Medical Policy

BlueCross BlueShield of Kansas
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Title: Circadian Rhythm Disorder

- **Prime Therapeutics will review Prior Authorization requests**

Prior Authorization Form:
http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6341KS-HETL.pdf

Link to Drug List (Formulary):
https://www.bcbsks.com/drugs/

Professional
Original Effective Date: September 1, 2015
Revision Date(s): September 1, 2015; June 1, 2016; July 1, 2017; June 15, 2018
Current Effective Date: June 15, 2018

Institutional
Original Effective Date: September 1, 2015
Revision Date(s): September 1, 2015; June 1, 2016; July 1, 2017; June 15, 2018
Current Effective Date: June 15, 2018

DESCRIPTION

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 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)

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

POLICY

Prior Authorization and Quantity Limits Criteria for Approval

Hetlioz (tasimelteon)will be approved when **ALL** of the following is 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 indications
      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

Length of Approval: 12 months

FDA Labeled Contraindications	
Agent	**Contraindications**
Hetlioz (tasimelteon)	None

Program Quantity Limits	
Brand (generic)	**Quantity Limit Per Day**
Hetlioz (tasimelteon)	
20 mg capsule	1 capsule

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.

REVISIONS

09-01-2015	Policy added to bcbsks.com on 08-25-2015 and effective 09-01-2015.
06-01-2016	Policy title change to "Circadian Rhythm Disorder" from "Hetlioz (tasimelteon)"
	Description section updated
	In Policy section: ▪ Added Item 1 added "ONE of the following:" ▪ Removed "The patient is greater than or equal to 18 years of age" ▪ Added Item 1 a "ALL of the following for Non-24-hour sleep wake disorder:" ▪ In Item 1 a i added "totally" and "(i.e. no light perception)" and removed "legally" to read "The patient is totally blind (i.e. no light perception)" ▪ Added b. "ALL of the following: i. The patient has another FDA labeled indications 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" ▪ In Item 2 added "the requested agent" and removed "therapy with Hetlioz (tasimelteon)" to read "The patient does not have any FDA labeled contraindications to the requested agent" ▪ Added 4 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"
	Rationale section updated
	References updated
07-01-2017	Description section updated
	In Policy section: ▪ In Item 1 a added "The patient has a diagnosis of" and "AND BOTH" and removed "ALL" to read "The patient has a diagnosis of Non-24-hour sleep-wake disorder AND BOTH ALL of the following:" ▪ Removed "The patient does not have severe hepatic impairment (Child-Pugh Class C)"
	Rationale section updated
	References updated
06-15-2018	Description section updated
	In Policy section ▪ In Policy header added "(tasimelteon)" to read "Hetlioz (tasimelteon) will be..."

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* (Minneap Minn). American Academy of Neurology. 2013;19(1):132-147.
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