BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.60.005

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	June 6, 2014
Subject:	Xyrem	**Page:**	1 of 6

Last Review Date: December 8, 2023

Xyrem

Description

Xyrem (sodium oxybate)

Background
Xyrem (sodium oxybate) is a central nervous system depressant used for the treatment of cataplexy in narcolepsy or excessive daytime sleepiness. The mechanism of action of Xyrem in the treatment of narcolepsy is unknown. Sodium oxybate is the sodium salt of gamma-hydroxyburtyrate (GHB) an endogenous compound and metabolite of the neurotransmitter GABA. It is hypothesized that the therapeutic effects of Xyrem on cataplexy and excessive daytime sleepiness are mediated through $GABA_B$ actions at noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons (1).

Regulatory Status
FDA-approved indications: Xyrem is a central nervous system depressant indicated for the treatment of cataplexy in narcolepsy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy (1).

Xyrem includes a boxed warning citing the risks of central nervous system depression and abuse and misuse. Use caution when considering the concurrent use of Xyrem with other CNS depressants. Because of the risks of CNS depression, abuse and misuse Xyrem is available only through a restricted distribution program called the Xywav and Xyrem REMS (1).

Xyrem has warnings for depression and suicidality, confusion/anxiety, parasomnias and high sodium content in Xyrem. In addition, patients should be instructed to not engage in activities

requiring mental alertness or motor coordination, including operating hazardous machinery, for at least 6 hours after taking Xyrem (1).

Xyrem is contraindicated in patients with succinic semialdehyde dehydrogenase deficiency and in combination with sedative hypnotics or alcohol (1).

Safety and effectiveness of Xyrem in patients less than 7 years of age have not been established (1).

Related policies
Hetlioz, Orexin Antagonists, Rozerem, Sedative Hypnotics, Xywav

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xyrem may be considered **medically necessary** if the conditions indicated below are met.

Xyrem may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 7 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Cataplexy in narcolepsy
2. Excessive daytime sleepiness (EDS) in narcolepsy

AND ALL of the following:

1. Patient and prescriber are both enrolled in the Xyrem REMS Program
2. Prescriber will monitor for signs of misuse, abuse, and addiction during therapy

AND NONE of the following:

1. Succinic semialdehyde dehydrogenase deficiency
2. Concurrent therapy with a Prior Authorization (PA) sleep aid (see Appendix 1) or with another oxybate product (see Appendix 2)

Prior – Approval *Renewal* Requirements

Age 7 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Cataplexy in narcolepsy
2. Excessive daytime sleepiness (EDS) in narcolepsy

AND ALL of the following:

1. Prescriber will continue to monitor for signs of misuse, abuse, and addiction during therapy
2. **NO** concurrent therapy with another Prior Authorization (PA) sleep aid (see Appendix 1) or with another oxybate product (see Appendix 2)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 810 grams (1620 ml) per 90 days

Duration 6 months

Prior – Approval *Renewal* Limits

Quantity 810 grams (1620 ml) per 90 days

Duration 12 months

Rationale

Summary

Xyrem (sodium oxybate) is a central nervous system depressant used for the treatment of cataplexy in narcolepsy or excessive daytime sleepiness. Xyrem includes a boxed warning

citing the risks of central nervous system depression and abuse and misuse. Xyrem has warnings for depression and suicidality, confusion/anxiety, parasomnias, and high sodium content in Xyrem. Xyrem is available only through a restricted distribution program called the Xywav and Xyrem REMS. Safety and effectiveness of Xyrem in patients less than 7 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Xyrem while maintaining optimal therapeutic outcomes.

References

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals Inc.; April 2023.

Policy History

Date	Action
May 2014	New addition to PA
September 2014	Annual review
June 2015	Annual review
September 2016	Annual editorial review and reference update Policy number change from 5.07.11 to 5.60.05
December 2017	Annual editorial review and reference update Addition of age to renewal
November 2018	Annual editorial review and reference update Age limit decreased to 7 years or older
December 2019	Annual review
May 2020	Revised no dual therapy requirement
June 2020	Annual review
March 2021	Annual editorial review and reference update
May 2021	Added no dual therapy with another oxybate product
June 2021	Annual editorial review. Revised Appendix 1
September 2022	Annual editorial review and reference update. Added Quviviq to Appendix 1
September 2023	Annual review and reference update
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.

Appendix 1 - List of Prior Authorization (PA) Sleep Aids

Generic Name	Brand Name
daridorexant	Quviviq
estazolam	Prosom
eszopiclone	Lunesta
flurazepam	Dalmane
lemborexant	Dayvigo
quazepam	Doral
ramelteon	Rozerem
tasimelteon	Hetlioz
suvorexant	Belsomra
temazepam	Restoril
triazolam	Halcion
zaleplon	Sonata
zolpidem	Ambien
zolpidem extended-release	Ambien CR
zolpidem oral spray	Zolpimist
zolpidem sublingual	Edluar
zolpidem sublingual	Intermezzo

Appendix 2 - List of Oxybate Products

Generic Name	Brand Name
sodium oxybate	Xyrem
calcium, magnesium, potassium, sodium oxybates	Xywav