Washington State Health Care Authority

Sleep Disorder Agents – Hetlioz (tasimelteon)

Medical policy no. 60.25.00.AA-1 Effective Date: 06/01/2024

Related medical policies:

Policy Name	Indications
N/A	N/A

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
tasimelteon (Hetlioz and Hetlioz LQ)	**Hetlioz (tasimelteon)** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Non-24-Hour Sleep-Wake Disorder (N24SWD) in adults tasimelteon capsules (Hetlioz)	Tasimelteon capsules (Hetlioz) may be approved when all of the following criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, a psychiatrist, neurologist, or sleep specialist; **AND** 3. Diagnosis of N24SWD defined as: a. History of insomnia or excessive daytime sleepiness alternating with asymptomatic episodes; **AND** b. Symptoms have persisted for at least 3 months; **AND** c. Documentation of gradually shifting sleep-wake times demonstrated by daily sleep logs or actigraphy for at least 14 consecutive days; **AND**

	4. Patient is blind in both eyes without light perception; **AND** 5. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Tasimelteon (Hetlioz) may be approved when all of the following criteria are met: 1. Documentation is submitted demonstrating positive clinical response from prior to initiating treatment with Hetlioz [e.g., Patient is maintaining regular or improved sleep intervals as documented by sleep logs, actigraphy, or medical records]; **AND** 2. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs. If ALL criteria are met, the request will be authorized for **12 months.**
Nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) tasimelteon capsules (Hetlioz) tasimelteon suspension (Hetlioz LQ)	Tasimelteon (Hetlioz and Hetlioz LQ) may be approved when all of the following criteria are met: 1. The patient meets the following age requirements: a. The patient is 16 years or older and the request is for tasimelteon (Hetlioz) capsules; **OR** b. The patient is 3 to 15 years old and the request is for tasimelteon (Hetlioz LQ) suspension; **AND** 2. Prescribed by, or in consultation with, a psychiatrist, neurologist, or sleep specialist; **AND** 3. Diagnosis of Smith-Magenis Syndrome (SMS) confirmed by one of the following: a. A heterozygous deletion of RAI1 on chromosome 17p11.2; **OR** b. Presence of a pathogenic variant involving RAI1 on chromosome 17p11.2; **AND** 4. Documentation of sleep disturbances (e.g frequent nocturnal arousals, early morning awakenings, daytime sleep attacks, inability to fall asleep); **AND**

	5. History of failure, contraindication, or intolerance to both (a and b) of the below (together or separately). Failure is defined as the inability to improve symptoms after 30 days. **a.** A beta-1 selective blocker (e.g. acebutolol)**; AND** b. At least one additional medication used to promote sleep (e.g ramelteon, clonidine, trazodone, diphenhydramine etc.); **AND** 6. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Tasimelteon (Hetlioz and Hetlioz LQ) may be approved when all of the following criteria are met: 1. Documentation is submitted demonstrating a positive clinical response from prior to initiating treatment with Hetlioz [e.g., improved sleep quality, decreased nighttime awakening, increased sleep time]; **AND** 2. Patients 17 years of age or younger require a second opinion review with the agency-designated mental health specialist from the Second Opinion Network (SON) when one of the following is met: a. The patient is prescribed five or more mental health drugs. If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Hetlioz **tasimelteon (generic)**	Non-24-Hour Sleep-Wake Disorder (N24SWD) in adults	20 mg orally once daily	• Capsule, 30 caps per 30 days
Hetlioz **tasimelteon (generic)**	Nighttime sleep disturbances in Smith-Magenis Syndrome (SMS)	20 mg orally once daily	• Capsule, 30 caps per 30 days

Hetlioz LQ	Nighttime sleep disturbances in Smith-Magenis Syndrome (SMS)	0.7 mg/kg orally daily (28 kg or less) 20 mg orally daily (greater than 28 kg)	• Suspension, 158 mL per 30 days

Coding:

HCPCS Code	Description
N/A	N/A

Background:

Non-24-Hour Sleep-Wake Disorder (N24SWD) occurs when individuals are unable to entrain to a regular 24-hour sleep-wake cycle.[1] This results in a progressively shifting sleep time that creates excessive sleepiness in the daytime and insomnia in the nighttime. Most individuals affected by N24SWD are totally blind without light perception. Per the 2015 American Academy of Sleep Medicine (AASM) guideline on the treatment of intrinsic circadian rhythm disorders, first line treatment is strategically timed melatonin.[1] The guidelines were unable to conclude that sleep promoting medications, light therapy, or other treatment options were effective in N24SWD. Two case reports encompassing three sighted individuals demonstrate that ramelteon may be effective for N24SWD, however, there is no evidence for its use in totally blind individuals.[2,3]

Hetlioz (tasimelteon) is the only medication approved by the FDA for the treatment of N24SWD.[4] It was approved based on two consecutive placebo-controlled trials involving totally blind adults aged 18 to 75 years (SET and RESET trials).[5] The SET trial randomized 84 participants to receive tasimelteon or placebo and were evaluated for entrainment (a circadian period of 24.1 hours or less). At one month circadian entrainment occurred in 20% and 3% of participants taking tasimelteon and placebo, respectively. The RESET trial evaluated 20 participants who had entrained while taking tasimelteon and randomized 10 to continue use and 10 to withdraw to placebo. After 4 weeks, 90% of participants who remained on tasimelteon were entrained while only 20% of participants withdrawn to placebo were entrained.[5] Hetlioz has not been compared to any other treatment option (e.g, melatonin); therefore, the comparative safety and efficacy is unknown.

Smith-Magenis Syndrome is a genetic disorder caused from the deletion or mutation of the RAI1 gene on chromosome 17p11.2.[6] It results in congenital anomalies, intellectual disability, behavioral challenges, and often sleep disturbances (e.g. frequent nocturnal arousals, early morning awakenings, and sleep attacks during the day). Sleep disturbances can exacerbate existing behavioral challenges. While there is very little robust clinical evidence to guide the treatment in this setting, several approaches have been used with at least moderate success. These include standard sleep hygiene practices, melatonin, ramelteon, acebutolol[6], and a variety of other sleep medications.[7]

Hetlioz (tasimelteon) is the only FDA-approved medication for sleep disturbances specific to the setting of Smith-Magenis Syndrome.[4] It was approved based on a double-blind, randomized, crossover study among 25 participants age 3 to 39 with genetically confirmed Smith-Magenis Syndrome.[8] Tasimelteon statistically improved sleep quality and sleep duration during the worst 50% of nights compared to placebo, however, clinical benefit remains questionable. Once again, Hetlioz has not been compared to any other treatment option (e.g, melatonin); therefore, the comparative safety and efficacy is unknown.[8]

Tasimelteon was associated with increased rates of headache, increased ALT levels, nightmares, upper respiratory tract infections, and urinary tract infections compared to placebo in clinical trials.[4]

References

1. Auger RR, Burgess HJ, Emens JS, Deriy LV, Thomas SM, Sharkey KM. Clinical practice guideline for the treatment of intrinsic circadian rhythm sleep-wake disorders: advanced sleep-wake phase disorder (Aswpd), delayed sleep-wake phase disorder (Dswpd), non-24-hour sleep-wake rhythm disorder (N24swd), and irregular sleep-wake rhythm disorder (Iswrd). An update for 2015: an american academy of sleep medicine clinical practice guideline. J Clin Sleep Med. 2015;11(10):1199-1236.
2. Watanabe A, Hirose M, Arakawa C, Iwata N, Kitajima T. A case of non-24-hour sleep-wake rhythm disorder treated with a low dose of ramelteon and behavioral education. *J Clin Sleep Med.* 2018;14(7):1265–1267.
3. Williams WPT, McLin DE, Dressman MA, Neubauer DN. Comparative review of approved melatonin agonists for the treatment of circadian rhythm sleep-wake disorders. Pharmacotherapy. 2016;36(9):1028-1041.
4. Hetlioz [Prescribing Information]. Washington, DC: Vanda Pharmaceuticals Inc. December 2020
5. Lockley SW, Dressman MA, Licamele L, et al. Tasimelteon for non-24-hour sleep-wake disorder in totally blind people (Set and reset): two multicentre, randomised, double-masked, placebo-controlled phase 3 trials. Lancet. 2015;386(10005):1754-1764.
6. De Leersnyder H, de Blois MC, Vekemans M, et al. Beta(1)-adrenergic antagonists improve sleep and behavioural disturbances in a circadian disorder, smith-magenis syndrome. J Med Genet. 2001;38(9):586-590.
7. Kaplan KA, Elsea SH, Potocki L. Management of sleep disturbances associated with smith-magenis syndrome. CNS Drugs. 2020;34(7):723-730.
8. 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. Genet Med. 2021;23(12):2426-2432.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
12/13/2023	06/01/2024	60.25.00.AA-1	Approved by DUR Board -New policy created