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Medication Policy Manual | **Policy No:** dru114

Topic: Lunesta®, eszopiclone | **Date of Origin:** January 10, 2005

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IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Eszopiclone (Lunesta®) is an orally administered hypnotic agent (sleep medicine) that is used for the treatment of insomnia. Eszopiclone is a controlled-substance.

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Policy/Criteria

I. Most contracts require prior authorization approval of eszopiclone prior to coverage of quantities greater than 14 tablets per month. Eszopiclone in quantities up to 14 tablets per month may be considered medically necessary in patients with insomnia and may be covered without prior authorization.

II. Eszopiclone in quantities between 15 to 34 tablets per month may be considered medically necessary in patients with primary insomnia when all criteria A through E below are met.

A. Difficulty initiating or maintaining sleep, or non-restorative sleep has occurred for at least one month.

AND

B. Specific measurable functional impairment due to insomnia is present.

AND

C. The sleep disturbance is not due to otherwise reversible conditions. Other reversible conditions may include, but are not limited to, another sleep disorder, mental disorder, or physiological effects of another substance.

AND

D. Non-pharmacologic therapies have been inadequate in improving functional impairments. Examples of non-pharmacologic therapies include, but are not limited to, stimulus control therapy, sleep restriction therapy, relaxation therapy, or cognitive therapy.

AND

E. Treatment with generic zolpidem and zaleplon has been inadequate or not tolerated.

III. Administration, Quantity Limitations and Authorization Period

A. Regence considers eszopiclone to be a self-administered medication.

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B. When prior authorization is approved, eszopiclone may be authorized in quantities up to 34 tablets per month. Doses exceeding 3 mg per day are considered not medically necessary.

C. Authorization shall be reviewed as follows to confirm that current medical necessity criteria are met and that there is clinical documentation of significantly improved functional impairment(s) due to treatment with eszopiclone.

1. **Initial Authorization -** Authorization shall be reviewed at 6 months

2. **Continued Authorization - C**ontinued authorization or re-authorization (after the initial 6 month period) shall be reviewed at least annually.

IV. Concomitant, alternating, or repeated sequential use of eszopiclone with either zolpidem (Ambien® Edluar™, ZolpiMist™), zolpidem (Ambien CR®), ramelteon (Rozerem®) or zaleplon (Sonata®) exceeding 14 tablets per month is considered duplication of therapy and not medically necessary.

V. Eszopiclone is considered investigational when used for all conditions other than those outlined in the policy criteria above.

Position Statement

- Sleep medications such as eszopiclone appear to help people fall asleep about 15 – 30 minutes faster than they would without medication. The impact of this additional 15 – 30 minutes of sleep on a person's overall health is uncertain.

- Patients with nighttime sleep disturbances do not necessarily experience functional impairment. [1] Data supporting improvements in daytime function resulting from treatment with eszopiclone are limited.

- The diagnosis of primary versus secondary insomnia can be difficult to determine. However, it is important to identify patients with secondary insomnia so that the underlying cause of insomnia can be treated. [36]

- Organizations such as the National Sleep Foundation, the American Academy of Sleep Medicine, and the National Heart, Lung, and Blood Institute recommend non-pharmacologic (non-drug) methods as options to improve sleep quality. [2-4]

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Clinical Efficacy

- Published data regarding long-term safety and efficacy of eszopiclone are limited. [67,8] In a study of long term use, the average patient taking eszopiclone for 6 months still experienced insomnia severe enough to have qualified for initial enrollment in the study: total sleep time less than 6.5 hours per night and/or sleep latency of greater than 30 minutes. [7]

- In a randomized controlled trial of women with insomnia related to menopause, eszopiclone reduced the time it took women to go to sleep by only 15 minutes compared to placebo. Though women may have received eszopiclone continuously for 4 weeks, the primary outcome was evaluated after 1 week of treatment. [9]

- In a study of elderly patients with insomnia, eszopiclone was administered continuously for14 days. No significant difference in functional outcomes was observed between eszopiclone and placebo group. [10]

- A randomized controlled trial of patients with concomitant depression and insomnia examined coadministration of eszopiclone with fluoxetine or placebo. Patients were treated for 8 weeks, though the primary outcome was evaluated after 1 week of treatment. [11]

    * The combination of fluoxetine and placebo decreased wake time after sleep onset (WASO) by 50 minutes. Fluoxetine and eszopiclone only improved WASO by an additional 15 minutes.

    * Thirty-two percent of patients did not complete the study.

- Eszopiclone has not been compared to other medications such as short-acting benzodiazepines in patients suffering from insomnia in randomized, controlled trials. Therefore, conclusions cannot be drawn regarding safety or effectiveness when compared to other medications, such as short-active benzodiazepines (e.g., triazolam or temazepam).

- Eszopiclone is the s-isomer (the biologically active component) of zopiclone, a sleep medication that has been extensively studied and widely-used in many countries. [3,12-32] Zopiclone does not have Food and Drug Administration approval for marketing in the United States. Zopiclone has been compared to several short-acting benzodiazepines in many randomized, controlled trials. This body of evidence suggests that zopiclone is not associated with any consistent clinically significant advantages in terms of safety, effectiveness or tolerance over short-acting benzodiazepines. [3,12-32]

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- Preliminary unpublished data suggests that short-term use of eszopiclone, limited to two consecutive days of treatment, may improve compliance in sleep apnea patients transitioning to CPAP. Larger, well controlled trials are needed to establish the efficacy of eszopiclone in this population. [5]

- A preliminary unpublished trial of eszopiclone in patients with rheumatoid arthritis and insomnia did not demonstrate a significant effect on pain or ability to function. It is unclear whether differences observed in wake time after sleep onset were clinically significant. [6]

Safety

- The quantity limit for eszopiclone is based on FDA labeling of hypnotics for short-term use in managing insomnia. The labeling states that "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." "Therefore, treatment of insomnia with hypnotic agents should generally be limited to 7 to 10 days of use, and reevaluation of the patient is recommended if treatment is to be extended for more than 2 to 3 weeks."[232]

- The FDA labeling of hypnotics includes the following safety information:

  * After taking Lunesta, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. Reported activities include:

    * driving a car ("sleep-driving")
    * making and eating food
    * talking on the phone
    * having sex
    * sleep-walking

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Appendix 1: Diagnostic criteria for 307.42 Primary Insomnia [33]	
A.	The predominant complaint is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least 1 month.
B.	The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C.	The sleep disturbance does not occur exclusively during the course of Narcolepsy, Breathing-Related Sleep Disorder, Circadian Rhythm Sleep Disorder, or a Parasomnia.
D.	The disturbance does not occur exclusively during the course of another mental disorder (e.g., Major Depressive Disorder, Generalized Anxiety Disorder, a delirium).
E.	The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

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Cross References
Ambien®, zolpidem dru062
Ambien CR®, zolpidem MR dru130
Edluar™ zolpidem sublingual tablets dru181
Rozerem®, ramelteon dru124
Sonata®, zaleplon dru061
ZolpiMist™, zolpidem oral spray dru182

Codes	Number	Description
N/A		

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