BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

HETLIOZ® (tasimelteon) oral capsule
HETLIOZ LQ™ (tasimelteon) oral suspension
Tasimelteon oral capsule
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Hetlioz (tasimelteon) capsule, Hetlioz LQ (tasimelteon) suspension, and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Specialist in Sleep Disorders

2. Request is for **ONE** of the following diagnosis and age

a. Tasimelteon (brand Hetlioz or generic) **capsule** for an individual 18 years of age or older who is totally blind with no light perception with a confirmed diagnosis of non-24-hour sleep wake disorder

b. Tasimelteon (brand Hetlioz or generic) **capsule** for an individual 16 years of age or older with a confirmed diagnosis of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS)

c. Hetlioz LQ **suspension** for an individual 3 years to 15 years of age with a confirmed diagnosis of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS)

3. Individual has a confirmed diagnosis that is supported by **ONE** of the following:
   a. For Non-24-hour sleep wake disorder
      i. Measurement of urinary melatonin levels
      ii. Actigraphy performed for ≥ 1 week plus evaluation of sleep logs recorded for ≥ 1 month
   b. For Smith-Magenis Syndrome
      i. Confirmed deletion 17p11.2 (cytogenetic analysis or microarray) or *RAI1* gene mutation is identified

4. Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for the following:
   a. For Non-24-hour sleep wake disorder: At least 3-months of timed melatonin (used nightly at same time, not to be used on an as needed basis)
   b. For Smith-Magenis Syndrome: At least 3-months of acebutolol or metoprolol tartrate in the morning and melatonin at bedtime

5. **For brand Hetlioz capsule:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **generic tasimelteon** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. **For brand Hetlioz LQ suspension if available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Capsule formulation and liquid formulation will not be used concurrently and will not be used in substitution for each other

8. Individual does not have severe hepatic impairment (Child-Pugh Class C)

9. There are no significant interacting drugs
   a. Strong CYP1A2 inhibitors such as fluvoxamine, others
   b. Strong CYP3A4 inducers such as rifampin, others

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Hetlioz (tasimelteon) capsule and Hetlioz LQ (tasimelteon) suspension, and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met: **(samples are not considered for continuation of therapy)**

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Specialist in Sleep Disorders

  2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
     a. For Non-24-hour sleep wake disorder, **BOTH** of the following:
        i. 45-minute increase in nighttime sleep and 45-minute decrease in daytime sleep
        ii. Entrainment to a 24-hour cycle has been achieved and is maintained
     b. For Smith-Magenis Syndrome, **BOTH** of the following:
        i. Improvement in sleep quality
        ii. Increase in nighttime sleep time

  3. Individual has been adherent with the medication, there must not be any gaps in usage

  4. **For brand Hetlioz capsule:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **generic tasimelteon** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  5. **For brand Hetlioz LQ suspension if available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

  6. Capsule formulation and liquid formulation will not be used concurrently and will not be used in substitution for each other

  7. Individual does not have severe hepatic impairment (Child-Pugh Class C)

  8. There are no significant interacting drugs
     a. Strong CYP1A2 inhibitors such as fluvoxamine, others
     b. Strong CYP3A4 inducers such as rifampin, others

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

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Description:

Hetlioz (tasimelteon) capsules are indicated for the treatment of Non-24-hour Sleep-Wake Disorder (Non-24) in adults and for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients 16 years of age and older. Generic tasimelteon is indicated for the treatment of Non-24-hour Sleep-Wake Disorder (Non-24) in adults.

Hetlioz (tasimelteon) LQ oral suspension is indicated for the treatment of nighttime sleep disturbances in SMS in pediatric patients 3 to 15 years of age.

Tasimelteon is an agonist of melatonin receptors MT1 and MT2; it has greater affinity for the MT2 receptor than the MT1 receptor. Stimulation of MT1 receptors is thought to preferentially induce sleepiness, while MT2 receptor activation preferentially influences regulation of circadian rhythms. Because of individual differences in circadian rhythms the effect of tasimelteon may not be seen for weeks or months.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Diagnostic criteria for non-24-hour sleep-wake rhythm disorder - American Academy of Sleep Medicine. International Classification of Sleep Disorders

Diagnostic criteria A-D must be met:	
A	There is a history of insomnia, excessive daytime sleepiness, or both, which alternate with asymptomatic episodes, due to misalignment between the 24-hour light-dark cycle and the non-entrained endogenous circadian rhythm of sleep-wake propensity.
B	Symptoms persist over the course of at least three months.
C	Daily sleep logs and actigraphy for at least 14 days, preferably longer for blind persons, demonstrate a pattern of sleep and wake times that typically delay each day, with a circadian period that is usually longer than 24 hours.
D	The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

Resources:

Hetlioz (tasimelteon) capsule and Hetlioz LQ (tasimelteon) suspension product information, revised by Vanda Pharmaceuticals, Inc. 12-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 25, 2024.

Tasimelteon capsule product information, revised by Amneal Pharmaceuticals NY, Inc. 01-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 25, 2024.

ORIGINAL EFFECTIVE DATE: 01/22/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/20/2025 | LAST CRITERIA REVISION DATE: 02/15/2024

Goldstein CA. Overview of circadian sleep-wake rhythm disorders. In: UpToDate, Benca R, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2024. Topic last updated December 27, 2023. Accessed January 02, 2025.

Abbott SM. Non-24-hour sleep-wake rhythm disorder. In: UpToDate, Goldstein CA, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2024. Topic last updated February 05, 2024. Accessed January 02, 2025.

Bacino CA. Microdeletion syndromes (chromosomes 12 to 22). In: UpToDate, Firth HV, Tehrani N (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2024. Topic last updated April 15, 2024. Accessed January 02, 2025.

Elsea SH, Girirajan S. Smith-Magenis syndrome. Euro J Human Genetics 2008; 16:412-421. Accessed January 12, 2021. Re-evaluated January 14, 2024. Re-evaluated January 02, 2025.

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. Genetics in Medicine 2021; 23: 2426–2432; https://doi.org/10.1038/s41436-021-01282-y. Accessed January 14, 2024. Re-evaluated January 02, 2025.