I. Medication Description

Sodium oxybate (also known as the sodium salt of 'GHB') is an endogenous 4-carbon fatty acid that is thought to act as a neurotransmitter in the regulation of sleep cycles, blood flow, emotion, and memory. Its actions are thought to be mediated through brain receptors specific for GHB as well as through binding to GABA-B receptors. At low doses, the drug inhibits presynaptic dopamine release, while at high doses, dopamine release may be stimulated. It is believed that sodium oxybate decreases the symptoms of narcolepsy by inducing REM sleep and increasing delta sleep. The precise mechanism by which sodium oxybate produces anti-cataplectic activity in patients with narcolepsy is unknown. Anesthetic induction is thought to occur from a general CNS depressant effect on the cerebrospinal axis, and occurs at higher dosages. Intoxication with sodium oxybate or GHB can produce severe symptoms including seizures, respiratory depression, CNS depression, coma, and death.

Because of the risks of CNS depression, abuse, and misuse, Xyrem is available only through a restricted distribution program call the Xyrem REMS Program.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Xyrem is available for the treatment of the following conditions:

- Cataplexy in patients with narcolepsy when the following criteria have been met:
  - Xyrem is prescribed by a sleep specialist or neurologist **AND**
  - Member is at least 7 years of age **AND**
  - The diagnosis of narcolepsy is confirmed by polysomnography and/or multiple sleep latency test (MSLT) **AND**
  - Clinical documentation is provided showing cataplexy that causes significant functional impairment **AND**
  - For members 18 years or age or older:
    - Member has tried therapy with at least ONE of the following medications: a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), or venlafaxine
  - For members 7 to 17 years of age:
When requesting coverage of a brand medication for which a plan-preferred A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results AND

- Member has tried therapy with at least ONE of the plan-preferred medications (a tricyclic antidepressant (TCA), a selective serotonin reuptake inhibitor (SSRI), or venlafaxine) first OR at least ONE of the following criteria have been met:
  - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
  - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member’s prescription drug regimen.
  - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
  - The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where “stable” is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected solely due to the availability of a drug sample or a coupon card and the member does not otherwise meet the definition of “stable”).
  - The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member’s adherence or to compliance with the member’s plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member’s ability to achieve or maintain reasonable functional ability in performing daily activities.

- Excessive daytime sleepiness in patients with narcolepsy when the following criteria have been met:
  - Xyrem is prescribed by a sleep specialist or neurologist AND
  - Member is at least 7 years of age AND
  - The diagnosis of narcolepsy is confirmed by polysomnography and/or multiple sleep latency test (MSLT) AND
  - Clinical documentation is provided showing excessive daytime sleepiness that significantly impacts activities of daily living AND
  - The patient has tried therapy with at least ONE of the following age-appropriate medications: modafinil, armodafinil, amphetamine/derivatives, or methylphenidate/derivatives

IV. Quantity Limitations

Xyrem is covered at a quantity of up to 540mL per month to allow for maximum daily dosing.

V. Coverage Duration
Coverage is initially granted for 3 months and may be renewed.

VI.  Coverage Renewal Criteria

Coverage can be renewed in 12 month intervals based upon the following criteria:

- Response to therapy is demonstrated as follows:
  - Narcolepsy with Cataplexy: documentation showing a reduction in frequency of cataplexy attacks compared to baseline
  - Narcolepsy with Excessive daytime sleepiness: documentation of improvement in excessive daytime sleepiness compared to baseline
- Absence of unacceptable toxicity from the drug

VII.  Billing/Coding Information

Available as a 500mg/1ml oral solution in 180mg bottles.

VIII.  Summary of Policy Changes

- 8/8/17: new policy
- 11/1/18: added minimum member age, added diagnostic confirmation of narcolepsy and documentation of functional impairment, updated initial approval duration and renewal criteria
- 2/15/19: updated indicated ages; added STEP criteria to cataplexy/narcolepsy criteria in pediatrics
- 11/15/19: no policy changes

IX.  References

2. Morgenthaler TI; Kapur VK; Brown TM; Swick TJ; Alessi C; Aurora RN; Boehlecke B; Chesson AL; Friedman L; Maganti R; Owens J; Pancer J; Zak R; Standards of Practice Committee of the AASM. Practice parameters for the treatment of narcolepsy and other hypersonnias of central origin. SLEEP 2007;30(12):1705-1711.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.