Clinical Policy Title:	zolpidem tartrate
Policy Number:	RxA.109
Drug(s) Applied:	Edluar®, Intermezzo®, Zolpimist®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Zolpidem tartrate (Edluar®, Intermezzo®, Zolpimist®) is a gamma-aminobutyric acid ($GABA_A$) agonist. Edluar® and Zolpimist® are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation.

Intermezzo® is indicated for use as needed for the treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep.

Limitation(s) of use: Intermezzo® is not indicated for the treatment of middle-of-the-night awakening when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
zolpidem tartrate (Edluar®)	short-term treatment of insomnia characterized by difficulties with sleep initiation	Adults: 5 mg SL for women and 5 or 10 mg for men SL HS PRN immediately before bedtime Elderly: 5 mg SL HS PRN immediately before bedtime	Adults: 10 mg/day Elderly: 5 mg/day
zolpidem tartrate (Intermezzo®)	middle-of-the-night awakening followed by difficulty returning to sleep	Women: 1.75 mg SL HS PRN Men: 3.5 mg SL HS PRN Elderly: 1.75 mg SL HS PRN	Adult women: 1.75 mg/day Adult men: 3.5 mg/day Elderly: 1.75 mg/day
zolpidem tartrate (Zolpimist®)	short-term treatment of insomnia characterized by difficulties with sleep initiation	Adults: 5 mg for women and 5 or 10 mg for men PO HS PRN immediately before bedtime Elderly: 5 mg PO HS PRN immediately before bedtime	Adults: 10 mg/day Elderly: 5 mg/day

Dosage Forms

- zolpidem tartrate (Edluar®) sublingual tablets: 5 mg, 10 mg
- zolpidem tartrate (Intermezzo®) sublingual tablets: 3.5 mg

- zolpidem tartrate (Zolpimist®) oral spray: 5 mg per actuation

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Insomnia (must meet all)**:**

1. Diagnosis of insomnia;
2. Age 18 years or more;
3. For Edluar® and Zolpimist®: Failure of zolpidem oral tablets, unless contraindicated or clinically significant adverse effects are experienced;
4. For Intermezzo®: Member has a history of insomnia with difficulty returning to sleep after middle-of-the-night awakening;
5. Dose does not exceed (a or b):
   a. Edluar®, Zolpimist®: 10 mg per day;
   b. Intermezzo®: 3.5 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Insomnia (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
   a. Edluar®, Zolpimist®: 10 mg per day;
   b. Intermezzo®: 3.5 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
SL: sub lingual
PRN: pro re nata (as needed)
HS: hora somni (at bedtime)
PO: per os (by mouth)

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

zolpidem tartrate (Ambien®)	Adults: 5-10 mg PO HS PRN Elderly: 5 mg PO HS PRN	10 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Zolpimist®: Patients who have experienced complex sleep behaviors after taking Zolpimist®, ; known hypersensitivity to zolpidem
  - Edluar®, Intermezzo®: Known hypersensitivity to zolpidem

- Boxed Warning(s):
  - Complex sleep behaviors

APPENDIX D: General Information

- Complex sleep behaviors including sleepwalking, sleep-driving, and engaging in other activities while not fully awake may occur following the first or any subsequent use of zolpidem. Patients can be seriously injured or injure others during complex sleep behaviors. Such injuries may result in a fatal outcome. Other complex sleep behaviors (e.g., preparing and eating food, making phone calls, or having sex) have also been reported. Patients usually do not remember these events. Post-marketing reports have shown that complex sleep behaviors may occur with zolpidem alone at recommended dosages, with or without the concomitant use of alcohol or other central nervous system (CNS) depressants. Discontinue immediately if a patient experiences a complex sleep behavior.

References

1. Edluar® Prescribing Information. Somerset, NJ: Meda Pharmaceuticals Inc.; August 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021997s011lbl.pdf. Accessed January 14, 2021.
2. Intermezzo® Prescribing Information. Stamford, CT: Purdue Pharma L.P.; August 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=913b6cfe-1fb0-44a8-817a-26374bbce995. Accessed January 14, 2021.
3. Zolpimist® Prescribing Information. Englewood, CO: Aytu BioScience Inc.; August 2019. Available at: https://myzolpimist.com/. Accessed January 14, 2021.
4. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. 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. Accessed January 14, 2021.
5. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed January 14, 2021.
6. Zolpidem, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed January 14, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed and updated: 1. Updated Maximum dose for Intermezzo® 2. Updated references	04/28/2020	05/20/2020

Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to 'zolpidem tartrate', Drug(s) Applied was updated to 'Edluar®, Intermezzo®, Zolpimist®', Line of business policy applies was updated to All lines of business. 2. Dosing information: Indications were added. Adult maximum dose for Zolpimist® was updated to 10 mg/day. 3. Dosage forms: discontinued strength for was updated to Intermezzo® 1.75 mg [DSC]. 4. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. Commercial approval duration was update to 6 months, from Length of benefit. 6. Appendix A was updated. 7. Appendix B verbiage was updated to 'Below are suggested therapeutic alternatives..' 8. Appendix C: contraindication(s) was updated as 'Patients who have experienced complex sleep behaviors after taking…' 9. Appendix C: boxed warning has been added as 'Complex sleep behaviors' 10. Appendix D was added. 11. References were updated.	01/25/2021	03/09/2021