

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)
 - Intermezzo® (zolpidem 1.75 and 3.5 mg sublingual tablets –Purdue, generic)
 - Lunesta® (eszopiclone tablets – Sepracor, generic)
 - Quviviq™ (daridorexant tablets – Idorsia)
 - Rozerem® (ramelteon tablets – Takeda, generic)
 - Silenor® (doxepin 3 mg and 6 mg tablets – Currax, generic)
 - Sonata® (zaleplon capsules – King, generic)
 - Zolpimist® (zolpidem oral spray – Aytu BioScience)
 - Zolpidem Capsule (Almatica Pharma)

REVIEW DATE: 08/30/2023

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**.^{1,3,5,6}
- 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.^{2,4,8,9}
- Zaleplon and Rozerem are specifically indicated for the treatment of insomnia characterized by difficulty with sleep onset.^{3,8}
- Zolpidem IR, zolpidem extended-release (ER), Silenor, and eszopiclone have also been shown to improve sleep maintenance or increase the duration of sleep.^{1,2,4,9}
- Belsomra, Dayvigo, and Quviviq, orexin receptor antagonists, are indicated for the **treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance**.¹⁰⁻¹²
- 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**.⁷ 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 Capsules is a branded product indicated for short-term treatment of transient insomnia in adults < 65 years of age.¹⁷

Eszopiclone, zaleplon, zolpidem, Belsomra, Dayvigo, and Quviviq are schedule IV controlled substances.^{1-7,10-12,17} Neither Rozerem nor Silenor are controlled substances.^{8,9}

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.

Use in the Elderly

08/30/2023

© 2023. All Rights Reserved.

This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

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.^{15,16} 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.^{1-7,9} Zolpidem capsules are not indicated for use in geriatric patients.¹⁷ The product labeling for Rozerem does not recommend a dosage adjustment in the elderly.⁸ Belsomra, Dayvigo, and Quviviq have been studied in patients ≥ 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.¹⁰⁻¹² 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.¹³ 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 ≥ 65 years (e.g., amitriptyline, benzodiazepines, doxepin [> 6 mg/day]); zolpidem, zaleplon, and eszopiclone should also be avoided.¹⁴

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 ≥ 65 years of age will not be targeted by this Step Therapy program.

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 Capsule, Zolpimist

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
2. If the patient has a documented of substance use disorder, approve Silenor or generic doxepin 3 mg or 6 mg tablets.
3. If the patient is ≥ 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; October 2020.
10. Belsomra® tablets [prescribing information]. Whitehouse Station, NJ: Merck; March 2021.
11. Dayvigo® tablets [prescribing information]. Woodcliff Lake, NJ: Eisai; March 2022.
12. Quviviq™ tablets [prescribing information]. Radnor, PA: Idorsia; October 2022.
13. Sateia MJ, Buysse DJ, Krystral 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 hypnotosedatives. 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.