Clinical Guideline

Oscar Clinical Guideline: sodium oxybate (Xyrem) (PG009, Ver. 8)

sodium oxybate (Xyrem)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Narcolepsy is a chronic neurological disorder characterized by excessive daytime sleepiness (EDS) and abnormal rapid eye movement (REM) sleep manifestations. It is classified into two types: narcolepsy type 1 (NT1), which includes cataplexy, and narcolepsy type 2 (NT2), without cataplexy. The disorder affects approximately 1 in 2,000 people and is caused by the loss of hypothalamic neurons that produce hypocretin (orexin), a neuropeptide that regulates wakefulness and REM sleep.

Treatment options for narcolepsy include central nervous system stimulants (e.g., modafinil, armodafinil, methylphenidate, amphetamines) for EDS, and antidepressants (e.g., SSRIs, SNRIs, TCAs) or sodium oxybate for cataplexy. Behavioral modifications, such as scheduled naps and sleep hygiene, are also important components of management.

Xyrem (sodium oxybate) is an oral solution of gamma-hydroxybutyrate (GHB), approved by the FDA for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with

narcolepsy. It is classified as a central nervous system depressant and is believed to act through GABA-B receptors, although its exact mechanism of action in narcolepsy is not fully understood. Xyrem (sodium oxybate) is typically administered in two equally divided doses: the first dose at bedtime and the second dose 2.5 to 4 hours later.

Definitions

"**Cataplexy**" refers to a sudden, transient episode of muscle weakness accompanied by full conscious awareness, typically triggered by emotions such as laughing, crying, or terror.

"**Excessive daytime sleepiness (EDS)**" is the inability to stay awake and alert during the day, resulting in unintended lapses into drowsiness or sleep.

"Hypocretin-1" is a natural chemical in the brain that helps regulate wakefulness.

"**Idiopathic hypersomnia (IH)**" is a neurological disorder characterized by excessive daytime sleepiness that is not caused by disturbed sleep at night, other medical conditions, or medications.

"**Multiple Sleep Latency Test (MSLT)**" is a sleep study that measures how quickly a person falls asleep during the day and whether they enter rapid eye movement (REM) sleep.

"**Narcolepsy**" is a chronic neurological disorder that affects the brain's ability to control sleep-wake cycles.

"Polysomnography (PSG)" is a sleep study used to diagnose sleep disorders by measuring certain components such as brain activity, oxygen levels, heart rate, breathing, eye movements, and leg movements.

"Sleep latency" is the amount of time it takes to fall asleep.

"**Sleep-onset REM periods (SOREMPs)**" are periods of rapid eye movement sleep that occur within 15 minutes of falling asleep, which are characteristic of narcolepsy.

Medical Necessity Criteria for Initial Authorization

The Plan considers **sodium oxybate (Xyrem)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a sleep medicine specialist, neurologist, psychiatrist, or pulmonologist with expertise in treating sleep disorders***; AND***
2. The member is 7 years of age or older; ***AND***
3. The member has a diagnosis of narcolepsy that has been confirmed by sleep lab testing or documented clinical symptoms including excessive daytime sleepiness (EDS) persisting for at least 3 months **AND** at least **ONE** of the following:
    a. Cataplexy episodes (for narcolepsy type 1)***; or***
    b. Hypocretin-1 (orexin A) deficiency (≤110 pg/mL or <1/3 of mean values of healthy individuals tested using the same standardized assay)***; or***
    c. Nocturnal sleep polysomnography showing rapid eye movement (REM) sleep latency ≤ 15 minutes, or a Multiple Sleep Latency Test (MSLT) showing a mean sleep latency ≤ 8 minutes and ≥ 2 sleep-onset REM periods (SOREMPs). A SOREMP within 15 minutes of sleep onset on the preceding nocturnal polysomnography may replace one of the SOREMPs on the MSLT***; AND***
4. The member has tried and failed prior treatments as follows:
    a. For members 18 years of age and older with narcolepsy, the member has tried and failed, or has a contraindication to, **ALL** of the following:
        i. Sunosi (solriamfetol); ***and***
        ii. Lumryz (sodium oxybate)***; and***
        iii. Wakix (pitolisant)***; or***
    b. For members 7 to 17 years of age with narcolepsy and excessive daytime sleepiness (EDS), the member has tried and failed, or has a contraindication to, **ALL** of the following:
        i. Wakix (pitolisant)***; and***
        ii. Lumryz (sodium oxybate); ***or***
    c. For members 7 to 17 years of age with narcolepsy and cataplexy, the member has tried and failed, or has a contraindication to, Lumryz (sodium oxybate)***; AND***
5. The member does **NOT** have **ANY** of the following:
    a. Succinic semialdehyde dehydrogenase (SSADH) deficiency***; or***
    b. Documentation indicating concomitant use with, or inability to abstain from, any of the following while taking Xyrem:
        i. Alcohol (e.g., beer, wine, whisky)***; or***
        ii. Sedative hypnotics (e.g., alprazolam, diazepam, lorazepam, zolpidem)***; or***

iii. Lumryz, Xywav, or other sodium oxybate products***; or***

c. A condition that better explains the hypersomnolence and/or MSLT findings, such as:

i. Insufficient sleep***; or***

ii. Obstructive sleep apnea***; or***

iii. Delayed sleep phase disorder***; or***

iv. The effect of medication or substances or their withdrawal***; AND***

6. Xyrem is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above prior authorization criteria are met, sodium oxybate (Xyrem) will be approved for 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if the member has recent (within the last 3-months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. The member has experienced a positive clinical response to sodium oxybate (Xyrem) therapy as demonstrated by a reduction in symptoms of cataplexy and/or EDS; ***AND***
2. The member continues to abstain from alcohol and sedative hypnotics; ***AND***
3. sodium oxybate (Xyrem) will not be used in combination with Lumryz, Xywav, Wakix, or other sodium oxybate products; ***AND***
4. sodium oxybate (Xyrem) continues to be prescribed at a dose and frequency that is within FDA approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines for the requested indication.

Experimental or Investigational / Not Medically Necessary

Sodium oxybate (Xyrem) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Sodium oxybate (Xyrem) has been studied for various indications beyond its approved uses. However, the current evidence is limited and inconclusive for these non-supported indications:

- Alcohol Dependence/Alcohol Use Disorders (AUD).
- Alcohol Withdrawal Syndrome.
- Alternating Hemiplegia of Childhood.
- Anxiety, Post Traumatic/Post Traumatic Stress Disorder (PTSD).

- Binge Eating Disorder (BED).
- Chronic Fatigue Syndrome/Myalgic Encephalitis (CFS/ME).
- Cluster Headache.
- Essential Tremor.
- Fibromyalgia.
- Hypersomnia.
- Idiopathic Hypersomnia.
- Insomnia Related to Schizophrenia/Schizophrenia.
- Laryngeal Tremor/Spasmodic Dysphonia.
- Obstructive Sleep Apnea (OSA).
- Parkinson's Disease (PD)/Rapid Eye Movement Sleep Behavior Disorder.
- Sedative Abuse Prevention.
- Sleep Initiation and Maintenance Disorders.
- Traumatic Brain Injury (TBI).
- When used in combination with alcohol, sedative hypnotics, or other medications containing sodium oxybate, gamma-hydroxybutyrate (GHB), or GHB precursors.
- When used in members with succinic semialdehyde dehydrogenase deficiency, a rare inborn error of metabolism.
- For members under 7 years of age, safety and efficacy have not been established in this pediatric population.

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