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

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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 7.5 mg capsules are a branded product indicated for **short-term treatment of transient insomnia** in adults < 65 years of age.[17]

Eszopiclone, zaleplon, zolpidem, Edluar, Zolpimist, Belsomra, Dayvigo, and Quviviq are all schedule IV controlled substances.[1-7,10-12,17] Neither ramelteon nor doxepin 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

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 $\geq$ 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.[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.

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

***Sedative Hypnotics Step Therapy Policy* product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.**

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 ≥ 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.

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 hypnosedatives. 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	**Zolpidem capsule:** 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