

## STEP THERAPY POLICY

- POLICY:** Sedative Hypnotics Step Therapy Policy
- Ambien® (zolpidem tablets – sanofi-aventis, generic)
  - Ambien CR® (zolpidem extended-release tablets – sanofi-aventis, generic)
  - Belsomra® (suvorexant tablets – Merck)
  - Dayvigo® (lemborexant tablets – Eisai)
  - Edluar® (zolpidem 5 and 10 mg sublingual tablets – Meda)
  - Lunesta® (eszopiclone tablets – Sepracor, generic)
  - Quviviq® (daridorexant tablets – Idorsia)
  - Rozerem® (ramelteon tablets – Takeda, generic)
  - Silenor® (doxepin 3 mg and 6 mg tablets – Currax, generic)
  - zaleplon capsules – generic only
  - zolpidem tartrate 7.5 mg capsules – Almatica, branded generic
  - zolpidem 1.75 and 3.5 mg sublingual tablets – generic only
  - Zolpimist® (zolpidem oral spray – Aytu BioScience) *[obsolete 05/31/2023]*

**REVIEW DATE:** 09/03/2025

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### OVERVIEW

The products included in this policy are indicated for the treatment of insomnia.

- Zolpidem immediate-release (IR), Edluar, Zolpimist, and zaleplon, non-benzodiazepine sedative hypnotics, are indicated for the **short-term treatment of insomnia**.<sup>1,3,5,6</sup>
- Eszopiclone, a non-benzodiazepine; Silenor, a tricyclic compound; and Rozerem, a melatonin receptor agonist, are also indicated for the treatment of **insomnia**, but their product labeling does not specifically limit their use to short-term.<sup>2,4,8,9</sup>
- Zaleplon and Rozerem are specifically indicated for the treatment of insomnia characterized by difficulty with sleep onset.<sup>3,8</sup>
- Zolpidem IR, zolpidem extended-release (ER), Silenor, and eszopiclone have also been shown to improve sleep maintenance or increase the duration of sleep.<sup>1,2,4,9</sup>
- Belsomra, Dayvigo, and Quviviq, orexin receptor antagonists, are indicated for the **treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance**.<sup>10-12</sup>
- Zolpidem sublingual tablets are indicated for use as needed for the treatment of insomnia when a **middle-of-the-night awakening is followed by difficulty returning to sleep**.<sup>7</sup> However, zolpidem sublingual tablets are not indicated for treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking.
- zolpidem 7.5 mg capsules are a branded product indicated for **short-term treatment of transient insomnia** in adults < 65 years of age.<sup>17</sup>

Eszopiclone, zaleplon, zolpidem, Edluar, Zolpimist, Belsomra, Dayvigo, and Quviviq are all schedule IV controlled substances.<sup>1-7,10-12,17</sup> Neither ramelteon nor doxepin are controlled substances.<sup>8,9</sup> Doxepin is also available generically as oral capsules (10, 25, 50, 75, 100, and 150 mg) and oral solution (10 mg/mL). These higher dose formulations are recommended for use in patients with depression and/or anxiety of varying etiologies.

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### **Use in the Elderly**

Although no specific adverse events (AEs) have been noted in elderly patients, changes in pharmacokinetics and/or use of high doses could put this population at increased risk of AEs. The general sensitivity of the elderly population to sedative hypnotics applies to all drugs with hypnotic effects.<sup>15,16</sup> However, because the potential for memory/cognitive/psychomotor impairment exists (primarily at peak concentrations) with certain non-benzodiazepine sedative hypnotics (the long-acting agents in particular), Rozerem's unique mechanism of action may be beneficial in older patients with or at risk for memory/cognitive/psychomotor impairment. Downward dosage adjustments of zolpidem IR, zolpidem ER, Edluar, zolpidem sublingual tablets, Zolpimist, zaleplon, Silenor, and eszopiclone are recommended when used in elderly or debilitated patients.<sup>1-7,9</sup> Zolpidem capsules are not indicated for use in geriatric patients.<sup>17</sup> The product labeling for Rozerem does not recommend a dosage adjustment in the elderly.<sup>8</sup> Belsomra, Dayvigo, and Quviviq have been studied in patients  $\geq 65$  years of age, and no clinically meaningful differences in safety or effectiveness were observed between these patients and younger patients at the recommended doses.<sup>10-12</sup> However, in addition to daytime somnolence, Belsomra and Dayvigo have the potential to cause sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms, which are not seen with the other agents.

### **GUIDELINES**

In 2017, an updated American Academy of Sleep Medicine (AASM) clinical guideline for the pharmacologic treatment of chronic insomnia in adults was published.<sup>13</sup> The guideline indicates that hypnotic medications, along with management of comorbidities and non-pharmacological interventions such as cognitive behavioral therapy for insomnia (CBT-I), are an important therapeutic option for chronic insomnia. The recommendations are intended as a guide for choosing a specific pharmacological agent (vs. no treatment) for treatment of chronic insomnia in adults, when such treatment is indicated. Each of the recommendations listed is weak, meaning it reflects a lower degree of certainty in the outcome and appropriateness of the patient-care strategy for all patients but should not be construed as an indication of ineffectiveness. The guideline suggests that clinicians can use Belsomra as a treatment for sleep maintenance insomnia; eszopiclone can be used as a treatment for sleep onset and sleep maintenance insomnia; zaleplon can be used as a treatment for sleep onset insomnia; zolpidem can be used as a treatment for sleep onset and sleep maintenance insomnia; triazolam can be used as a treatment for sleep onset insomnia; temazepam can be used as a treatment for sleep onset and sleep maintenance insomnia; Rozerem can be used as a treatment for sleep onset insomnia; and Silenor can be used as a treatment for sleep maintenance insomnia. The authors note that CBT-I is a standard of care for this condition; however, the AASM guideline does not address the relative benefits of CBT-I vs. pharmacotherapy.

In addition, several agents used for insomnia are on the 2023 Beers list of medications that are categorized as potentially inappropriate agents for elderly persons aged  $\geq 65$  years (e.g., amitriptyline, benzodiazepines, doxepin [ $> 6$  mg/day]); zolpidem, zaleplon, and eszopiclone should also be avoided.<sup>14</sup>

### **POLICY STATEMENT**

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

**Automation:** A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy. For Silenor and generic doxepin 3 mg and 6 mg tablets, a patient who is  $\geq 65$  years of age will not be targeted by this Step Therapy program.

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**Step 1:** generic eszopiclone tablets, generic ramelteon tablets, generic zaleplon capsules, generic zolpidem immediate-release tablets, generic zolpidem extended-release tablets, generic zolpidem sublingual tablets

**Step 2:** Ambien, Ambien CR, Belsomra, Dayvigo, Edluar, Intermezzo, Lunesta, Quviviq, Rozerem, Silenor, generic doxepin 3 mg and 6 mg tablets, Sonata, zolpidem 7.5 mg capsules, Zolpimist

## CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
2. If the patient has a documented history of substance use disorder, approve Silenor or generic doxepin 3 mg or 6 mg tablets.
3. If the patient is  $\geq 65$  years of age, approve Silenor or generic doxepin 3 mg or 6 mg tablets.
4. If the patient has difficulty swallowing or cannot swallow tablets/capsules, approve Edluar or Zolpimist.
5. No other exceptions are recommended.

## REFERENCES

1. Ambien® tablets [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; February 2022.
2. Ambien CR® tablets [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; February 2022.
3. Sonata® capsules [prescribing information]. New York, NY: Pfizer; August 2019.
4. Lunesta® tablets [prescribing information]. Marlborough, MA: Sunovion; August 2019.
5. Edluar® sublingual tablets [prescribing information]. Somerset, NJ: Meda; August 2019.
6. Zolpimist® oral spray [prescribing information]. Englewood, CO: Aytu BioScience; August 2019.
7. Intermezzo® sublingual tablets [prescribing information]. Stamford, CT: Purdue; August 2019.
8. Rozerem® tablets [prescribing information]. Lexington, MA: Takeda; November 2021.
9. Silenor® tablets for oral administration [prescribing information]. Morristown, NJ: Currax; December 2022.
10. Belsomra® tablets [prescribing information]. Whitehouse Station, NJ: Merck; February 2023.
11. Dayvigo® tablets [prescribing information]. Woodcliff Lake, NJ: Eisai; December 2023.
12. Quviviq™ tablets [prescribing information]. Radnor, PA: Idorsia; October 2023.
13. Sateia MJ, Buysse DJ, Krystal AD, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2017;13(2):307–349.
14. The American Geriatrics Society 2023 Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.
15. Drover DR. Comparative pharmacokinetics and pharmacodynamics of short-acting hypnotics. Zaleplon, zolpidem and zopiclone. *Clin Pharmacokinet.* 2004;43(4):227-238.
16. Patel D, Steinberg J, Patel P. Insomnia in the elderly: a review. *J Clin Sleep Med.* 2018;14(6):1017-1024.
17. Zolpidem tartrate capsules [prescribing information]. Morristown, NJ. Almatica Pharma. May 2023.

## History

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	<b>Zolpidem capsule:</b> Zolpidem capsule was added to the list of Step 2 medications.	08/30/2023
Annual Revision	No criteria changes.	09/04/2024
Annual Revision	No criteria changes.	09/03/2025