**Medication Policy Manual**

**Policy No:** dru349

**Topic:** Hetlioz®, tasimelteon (Hetlioz)

**Date of Origin:** May 9, 2014

**Committee Approval Date:** April 8, 2016

**Next Review Date:** April 2017

**Effective Date:** May 1, 2016

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Tasimelteon (Hetlioz) is an oral, self-administered medication similar to melatonin used to manage poor sleep patterns and daytime sleepiness due to disruptions in circadian rhythms (“master body clock”), in people who are blind. This condition is sometimes referred to as free-running disorder (FRD) or Non-24-Hour Sleep-Wake Disorder (“Non-24”).
Policy/Criteria

I. Most contracts require prior authorization approval of tasimelteon (Hetlioz) prior to coverage. Tasimelteon (Hetlioz) may be considered medically necessary in patients when criteria A through E below are met.
   
   A. The patient has total blindness without light perception.

   AND

   B. A diagnosis of free-running disorder (FRD), also known as Non-24-Hour Sleep-Wake Disorder (“Non-24”).

   AND

   C. Specific measurable functional impairment due to FRD or “Non-24” is present.

   AND

   D. Documentation is provided that other therapies have been inadequate in improving functional impairment. Examples include, but are not limited to, timed melatonin administration and planned social and physical activities.

   AND

   E. Treatment with one prescription medication used for sleep has been inadequate or not tolerated. (See Appendix 1)

II. Administration, Quantity Limitations, and Authorization Period

   A. OmedaRx considers tasimelteon (Hetlioz) to be a self-administered medication.

   B. When prior authorization is approved, tasimelteon (Hetlioz) may be authorized in quantities of up to thirty 20-mg capsules per 30 days.

   C. Authorization shall be reviewed as follows to confirm that medical necessity criteria are met and that the medication is effective.

   1. Initial authorization shall be reviewed at 6 months.

   2. Continued authorization or re-authorization (after the initial 6 month period) shall be reviewed at least annually.

III. Tasimelteon (Hetlioz) is considered not medically necessary when used in sighted individuals or blind individuals with light perception.

IV. Tasimelteon (Hetlioz) is considered investigational when used for all other conditions including, but not limited to:

   A. Jet lag disorder.

   B. Shift work sleep disorder.

   C. Major depressive disorder.
Position Statement

- Tasimelteon (Hetlioz) is an oral, self-administered melatonin receptor agonist indicated for managing poor sleep patterns and daytime sleepiness due to disruptions in circadian rhythms (“master body clock”), in people who are blind. This condition is sometimes referred to as free-running disorder (FRD) or Non-24-Hour Sleep-Wake Disorder (“Non-24”).

- It is estimated that approximately 80,000 to 100,000 totally blind individuals in the United States may have FRD.[1]

- The efficacy of tasimelteon (Hetlioz) was evaluated in two clinical trials in 104 totally blind patients. It resulted in a minor improvement in the duration of nighttime sleep and reduction of the duration of daytime napping.

- Although this is a disorder of circadian rhythm, these endpoints did not demonstrate that tasimelteon (Hetlioz) improved circadian rhythm function. Thus, it is reasonable to attempt all feasible modalities where a potential benefit exists (such as prescription medications used for sleep).

- Therapies such as timed melatonin administration and planned social and physical activities are recommended by guidelines and sleep specialists for treatment of FRD in blind individuals.

- Tasimelteon (Hetlioz) has not been evaluated for the treatment of FRD in sighted individuals or blind individuals with light perception.

- Tasimelteon (Hetlioz) can potentially impair the performance of activities requiring complete mental alertness. After taking tasimelteon (Hetlioz), patients should limit their activity to preparing for going to bed.

- The recommended dosage of tasimelteon (Hetlioz) is 20 mg (one capsule) per day taken before bedtime, at the same time every night.

Clinical Efficacy

FRD IN BLIND INDIVIDUALS WITHOUT LIGHT PERCEPTION

- The efficacy of tasimelteon (Hetlioz) was evaluated in two randomized, double-blind, placebo-controlled, parallel group studies in 104 totally blind patients with poor sleep patterns and daytime sleepiness due to disruptions in circadian rhythms (“master body clock”).[2,3]

- Treatment with tasimelteon (Hetlioz) 20 mg one hour prior to bedtime, at the same time every night, improved the duration of nighttime sleep by 28 minutes and reduced the duration of daytime napping by 27 minutes, while each worsened when treatment was withdrawn.
  
  o Although this is a disorder of circadian rhythm, these endpoints did not demonstrate that tasimelteon (Hetlioz) improved circadian rhythm function.
  
  o Due to uncertain benefit, it is reasonable to attempt all feasible modalities where a potential benefit exists (such as prescription medications used for sleep).
- Therapies such as timed melatonin administration, and planned social and physical activities are recommended for treatment of FRD in blind individuals.
  
  o Timed melatonin administration is a “guideline” recommendation by the American Academy of Sleep Medicine [4] and reflects a moderate degree of clinical certainty based on four case reports [5-8] and five cohort studies or clinical trials [9-13].
  
  o Timed exposure to non-photic entraining agents, such as planned social and physical activities, is also recommended for blind people with FRD. [14]

FRD IN SIGHTED INDIVIDUALS OR BLIND INDIVIDUALS WITH LIGHT PERCEPTION
- The trials submitted as evidence for efficacy of tasimelteon (Hetlioz) in FRD did not include sighted individuals or blind individuals with light perception. [2]

OTHER USES
- A phase II/III single-dose trial of tasimelteon (Hetlioz) for transient insomnia following a 5-hour sleep-time shift induced in healthy individuals in a sleep lab demonstrated “increased sleep efficiency” compared to placebo. [15] Trials of longer duration are necessary to establish safety and effectiveness in this population.
- A phase II/III trial evaluating tasimelteon (Hetlioz) for major clinical depressive disorder did not meet its primary endpoint of change from baseline in the Hamilton Depression Scale (HAMD-17) after 8 weeks of treatment as compared to placebo.

Safety
- The most common adverse reactions (incidence > 5% and at least as twice as high on tasimelteon (Hetlioz) than on placebo) were headache, increased liver enzymes, nightmares or unusual dreams, and upper respiratory or urinary tract infection.
- Exposure to tasimelteon (Hetlioz) is two-fold higher in older patients than younger patients, but no overall differences in safety or efficacy were observed in older patients.
- Mean overall exposure is 20-30% greater in females than in male subjects, but the significance of this is unknown. No differences in safety or efficacy were observed between females and males.

Dosing and Administration Considerations
- The recommended dosage of tasimelteon (Hetlioz) is 20 mg per day taken before bedtime, at the same time every night.
- Due to individual differences in circadian rhythms, daily use for several weeks or months may be necessary before benefit from tasimelteon (Hetlioz) is observed.
- Tasimelteon (Hetlioz) should be taken on an empty stomach.
- After taking tasimelteon (Hetlioz), patients should limit their activity to preparing for going to bed. Tasimelteon (Hetlioz) can potentially impair the performance of activities requiring complete mental alertness.
Appendix 1: Prescription Medications Used for Sleep [16]

**Benzodiazepines**

- estazolam
- flurazepam
- lorazepam
- temazepam
- triazolam
- quazepam

**Non-Benzodiazepines**

- doxepin
- eszopiclone
- zaleplon
- zolpidem immediate-release
- zolpidem sublingual (Edluar, Intermezzo)
- zolpidem extended-release
- zolpidem oral spray (ZolpiMist)

**Melatonin Agonists**

- ramelteon (Rozerem)

Cross References

None

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<td>ICD-9</td>
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References


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