MEDICAL MUTUAL®

Drug Policy

Policy:	**Hetlioz (tasimelteon) capsules** **Hetlioz LQ (tasimelteon) oral suspension**	**Annual Review Date: 01/16/2025** **Last Revised Date: 01/16/2025**

OVERVIEW

Hetlioz, a melatonin receptor agonist, is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) and patients with nighttime disturbances due to Smith-Magenis Syndrome.

Non-24 is a chronic, circadian rhythm disorder that is due to the misalignment of the endogenous master body clock to the 24-hour day which disrupts the sleep-wake cycle and commonly is thought to be caused by the failure of light to reach the suprachiasmatic nuclei. Patients who are completely blind are particularly susceptible to this condition. It has been estimated that of the 1.3 million people in the US who are blind, 10% of people have no light perception, a risk factor for this disorder, and reports suggest that as many as one-half to three-quarters of totally blind patients have Non-24, which is approximately 65,000 to 95,000 Americans.

Smith-Magenis Syndrome is a rare genetic disorder that causes physiologic, circadian defects. It is associated with significant sleep problems that include; difficulty falling asleep, shortened sleep cycles, frequent and prolonged nocturnal awakenings (altered rapid eye movement [REM] sleep), excessive daytime sleepiness, daytime napping, snoring, and bedwetting.

Hetlioz has a Warning and Precaution regarding somnolence and that it can potentially impair performance if doing activities that require complete mental alertness.

POLICY STATEMENT

This policy involves the use of Hetlioz and tasimelteon. Prior authorization is recommended for pharmacy benefit coverage of Hetlioz or Tasimelteon. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Hetlioz as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Hetlioz be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Hetlioz is recommended in those who meet the following criteria:

For all indications: If Brand Hetlioz is being requested, the patient must have tried generic tasimleteon AND the brand product is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand product and the bioequivalent generic product which, per the prescribing provider, would result in a significant allergy or serious adverse reaction; AND

Food and Drug Administration (FDA)-Approved Indications

1. Non-24-Hour Sleep Wake Disorder (Non-24), Initial Therapy. Approve for 6 months if the patient meets all the following criteria (A, B, C, D, E and F):

A) The patient is ≥ 18 years of age; AND
B) The patient is totally blind with no perception of light; AND
C) The medication is prescribed by, or in consultation with, a physician who specializes in the treatment of sleep disorders; AND
D) The diagnosis of Non-24 is confirmed by meeting ONE of the following conditions (i or ii):
  i. Assessment of at least one physiologic circadian phase marker (e.g., measurement of urinary melatonin levels, dim light melatonin onset [as measured in blood or saliva], assessment of core body temperature); OR
  ii. If assessment of at least one physiologic circadian phase marker cannot be done, the diagnosis must be confirmed by actigraphy performed for ≥ 1 week plus evaluation of sleep logs recorded for ≥ 1 month; AND
E) The patient meets both conditions below (i and ii):
  i. The patient has received at least 6 months of continuous therapy (i.e., 6 consecutive months of daily treatment) with melatonin under the guidance of a physician who specializes in the treatment sleep disorders; AND
  ii. The patient did not achieve adequate results with melatonin therapy according to the prescribing physician (e.g., entrainment, clinically meaningful or significant increases in nighttime sleep, clinically meaningful or significant decreases in daytime sleep).

2. Non-24-Hour Sleep Wake Disorder (Non-24), Continuation Therapy. Approve for 12 months if the patient meets all of the following criteria (A, B, C, D, and E):

A) The patient is ≥ 18 years of age; AND
B) The patient is totally blind with no perception of light; AND
C) The medication is prescribed by, or in consultation with, a physician who specializes in the treatment of sleep disorders; AND
D) The patient has received at least 6 months of continuous therapy (i.e., 6 consecutive months of daily treatment) with Hetlioz under the guidance of a physician who specializes in the treatment of sleep disorders (Note: Patients who have not received at least 6 months of continuous Hetlioz therapy, or if the therapy has not been continuous [i.e., 6 consecutive months of daily treatment], should follow criteria 1 [initial therapy]); AND

E) The patient has achieved adequate results with Hetlioz therapy according to the prescribing physician (e.g., entrainment, clinically meaningful or significant increases in nighttime sleep, clinically meaningful or significant decreases in daytime sleep).

Initial Approval/ Extended Approval.
A) Initial Approval: 6 months (180 days)
B) Extended Approval: 12 months (365 days)

3. Nighttime Disturbances due to Smith-Magenis Syndrome Initial Therapy. Approve for 6 months if the patient meets all the following criteria (A, B, and C):
A) The patient is greater than 3 years old and meets one of the following criteria (i or ii):
  i. Patient is aged 3 to 15 years old and will use the Hetlioz oral suspension formulation; OR
  ii. Patient is aged 16 or older and will use the Hetlioz capsule.
B) Molecular genetic testing has confirmed mutation or microdeletion of the chromosome 17p11.2, indicative of Smith-Magenis Syndrome.
C) Hetlioz is prescribed by or in consultation with a physician who specializes in the treatment of sleep disorders, a neurologist or medical geneticist.

4. Nighttime Disturbances due to Smith-Magenis Syndrome, continuation of therapy. Approve for 12 months if the patient meets all the following criteria (A and B):
A) The patient has received at least 6 months of continuous therapy with Hetlioz under the guidance of a physician who specializes in the treatment of sleep disorders, neurologist or medical geneticist.
B) According to the prescriber, the patient has achieved adequate results with Hetlioz therapy.

Initial Approval/ Extended Approval.
A) Initial Approval: 6 months (180 days)
B) Extended Approval: 12 months (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Hetlioz has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Insomnia, Primary**. Only limited data have investigated use of Hetlioz in patients with primary insomnia. Further data are needed to establish the safety and efficacy of Hetlioz

2. **Rozerem™ (ramelteon tablets), Concomitant Therapy**. Rozerem is a melatonin receptor agonist indicated for the treatment of insomnia characterized by difficulty with sleep onset. The safety and efficacy of concomitant use of Rozerem and Hetlioz have not been studied and it is suspected that the AEs with use of these agents with a similar mechanism of action taken together may be additive (e.g., central nervous system effects [somnolence], hepatic

impairment). Rozerem has not been studied in Non-24. In the clinical trials with Hetlioz, patients were not permitted to use medications that could interfere with the assessment of circadian rhythms.

3. **Sedative Hypnotic Medications or Other Medications for Insomnia or Other Sleep-Related Disorders**, Concomitant Therapy (e.g., benzodiazepines [triazolam, temazepam], nonbenzodiazepine hypnotics [e.g., zolpidem, zaleplon], chloral hydrate). There are no data to evaluate the safety and efficacy of hypnotic medications in patients who are blind with Non-24. Also, there are not data to determine the safety and efficacy of Hetlioz when used with other sedative hypnotic medications or other medications for insomnia or sleep-related disorders.

4. **Sleep-Related Disorders, Other Types** (e.g. shift work disorder, jet lag disorder, advanced sleep phase disorder, delayed sleep phase disorder, irregular sleep-wake rhythm disorder). A published investigation details a Phase II study (n = 29) and a Phase III study (n = 411) assessing Hetlioz treatment in adults with transient insomnia associated with shifted sleep and wake time. Further studies are needed to establish the efficacy and safety of Hetlioz in patients with other types of sleep-related disorders.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Hetlioz™ [prescribing information]. Washington, DC: Vanda Pharmaceuticals; December 2020.
2. Johnsa JD, Neville MW. Tasimelteon: a melatonin receptor agonist for non-24-hour sleep-wake disorder. *Ann Pharmacother*. 2014;48(12):1636-1641.
3. Dhillon S, Clarke M. Tasimelteon: first global approval. *Drugs*. 2014;74:505-511.
4. Emens JS, Amber LL, Songer JB, Lewy AJ. Non-24-hour disorder in blind individuals revisited: variability and the influence of environmental time cures. *Sleep*. 2013;36(7):1091-1100.
5. Bonacci JM, Venci JV, Gandhi MA. Tasimelteon (Hetlioz): a new melatonin receptor agonist for the treatment of non-24-hour sleep-wake disorder. *J Pharm Pract*. 2014 Aug 3. [Epub ahead of print].
6. National Sleep Foundation [Internet]. Non-24-hour Sleep Wake Disorder Facts and Prevalence. Available at: http://sleepfoundation.org/non-24/facts_prevalence.html. Accessed on April 2, 2015.
7. Morgenthaler TI, Lee-Chong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. *Sleep*. 2007;30(11):1445-1459. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2082098/pdf/aasm.30.11.1445.pdf. Accessed on April 1, 2015.

8. Sack RL, Auckley D, Auger R, et al. Circadian rhythm sleep disorders: part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. An American Academy of Sleep Medicine review. *Sleep*. 2007;30(11):1484-1501.
9. Feeney J, Birznieks G, Scott C, et al. Melatonin agonist tasimelteon improves sleep in primary insomnia characterized by difficulty falling asleep. *Sleep*. 2009;32(Suppl):43.
10. Rozerem™ tablets [prescribing information]. Deerfield, IL: Takeda; November 2010.
11. No authors listed. Drugs for insomnia. *Treat Guidel Med Lett*. 2012;10(119):57-60.
12. Rajartnam SMW, Polymeropoulos MH, Fisher DM, et al. Melatonin agonist tasimelteon (VEC-162) for transient insomnia after sleep-time shift: two randomized controlled multicenter trials. *Lancet*. 2009;373:482-491.
13. Tasimelteon. In: DRUGDEX (online database). Truven Health Analytics: Greenwood Village, CO. Last updated 12 December 2019. Accessed on 20 January 2020.
14. Auger RR, Burgess HJ, Emens JS, et al. Clinical practice guideline for the treatment of intrinsic circadian rhythm sleep-wake disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder (DSWPD), Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD). An update for 2015. *J Clin Sleep Med*. 2015;11(10):1199-1236. Available at: http://www.aasmnet.org/Resources/clinicalguidelines/CRSWD-intrinsic.pdf Accessed on 17 January 2018.