Clinical Policy: Sodium Oxybate (Xyrem, Lumryz) and Calcium, Magnesium, Potassium, and Sodium Oxybate (Xywav)

Reference Number: CP.PMN.42
Effective Date: 05.01.11
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

Sodium oxybate (Xyrem®, Lumryz™) and calcium, magnesium, potassium, and sodium oxybate (Xywav®) are central nervous system (CNS) depressants.

FDA Approved Indication(s)

Lumryz, Xyrem/generic Xyrem, and Xywav are indicated for the treatment of patients 7 years of age and older with:

- Cataplexy in narcolepsy
- Excessive daytime sleepiness (EDS) in narcolepsy

Xywav is also indicated for the treatment of idiopathic hypersomnia (IH) in adults.

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 Xyrem/generic Xyrem, Xywav, and Lumryz are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Narcolepsy with Cataplexy (must meet all)**:**

1. Prescribed for the treatment of cataplexy in narcolepsy;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age ≥ 7 years;
4. For Lumryz requests, one of the following (a or b):
   a. Member weighs ≥ 45 kg;
   b. Member weighs < 45 kg, and dose has been titrated to ≥ 4.5 mg per day with an alternative sodium oxybate product;
5. Documentation of one of the following (a or b):
   a. EDS associated with narcolepsy as confirmed by documented multiple sleep latency test (MSLT) and one of the following (i or ii):
      i. Mean sleep latency ≤ 8 minutes with evidence of two or more sleep-onset rapid eye movement periods (SOREMPs);
      ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight polysomnography (PSG);

b. Lumbar puncture shows cerebrospinal fluid (CSF) hypocretin-1 level ≤ 110 pg/mL;

6. Failure of 2 of the following agents, each used for ≥ 1 month, unless member's age is ≥ 65, clinically significant adverse effects are experienced, or all are contraindicated: venlafaxine, fluoxetine, atomoxetine, clomipramine*, protriptyline*;
   **If member's age is ≥ 65 years, tricyclic antidepressants are not required for trial.*
7. If member is ≥ 18 years of age, failure of a 1-month trial of Wakix® at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
   **Prior authorization may be required for Wakix*
8. For brand Xyrem requests, member must use generic Xyrem, unless contraindicated or clinically significant side effects are experienced;
9. For Xywav or Lumryz requests: If member has failed Wakix, then failure of sodium oxybate (Xyrem) at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
10. Dose does not exceed 9 grams per day.

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

B. Narcolepsy with Excessive Daytime Sleepiness (must meet all)**:**

1. Diagnosis of narcolepsy with EDS;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age ≥ 7 years;
4. For Lumryz requests, one of the following (a or b):
   a. Member weighs ≥ 45 kg;
   b. Member weighs < 45 kg, and dose has been titrated to ≥ 4.5 mg per day with an alternative sodium oxybate product;
5. Documentation of both of the following (a and b):
   a. EDS associated with narcolepsy as confirmed by documented MSLT and one of the following (i or ii):
      i. Mean sleep latency ≤ 8 minutes with evidence of two or more SOREMPs;
      ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight PSG;
   b. Member has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months;
6. Failure of a 1-month trial of one of the following generic central nervous system stimulant-containing agents at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: amphetamine, dextroamphetamine, methylphenidate;
   **Prior authorization may be required for CNS stimulants*
7. If member is ≥ 17 years of age, failure of a 1-month trial of armodafinil or modafinil at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for armodafinil and modafinil*

8. If member is ≥ 18 years of age, failure of a 1-month trial of Sunosi™ at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
   **Prior authorization may be required for Sunosi*
9. If member has failed Sunosi, then failure of a 1-month trial of Wakix at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
   **Prior authorization may be required for Wakix*
10. For brand Xyrem requests, member must use generic Xyrem, unless contraindicated or clinically significant side effects are experienced;
11. For Xywav and Lumryz requests: If member has failed Sunosi and Wakix, then failure of sodium oxybate (Xyrem) at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
12. If request is for concomitant therapy with other antinarcoleptic agents (e.g., Wakix, Sunosi) for members ≥ 18 years of age, failure of combination therapy with modafinil or armodafinil and Sunosi, unless clinically significant adverse effects are experienced or all are contraindicated;
13. Dose does not exceed 9 grams per day.

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

C. Idiopathic Hypersomnia (must meet all)**:**

1. Diagnosis of IH;
2. Request is for Xywav;
3. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
4. Age ≥ 18 years;
5. All of the following have been excluded (a, b, and c):
   a. Narcolepsy of cataplexy;
   b. Narcolepsy of EDS;
   c. Insufficient sleep syndrome;
6. Documentation of both of the following (a and b):
   a. MSLT documents either (i or ii):
      i. Fewer than two SOREMPs;
      ii. No SOREMPs if the REM sleep latency on the preceding PSG was ≤ 15 minutes;
   b. Presence of at least one of the following (i or ii):
      i. MSLT shows a mean sleep latency of ≤ 8 minutes;
      ii. Total 24-hour sleep time is ≥ 660 minutes on 24-hour PSG or by wrist actigraphy in association with a sleep log;
7. Failure of a 1-month trial of armodafinil or modafinil at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for armodafinil and modafinil*
8. Failure of a 1-month trial of one of the following generic central nervous system stimulant-containing agents at up to maximally indicated doses, unless clinically

significant adverse effects are experienced or all are contraindicated: amphetamine, dextroamphetamine, methylphenidate;
**Prior authorization may be required for CNS stimulants*

9. Dose does not exceed both of the following (a and b):
   a. Both i and ii:
      i. 6 grams per day for once nightly dosing;
      ii. 12 mL per day for once nightly dosing;
   b. Both i and ii:
      i. 9 grams per day for twice nightly dosing;
      ii. 18 mL per day for twice nightly dosing.

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

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, but not limited to, improvement in <u>any</u> of the following parameters: reduction in frequency of cataplexy attacks, reported daytime improvements in wakefulness;
3. If request is for a dose increase, new dose does not exceed 9 grams per day.

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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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

CNS: central nervous system
CSF: cerebrospinal fluid
EDS: excessive daytime sleepiness
ESS: Epworth Sleepiness Scale
FDA: Food and Drug Administration
IH: idiopathic hypersomnia
IHSS: Idiopathic Hypersomnia Severity Scale
MSLT: multiple sleep latency test
PSG: polysomnography
SOREMP: sleep-onset rapid eye movement period

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
Cataplexy		
venlafaxine (Effexor®)†	75–150 mg PO BID, or 75–150 mg (extended release) PO QAM	375 mg/day* (IR tablets); 225* mg/day (extended release)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fluoxetine (Prozac®)†	20 to 80 mg PO QAM	80 mg/day
clomipramine (Anafranil®)†	10 to 150 mg PO as a single dose every morning or in divided doses	250 mg/day*
protriptyline (Vivactil®)†	5 to 60 mg PO as a single dose every morning or in divided doses	60 mg/day
atomoxetine (Strattera®)†	40–60 mg PO QD	100 mg/day*
EDS		
amphetamine (Evekeo®)	5 to 60 mg/day PO in divided doses	60 mg/day
amphetamine/ dextroamphetamine (Adderall®)		
dextroamphetamine ER (Dexedrine® Spansule®)		
dextroamphetamine IR (Zenzedi®, Procentra®)		
methylphenidate (Ritalin® LA or SR, Concerta®, Metadate® CD or ER, Methylin® ER, Daytrana®)	Dosing varies; 10-60 mg PO divided 2 to 3 times daily 30-45 min before meals	60 mg/day
armodafinil (Nuvigil®)	150 mg to 250 mg PO once a day	250 mg/day
modafinil (Provigil®)	200 mg PO QD as a single dose in the morning	400 mg/day
Sunosi™ (solriamfetol)	Initiate at 75 mg PO once a day; dose may be doubled at intervals of at least 3 days	150 mg/day
Wakix® (pitolisant)	Dose range is 17.8 to 35.6 mg PO once daily in the morning upon wakening. Titrate dosage as follows: • Week 1: Initiate with a dosage of 8.9 mg once daily • Week 2: Increase dosage to 17.8 mg once daily • Week 3: May increase to the maximum recommended dosage of 35.6 mg once daily	35.6 mg/day
IH		
modafinil (Provigil®)†	200 mg PO Q AM	400 mg/day
armodafinil (Nuvigil®)†	150 mg to 250 mg PO once a day	250 mg/day
methylphenidate (Ritalin® LA or SR, Concerta®, Metadate® CD or ER, Methylin® ER, Daytrana®)†	Dosing varies; 10-60 mg PO divided 2 to 3 times daily 30-45 min before meals	60 mg/day
amphetamine (Evekeo®)†		60 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
amphetamine/ dextroamphetamine (Adderall®)†	5 to 60 mg/day PO in divided doses	
dextroamphetamine ER (Dexedrine® Spansule®)†		
dextroamphetamine IR (Zenzedi®, Procentra®)†		

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.
**Non-indication specific (maximum dose for the drug)*
†Off-label indication

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In combination with sedative hypnotics or alcohol
  - Succinic semialdehyde dehydrogenase deficiency
- Boxed warning(s):
  - Central nervous system depression: Respiratory depression can occur.
  - Abuse and misuse: Xyrem/generic Xyrem, Xywav, and Lumryz are a sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB is associated with CNS adverse reactions, including seizure, respiratory depression, decreased consciousness, coma, and death.
  - Xywav and Xyrem/generic Xyrem are available only through a restricted program called the Xywav and Xyrem REMS (*Xywav and Xyrem/generic Xyrem only*).
  - Lumryz is available only through a restricted program called Lumryz REMS (*Lumryz only*).

Appendix D: General Information

- PSG:
  - In IH, PSG may show a short sleep latency, increased total sleep time, increased sleep spindles, and variable changes in sleep efficiency and sleep stage distribution
  - Used in diagnostic criteria of IH
    - If no SOREMPs are present on MSLT, REM sleep latency on preceding PSG can be ≤ 15 minutes for diagnosis
    - Presence of total 24-hour sleep time ≥ 660 minutes on 24-hour PSG or by wrist actigraphy in association with a sleep log
- MSLT:
  - This test is a series of five daytime nap opportunities that allow objective characterization of the patient's level of daytime sleepiness, physiological sleep tendency, as reflected by the mean sleep latency
  - In IH, mean sleep latency is shortened and less than 8 minutes and number of SOREMPs is less than two

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cataplexy in narcolepsy EDS in narcolepsy	**sodium oxybate (Xyrem), Xywav:** Adults: The recommended starting dose is 4.5 grams (g) per night administered orally in two equal, divided doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later. Increase the dose by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to the effective dose range of 6 g to 9 g per night orally Pediatrics: Dosing is weight-based as follows: • *20 to < 30 kg*: ≤ 1 g at bedtime and ≤ 1 g taken 2.5 to 4 hours later. Increase the dose by 1 g per night at weekly intervals (additional 0.5 g at bedtime and 0.5 g taken 2.5 to 4 hours later) to a maximum dose of 6 g per night orally • *30 to < 45 kg*: ≤ 1.5 g at bedtime and ≤ 1.5 g taken 2.5 to 4 hours later. Increase the dose by 1 g per night at weekly intervals (additional 0.5 g at bedtime and 0.5 g taken 2.5 to 4 hours later) to a maximum dose of 7.5 g per night orally • ≥ *45 kg*: ≤ 2.25 g at bedtime and ≤ 2.25 g taken 2.5 to 4 hours later. Increase the dose by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to a maximum dose of 9 g per night orally **Lumryz:** Adults: The recommended starting dosage is 4.5 g per night administered orally. Increase the dosage by 1.5 g per night at weekly intervals to the recommended dosage range of 6 g to 9 g once per night orally Pediatrics: Dosing is weight-based as follows: • < *45 kg*: Because the recommended starting dosage cannot be achieved with the available strengths of Lumryz, use another sodium oxybate product to initiate treatment. The maximum recommended dosage for patients weighing 20 kg to < 30 kg is 6 g once per night orally, and the maximum recommended dosage for patients weighing 30 kg to < 45 kg is 7.5 g once per night orally • ≥ *45 kg*: The recommended starting dosage is 4.5 g once per night administered orally. Increase the dosage by 1.5 g per night at weekly intervals to the maximum recommended dosage of 9 g once per night orally	9 g/night
IH	**Xywav:** Adults: Administered twice or once nightly regimen in adults. For twice nightly, initiate dose at 4.5 g or less per	9 g/night

Indication	Dosing Regimen	Maximum Dose
	night PO, divided into two doses. Titrate to effect in increments of up to 1.5 g per night per week, up to 9 g total nightly dose. For once nightly, initiate dosage at 3 g or less per nightly PO, as one dose. Titrate to effect in increments of up to 1.5 g per night per week, up to 6 g total nightly dose.	

VI. Product Availability

Drug Name	Availability
sodium oxybate (Xyrem)	Oral solution: 0.5 g per mL in 180 mL bottle
Xywav (calcium, magnesium, potassium, and sodium oxybate)	Oral solution: 0.5 g per mL in 180 mL bottle
Lumryz (sodium oxybate)	Extended-release oral suspension: 4.5 g, 6 g, 7.5 g, 9 g powder in packets

VII. References

1. Xyrem Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; April 2023. Available at: https://pp.jazzpharma.com/pi/xyrem.en.USPI.pdf. Accessed January 14, 2025.
2. Xywav Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; April 2023. Available at: https://pp.jazzpharma.com/pi/xywav.en.USPI.pdf. Accessed January 14, 2025.
3. Lumryz Prescribing Information. Chesterfield, MO. Avadel CNS Pharmaceuticals, LLC.; October 2024. Available at: https://www.avadel.com/lumryz-prescribing-information.pdf. Accessed January 14, 2025.
4. Sodium Oxybate Prescribing Information. Bridgewater, NJ. Amneal Pharmaceuticals, LLC.; April 2023. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a6c17f6f-46bc-4852-a825-07f49cc08495. Accessed January 14, 2025.
5. Morgenthaler TI, Kapur VK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin An American Academy of Sleep Medicine Report: An American Academy of Sleep Medicine Report. Sleep. 2007;30(12):1705-1711.
6. Bassetti CL, Kallweit U, Vignatelli, et al. European guideline and expert statements on the management of narcolepsy in adults and children. J Sleep Res. 2021;00:e13387. DOI: 10.1111/jsr.13387.
7. Wise MS, Arand DL, Auger RR, Brooks SN, Watson NF. Treatment of Narcolepsy and other Hypersomnias of Central Origin: An American Academy of Sleep Medicine Review. Sleep. 2007;30(12):1712-1727.
8. Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. Nat Sci Sleep. 2015; 7:159-169.
9. Trotti LM, Staab BA, Rye DB. Test-retest reliability of the multiple sleep latency test in narcolepsy without cataplexy and idiopathic hypersomnia. J Clin Sleep Med. 2013 Aug 15;9(8):789-95. doi: 10.5664/jcsm.2922. PMID: 23946709; PMCID: PMC3716670.
10. Lopez R, Doukkali A, Barateau L, Evangelista E, Chenini S, Jaussent I, Dauvilliers Y. Test-Retest Reliability of the Multiple Sleep Latency Test in Central Disorders of Hypersomnolence. Sleep. 2017 Dec 1;40(12). doi: 10.1093/sleep/zsx164. PMID: 29099966.

11. Anderson KN, Pilsworth S, Sharples LD, Smith IE, Shneerson JM. Idiopathic hypersomnia: a study of 77 cases. Sleep. 2007 Oct;30(10):1274-81. doi: 10.1093/sleep/30.10.1274. PMID: 17969461; PMCID: PMC2266276.
12. Lavault S, Dauvilliers Y, Drouot X, Leu-Semenescu S, Golmard JL, Lecendreux M, Franco P, Arnulf I. Benefit and risk of modafinil in idiopathic hypersomnia vs. narcolepsy with cataplexy. Sleep Med. 2011 Jun;12(6):550-6. doi: 10.1016/j.sleep.2011.03.010. Epub 2011 May 14. PMID: 21576035.
13. Dauvilliers Y, Evangelista E, Barateau L, Lopez R, Chenini S, Delbos C, Beziat S, Jaussent I. Measurement of symptoms in idiopathic hypersomnia: The Idiopathic Hypersomnia Severity Scale. Neurology. 2019 Apr 9;92(15):e1754-e1762. doi: 10.1212/WNL.0000000000007264. Epub 2019 Mar 13. PMID: 30867266.
14. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021 Sep 1;17(9):1881-1893. doi: 10.5664/jcsm.9328.
15. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Available at: https://www.clinicalkey.com/pharmacology. Accessed January 27, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added diagnostic criteria for narcolepsy with cataplexy and narcolepsy associated with excessive daytime sleepiness; added prescriber requirements for neurologist or sleep medicine specialist for all indications; for narcolepsy with excessive daytime sleepiness: added trial of Sunosi, and added requirement for combination use of preferred agents if request is for concomitant use; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	04.13.21	05.21
RT4: criteria added for new FDA indication of IH for Xywav; revised bypassing of redirections for age 65 years and older to apply only to TCAs for narcolepsy with cataplexy.	09.03.21	11.21
Per November SDC and prior clinical guidance, for narcolepsy with cataplexy added redirection to Xyrem for Xywav requests; for narcolepsy with EDS added requirement for redirection to Wakix (and for Xywav additional redirection to Xyrem) in a step-wise fashion; revised Commercial auth duration from length of benefit to 12 months or duration of request, whichever is less.	11.30.21	02.22
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.31.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.26.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.07.23	05.23
RT4: added new extended-release oral suspension formulation Lumryz to policy; for narcolepsy with cataplexy and narcolepsy associated with EDS, updated age requirement in initial criteria to	06.12.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
reflect minimum age Lumryz use per PI; removed "antidepressant" classification for redirected agents for narcolepsy with cataplexy initial criteria since atomoxetine (although a SNRI) is not considered an antidepressant; per SDC: for narcolepsy with cataplexy and narcolepsy with EDS, added requirement for redirection to Sunosi, Wakix, and Xyrem for Lumryz requests in a step-wise fashion.		
2Q 2024 annual review: for Narcolepsy with Cataplexy, revised antidepressant redirection criteria by adding "unless member's age is ≥ 65" to align with Wakix criteria; for boxed warnings, updated central nervous system depression description to "respiratory depression can occur" and added "available only through a restricted REMS program" per prescriber information; references reviewed and updated.	01.12.24	05.24
Per SDC: for narcolepsy with cataplexy and narcolepsy with EDS, added redirection to generic Xyrem for brand Xyrem requests and "for Xywav or Lumryz requests" modified failure of "Xyrem" to failure of "sodium oxybate (Xyrem)"; added generic Xyrem to criteria and Xyrem to REMS program information in Appendix C.	06.17.24	
RT4: updated criteria to reflect newly approved pediatric extension for Lumryz.	10.23.24	
2Q 2025 annual review: for narcolepsy with cataplexy: clarified if member is ≥ 65 years then trial of tricyclic antidepressants are not required apply to clomipramine and protriptyline only, added "if member is ≥ 18 years of age" to trial of Wakix; for narcolepsy with EDS: added "if member is ≥ 18 years of age" to trial of Sunosi; for IH, removed criteria requiring minimal scoring for ESS or IHSS to align with competitor analysis; for Appendix D, removed supplemental information on ESS and IHSS; references reviewed and updated.	01.14.25	05.25

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.