CareSource

PHARMACY POLICY STATEMENT
North Carolina Marketplace

DRUG NAME	Hetlioz and Hetlioz LQ (tasimelteon)
BILLING CODE	Must use valid NDC
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home
STATUS	Prior Authorization Required

Hetlioz is a melatonin receptor agonist that was originally FDA approved in 2014 for the treatment of Non-24-Hour Sleep-Wake Disorder (non-24), and later approved in 2020 for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS). It acts upon MT1 and MT2 receptors to entrain circadian sleep phase timing.
Non-24 is a type of circadian rhythm sleep-wake disorder that is often present in blind individuals due to the inability to perceive light, causing the hypothalamic circadian pacemaker to fail to entrain (synchronize) with the 24-hour day. This results in nighttime insomnia and excessive daytime sleepiness.
SMS is a rare genetic neurodevelopmental disorder that affects multiple organ systems and is characterized by cognitive impairment, behavioral problems, and sleep disturbances. The sleep disturbances are caused by an inverted circadian rhythm with abnormal timing of melatonin release.

Hetlioz (tasimelteon) will be considered for coverage when the following criteria are met:

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

For **initial** authorization:
1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a sleep specialist; AND
3. Member has a diagnosis of non-24 confirmed by at least one of the following:
   a) Daily sleep logs and/or actigraphy for at least 14 days
   b) Measurements of at least one circadian biomarker (e.g., 6-sulfatoxymelatonin (aMT6s)); AND
4. Member has at least a 3-month history of insomnia, excessive daytime sleepiness, or both, which alternate with asymptomatic episodes; AND
5. Member is totally blind (has no perception of light); AND
6. Member has had at least a 3-6 month trial and failure of melatonin.
7. **Dosage allowed/Quantity limit:** 20 mg (1 capsule) one hour before bedtime, at the same time every night.
   (QL: 30 capsules per 30 days)

If all the above requirements are met, the medication will be approved for 4 months.

For **reauthorization**:
1. Chart notes must show improvement of signs and symptoms compared to baseline, including entrainment, increased duration of nighttime sleep, and/or decreased unwanted daytime sleep.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Smith-Magenis Syndrome (SMS)

For **initial** authorization:
1. Member is at least 3 years of age; AND
2. Medication is prescribed by or in consultation with a sleep specialist, geneticist, or neurologist; AND
3. Member has documentation of nighttime sleep disturbance with diagnosis of SMS; AND
4. Molecular genetic testing confirms one of the following:
   a) Chromosome 17p11.2 microdeletion (encompasses the RAI1 gene)
   b) Pathogenic variant in the RAI1 gene; AND
5. Member has had at least a 4-6 week trial and failure of melatonin.
6. **Dosage allowed/Quantity limit:**
   Age 16 years and older: 20 mg (1 capsule) one hour before bedtime, at the same time every night. (QL: 30 capsules per 30 days)
   Age 3 to 15 years: Hetlioz LQ oral suspension, based on body weight:

Body Weight	Daily Dose (oral suspension)
≤28 kg	0.7 mg/kg one hour before bedtime
>28 kg	20 mg one hour before bedtime

   (QL: 3 bottles per 30 days for the 48 mL bottle; 1 bottle per 30 days for the 158 mL bottle)

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:
1. Chart notes must document improved nighttime sleep disturbances compared to baseline, such as improved sleep quality.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Hetlioz (tasimelteon) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
01/31/2022	New policy for Hetlioz created.

References:

1. Hetlioz [prescribing information]. Vanda Pharmaceuticals, Inc.; December 2020.
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Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med*. 2015;11(10):1199-1236. Published 2015 Oct 15. doi:10.5664/jcsm.5100
3. Steele TA, St Louis EK, Videnovic A, Auger RR. Circadian Rhythm Sleep-Wake Disorders: a Contemporary Review of Neurobiology, Treatment, and Dysregulation in Neurodegenerative Disease. *Neurotherapeutics*. 2021;18(1):53-74. doi:10.1007/s13311-021-01031-8
4. Lockley SW, Dressman MA, Licamele L, et al. Tasimelteon for non-24-hour sleep-wake disorder in totally blind people (SET and RESET): two multicentre, randomised, double-masked, placebo-controlled phase 3 trials. *Lancet*. 2015;386(10005):1754-1764. doi:10.1016/S0140-6736(15)60031-9
5. Johnsa JD, Neville MW. Tasimelteon: a melatonin receptor agonist for non-24-hour sleep-wake disorder. *Ann Pharmacother*. 2014;48(12):1636-1641. doi:10.1177/1060028014550476
6. Emens JS, Eastman CI. Diagnosis and Treatment of Non-24-h Sleep-Wake Disorder in the Blind. *Drugs*. 2017;77(6):637-650. doi:10.1007/s40265-017-0707-3
7. Quera Salva MA, Hartley S, Léger D, Dauvilliers YA. Non-24-Hour Sleep-Wake Rhythm Disorder in the Totally Blind: Diagnosis and Management. *Front Neurol*. 2017;8:686. Published 2017 Dec 18. doi:10.3389/fneur.2017.00686
8. Polymeropoulos CM, Brooks J, Czeisler EL, et al. Tasimelteon safely and effectively improves sleep in Smith-Magenis syndrome: a double-blind randomized trial followed by an open-label extension. *Genet Med*. 2021;23(12):2426-2432. doi:10.1038/s41436-021-01282-y
9. Smith ACM, Boyd KE, Brennan C, et al. Smith-Magenis Syndrome. 2001 Oct 22 [Updated 2019 Sep 5]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1310/

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