Clinical Policy: Sodium Oxybate (Xyrem)
Reference Number: ERX.NPA.23
Effective Date: 06.01.15
Last Review Date: 05.18

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

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

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 Envolve Pharmacy Solutions™ that Xyrem is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Narcolepsy with Cataplexy (must meet all):
      1. Diagnosis of narcolepsy with cataplexy;
      2. Age ≥ 18 years;
      3. Failure of 2 of the following, each used for ≥ 1 month unless contraindicated or clinically significant adverse effects are experienced: venlafaxine, fluoxetine, atomoxetine, clomipramine, or protriptyline;
      4. Dose does not exceed 9 grams/day (18 mL/day).
      
      Approval duration: 6 months

   B. Narcolepsy with Excessive Daytime Sleepiness (must meet all):
      1. Diagnosis of narcolepsy with EDS;
      2. Age ≥ 18 years;
      3. 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 may require prior authorization
      4. Failure of a 1 month trial of one of the following CNS stimulants at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
         amphetamine immediate release (IR), amphetamine/dextroamphetamine IR, dextroamphetamine, methylphenidate IR, or Metadate ER;
      5. Dose does not exceed 9 grams/day (18 mL/day).
      
      Approval duration: 6 months

   C. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. All Indications in Section I (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request does not exceed 9 grams/day (18 mL/day).

**Approval duration: 12 months**

B. **Other diagnoses/indications** (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   
   **Approval duration: Duration of request or 12 months (whichever is less); or**
   2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

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
   REMS: Risk Evaluation and Mitigation Strategy

   **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 and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cataplexy</strong></td>
<td></td>
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</tr>
<tr>
<td>venlafaxine (Effexor®)†</td>
<td>75–150 mg PO BID, or 75–150 mg (extended release) PO QAM</td>
<td>375 mg/day* (IR tablets); 225* mg/day (extended release)</td>
</tr>
<tr>
<td>fluoxetine (Prozac®)†</td>
<td>20 to 80 mg PO QAM</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>clomipramine (Anafranil®)†</td>
<td>10 to 150 mg PO as a single dose every morning or in divided doses</td>
<td>250 mg/day*</td>
</tr>
<tr>
<td>protriptyline (Vivactil®)†</td>
<td>5 to 60 mg PO as a single dose every morning or in divided doses</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>atomoxetine (Strattera®)†</td>
<td>40–60 mg PO QD</td>
<td>100 mg/day*</td>
</tr>
<tr>
<td><strong>Excessive daytime sleepiness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evekeo® (amphetamine)</td>
<td>5 to 60 mg/day PO in divided doses</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>amphetamine/dextroamphetamine (Adderall®)</td>
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<td></td>
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<tr>
<td>dextroamphetamine ER (Dexedrine® Spansule®)</td>
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<tr>
<td>dextroamphetamine IR (Zenzedi®, Procentra®)</td>
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<tr>
<td>methylphenidate IR (Ritalin®, Methylin®)</td>
<td>10 to 60 mg/day PO in 2 to 3 divided doses</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>armodafinil (Nuvigil®)</td>
<td>150 mg to 250 mg orally once a day</td>
<td>250 mg/day</td>
</tr>
<tr>
<td>modafinil (Provigil®)</td>
<td>200 mg PO QD as a single dose in the morning</td>
<td>400 mg/day</td>
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</table>

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataplexy in narcolepsy</td>
<td>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</td>
<td>9 g per night</td>
</tr>
<tr>
<td>EDS in narcolepsy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

Oral solution: 0.5 g per mL

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
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<th>Date</th>
<th>P&amp;T Approval Date</th>
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<td>08.17</td>
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<td>01.23.18</td>
<td>05.18</td>
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</tbody>
</table>

Updated to new template (converted algorithm to bulleted criteria, added background and references). Removed age restriction since age is not an absolute contraindication per PI and safety concerns with this drug are addressed by REMS program (required enrollment to receive therapy). Modified trial/failure criteria to include specific agents (rather than general drug classes which do not have demonstrated efficacy across the board) used in the treatment of cataplexy in narcolepsy per literature review.

Converted to new template. Added age restriction; added safety requirement related to contraindications not addressed by REMS program. Cataplexy: modified to require trial/failure of 2 agents instead of 1; On re-auth, added that member is responding positively to therapy; Updated references.

2Q 2018 annual review: Modified age requirement from ≥ 16 years to ≥ 18 years as safety and efficacy in pediatric patients have not been established per PI. Removed safety requirement related to contraindications per safety guidance. References reviewed and updated.

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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