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/or 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.

Medical Necessity Requirements for HETLIOZ (tasimelteon) oral capsule, HETLIOZ LQ (tasimelteon) oral suspension, and Tasimelteon oral capsule generic

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in sleep disorders or is in consultation with a specialist in sleep disorders

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Indication

- **ONE** of the following:
  - Non 24 hour sleep wake disorder
  - Smith Magenis Syndrome (SMS)

Age Requirement

- **Non 24 hour sleep wake disorder:** Capsule formulation for 18 years or older
- **Smith Magenis Syndrome (SMS): ONE** of the following:
  - Capsule formulation: 16 years or older
  - Suspension formulation: 3 to 15 years of age

Baseline Clinical Evaluation

- **Non 24 hour sleep wake disorder**
  - Totally blind with no light perception
  - Measurement of urinary melatonin levels
  - Actigraphy performed for greater than 1 week plus evaluation of sleep logs recorded for greater than 1 month
- **Smith Magenis Syndrome**
  - Confirmed deletion 17p11.2 (cytogenetic analysis or microarray) or RAI1 gene mutation identified
  - Nighttime sleep disturbances

Alternative Therapies

- **Non 24 hour sleep wake disorder**
  - Failure (trial for at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for timed melatonin used nightly at the same time (not on an as needed basis)
- **Smith Magenis Syndrome**
  - At least 3 months of acebutolol or metoprolol tartrate in the morning and melatonin at bedtime

Brand Specific Criteria

- **For brands Hetlioz capsule** and **Hetlioz LQ suspension**
  - Failure (trial for at least three months duration), 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)
- **For brand Hetlioz LQ suspension if available**
  - Failure (trial for at least three months duration), 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)

Safety

- Capsule and liquid formulations will not be used concurrently or substituted for each other
- No severe hepatic impairment (Child Pugh Class C)
- No concomitant use of:
  - Strong CYP1A2 inhibitors (e.g., fluvoxamine)

ORIGINAL EFFECTIVE DATE: 01/22/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

- Strong CYP3A4 inducers (e.g., rifampin)

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (urinary melatonin levels, actigraphy data, genetic testing results)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by a physician specializing in sleep disorders or is in consultation with a specialist in sleep disorders

Clinical Response

- **Non 24 hour sleep wake disorder**
  - **BOTH** of the following:
    1. 5 minute increase in nighttime sleep and 45 minute decrease in daytime sleep
    2. Entrainment to a 24 hour cycle has been achieved and is maintained
- **Smith Magenis Syndrome**
  - **BOTH** of the following:
    1. Improvement in sleep quality
    2. Increase in nighttime sleep time

Adherence

- Adherence to the prescribed therapy regimen has been documented; no gaps in usage

Brand Specific Criteria

- **For brand Hetlioz capsule**
  - Failure (trial for at least three months duration), 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)
- **For brand Hetlioz LQ suspension if available**
  - Failure (trial for at least three months duration), 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)

Safety

- Capsule and liquid formulations will not be used concurrently or substituted for each other

- No severe hepatic impairment (Child Pugh Class C)
- No concomitant use of:
  - Strong CYP1A2 inhibitors (e.g., fluvoxamine)
  - Strong CYP3A4 inducers (e.g., rifampin)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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

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

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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 07, 2025.

Tasimelteon capsule product information, revised by Amneal Pharmaceuticals NY, Inc. 01-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 07, 2025.

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 2025. Topic last updated October 27, 2025. Accessed January 21, 2026.

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 2025. Topic last updated October 28, 2025. Accessed January 21, 2026.

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 2025. Topic last updated August 15, 2024. Accessed January 21, 2026.

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 21, 2026.

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 21, 2026.