Original Effective Date: 04/01/2016
Current Effective Date: 06/21/2023
Last P&T Approval/Version: 04/26/2023
Next Review Due By: 04/2024
Policy Number: C8920-A

Hetlioz (tasimelteon)

PRODUCTS AFFECTED

Hetlioz (tasimelteon), Tasimelteon

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Diagnosis of Non-24-Hour Sleep-Wake Disorder

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. NON-24 HOUR SLEEP-WAKE DISORDER (N24SWD):
   1. Documented diagnosis of Non-24-Hour Sleep- Wake Disorder
      AND
   2. Member is totally blind; defined by the inability to perceive light (completely blind with NO light perception). Documentation confirming member's total blindness

*** Hetlioz has not been studied in patients with N24SWD with light perception
AND

3. Prescriber attestation that member's sleep disturbance is not attributed to concomitant sleep disorder (i.e., sleep apnea, insomnia), medical or neurological disorder, mental disorder, medication use, or substance abuse disorder
   AND
4. History of failure* of at least 6 months of continuous therapy (i.e., uninterrupted daily treatment) or contraindication or intolerance to melatonin
   * Failure defined as: Lack of improvement in overall sleep quality or inadequate results (e.g., entrainment, clinically meaningful or significant increases in nighttime sleep, clinically meaningful or significant decreases in daytime sleep)
   AND
5. Prescriber attests that Hetlioz (tasimelteon) will not be used concurrently with melatonin or ramelteon (Rozerem), Strong CYP1A2 inhibitors (e.g., fluvoxamine) OR Strong CYP3A4 inducers (e.g., rifampin)
   AND
6. FOR BRAND NAME CAPSULE REQUESTS: Documentation of trial and failure of the generic AND Documentation the member experienced a documented adverse drug reaction with the generic agent (e.g., rash, anaphylaxis) that is NOT a known side effect of the medication and/or the prescriber has submitted a completed FDA MedWatch form [DOCUMENTATION REQUIRED]

B. NIGHTTIME SLEEP DISTURBANCES WITH SMITH-MAGENIS SYNDROME:

1. Documented diagnosis of Smith-Magenis syndrome
   AND
2. History of failure* of at least 6 months of continuous therapy (i.e., uninterrupted daily treatment) or contraindication or intolerance to melatonin
   *Failure defined as: Lack of improvement in overall sleep quality or inadequate results (e.g., entrainment, clinically meaningful or significant increases in nighttime sleep, clinically meaningful or significant decreases in daytime sleep)
   AND
3. Prescriber attests that Hetlioz (tasimelteon) will not be used concurrently with melatonin or ramelteon (Rozerem), Strong CYP1A2 inhibitors (e.g., fluvoxamine) OR Strong CYP3A4 inducers (e.g., rifampin)
   AND
4. FOR BRAND NAME CAPSULE REQUESTS: Documentation of trial and failure of the generic AND Documentation the member experienced a documented adverse drug reaction with the generic agent (e.g., rash, anaphylaxis) that is NOT a known side effect of the medication and/or the prescriber has submitted a completed FDA MedWatch form [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. ALL INDICATIONS

1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
   AND
2. Documented positive response or improvement on therapy of overall sleep quality (based on objective evaluation of the member's sleep quality) including but not limited to entrainment, significant increase in nighttime sleep, and/or significant decreases in daytime sleep
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a neurologist, board-certified sleep medicine specialist OR physician who specializes in the treatment of sleep disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
Non-24: 18 years and older
Smith-Magenis Syndrome: 3 years and older

QUANTITY:
Age ≥16 years: 20 mg daily; Dispensing limit: Only a one month supply may be dispensed at a time (#30 capsules per 30 days)
Age 3 to 15 years, >28 kg: 20 mg (5 mL) daily; Dispensing limit: Only a one month supply may be dispensed at a time (158 mL per month)
Age 3 to 15 years, ≤28 kg: 0.7 mg/kg daily; Dispensing limit: Only a one month supply may be dispensed at a time. *Note: Suspension available in 48 mL bottle (discard 5 weeks after opening) and 158 mL bottle (discard 8 weeks after opening).*

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Selective Melatonin Receptor Agonists

FDA-APPROVED USES:
HETLIOZ capsules are indicated for the treatment of:
- Non-24-Hour Sleep-Wake Disorder (Non-24) in adults
- Nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients 16 years of age and older

HETLIOZ LQ oral suspension is indicated for the treatment of:
- Nighttime sleep disturbances in SMS in pediatric patients 3 years to 15 years of age

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Smith-Magenis Syndrome (SMS).

December 2020 the Food and Drug Administration (FDA) approved Hetlioz® (tasimelteon; Vanda)for the treatment of adults and pediatric patients with nighttime sleep disturbances associated with Smith- Magenis Syndrome (SMS).

The approval was based on data from a 9-week, double-blind, placebo-controlled, crossover study which assessed the effects of Hetlioz in patients with SMS. The study included two 4-week periods, separated by a 1-week washout interval. Patients aged 16 years and older received Hetlioz 20mg capsules, and patients aged 3 to 15 years received a weight-based dose of oral suspension. The primary end points were nighttime total sleep time and nighttime sleep quality from a parent/guardian-recorded diary; efficacy comparisons were based on the 50% of nights with the worst sleep quality and the 50% of nights with the least nighttime sleep in each 4-week period.

Results showed that treatment with Hetlioz was associated with a statistically significant improvement in the 50% worst nights' sleep quality compared with placebo. While Hetlioz demonstrated improvements in the 50% worst total nighttime sleep time, the difference was not found to be statistically significant. The safety profile of Hetlioz was similar to that seen in previous studies for non-24-hour sleep-wake disorder. Hetlioz 20mg capsules are indicated for the treatment of nighttime sleep disturbances in patients 16years of age and older with SMS. Hetlioz LQ oral suspension, supplied as 4mg/mL in 48mL and 158mL bottles, is indicated for the treatment of nighttime sleep disturbances in pediatric patients 3 to 15 years of age with SMS.

Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD)

(also known as free-running disorder, free- running or non-entrained type circadian rhythm sleep disorder, or hyper nychthemeral syndrome) is a chronic primary circadian rhythm sleep disorder (CSRD) that alters sleep patterns, causes daytime sleepiness, and results in impaired social and occupational functioning. Non-24 occurs primarily among blind individuals, though some sighted persons have the disorder also. Most blind individuals perceive enough light to prevent non-24; however, some have no light perception. Since light cannot enter their eyes, people with N24SWD cannot synchronize or "entrain" the suprachiasmatic nucleus. The presence of light in the daytime stimulates the SCN to inhibit melatonin secretion from the pineal gland, while the absence of light at night stimulates melatonin secretion. Thus, in absence of any light, the SCN cannot set the circadian "body clock" to a 24-hour light-dark cycle. N24SWD is a circadian rhythm disorder occurs most commonly in blind patients with no light perception. It occurs when the individual's own biologic circadian period is not aligned to the external 24- hour environment. External cues, primarily the light/dark cycle which normally entrains the circadian rhythm to the 24-hour clock is absent in individuals with no light perception. Due to absence of input from environmental light to the eyes in patients with no light perception, it causes a constant gradual shifting of the sleep-wake cycle approximately 30 minutes each day thus returning to re- alignment with the 24- hour clock only once every 48 days. Due to the lack of entrainment of the circadian rhythm, patients with no light perception suffer from sleep deprivation resulting in long periods of excessive daytime sleepiness, nighttime insomnia, alterations in secretion of melatonin and cortisol, and impairment of social and occupational functioning.

There are approximately 1,300,000 blind people in the United States. Ten percent of these individuals have no light perception. The estimated prevalence of non-24 in the totally blind is approximately 100,000 individuals in the U.S. Disturbances in people who are blind are common, and approximately 50% may have Non-24 according to the American Academy of Neurology.

Diagnosis

The American Academy for Sleep Medicine CSRD practice parameters recommend (based on consensus) sleep logs to determine sleep patterns and also recommend measurement of circadian phase markers (including the urinary biomarker 6-sulfatoxy-melatonin or aMT6s) to determine the

circadian phase (τ) and confirm the diagnosis. Entrainment is a measure of synchronization of an individual's intrinsic master clock (τ) to the 24-hour day. Entrainment can be measured by 2 distinct circadian rhythms: melatonin (or aMT6s in urine),and cortisol. For aMT6smeasurement, urine is collected every 4 hours (every 8 hours overnight) over a 48- hour period and the acrophase, or peak timing of analyte secretion, determined. Quartile-nighttime Total Sleep Time(LQ-nTST), Upper Quartile-daytime Total Sleep Duration (UQ-dTSD), Midpoint of Sleep Time (MoST), and Clinician Global Impression-Change (CGI-C) assessments. Q-nTST and UQ-dTSD correlate with the most symptomatic phases of circadian cycle (maximum misalignment), reflecting the 25% most symptomatic days of nighttime sleeplessness or daytime sleepiness, respectively. The CGI-C is a 7-point clinician-performed evaluation of global functioning ranging from 1 (very much improved) to 7 (very much worse). Each assessment on the scale is scored as a 1 or 0 depending on whether the prespecified threshold was achieved or not. The score for each assessment is summarized with a range of 0 to 4.

Pivotal Trials

Efficacy for tasimelteon consists of 2 distinct pivotal trials called SET (N=84) and RESET (N=20).Both were randomized, placebo-controlled, double-blind trials with an overlapping patient population in totally blind patients with a diagnosis of Non-24.[a]

- Study 1 and Study 2 evaluated the duration and timing of nighttime sleep and daytime naps via patient- recorded diaries. • Because symptoms of nighttime sleep disruption and daytime sleepiness are cyclical in patients with Non-24, with severity varying according to the state of alignment of the individual patient's circadian rhythm with the 24-hour day (least severe when fully aligned, most severe when 12 hours out of alignment), efficacy endpoints for nighttime total sleep time and daytime nap duration were based on the 25% of nights with the least nighttime sleep, and the 25% of days with the most daytime nap time. • Treatment with tasimelteon resulted in an improvement, compared with placebo, for both of these end points in both SET and RESET. • Tasimelteon was generally well- tolerated in SET and RESET. Adverse effects that occurred in at least 5% of patients in the tasimelteon group and at a two-fold higher rate than placebo were headache (17% vs. 7%), increased alanine aminotransferase (10% vs. 5%),

nightmare/abnormal dreams (10% vs. 0%), upper respiratory tract infection (7% vs. 0%), and urinary tract infection (7% vs. 2%). There were no withdrawal symptoms, next day residual effect, or increase in suicidality observed in patients receiving tasimelteon.

Study 1: SET (Safety and Efficacy of Tasimelteon)

Randomized, double-blind, placebo-controlled, multicenter, phase 3 study

The SET trial evaluated Hetlioz in 84 patients with non-24 compared tasimelteon and placebo for 6 months.; 84 patients (n=84) with non-24-hour sleep-wake disorder (median age, 54 years) were randomized to receive tasimelteon 20 mg or placebo, one hour prior to bedtime, at the same time every night for up to 6 months.[a]

Design: Phase III, multicenter, randomized, double-masked, placebo-controlled trial conducted between August 2010 and October 2012. Patients ineligible for randomization or unable to complete the trial could elect to participate in the open-label extension phase.

Objective: To investigate the safety and efficacy of tasimelteon in patients with Non-24 Population:84 totally blind patients, 18 to 75 years of age, with confirmed Non-24 6- sulfatoxy melatonin rhythms (tau at least 24.25 hours) and history of sleep disturbance. Mean age was 50.7 years (range, 23 to 74 years), 83% were white, and 58% were male. Mean tau was 24.47 hours (circadian cycle lengths ranged from 30 to 114 days corresponding to tau 24.21 to 24.8 hours). Average nighttime sleep time was 3.25 hours in the worst 25% of nights (lower quartile of nighttime total sleep time [LQ-nTST]) and 5.33 hours overall and average daytime sleep time was 2.41 hours in the worst 25% of days (upper quartile of daytime total sleep duration [UQ-dTSD]) and 0.92 hours overall.

Primary endpoint: Significantly more patients treated with tasimelteon 20mg (8/40) compared to placebo (1/38) achieved entrainment measured by aMT6s in one month (20% vs 2.6%, p=0.0171) Result: Significantly more tasimelteon-treated patients (20% vs. 3%) achieved entrainment (synchronization) of the circadian rhythm as measured by urine levels of a melatonin metabolite. Mean total nighttime sleep was 28

minutes longer and daytime nap time was 27 minutes shorter inpatients taking tasimelteon than in patients taking placebo.1 In totally blind patients, tasimelteon, compared with placebo, significantly increased nighttime sleep (50 vs. 22 minutes) and significantly decreased daytime napping (49 vs. 22 minutes) compared with baseline. The duration and timing of night-time 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). Twenty-two patients did not complete the study: adverse events (n=6), protocol deviation (n=1), withdrawal of consent (n=5), and unsatisfactory response (n=1); travel issues (n=1); study closed by sponsor, but patients had adequate data for primary and secondary endpoints in the double- masked phase (n=8; 4-tasimelteon; 4 placebo).

Adverse reactions with tasimelteon compared with placebo included headache (17% vs. 7%), increased ALT (10% vs. 5%), abnormal dreams (10% vs. 0%), upper respiratory tract infection (7% vs. 0%), and urinary tract infection (7% vs. 2%).

- Entrainment of the circadian rhythm to a 24-hour day was achieved in 20% of the patients taking tasimelteon compared to 2.6% with placebo as measured by aMT6s by the first month. Assessing entrainment early per trial design may underestimate the entrainment rate effect.
- Entrainment of the circadian rhythm to a 24-hour day was achieved in 17.5% of the patients taking tasimelteon compared to 2.6% with placebo as measured by cortisol by the first month.
- Tasimelteon had a clinically meaningful improvement as measured by the assessment of clinical response and the Non-24 Clinical Response Scale • Tasimelteon once daily was generally well-tolerated and safe in the studied population. The majority of adverse events were mild or moderate and discontinuation due to adverse events was similar between treatment groups. *Study 2: RESET (Randomized withdrawal study of the Efficacy and Safety of Tasimelteon)* Randomized, double-blind, placebo-controlled, multicenter, phase 3 study

Design: Phase III, multicenter, randomized withdrawal, double-masked, placebo- controlled, parallel group designed to determine the long-term maintenance effect and safety of tasimelteon 20mg in patients with Non-24. The study consisted of two phases: 1) open label pre-randomization phase (~12 weeks), and 2) placebo-controlled randomized withdrawal phase (~8 weeks).

Objective: Demonstrate effectiveness and safety of tasimelteon 20mg in maintaining entrainment when treatment was withdrawn.

Population: Patients meeting inclusion criteria and who had previously participated in, or were screened for SET trial, were eligible to participate. Twenty entrained totally blind individuals (as defined by aMT6 rhythms) were randomized (aged 27-68 years; (mean age 51.7years; 60% male;90% Caucasian, 5% African American, mean BMI 28.64 kg/m2; mean circadian rhythm= 24.0 hours). No demographic or patient characteristics differences between the two groups exist.

Primary End Point(s): • The primary endpoint of the RESET to treat N24SWD was the proportion of patients who did not maintain entrainment of an aMT6s rhythm to 24 hours after therapy was withdrawn. Twenty blind patients (median age 54 years) with N24SWD were randomized. • The discontinuation of therapy following achievement of entrainment caused a loss in circadian rhythm synchronization in 80% of patients within 8 weeks.

In totally blind patients treated with tasimelteon, continued maintenance therapy with tasimelteon, compared with placebo, produced significant differences in nighttime sleep (-7 vs. -74 minutes) and daytime napping (-9 vs. +50 minutes) compared with baseline.

Conclusion • Discontinuation of tasimelteon therapy resulted in a loss of entrainment that corresponded with an approximately 50-minute decrease in nighttime sleep and 60-minute increase in daytime napping. • Chronic therapy with tasimelteon is required to maintain entrainment in totally blind patients with Non-24

GUIDELINES

The International Classification of Sleep Disorders defines non-24-hour sleep wake disorder as a circadian rhythm sleep disorder characterized by complaints of insomnia or excessive sleepiness related to abnormal synchronization between the 24-hour light–dark cycle and the endogenous circadian rhythms of sleep and wake propensity.

Patients with non-24 experience a steady pattern composed of 1- to 2-hour daily delays in sleep onset and wake times. More than half of all totally blind individuals have non-24. The lack of sight and the ability of light cues to be given to the brain prevent synchronization of the sleep-wake cycle by the suprachiasmatic nucleus of the hypothalamus in the brain. A

The National Organization for Rare Disorders (NORD) states that the condition is characterized by the failure of a person's biological clock to synchronize to a 24-hour day light-dark cycle because light does not enter their eyes. Those with the disorder may have difficulty falling or staying asleep and may wake up feeling as if they need more rest. People with non-24 may find their sleep patterns reversed (e.g., needing to sleep during the day and to be awake at night). Due to differences in circadian rhythms, it can take weeks or months of daily use of tasimelteon before the patient experiences any benefit.

Melatonin

American Academy of Neurology (2013) review on circadian rhythm disorders suggests that melatonin is the therapeutic mainstay in blind patients with Non-24, together with strong structured behavioral and social cues (e.g., timing of meals, planned activities, and regular physical exercise).C This same approach is recommended for sighted persons, with the additional option of bright light exposure in the morning shortly after awakening.

Although the dose of melatonin for the treatment of Non-24 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.

The American Sleep Disorder Association considers melatonin an experimental drug and does not recommend its use without medical supervision. Melatonin has been classified as an orphan drug by the US FDA since 1993 for circadian rhythm sleep disorders in blind patients who have no light perception. Melatonin is also available over the counter (OTC) in the US, and products are marketed under the Dietary Supplement and Health Education Act of1994 (DSHEA). In Europe melatonin is available by prescription only.[F,G]

A meta-analysis with the critical outcome of entrainment using melatonin was included in the recent American Academy of Sleep Medicine Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders.3 Three placebo-controlled, crossover studies using timed oral melatonin for patients with N24SWD (n=36) were included in the meta-analysis. The dose of melatonin studied included 0.5mg, 5 mg, and 10mg and the duration of melatonin treatment ranged from 26- 81 days. The odds ratio for entrainment was 21.18 (95% CI 3.22-139.17) in favor of melatonin. Although the quality of evidence was low and the strength of the recommendation was weak for, the recommendation that clinicians use strategically timed melatonin for the treatment of N24SWD in blind adults (versus no treatment) was made based on the assessment of evidence, benefits versus harms analyses, and patient values and preferences.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Hetlioz (tasimelteon) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Hetlioz (tasimelteon) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:

Hetlioz (tasimelteon) should be taken 1 hour prior to bedtime.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Hetlioz CAPS 20MG
Hetlioz LQ SUSP 4MG/ML (48mL or 158mL bottle)
Tasimelteon CAPS 20MG

REFERENCES

1. Hetlioz (tasimelteon) [prescribing information]. Washington, DC: Vanda Pharmaceuticals; January 2023.
2. Rozerem [package insert]. Deerfield, IL: Takeda Pharmaceuticals America Inc; November 2021.
3. SW Lockley et al. Tasimelteon treatment entrains the circadian clock and demonstrates a clinically meaningful benefit in totally blind individuals with non-24-hour circadian rhythms. The Endocrine Society 95th annual meeting (ENDO), San Francisco, June 15-18, 2013. Poster SUN-134.
4. SW Lockley et al. RESET study demonstrates that tasimelteon maintains entrainment of melatonin and cortisol in totally blind individuals with non-24-hour circadian rhythms. The Endocrine Society 95th annual meeting (ENDO), San Francisco, June 15-18, 2013. PosterSUN- 137.
5. Auger RR, Burgess HJ, Emens JS et al. Clinical practice guideline for the treatment of intrinsic circadian rhythm sleep-wake disorders: advance 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.J Clin Sleep Med 2015;11:1199-1236.
6. International Classification of Sleep Disorders: Diagnostic & Coding Manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
7. Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders: an American Academy of Sleep Medicine report. Sleep 2007;30(11):1445-1459.
8. 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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10. Circadian Sleep Disorders Network. Non-24-Hour Sleep-Wake Disorder Questions and Answers. Available at: http://www.circadiansleepdisorders.org/docs/N24-QandA.php. Accessed on April 2016.
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12. 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.
13. American Academy of Sleep Medicine (AASM). An American Academy of Sleep Medicine Clinical Practice Guideline: 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. Journal of Clinical Sleep Medicine, Vol. 11, No. 10, 2015. Available at: http://www.aasmnet.org/Resources/clinicalguidelines/CRSWD- intrinsic.pdf. Accessed on April 2016.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Prescriber requirements Quantity Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q2 2023
REVISION- Notable revisions: Duration of Approval	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file