducers: Avoid the use.
- Concomitant use of other CNS depressants (e.g., benzodiazepine, opioid, tricyclic antidepressants, alcohol): Dosage adjustment to daridorexant or the CNS depressant may be needed.

**Indicated for pediatrics:**

Safety and effectiveness not established in pediatric patients.

**Pharmacokinetic:**

Absorption

- Bioavailability: 62%.
- Effects of food: Delayed Tmax by 1.3 hr and decreased Cmax by 16%; no effect on AUC.
- Tmax, oral: 1 to 2 hr.

Distribution

- Protein binding: 99.7%
- Vd: 31 L.

Metabolism

- Extensive, primarily via CYP3A4.
- Substrate of CYP3A4.

Excretion

- Fecal excretion: Approximately 57%, primarily as metabolites.
- Renal excretion: Approximately 28%, primarily as metabolites.

Elimination Half-Life: 8 hrs

**Safety:**

**Common Adverse Reactions (%):**

**Neurologic:** Headache (6% to 7%), Somnolence.

Severe/rare adverse Reactions (%):

**Neurologic:** Dizziness (2% to 3%), Hypnagogic hallucinations and hypnopompic (0.6%), Sleep paralysis (0.3% to 0.5%), Sleepwalking disorder.

**Psychiatric:** Complex mannerisms - behavior, Sleep, Depression.

**Drug Interactions**

There are 386 drugs known to interact: *amlodipine, gabapentin, and sertraline*.

**Contraindications/Precautions:** Narcolepsy.

**Monitoring Requirements:**

A) Therapeutic.

1) Physical Findings:

a) Decrease in the time to falling asleep and maintaining sleep indicates efficacy.

b) Reevaluate the patient for the presence of a primary psychiatric and medical illness if insomnia symptoms persist after 7 to 10 days of management.

B) Toxic.

1) Physical Findings:

Assess for worsening of depression, suicidality, or new or unusual changes in behavior.

**Sound-Alikes/ Look-Alikes:** Not available.

**High Alert:** Not available.

**Boxed warnings or alerts issue:** Not available.

**Toxicity if antidote required:** Not available.

**Storage if there is a specific condition**

Store at a controlled room temperature between 20 – 25°C excursions is permitted between 15 - 30°C.

**Patient counseling**

**How to Use This Medicine:**

1. Follow the doctor’s instruction.
2. Take this medicine in the evening within 30 min before bed.
3. This medicine works better without food or right after a meal.
4. This medicine is used for insomnia only.
5. Store the medicine at room temperature in a closed container, keeping it away from moisture, heat, and direct light.

**Drugs and Foods to Avoid:**

1. Some medicines, such as itraconazole or rifampin, can affect how daridorexant works.
2. Avoid alcohol drinking when using this medicine.

**Warnings While Using This Medicine:**

1. Pregnant or breastfeeding,
2. kidney disease, liver disease, breathing or lung problems (including COPD, sleep apnea), history of drug or alcohol addiction, daytime sleepiness, depression, mental health problems, or muscle weakness.

**This medicine might cause the following problems:**

- Unusual changes in mood or behavior.
- Sleep paralysis (while you are going to sleep or waking up).
- This medicine may cause drowsy or alertness the following day.

**Summary of Cost Analysis:**

|           | Drug classes  | Approval Indication                           | Dose  | Cost per unit (USD) | Cost (USD)        | Insurance drug formulary (SCHI) |
|-----------|---|---|-------|---------------------|-------------------|---------------------------------|
| Quviviq   | Miscellaneous anxiolytics, sedatives, and hypnotics | Insomnia                                      | 25 mg | \$17.16             | \$514.78          | Not Covered                     |
| Trazadone | Phenylpiperazine antidepressants                    | Depression Sedation Major Depressive Disorder | 50 mg | \$0.22 - \$0.23     | \$22.09 - \$22.76 | Not Covered                     |
| Zolpidem  | Miscellaneous anxiolytics, sedatives, and hypnotics | Insomnia                                      | 10 mg | \$22.72             | \$2,271.99        | Covered                         |

**REFERENCES**

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2. QUVIVIQ (Daridorexant) oral tablets. Idorsia Pharmaceuticals US Inc (per FDA). Radnor, PA; 2022.
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**Juman Alsaab**, Pharm D  
Ministry of Health, Riyadh, SAUDI ARABIA.

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