Clinical Policy: Sodium Oxybate (Xyrem)
Reference Number: CP.PMN.42
Effective Date: 05/11
Last Review Date: 05/17
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description
Sodium oxybate (Xyrem®) is a central nervous system (CNS) depressant.

FDA approved indication
Xyrem is indicated:
- For the treatment of cataplexy in narcolepsy
- For the treatment of excessive daytime sleepiness (EDS) in narcolepsy

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Xyrem is **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. Failure of 2 of the following antidepressants: venlafaxine, fluoxetine, tricyclic antidepressant (e.g., protriptyline, clomipramine), each trialed for ≥ 1 month, unless all are contraindicated or clinically significant adverse effects are experienced;

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~~5.~~3. Dose ~~within FDA approved limit with starting doses of no more than 4.5 grams/day and titration not more often than every two weeks up to a maximum of~~does not exceed 9 grams/day.

Approval duration: 3 months

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

1. Diagnosis of narcolepsy with EDS;
2. Failure of a 1 month trial of one of the following CNS stimulants: ~~-~~amphetamine immediate release (IR), amphetamine; dextroamphetamine IR, dextroamphetamine, methylphenidate IR, or Metadate ER at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced; **Note: CNS stimulants may require prior authorization.*
~~2.~~3. ~~a -~~Failure of a 1 month trial of armodafinil or modafinil at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced; **Note: Armodafinil and modafinil require prior authorization*
~~3.~~4. Dose does not exceed 9 grams/day.

Approval duration: 3 months

C. Other diagnoses/indications

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria; ~~Member is currently receiving this medication through Centene benefit per provider's documentation or pharmacy record;~~
2. Documentation of positive response to therapy (e.g., 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/day.
~~2. Dose must not exceed FDA approved limit of 9 grams per day.~~

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12 months

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 policy – CP.PMN.53 or evidence of coverage documents~~;~~

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IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CNS: central nervous system
EDS: excessive daytime sleepiness
FDA: Food and Drug Administration
IR: immediate release

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cataplexy in narcolepsy	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.	9 g per night
Excessive daytime sleepiness in narcolepsy		

VI. Product Availability

Oral solution: 0.5 g per mL

VII. Workflow Document

CP.PMN.42.sodium oxybate (Xyrem) Q2 2

VIII. References

1. Xyrem Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; September 2016. Available at: https://www.xyrem.com/. Accessed January 10, 2017.
1. ~~Xyrem® prescribing information. Accessed February, 2016. http://www.xyrem.com/xyrem_pi.pdf~~
2. 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.

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3. 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.
4. Scammell TE. The neurobiology, diagnosis and treatment of narcolepsy. Ann Neurol 2003;53:154 –166.
5. Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. Nat Sci Sleep. 2015; 7:159-169.

~~2. Sodium oxybate monograph. Clinical Pharmacology. Accessed February 2016.~~
~~3. Billiard M, Dauvilliers Y, Dolenc-Groselj L, et al. Management of Narcolepsy in Adults. European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 513-28. http://www.guideline.gov/content.aspx?id=34901&search=narcolepsy~~
~~4. Morgenthaler T, Kapur V, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. Sleep 2007; 30(12):1705-1711. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2276123/~~
~~5. Scammell TE. Treatment of narcolepsy. Benca R. (Ed). UpToDate, Waltham MA. Last literature review, January 2016. Accessed February 2016.~~
~~6. Scammell TE. Clinical Features and diagnosis of narcolepsy in adults. Benca R. (Ed), UpToDate, Waltham MA. Accessed February 2016.~~
~~7. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. American Academy of Sleep Medicine Report.~~
~~8. Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. Nat Sci Sleep. 2015; 7:159-169. Published online 2015 Dec 11. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4686331/.~~
~~9. Sodium Oxybate DrugPoint Summary. Micromedex. Accessed February 2016.~~
~~10. Ali Bozorg, MD. Treatment and Management of Narcolepsy. Medscape. November 2012. http://emedicine.medscape.com/article/1188433-treatment. Accessed February 2016.~~

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Previous criteria consolidated under an umbrella diagnosis of narcolepsy with associated cataplexy. Trial and failure for antidepressant therapy changed from one month to two months. Only a single therapeutic category trial is required. References updated to reflect a current literature search.	05/12	05/12
Description to include receptor binding and effects on sleep cycle FDA approved indications to include narcolepsy with EDS Criteria for approval to exclude patients < 16 years of age, Fluoxetine and Clomipramine alternative antidepressants, combined use with alcohol excluded; added specific requirement for diagnostic tests (PSG/MSLT) Special Instructions to include contraindication with alcohol	05/13	05/13

Reviews, Revisions, and Approvals	Date	P&T Approval Date
References updated.		
Updated Approval to include recommended dosing information. References updated.	05/14	05/14
References updated.	05/15	05/15
Converted into new policy template Removed requirement for proof of diagnosis based on DSM-V criteria and requirement of polysonmogram as this subjective and not within scope of practice for pharmacist to accurate interpret or measure results of sleep study; Removed bullet point #C as this subjective and not within scope of practice for accurate measure or interpretation by pharmacist as reviewer of sleep study results no measure to verify requirements; Created separate bullet point for trial and failure of SSRI or TCA if member intolerant to venlafaxine; Removed concomitant stimulant plus antidepressant therapy as research did not reflect two classes must be used together; Removed use of alcohol because although a safety requirement, no accurate means to measure alcohol use therefore considered subjective; Added that sedative hypnotic use will be reviewed by pharmacy claim history as this is an objective measure ; Removed renewal criteria requiring show of improvement of daytime wakefulness and Epworth Sleepiness Scale as this is subjective; Added the following to renewal criteria: Member must be currently on medication AND Dose does not exceed FDA approved limit; Updated background section to include mechanism of action and FDA approved indications. Updated reference to reflect current literature search.	02/16	05/16
~~Clinical changes made to criteria:~~ -Created separate criteria for diagnosis of narcolepsy with cataplexy and diagnosis of narcolepsy with EDS -Narcolepsy with cataplexy: removed requirements related to trial and failure of stimulants and armodafinil/modafinil for narcolepsy with cataplexy since these agents used to treat excessive sleepiness have little effect on cataplexy per American Academy of Sleep Medicine report; modified criteria to require trial and failure of 2 antidepressants, instead of 1 for cataplexy	03~~1~~/17	05/17

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
-Narcolepsy with EDS: modified criteria to require failure of one CNS stimulant indicated for narcolepsy at up to maximally indicated doses instead of failure of 2 stimulants, one from each class (amphetamine and methylphenidate) ~~Non-clinical changes to criteria:~~ -Converted to new template		
-Removed requirements related to age restriction and "No concurrent use of sedative hypnotics as evidenced by review of pharmacy claim history" per template update, and since age is not an absolute contraindication per PI and safety concerns are addressed by Xyrem REMS Program -Added "documentation of positive response to therapy" for re-auth -Updated references		

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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.