Clinical Policy: sodium oxybate (Xyrem®)
Reference Number: HIM.PA.69
Effective Date: 12/14
Last Review Date: 08/17
Line of Business: Health Insurance Marketplace

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

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

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

Limitation of use: Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program.

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

I. Initial Approval Criteria
   A. Narcolepsy with Cataplexy (must meet all)**:**
   1. Diagnosis of narcolepsy with cataplexy;
   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;
   3. Dose does not exceed 9 grams per day (18 mL/day).
   Approval duration: 3 months

   B. Narcolepsy with Excessive Daytime Sleepiness (EDS) (must meet all)**:**
   1. Diagnosis of narcolepsy with EDS;
   2. Failure of ≥ 1 month trial of one formulary CNS stimulant indicated for narcolepsy (e.g., amphetamine; dextroamphetamine IR, dextroamphetamine, methylphenidate IR) at up to maximally indicated doses unless all are contraindicated or clinically significant adverse effect are experienced;
   3. Failure of ≥ 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.
   4. Dose does not exceed 9 grams per day (18 mL/day).
   Approval duration: 3 months

   C. Other diagnoses/indications

1. Refer to HIM.PHAR.21 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;
      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 per day (18 mL/day).
      Approval duration: 12 months

   B. **Other diagnoses/indications** (must meet 1 or 2)**:**
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
         Approval duration: Duration of request or 12 months (whichever is less); or
      2. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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 – HIM.PHAR.21or evidence of coverage documents

IV. **Appendices/General Information**
   CNS: central nervous system
   EDS: excessive daytime sleepiness
   FDA: Food and Drug Administration
   IR: immediate release
   REMS: Risk Evaluation and Mitigation Strategy

V. **References**
   1. Xyrem Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; January 2017. Available at: https://www.xyrem.com/. Accessed April 7, 2017.
   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.
   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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Reformatted guideline to new format. Adjusted criteria for flow. Added Workflow reference document.	12/15	12/15
Removed age requirement. Created separate criteria for diagnosis of narcolepsy with cataplexy and diagnosis of narcolepsy with EDS. Removed requirements related to *polysomnography* and multiple sleep latency tests for confirmation of diagnosis. Removed drug safety requirement related to no concurrent use of sedative hypnotics or alcohol. Removed workflow document. Updated references to reflect current literature search	08/16	11/16
Converted to new template. Narcolepsy with cataplexy: removed requirements related to trial and failure of stimulants and armodafinil/modafinil 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. Narcolepsy with EDS: modified criteria to require failure of one CNS stimulant at up to maximally indicated doses instead of 2 stimulants, one from each class (amphetamine and methylphenidate) since modafinil and Xyrem are recommended as standard therapy per guideline. Updated references.	04/17	08/17

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.