Pharmacy Policy Bulletin: J-0403 Hetlioz (tasimelteon) and Hetlioz LQ (tasimelteon) – Commercial and Healthcare Reform	
Number: J-0403	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral= Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0403-016	**Original Date:** 09/03/2014
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Hetlioz (tasimelteon) • Hetlioz LQ (tasimelteon)
FDA-Approved Indication(s):	**Hetlioz Capsules** • Treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in adults • Treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients 16 years of age and older **Hetlioz LQ Oral Suspension** • Treatment of nighttime sleep disturbances in SMS in pediatric patients 3 years to 15 years of age

Background:	• Hetlioz is a melatonin agonist acting at the MT_1 and MT_2 receptors. The precise mechanism in which it exerts its effect is unknown. The MT_1 and MT_2 receptors are believed to be involved in the promotion of sleep and the maintenance of the normal circadian rhythm (shift between day and night). • Non-24 is a disorder that affects the normal 24-hour synchronization of circadian rhythms. In mammals, circadian rhythms are generated by the suprachiasmatic nuclei (SCN) in the hypothalamus with the day-night cycle as the primary environmental time cue that synchronizes the circadian system to the 24-hour day. People with Non-24 have circadian rhythms that are not synchronized with the 24-hour day-night cycle. In totally blind patients, this occurs because of a failure of light to reach the SCN. • Generic Hetlioz capsules are only indicated for the treatment of Non-24 in adults. • All patients in the Hetlioz Non-24 clinical trials were totally blind. • The 2015 Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder, Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD) Update for 2025 suggests that clinicians use strategically timed melatonin for the treatment on non-24 hour sleep wake disorder in blind adults.

	• SMS is a rare, genetic, neurodevelopmental disorder characterized by cognitive impairment of variable severity, behavioral abnormalities, and sleep disturbance. Most patients with SMS have a deletion of genetic material in each cell from a specific region of chromosome 17. The sleep disturbance that occurs in affected individuals is a chronic life-long problem. These sleep abnormalities are associated with an inverted circadian rhythm of melatonin. In individuals with an inverted circadian rhythm, the rising and falling of melatonin levels is reversed (daytime highs). • The diagnosis of SMS is confirmed when deletion 17p11.2 (cytogenetic analysis or microarray) or *RAI*1 gene mutation is identified. • An ICD-10 code of Q93.88 (other microdeletions) may apply to SMS, however the prescriber must confirm the patient has SMS. • Hetlioz capsules and Hetlioz LQ oral suspension are not substitutable. • Prescribing considerations: ○ Avoid use with strong CYP1A2 inhibitors (e.g. fluvoxamine) and strong CYP3A4 inducers (e.g. rifampin). ○ Hetlioz can impair the performance of activities requiring complete mental alertness, patients should limit their activity to prepare for going to bed after taking Hetlioz.

Approval Criteria

I. Initial Authorization

A. Hetlioz Capsules

1. Non-24-Hour Sleep-Wake Disorder (Non-24)

When a benefit, coverage of Hetlioz capsules (tasimelteon) may be approved when all of the following criteria are met **(a. through f.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of Non-24 Hour Sleep-Wake Disorder (ICD-10: G47.24).

c. The member meets all of the following diagnostic criteria for Non-24 Hour Sleep-Wake Disorder **(i. through iv.)**:

i. A history of insomnia, excessive daytime sleepiness, or both alternating with asymptomatic episodes.

ii. Symptoms persisting for at least 3 months.

iii. Daily sleep logs of at least 14 days that demonstrate a sleep/wake pattern that delays each day.

iv. The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance abuse disorder.

d. The member is totally blind and has no light perception.

e. The member has experienced therapeutic failure, contraindication or intolerance to melatonin.

f. If the request is for brand Hetlioz, the member has experienced therapeutic failure or intolerance to generic tasimelteon.

2. Nighttime Sleep Disturbances in SMS

When a benefit, coverage of Hetlioz capsules may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 16 years of age and older.

b. The member has a diagnosis of Smith-Magenis Syndrome (no ICD-10 code) confirmed by one (1) of the following **(i. or ii.):**

i. deletion of chromosome 17p11.2

ii. variant in the *RAI1* gene

c. The member is experiencing nighttime sleep disturbances which includes difficulty falling asleep, shortened sleep cycles, inability to enter REM sleep, or frequent awaking during the night and early in the morning.

B. Hetlioz LQ Oral Suspension

1. Nighttime Sleep Disturbances in SMS

When a benefit, coverage of Hetlioz LQ Oral Suspension may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 3 to 15 years of age.

b. The member has a diagnosis of Smith-Magenis Syndrome (no ICD-10 code) confirmed by one (1) of the following **(i. or ii.):**

i. deletion of chromosome 17p11.2

ii. variant in the *RAI1* gene

c. The member is experiencing nighttime sleep disturbances which includes difficulty falling asleep, shortened sleep cycles, inability to enter REM sleep, or frequent awaking during the night and early in the morning.

II. Reauthorization

A. Hetlioz Capsules

1. Non-24 Hour Sleep-Wake Disorder (Non-24)

When a benefit, reauthorization of Hetlioz capsules (tasimelteon) may be approved when all of the following criteria are met **(a. and b.)**:

a. One (1) of the following criteria is met **(i. or ii.)**:

i. The prescriber attests that the member has experienced an increase in total nighttime sleep time.

ii. The prescriber attests that the member has experienced a decrease in daytime nap duration.

b. If the request is for brand Hetlioz, the member has experienced therapeutic failure or intolerance to generic tasimelteon.

2. Nighttime Sleep Disturbances in SMS

When a benefit, reauthorization of Hetlioz capsules may be approved when the following criterion is met **(a.)**:

a. One (1) of the following criteria is met **(i. or ii.)**:

i. The prescriber attests that the member has experienced an increase in total nighttime sleep time.

ii. The prescriber attests that the member has experienced an increase in sleep quality.

B. Hetlioz LQ Oral Suspension

1. Nighttime Sleep Disturbances in SMS

When a benefit, reauthorization of Hetlioz LQ oral suspension may be approved when all of the following criteria are met **(a. and b.)**:

a. The member is between 3 and 15 years of age.

b. The member meets one (1) of the following criteria **(i. or ii.)**:

i. The prescriber attests that the member has experienced an increase in total nighttime sleep time.

ii. The prescriber attests that the member has experienced an increase in sleep quality.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Hetlioz should not be used for sighted individuals with Non-24 as they may be treated with timed light therapy.
II. Hetlioz should not be initiated in blind individuals without Non-24.
III. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
IV. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Hetlioz [package insert]. Washington, DC: Vanda Pharmaceuticals Inc. December 2020.
2. Sleep Wake Disorder. Available at: https:/www.sleepfoundation.org/non-24-sleep-wake-disorder. Accessed January 7, 2025.
3. Smith Magenis Syndrome. Available at: https://rarediseases.org/rare-diseases/smith-magenis-syndrome/. Accessed January 7, 2025.
4. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2023.
5. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic & coding manual (2nded.). West-Chester, IL: American Academy of Sleep Medicine, 2005.
6. Guidelines for the Management of Children and Adults with Smith-Magenis Syndrome. Available at: https://smith-magenis.org/wp-content/uploads/Guidelines_for_Mgtment_of_Child_and_Adults_with_SMS_14.03.05.pdf. Accessed January 6, 2024.
7. 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.
8. 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*. Nov 2007;30(11):1445-1459. PMID 180414479.
9. UpToDate. Non-24-hour sleep-wake rhythm disorder. Available at: https://www-uptodate-com.pitt.idm.oclc.org/contents/non-24-hour-sleep-wake-rhythm-disorder. Accessed January 7, 2025.