



**BlueCross BlueShield
of Alabama**

Circadian Rhythm Disorder Prior Authorization with Quantity Limit Program Summary

This program is implemented on the Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Circadian Rhythm Disorder prior authorization criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling. Approvals will be for use in totally blind patients (i.e. no light perception) with Non-24-Hour Sleep-Wake Disorder (Non-24), or another FDA approved indication. Requests for the requested agent will be reviewed when patient-specific documentation is provided.

TARGET AGENTS

Hetlioz® (tasimelteon)

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Limit per day
Hetlioz (tasimelteon)			
20 mg capsule	60250070000130	M, N, O, or Y	1 capsule

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

Hetlioz (tasimelteon) will be approved when ALL of the following are met:

1. ONE of the following:
 - a. The patient has a diagnosis of Non-24-hour sleep-wake disorder AND BOTH of the following:
 - i. The patient is totally blind (i.e. no light perception)
AND
 - ii. The prescriber is a sleep specialist or has consulted with a sleep specialist
OR
 - b. BOTH of the following:
 - i. The patient has another FDA labeled indication
AND
 - ii. The prescriber is a specialist in the area of the patient’s diagnosis or has consulted with a specialist in the area of the patient’s diagnosis
AND
2. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
3. ONE of the following:
 - a. The quantity requested is less than or equal to the program quantity limit
OR
 - b. The quantity (dose) requested is above the program limit, less than or equal to the maximum dose recommended in FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength
OR
 - c. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE¹

Agent	Indication	Dosing and Administration
Hetlioz [®] (tasimelteon) capsules	Treatment of Non-24-Hour Sleep-Wake Disorder (Non-24)	20 mg prior to bedtime, at same time every night Take without food

CLINICAL RATIONALE

Tasimelteon (Hetlioz) is a melatonin receptor agonist indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). Non-24 is a rare, chronic circadian rhythm disorder characterized by the inability to synchronize (entrain) the master body clock with the 24 hour day-night cycle, resulting in significant disruption of the sleep-wake cycle which affects nighttime sleep patterns and causes excessive daytime sleepiness.

Non-24 occurs almost exclusively in people who are deprived of light, which is needed to synchronize the body's internal clock. When light does not enter the eyes, the body cannot synchronize to the 24 hour light-dark cycle. Totally blind is defined as when there is no light perception.⁶⁻⁸ Those affected may have difficulty falling asleep or staying asleep and may wake up feeling as if they need more sleep. Many people may have their sleep patterns reversed, needing to sleep during the day and to be awake at night. Those individuals with Non-24 may experience severe disruptions to essential activities such as school, work, and parenting due to the condition.^{2,3}

Guidelines, Reviews

The American Academy of Sleep Medicine guidelines on treatment of circadian rhythm disorders (AASM, 2015) recommends clinicians use strategically timed administration of melatonin for treatment of Non-24-Hour Sleep-Wake Disorder in blind adults (vs. no treatment) [Weak]. No serious adverse reactions to melatonin have been described to date and therefore benefits of use appear to outweigh any potential harm.⁴

A review on circadian rhythm disorders (American Academy of Neurology, 2013) suggests that melatonin is the therapeutic mainstay in blind patients with Non-24-Hour Sleep-Wake Disorder, together with strong structured behavioral and social cues (e.g., timing of meals, planned activities, and regular physical exercise). Although the dose of melatonin for the treatment of Non-24-Hour Sleep-Wake Disorder varies among studies, a practical recommendation is to start with a higher dose (3 mg to 10 mg) 1 hour before bedtime or a few hours before predicted melatonin onset measured in a dim light environment for the first month. Entrainment usually occurs within 3 to 9 weeks but must be maintained by regular low-dose (0.5 mg) melatonin to prevent a relapse. If the initiation dose fails, an alternate method is a 0.5-mg dose over a period of several months. Most blind patients whose circadian period is close to 24 hours can maintain entrainment with very low nightly doses of 20 µg to 300 µg. Evidence from case reports suggests that a combination of timed melatonin doses of 0.5 mg to 5.0 mg taken nightly at 9:00 PM, exposure to bright light, and a regular sleep-wake schedule is successful in entraining these patients.³

An evidence base review suggested appropriately timed melatonin, in doses from 0.5 mg to 10 mg, have been shown to entrain totally blind people who have Non-24-Hour Sleep-Wake Disorder. The effective dose may be even less than 0.5 mg (the dose that approximates a physiological plasma concentration). Treatment must be sustained or relapse will occur. Entrainment may not occur for weeks or months after initiating treatment, depending on the phase of the patient's rhythm when treatment is started and the period of the patient's free-running rhythm.⁵

Safety

Tasimelteon has no FDA labeled contraindications or black box warnings.

REFERENCES

1. Hetlioz prescribing information. Vanda Pharmaceuticals Inc. December 2014.
2. Shirani A, St. Louis EK. Illuminating rationale and uses for light therapy. *J Clin Sleep Med*. 2009;5(2):155-163.
3. Zee P, Attarian H, Videnovic A. Circadian rhythm disorders. *Continuum* (Minneapolis, Minn). American Academy of Neurology. 2013;19(1):132-147.
4. American Academy of Sleep Medicine (AASM). Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders. 2015. [Draft] Accessed 10.6.2015 at: <http://www.aasmnet.org/resources/doc/TreatmentofIntrinsicCRSWDsDraftGuideline.pdf>
5. Sack R, Auckley D, Auger R, et al. Circadian rhythm-sleep disorders: part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. An American Academy of Sleep Medicine Review. *Sleep*. 2007;30(11):1484-1501.
6. American Foundation of Blindness. Low Vision and Legal Blindness Terms and Descriptions. Accessed 01/28/2015. <http://www.visionaware.org/info/your-eye-condition/eye-health/low-vision/low-vision-terms-and-descriptions/1235#TotalBlindness>
7. International Council of Ophthalmology. Visual Standards: Aspect and Ranges of Vision Loss with Emphasis on Population Surveys. Accessed 01/28/2015. <http://www.icoph.org/downloads/visualstandardsreport.pdf>
8. American Academy of Ophthalmology. Accessed 01/28/2015 <http://www.aao.org/aaof/coding/upload/visionrehabilitationcm2012.pdf>.

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