The Regence Group

Regence BlueCross BlueShield of Oregon · Regence BlueShield
Regence BlueCross BlueShield of Utah · Regence BlueShield of Idaho
Independent licensees of the Blue Cross and Blue Shield Association

Medication Policy Manual | **Policy No:** dru130

Topic: Ambien CR®, zolpidem MR | **Date of Origin:** March 10, 2006

Revised/Effective Date: May 8, 2009 | **Next Review Date:** May 2010

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

Zolpidem modified-release "MR" (Ambien CR®) is an orally administered hypnotic agent (sleep medicine) that is used for the treatment of insomnia. Zolpidem MR is a controlled-substance.

© 2008 The Regence Group. All rights reserved.

Policy/Criteria

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

II. Zolpidem MR in quantities between 15 and 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 zolpidem MR to be a self-administered medication.

© 2008 The Regence Group. All rights reserved.

B. When prior authorization is approved, zolpidem MR may be authorized in quantities up to 34 tablets per month. Doses exceeding 12.5 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 zolpidem MR.

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 zolpidem MR with either zolpidem (Ambien®, Edluar™, ZolpiMist™), eszopiclone (Lunesta®), ramelteon (Rozerem®) or zaleplon (Sonata®) exceeding 14 tablets per month is considered duplication of therapy and not medically necessary.

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

Position Statement

- Sleep medications such as zolpidem MR 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 zolpidem MR 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. [10]

© 2008 The Regence Group. All rights reserved.

- The only reliable evidence supporting the efficacy of zolpidem MR is in patients who meet the Diagnostic and Statistical Manual of Mental Disorders "DSM-IV" criteria for primary insomnia. Regence coverage policy criteria are based on the DSM-IV criteria for primary insomnia. [2]
- The benefit of treating secondary insomnia with zolpidem MR is uncertain. Sleep medications alone may not address the most common underlying causes of insomnia.
- 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]

Clinical Efficacy

- A published randomized trial comparing zolpidem MR to placebo for up to 16 days of continuous administration demonstrated a decrease in wake time after sleep onset and sleep latency with zolpidem MR.[5]
  * Groups were unbalanced at baseline. The zolpidem MR group slept longer and spent less time awake each night.
  * Effects of zolpidem MR appear to lessen with time. The time spent awake after sleep onset increased between nights 1 and 2 and nights 15 and 16.
- Zolpidem MR 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 such as triazolam or temazepam.
- Zolpidem MR contains zolpidem, a sleep medication that has been extensively studied and widely-used in many countries. [3] A recent review of the scientific studies of zolpidem failed to produce any evidence of clinically meaningful improvements in health of patients.
- The US Agency for Healthcare Research and Quality (AHRQ) published a technical review on the management of chronic insomnia in adult patients and concluded that: [6]
  * Benzodiazepines and non-benzodiazepines are effective in the treatment of chronic insomnia and they pose a risk of harm.

© 2008 The Regence Group. All rights reserved.

* Benzodiazepines pose a greater risk of harm than non-benzodiazepines. However, this conclusion is drawn upon indirect comparisons and do not take differences in benzodiazepines (such as those with very long half lives or active metabolites) into consideration.

Safety

- Zolpidem MR is approved for the treatment of insomnia in patients with difficulty initiating or maintaining sleep.

- The quantity limit for zolpidem MR is based on:

    * No clinical studies of zolpidem MR of effectiveness beyond 16 days of continuous therapy.

    * The 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."[7]

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

    * After taking Ambien CR, 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

© 2008 The Regence Group. All rights reserved.

Appendix 1: Diagnostic criteria for 307.42 Primary Insomnia [1]	
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.

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV*, 4th Edition. Washington, DC. 1994.
2. American Academy of Sleep Medicine. Practice parameters for the nonpharmacologic treatment of chronic insomnia. *Sleep* 1999;22:1128-33.
3. National Institute for Clinical Excellence. Guidance on the use of zaleplon, zolpidem, and zopiclone for the short-term management of insomnia. Technology Appraisal 77. April 2004. National Institute for Clinical Excellence Web site at http://www.nice.org.uk/pdf/TA077fullguidance.pdf. Accessed 1/7/2005.
4. National Heart, Lung, and Blood Institute. Facts about problem sleepiness. National Heart, Lung, and Blood Institute Web site at http://www.nhlbi.nih.gov/health/public/sleep/pslp_fs.htm. Accessed 1/7/2005.
5. Roth T, Soubrane C, Titeux, et al. Efficacy and safety of zolpidem-MR: a double-blind, placebo-controlled study in adults with primary insomnia. *Sleep Medicine* 2006;7:397-406.
6. Buscemi N, et al. (University of Alberta Evidence-Based Practice Center, Edmonton, Alberta, Canada.) Manifestations and management of chronic insomnia in adults. Agency for Healthcare Research and Quality. Contract No. 40000021.
7. Ambien CR (zolpidem MR) prescribing information. Sanofi-Adventis Inc. Bridgeport, NJ. January 2008.

© 2008 The Regence Group. All rights reserved.

8. Krystal AD et al. Long-term efficacy and safety of zolpidem extended-release 12.5 mg, administered 3 to 7 nights per week for 24 weeks, in patients with chronic primary insomnia: a 6-month, randomized, double-blind, placebo-controlled, parallel-group, multicenter study. *Sleep Medicine* 2008; 31:79 - 89.

9. Walsh JK et al. Efficacy and safety of zolpidem extended release in elderly primary insomnia patients. *Am J Geriatr Psychiatry* 2008;16:44 – 57.

10. NIH State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults. *NIH Consens Sci Statements*. 2005. June 13 – 15;22(2) 1 – 30.

Cross References
Ambien®, zolpidem dru062
Edluar™ zolpidem sublingual tablets dru181
Lunesta®, eszopiclone dru114
Rozerem®, ramelteon dru124
Sonata®, zaleplon dru061
ZolpiMist™, zolpidem oral spray dru182

Codes	Number	Description
N/A		

© 2008 The Regence Group. All rights reserved.