

➤ **Prime will review Prior Authorization requests**

**Prior Authorization Form:**

<https://www.bcbsks.com/CustomService/Forms/pdf/PriorAuth-6058KS-ST-IPPI.pdf>

**Link to Drug List (Formulary):**

<https://www.bcbsks.com/drugs/>

**FDA APPROVED INDICATIONS AND DOSAGE<sup>1-10</sup>**

Agent	Indication <sup>a</sup>	Dosing and Administration
<b>Ambien<sup>®</sup></b> (zolpidem) <sup>bc</sup>  tablets	Short-term treatment of insomnia characterized by difficulties with sleep initiation  Shown to decrease sleep latency for up to 35 days in controlled clinical studies. Clinical trials supporting efficacy were 4-5 weeks in duration with final formal assessments of sleep latency performed at the end of treatment	Maximum daily dose is 10 mg. Use the lowest effective dose. Recommended doses below: <b>Women:</b> 5 mg once daily immediately before bedtime. May increase to 10 mg if needed <sup>d</sup> <b>Men:</b> 5 mg provides sufficient efficacy for many men. May increase to 10 mg if needed <sup>d</sup> <b>Elderly, debilitated, or hepatically impaired patients:</b> 5 mg once daily
<b>Ambien CR<sup>®</sup></b> (zolpidem CR) <sup>bc</sup>  tablets	Treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance  Clinical trials performed in support of efficacy were up to 3 weeks & 24 wks in duration	Maximum daily dose is 12.5 mg. Use the lowest effective dose. Recommended doses below: <b>Women:</b> 6.25 mg once daily immediately before bedtime. May increase to 12.5 mg if needed <sup>d</sup> <b>Men:</b> 6.25 mg provides sufficient efficacy for many men. May increase to 12.5 mg if needed <sup>d</sup> <b>Elderly, debilitated, or hepatically impaired patients:</b> 6.25 mg once daily
<b>Belsomra<sup>®</sup></b> (suvorexant)  tablets	Treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance	Recommended dose is 10 mg, no more than once per night taken within 30 minutes of going to bed, with at least 7 hours remaining before the planned time of awakening. If the 10 mg dose is well tolerated but not effective, the dose can be increased, not to exceed 20 mg once daily

Agent	Indication <sup>a</sup>	Dosing and Administration
<b>Edluar®</b> (zolpidem) <sup>b</sup>  sublingual tablets	Short-term treatment of insomnia characterized by difficulties with sleep initiation  Clinical trials supporting efficacy were 4-5 weeks in duration with final formal assessments of sleep latency performed at the end of treatment	Maximum daily dose is 10 mg. Use the lowest effective dose. Recommended doses below: <b>Women:</b> 5 mg once daily immediately before bedtime. May increase to 10 mg if needed. <sup>d</sup> <b>Men:</b> 5 mg provides sufficient efficacy for many men. May increase to 10 mg if needed. <sup>d</sup> <b>Elderly, debilitated, or hepatically impaired patients:</b> 5 mg
<b>Intermezzo®</b> (zolpidem) <sup>bc</sup>  sublingual tablet	For use as needed for the treatment of insomnia when a middle of the night awakening is followed by difficulty returning to sleep  Clinical trials supporting efficacy was shown in two clinical trials: Sleep Laboratory Study (3-period crossover) and an Outpatient Study (double blind placebo controlled 4 weeks).	1.75mg for women and 3.5mg for men, taken only once per night as needed  Geriatric patients and patients with hepatic impairment: 1.75 mg once nightly
<b>Lunesta®</b> (eszopiclone) <sup>bc</sup>  tablet	Treatment of insomnia  Clinical trials performed in support of efficacy were up to 6 months in duration. Final formal assessments of sleep latency and maintenance were performed at 4 weeks in the 6-week study, at the end of both 2-week studies and at the end of the 6-month study.	1 mg, immediately before bedtime. May increase to maximum of 3 mg if needed  Geriatric or debilitated patients: Maximum 2 mg daily  Severe hepatic impairment or on CYP3A4 inhibitors: Maximum 2 mg daily
<b>Rozerem®</b> (ramelteon)  tablet	Treatment of insomnia characterized by difficulty with sleep onset  Clinical trials performed in support of efficacy were up to 6 months in duration. Final formal assessments of sleep latency were performed after 2 days of treatment during the crossover study, at 5 weeks in the 6-week studies, and at the end of the 6-month study.	8 mg taken within 30 minutes of going to bed  Total Rozerem dose should not exceed 8 mg per day
<b>Silenor®</b> (doxepin)  tablet	Treatment of insomnia characterized by difficulty with sleep maintenance  The clinical trials performed in support of efficacy were up to 3 months in duration.	6 mg once daily  Total daily dose should not exceed 6mg  Elderly: 3 mg once daily
<b>Sonata®</b> (zaleplon) <sup>bc</sup>  capsule	Short-term treatment of insomnia  Shown to decrease the time to sleep onset for up to 30 days in controlled clinical studies. Not shown to increase total sleep time or decrease the number of awakenings. Clinical trials performed in support of efficacy ranged from a single night to 5 weeks in duration. Final formal assessments of sleep latency were performed at the end of treatment.	10 mg once daily; 5 mg once daily may be sufficient for low weight individuals and elderly or debilitated patients; 20 mg may be considered for occasional patients not responding to lower doses Dosage should be individualized Maximum daily dose is 20 mg (10 mg in elderly)

Agent	Indication <sup>a</sup>	Dosing and Administration
<b>Zolpimist™</b> (zolpidem) <sup>b</sup>  oral spray	Short-term treatment of insomnia characterized by difficulties with sleep initiation  Shown to decrease sleep latency for up to 35 days in controlled clinical studies. Clinical trials performed in support of efficacy were 4-5 weeks in duration with final formal assessments of sleep latency performed at the end of treatment.	Maximum daily dose is 10 mg. Use the lowest effective dose. Recommended doses below: <b>Women:</b> 5 mg once daily immediately before bedtime. May increase to 10 mg if needed. <sup>d</sup> <b>Men:</b> 5 mg provides sufficient efficacy for many men. May increase to 10 mg if needed. <sup>d</sup> <b>Elderly, debilitated, or hepatically impaired patients:</b> 5 mg

a – Prescribing information for all products contains the following: Failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated.

b – Hypnotics classified as Schedule IV controlled substances

c – Generics available

d - Compared to lower doses, zolpidem 10 mg (immediate release) or 12.5 mg (extended release) is more likely to impair next-morning activities requiring alertness (e.g., driving).

## OBJECTIVE

The intent of the Insomnia Agents Step Therapy (ST) program is to encourage the use of cost-effective generic insomnia agents over the more expensive brand agents and to accommodate for use of brand nonbenzodiazepine hypnotics (Ambien, Ambien CR, Belsomra, Edluar, Intermezzo, Lunesta, Sonata, and Zolpimist), melatonin receptor agonist (Rozerem), and histamine H<sub>1</sub> receptor antagonist (Silenor) when generic agents cannot be used due to documented intolerance, FDA labeled contraindication, or hypersensitivity. All dosage forms of the brand agents listed will be included as targets in the step therapy program. If the patient cannot be treated with a controlled substance, Rozerem or Silenor may be approved for use. The program allows continuation of therapy when there is documentation that the patient is receiving the requested agent.

## TARGET AGENTS

- **Ambien®** (zolpidem)<sup>a</sup>
- **Ambien CR®** (zolpidem)<sup>a</sup>
- **Belsomra®** (suvorexant)
- **Edluar®** (zolpidem)
- **Intermezzo®** (zolpidem)<sup>a</sup>
- **Lunesta®** (eszopiclone)<sup>a</sup>
- **Rozerem®** (ramelteon)
- **Silenor®** (doxepin)
- **Sonata®** (zaleplon)<sup>a</sup>
- **Zolpimist™** (zolpidem)

a – generic available that is a prerequisite agent for step therapy program

## PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Brand Insomnia Agents** will be approved when ONE of the following is met:

1. The patient's medication history includes the use of a generic nonbenzodiazepine hypnotic agent in the past 90 days  
**OR**
2. There is documentation that the patient is currently being treated with the requested agent  
**OR**
3. The prescriber states the patient is currently being treated with the requested agent AND is at risk if therapy is changed  
**OR**
4. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the available generic nonbenzodiazepine hypnotic agents  
**OR**
5. The patient requires therapy with a non-controlled agent, Rozerem or Silenor

**Length of approval:** 12 months

## CLINICAL RATIONALE

Cognitive behavioral therapy (CBT) is the first line treatment for chronic insomnia.<sup>11-14</sup> This treatment comprises advice on sleep-wake behavior (sleep hygiene), stimulus control and sleep restriction, and relaxation and cognitive techniques. Efficacy of CBT has been shown to be equal to pharmacotherapy during acute treatment and more effective for long term treatment.<sup>11,13</sup> Evidence is insufficient to evaluate the balance of the benefits and harms of long-term use of pharmacologic treatments in adults with chronic insomnia disorder.<sup>12</sup>

For patients with sleep onset insomnia, a short-acting medication is a reasonable choice for an initial trial of pharmacologic therapy. This may improve the insomnia with less residual somnolence the following morning. Examples of short-acting medications (duration of effect  $\leq 8$  hours) include zaleplon, zolpidem, triazolam, lorazepam, and ramelteon. For patients with sleep maintenance insomnia, a longer-acting medication is preferable for an initial trial of pharmacologic therapy. Examples of longer-acting medications include zolpidem extended release, eszopiclone, temazepam, estazolam, low dose doxepin, and suvorexant. However, these medications may increase the risk for hangover sedation and patients must be warned about this possibility. For patients with awakening in the middle of the night, both zaleplon and a specific sublingual tablet form of zolpidem have been developed for use during the night, with the constraint that there will be at least four hours of time in bed remaining after administration.<sup>13</sup>

All insomnia drugs can impair activities requiring alertness (e.g., driving) the morning after use. Patients can experience impairment of mental alertness the morning after use, even if they feel fully awake. Women appear more susceptible to this risk due to slower elimination of zolpidem vs men.<sup>15</sup>

## Use in the Elderly

Zolpidem, zaleplon, and eszopiclone are all included in the list of Potentially Inappropriate Medications (for use in the elderly) in the Beers List published by the American Geriatrics Society.<sup>16</sup> Benzodiazepine-receptor agonists have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency department visits and hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration. Beers provides a strong recommendation that these drugs be avoided in the elderly.<sup>16</sup>

## REFERENCES

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15. FDA Drug Safety Communication: Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem (Ambien, Ambien CR, Edluar, and Zolpimist). January 10, 2013. Accessed January 17, 2013 at: <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM335007.pdf>.
16. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc* 2015: 1-20.

### Document History

Prime Standard Initial Review, BCBS KS 03/2014  
Administrative Action (addition of generic Lunesta as a prerequisite) 05/2014  
Administrative Action (addition of Belsomra as a target) 12/2014  
Annual Review, Prime Standard criteria maintained, approved by P&T UM Committee 04/2015  
Client Specific Annual Review, Prime Standard criteria maintained, approved by BCBS KS Review Committee 04/2015  
Administrative Action (note generic availability of Intermezzo) 03/2016  
Annual Review, Prime Standard criteria with changes, approved by P&T UM Committee 04/2016  
Client Specific Annual Review, Prime Standard criteria with changes, approved by BCBSKS Committee 04/2016  
Annual Review, Prime Standard criteria with changes, approved by P&T UM Committee 04/2017  
Client Specific Annual Review, Prime Standard criteria with changes, approved by BCBS KS 05/2017  
Annual Review, Prime Standard criteria with changes, approved by P&T UM Committee 03/2018  
Client Specific Annual Review, Prime Standard criteria with changes, approved by BCBS KS 04/2018

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