Oxybate Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date
05-01-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Lumryz™ (sodium oxybate extended release) Oral suspension	Treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy		11
Xyrem ®, Sodium Oxybate Oral solution	Treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy		1
Xywav ® (calcium, magnesium, potassium, and sodium oxybate) Oral solution	Treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy Treatment of idiopathic hypersomnia (IH) in adults		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Narcolepsy	Narcolepsy is a chronic neurological disorder caused by the inability to regulate sleep-wake cycles. At various times throughout the day, patients with narcolepsy experience irresistible bouts of sleep and could fall asleep. If left undiagnosed or untreated, narcolepsy can interfere with psychological, social, and cognitive function and development and can inhibit academic, work, and social activities.(3) Symptoms may include excessive daytime sleepiness (EDS), cataplexy, sleep paralysis, and hallucinations. All patients diagnosed with narcolepsy will have excessive daytime sleepiness. However, sleepiness in narcolepsy is more like a "sleep attack", where an overwhelming sense of sleepiness comes on quickly.(3) There is limited evidence to advise on treatment of special populations such as children, pregnant women, and breastfeeding mothers.(6) The American Family Physician recommends referral to a sleep clinic if narcolepsy is suspected.(4) The American Academy of Sleep Medicine indicates treatment goals

	should be to alleviate daytime sleepiness and produce the fullest possible return of normal function for patients at work, school, home, and socially.(5)
	
	Excessive daytime sleepiness (EDS) is characterized by persistent sleepiness regardless of how much sleep an individual gets at night. In between sleep attacks, individuals have normal levels of alertness, particularly if doing activities that keep their attention. The most common causes of EDS include narcolepsy, obstructive sleep apnea, shift work disorder, sleep deprivation, medication effects, and other medical and psychiatric conditions.(6) Narcolepsy has two types, narcolepsy with cataplexy and without cataplexy. Narcolepsy with cataplexy involves the sudden loss of voluntary muscle tone while awake. It is often triggered by sudden, strong emotions such as laughter, fear, anger, stress, or excitement. The symptoms of cataplexy may appear weeks or even years after the onset of EDS.(3) The American Academy of Sleep Medicine (AASM) 2021 guidelines combined the recommendations for narcolepsy with cataplexy and EDS associated with narcolepsy. The AASM recommend the following for the pharmacologic treatment of narcolepsy:(7)
	
	• Strong treatment recommendations:
	  o Modafinil
	  o Pitolisant
	  o Sodium oxybate
	  o Solriamfetol
	• Conditional treatment recommendations:
	  o Armodafinil
	  o Dextroamphetamine
	  o Methylphenidate
	• There was insufficient evidence to make recommendations for SSRI and SNRIs for the treatment of narcolepsy.(7)

Efficacy	Lumryz The effectiveness of Lumryz for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy has been established based on a double-blind, randomized, placebo-controlled, two-arm multi-center study to assess the efficacy and safety of a once nightly administration of Lumryz in patients with narcolepsy. The three co-primary endpoints were the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I), and mean change in weekly cataplexy attacks.(11) The mean number of cataplexy attacks per week at baseline was 18.9 in the Lumryz group and 19.8 in the placebo group. A statistically significant improvement was seen on the MWT, CGI-I, and mean weekly cataplexy attacks, for the 6 g (Week 3), 7.5 g (Week 8), and 9 g (Week 13) dose of Lumryz, compared to the placebo group.(11) The effectiveness of Lumryz in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy was established in a double-blind, placebo-controlled, randomized-withdrawal study (NCT02221869). The study was conducted in 106 pediatric patients (median age: 12 years; range: 7 to 17 years) with a baseline history of at least 14 cataplexy attacks in a typical 2-week period prior to any treatment for narcolepsy symptoms.(11) Pediatric patients taking stable dosages of immediate-release sodium oxybate who were withdrawn from immediate-release sodium oxybate treatment and were randomized to placebo during the double-blind treatment period experienced a statistically significant increase in weekly cataplexy attacks compared with patients who were randomized to continue treatment with immediate-release sodium oxybate. Patients randomized to receive placebo during the double-blind treatment period experienced a statistically significant worsening of cataplexy severity and narcolepsy overall according to the clinician's assessment compared with patients randomized to continue receiving immediate-release sodium oxybate.(11)

	Xyrem The effectiveness of sodium oxybate in the treatment of EDS in narcolepsy was established in two 8-week, randomized, double-blind, placebo-controlled trials in patients with narcolepsy. Patients were randomized to one of four groups: placebo, sodium oxybate 4.5 grams per night, sodium oxybate 6 grams per night, or sodium oxybate 9 grams per night. The primary efficacy was extent of sleepiness in everyday situations (determined using Epworth Sleepiness Scale) and change in symptoms of EDS (evaluated using Clinical Global Impression of Change tool). Sodium oxybate was associated with statistically significant differences for both primary outcomes when compared to placebo.(1) The effectiveness of sodium oxybate in the treatment of cataplexy was established in two 4-week, randomized, double-blind, placebo-controlled trials in patients with narcolepsy. Patients were randomized to receive placebo or sodium oxybate dosed at 3 grams to 9 grams nightly. The primary efficacy endpoint for both trials was frequency of cataplexy attacks. Both trials found that dose of 6 grams to 9 grams resulted in statistically significant reduction in frequency of cataplexy attacks. The trials also found that discontinuation of sodium oxybate in patients who had been treated with it long term resulted in a significant increase in cataplexy attacks.(1) Xywav Efficacy of Xywav for the treatment of cataplexy and excessive daytime sleepiness in adult patients with narcolepsy was established in a double-blind, placebo-controlled, randomized-withdrawal study (Study 1; NCT03030599). This study had two parts, consisting of the main study, followed by an optional 24-week open-label extension (OLE). The main study consisted of a 12-week open-label optimized treatment and titration period (OL OTTP), followed by a 2-week stable-dose period (SDP), and finally a 2-week double-blind randomized-withdrawal period (DB RWP).(2) Patients entering the study were taking a stable dosage of 1) Xyrem only, 2) Xyrem + another anticataplectic, 3) a non-Xyrem anticataplectic, or 4) were cataplexy-treatment naïve. The primary efficacy endpoint was the change in frequency of cataplexy attacks from the 2 weeks of the SDP to the 2 weeks of the DB RWP. The key secondary endpoint was the change in the Epworth Sleepiness Scale (ESS) score, as a measure of reduction in EDS from the end of the SDP to the end of the DB RWP. Patients taking stable doses of Xywav who discontinued Xywav treatment and were randomized to placebo during the DB RWP experienced a significant worsening in the average weekly number of cataplexy attacks and in ESS score, compared with patients randomized to continue treatment with Xywav.(2) The effectiveness of Xywav in pediatric patients is based upon a clinical study in patients treated with Xyrem.(2)

Idiopathic Hypersomnia	Idiopathic hypersomnia (IH) is a sleep disorder characterized by excessive daytime sleepiness despite adequate quantity and quality of sleep, and difficulty waking up from nocturnal sleep and daytime naps. IH often develops in adolescents and can be lifelong with some instances of remission. The diagnosis is one of exclusion by ruling out other causes, such as sleep apnea, restless leg syndrome, narcolepsy, periodic limb movement disorder, medications, substance use/abuse, or other medical, neurological, or psychiatric conditions. The diagnosis should be made by a sleep specialist and a sleep study completed.(8)
	
	Treatment focuses on the symptoms of sleepiness due to the underlying causes being unknown. The American Academy of Sleep Medicine recommend the following for the pharmacologic treatment of IH:(7)
	
	• Strong treatment recommendations:
	  o Modafinil
	• Conditional treatment recommendations:
	  o Clarithromycin

	o Methylphenidate o Pitolisant o Sodium oxybate(7)
Efficacy	Xywav Efficacy of Xywav for the treatment of idiopathic hypersomnia (IH) in adult patients as a once or twice nightly regimen was established in a double-blind, placebo-controlled, randomized-withdrawal, study (Study 2, NCT03533114). This study consisted of a minimum of 10-week open-label treatment titration and optimization period (OL OTTP), (with up to 4 additional weeks) to allow for an optimally effective and tolerable dose and regimen followed by a 2-week stable dose period (SDP), a 2-week double-blind, randomized withdrawal period (DB RWP), and a 24-week open label safety extension period (OLE).(2) Study 2 enrolled 154 patients with idiopathic hypersomnia, 19 to 75 years of age. Of the 154 patients, 115 were evaluable for efficacy data and were randomized 1:1 to continue treatment with Xywav or to placebo in the 2-week DB RWP. The primary efficacy endpoint was the change in Epworth Sleepiness Scale (ESS) score, as a measure of reduction in EDS from the end of the SDP to the end of the DB RWP.(2) Patients in Study 2 taking stable doses of Xywav who were withdrawn from Xywav treatment and randomized to placebo during DB RWP experienced significant worsening in ESS score compared with patients randomized to continue treatment with Xywav ($p<0.0001$) across all dosing regimens.(2)
Safety	*Lumryz* Lumryz carries the following contraindications: • Use in combination with sedative hypnotics (i.e., benzodiazepines, butabarbital, eszopiclone, Rozerem [ramelteon], Silenor [doxepin], zaleplon, zolpidem) • Use in combination with alcohol • Use in patients with succinic semialdehyde dehydrogenase deficiency(11) Boxed warnings include: • Central Nervous System Depression. Lumryz is a CNS depressant and respiratory depression can occur with Lumryz use • Abuse and Misuse. Lumryz is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB is associated with CNS adverse reactions, including seizure, respiratory depression, decreased consciousness, coma, and death Lumryz is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) due to the risks of CNS depression, abuse, and misuse. This program is called the Lumryz REMS.(11) Xyrem Xyrem carries the following contraindications: • Use in combination with sedative hypnotics • Use in combination with alcohol • Use in patients with succinic semialdehyde dehydrogenase deficiency(1) Boxed warnings include:

	• Central Nervous System Depression. Sodium oxybate is a CNS depressant. Clinically significant respiratory depression occurred in adult patients treated with Xyrem at recommended doses • Abuse and Misuse. Sodium oxybate is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death(1) Xyrem is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) due to the risks of CNS depression, abuse, and misuse. This program is called the Xywav and Xyrem REMS.(1) Xywav Xywav carries the following contraindications: • Use in combination with sedative hypnotics • Use in combination with alcohol • Use in patients with succinic semialdehyde dehydrogenase deficiency(2) Boxed warnings include: • Central Nervous System Depression. Xywav is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with Xywav at recommended doses • Abuse and Misuse. The active moiety of Xywav is oxybate or gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death(2) Xywav is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) due to the risks of CNS depression, abuse, and misuse. This program is called the Xywav and Xyrem REMS.(2)

REFERENCES

Number	Reference
1	Xyrem prescribing information. Jazz Pharmaceuticals, Inc. April 2023.
2	Xywav prescribing information. Jazz Pharmaceuticals, Inc. April 2023.
3	National Institute of Neurological Disorders and Stroke. Narcolepsy. NIH Publication No. 17-1637.
4	Ramar, Kannan MD and Olson, Eric MD. Management of Common Sleep Disorders. Am Fam Physician . 2013 Aug 15; 88(4): 231-238.
5	Krahn, Lois MD, et al. Quality Measures for the Care of Patients with Narcolepsy. Journal of Clinical Sleep Medicine. 2015; Vol. 11(3).
6	Pagel J. Excessive daytime sleepiness. Am Fam Physician. 2009;79(5): 391-395.
7	Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021;17(9):1881–1893.
8	Idiopathic hypersomnia. Sleep Education. (2021, May 6).
9	Reference no longer in use
10	Reference no longer in use.
11	Lumryz prescribing information. Avadel CNS Pharmaceuticals, LLC. October 2024

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Xywav	calcium, mag, potassium, & sod oxybates oral soln	500 MG/ML	M ; N ; O ; Y	N		
Lumryz ; Lumryz starter pack ; Sodium oxybate ; Xyrem	sodium oxybate oral solution ; sodium oxybate pack for er susp ; sodium oxybate pack for oral er susp	4.5 & 6 & 7.5 GM ; 4.5 GM ; 500 MG/ML ; 6 GM ; 7.5 GM ; 9 GM	M ; N ; O ; Y	M ; N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Lumryz	sodium oxybate pack for oral er susp	4.5 GM ; 6 GM ; 7.5 GM ; 9 GM	30	Packets	30	DAYS			
Lumryz starter pack	sodium oxybate pack for er susp	4.5 & 6 & 7.5 GM	28	Packets	180	DAYS			
Sodium oxybate ; Xyrem	Sodium Oxybate Oral Solution 500 MG/ML	500 MG/ML	540	mLs	30	DAYS			
Xywav	Calcium, Mag, Potassium, & Sod Oxybates Oral Soln	500 MG/ML	540	mLs	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Lumryz ; Lumryz starter pack ; Sodium oxybate ; Xyrem	sodium oxybate oral solution ; sodium oxybate pack for er susp ; sodium oxybate pack for oral er susp	4.5 & 6 & 7.5 GM ; 4.5 GM ; 500 MG/ML ; 6 GM ; 7.5 GM ; 9 GM	Commercial ; HIM ; ResultsRx
Xywav	calcium, mag, potassium, & sod oxybates oral soln	500 MG/ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Lumryz	sodium oxybate pack for oral er susp	4.5 GM ; 6 GM ; 7.5 GM ; 9 GM	Commercial ; HIM ; ResultsRx
Lumryz starter pack	sodium oxybate pack for er susp	4.5 & 6 & 7.5 GM	Commercial ; HIM ; ResultsRx
Sodium oxybate ; Xyrem	Sodium Oxybate Oral Solution 500 MG/ML	500 MG/ML	Commercial ; HIM ; ResultsRx
Xywav	Calcium, Mag, Potassium, & Sod Oxybates Oral Soln	500 MG/ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of narcolepsy with cataplexy OR narcolepsy with excessive daytime sleepiness AND ONE of the following: 1. The patient has tried and had an inadequate response to modafinil OR armodafinil OR 2. The patient has an intolerance or hypersensitivity to modafinil OR armodafinil OR 3. The patient has an FDA labeled contraindication to BOTH modafinil AND armodafinil OR B. The patient has a diagnosis of idiopathic hypersomnia AND ALL of the following: 1. The requested agent is Xywav AND 2. The patient has completed a sleep study AND 3. All other causes of hypersomnia have been ruled out AND 4. ONE of the following: A. The patient has tried and had an inadequate response to modafinil OR B. The patient has an intolerance or hypersensitivity to modafinil OR C. The patient has an FDA labeled contraindication to modafinil OR C. The patient has another FDA approved indication for the requested agent and route of administration AND 2. If the patient has an FDA labeled indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent OR B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication AND 3. If the request is for brand Xyrem, then ONE of the following: A. The patient has an intolerance or hypersensitivity to authorized generic Sodium Oxybate that is not expected to occur with the requested agent OR B. The patient has an FDA labeled contraindication to authorized generic Sodium Oxybate that is not expected to occur with the requested agent **OR** C. There is support for the use of the requested agent over authorized generic Sodium Oxybate AND 4. The patient will NOT be using the requested agent in combination with another oxybate agent, Sunosi, OR Wakix for the requested indication AND 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., sleep specialist, neurologist, psychiatrist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis AND 6. The patient does NOT have any FDA labeled contraindications to the requested agent Length of Approval: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	Quantity limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit OR 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication AND 2. There is support for therapy with a higher dose for the requested indication OR B. BOTH of the following:

Module	Clinical Criteria for Approval
	1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication AND 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** up to 12 months