Clinical Policy: Tasimelteon (Hetlioz, Hetlioz LQ)

Reference Number: CP.PMN.104
Effective Date: 03.01.17
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Tasimelteon (Hetlioz®, Hetlioz LQ™) is a melatonin receptor agonist.

FDA Approved Indication(s)

Hetlioz is indicated for 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 is indicated for the treatment of nighttime sleep disturbances in SMS in pediatric patients 3 to 15 years of age.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Hetlioz is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-24-Hour Sleep-Wake Disorder (must meet all)**:**

1. Diagnosis of non-24-hour sleep-wake disorder;
2. Request is for Hetlioz capsules;
3. Age ≥ 18 years;
4. Prescribed by or in consultation with a specialist in sleep disorders;
5. Failure of melatonin and ramelteon (Rozerem®), unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for ramelteon*
6. Member has total blindness (e.g., nonfunctioning retinas) and is unable to perceive light in both eyes;
7. Dose does not exceed 20 mg (1 capsule) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Nighttime sleep disturbances in Smith-Magenis Syndrome (must meet all)**:**
1. Diagnosis of SMS confirmed by genetic testing (e.g., deletion 17p11.2 or RAI1 mutation);
2. Request is for treatment of nighttime sleep disturbances;
3. Prescribed by or in consultation with a specialist in sleep disorders;
4. One of the following (a or b):
   a. Request is for Hetlioz capsules and member is ≥ 16 years old;
   b. Request is for Hetlioz LQ and member is 3 to 15 years of age;
5. Dose does not exceed one of the following (a or b):
   a. Hetlioz: 20 mg (1 capsule) per day;
   b. Hetlioz LQ: 0.7 mg per kg per day if weight ≤ 28 kg, 20 mg per day if weight > 28 kg.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All FDA-Approved Indications (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Hetlioz: 20 mg (1 capsule) per day;
   b. Hetlioz LQ: 0.7 mg per kg per day if weight ≤ 28 kg, 20 mg per day if weight > 28 kg.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
SMS: Smith-Magenis Syndrome

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
melatonin	Non-24: 5 to 10 mg PO QHS	N/A
ramelteon (Rozerem)	Non-24: 8 mg PO QHS	8 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Hetlioz	Non-24-hr-sleep-wake disorder, nighttime sleep disturbances in SMS	20 mg PO QD one hour before bedtime, at the same time each night	20 mg/day
Hetlioz LQ	Nighttime sleep disturbances in SMS	Weight ≤ 28 kg: 0.7 mg per kg per day PO Weight > 28 kg: 20 mg per day Dose should be given one hour before bedtime, at the same time each night	See dosing regimen

VI. Product Availability

- Capsule (Hetlioz): 20 mg
- Oral suspension (Hetlioz LQ): 4 mg/mL (158 mL bottle)

VII. References

1. Hetlioz Prescribing Information. Washington, D.C.: Vanda Pharmaceuticals Inc.; December 2020. Available at: www.hetlioz.com. Accessed September 27, 2021.
2. Auger RR, Burgess HJ, Emens JS, Deriy LV, Thomas SM, and 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. J Clin Sleep Med. 2015; 11(10): 1199-1236.
3. Williams WP 3rd, McLin DE 3rd, Dressman MA, Neubauer DN. Comparative review of approved melatonin agonists for the treatment of circadian rhythm sleep-wake disorders. Pharmacotherapy. 2016 Sep;36(9):1028-41.
4. PRISMS Professional Advisory Board. Medical management guidelines for an individual diagnosed with SMS. Approved January 24, 2018. Available at: https://www.prisms.org/wp-content/uploads/pdf/mmg/PRISMS_Medical_Management_Guidelines2018.pdf. Accessed September 27, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Policies combined for HIM and commercial; Medicaid line of business was added to criteria; Added specialist requirement; Added trial and failure of melatonin; Removed diagnosis with "confirmed by at least 14 days of documentation of progressively shifting sleep-wake times" due to added specialist requirement; References reviewed and updated	11.20.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.20.18	02.19
Added trial and failure of Rozerem including therapeutic alternatives table information; references reviewed and updated.	05.15.19	08.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	09.26.19	02.20
1Q 2021 annual review: modified initial approval duration from 6 to 12 months; references reviewed and updated. RT4: added new dosage form Hetlioz LQ and new indication for nighttime sleep disturbances in SMS; for non-24 added age 18 or older and requirement that request is for Hetlioz per updated prescribing information.	12.08.20	02.21
1Q 2022 annual review: revised Commercial auth duration from Length of Benefit to 12 months or duration of request, whichever is less; clarified that request for non-24 must be for capsules; references reviewed and updated.	09.27.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.