



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

tasimelteon (Hetlioz)

Policy # 00431

Original Effective Date: 09/17/2014

Current Effective Date: 09/17/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider tasimelteon (Hetlioz) for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for tasimelteon (Hetlioz) will be considered when all of the following criteria are met:

- Patient is totally blind without light perception; and
- Patient has a diagnosis of Non-24-Hour Sleep-Wake Disorder (Non-24), defined as meeting all of the following:
 - o Patient has a history of insomnia, excessive daytime sleepiness, or both, which alternate with asymptomatic episodes, due to misalignment of the 24-hour light-dark cycle and the non-entrained endogenous circadian rhythm of sleep-wake propensity; and
 - o Patient's symptoms persist over the course of at least 3 months; and
 - o Patient sleep logs are submitted (at least 14 days) that demonstrate a pattern of sleep and wake times that typically delay each day, with a circadian period that is usually longer than 24 hours; and
 - o Patient's sleep disturbance is not attributed to another current sleep disorder or other disorder (ie substance abuse, medications, etc); and
- Patient has tried and failed another sleep medication after at least 3 months of use.

*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of tasimelteon (Hetlioz) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary****).

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of tasimelteon (Hetlioz) when a patient has not tried and failed another sleep medication after at least 3 months of use to be **not medically necessary****.

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Background/Overview

Hetlioz is a melatonin agonist that is approved for the treatment of Non-24, also known as Non-24. Hetlioz is dosed at 20mg by mouth prior to bedtime, at the same time every night, and it should be taken without food.

Non-24 is a chronic circadian rhythm disorder that occurs when the endogenous circadian pacemaker is not aligned with the 24-hour clock. The major environmental factor that synchronizes the circadian rhythm is the light-dark cycle, which is detected exclusively by the eyes, and signals are then directed to the suprachiasmatic nuclei (SCN). Exposure to light causes adjustments, or phase shifts, in the circadian rhythm via melatonin. Melatonin synthesis, signaled by the SCN, occurs in the pineal gland. Light causes the SCN to inhibit the production of melatonin and darkness has the opposite effect. In an individual entrained to the 24 hour clock, melatonin levels are typically elevated at night and lower during the day. Melatonin affects the initiation of sleep (via the MT₁ receptor) as well as entrainment (via the MT₂ receptor). In patients without light perception, this "normal" process isn't able to take place. The misalignment causes a gradual shift of the sleep-wake cycle to become out of sync with the 24 hour clock. Hetlioz works in patients with Non-24 to bind to the MT₂ and cause entrainment to the 24 hour clock. Hetlioz also has an affinity to the MT₁ receptor, however the affinity to the MT₂ receptor is much greater.

Non-24 is common in individuals that are totally blind without light perception. Studies have found that 57-70% of blind patients without light perception have Non-24. In totally blind patients without light perception, the endogenous circadian rhythm can range from 24.2-24.5 hours. The diagnosis of Non-24 is mainly clinical, but the International Classification of Sleep Disorders, which is published by the American Academy of Sleep Medicine (AASM), gives guidance on characteristics of the diagnosis. The AASM also released a guideline document that concluded that the use of appropriately timed melatonin has been shown to entrain totally blind patients with Non-24.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Hetlioz was approved in January of 2014 by the FDA for the treatment of Non-24. It is the first product approved for this indication.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Hetlioz was studied in two randomized double-masked, placebo-controlled, multicenter, parallel group studies in totally blind patients with Non-24. In Study 1 (n=84), patients with Non-24 were randomized to receive Hetlioz 20mg or placebo one hour prior to bedtime. The duration and timing of nighttime sleep and daytime naps were evaluated using patient-recorded diaries. At month 1, more patients receiving Hetlioz were entrained (20%) compared with patients randomized to placebo (2.6%, p=0.0171).

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Entrainment is defined as the synchronization of the circadian rhythm of the body to the 24 hour day. In the Hetlioz group, 29% of patients met responder criteria, defined as patients with both a \geq 45 minute increase in nighttime sleep and a \geq 45 minute decrease in daytime nap time, compared with 12% of patients who received placebo.

Study 2 involved patients who received Hetlioz for 12 weeks and became entrained during Study 1. The patients were then randomized to either continue Hetlioz or switch to placebo. Ninety percent of patients who continued Hetlioz remained entrained compared with 20% of patients that were randomized to placebo.

References

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Policy History

Original Effective Date: 09/17/2014
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09/04/2014 Medical Policy Committee review
09/17/2014 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 09/2015



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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. in accordance with nationally accepted standards of medical practice;
- B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.