UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 2021-17
Program	Prior Authorization/Medical Necessity
Medication	Lumryz™ (sodium oblate), sodium oxybate [Xyrem authorized generic (manufactured by Amneal)]*, sodium oxybate [Xyrem authorized generic (manufactured by Hikma)], Xyrem® (sodium oxybate), Xywav™ (calcium, magnesium, potassium, and sodium oxybates)
P&T Approval Date	4/2014, 8/2014, 4/2015, 2/2016, 4/2016, 7/2016, 7/2017, 7/2018, 8/2019, 1/2020, 4/2020, 12/2020, 11/2021, 11/2022, 11/2023
Effective Date	2/1/2024

1. Background:

Lumryz, Xyrem® (sodium oxybate) and Xywav™ are central nervous system depressants indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in patients with narcolepsy. Xyway is also indicated for idiopathic hypersomnia (IH) in adults.

Lumryz, Xyrem and Xywav are classified as a Schedule III controlled substance by Federal law. The active ingredient, sodium oxybate or gamma-hydroxybutyrate (GHB), is listed in the most restrictive schedule of the Controlled Substances Act (Schedule I). Thus, non-medical uses are classified under Schedule I.

Lumryz, Xyrem and Xywav are available only through a REMS program with restricted distribution. The REMS Program provides educational materials to the prescriber and the patient explaining the risks and proper use of Lumryz, Xyrem and Xywav, and the required prescription form. Once it is documented that the patient has read and/or understood the materials, the drug will be shipped to the patient. The REMS Program also recommends patient follow-up every 3 months. Physicians are expected to report all serious adverse events to the manufacturer.

Members will be required to meet the coverage criteria below.

2. Coverage Criteria[a]:

A. Narcolepsy with Cataplexy (i.e., Narcolepsy Type 1)

1. **Initial Authorization**

a. **Lumryz, sodium oxybate [Xyrem authorized generic (manufactured by Amneal)]*, sodium oxybate [Xyrem authorized generic (manufactured by Hikma)], Xyrem*** or **Xywav** will be approved based on **all** of the following criteria:

(1) Submission of medical records (e.g. chart notes, laboratory values) documenting a diagnosis of narcolepsy *with* cataplexy (i.e., Narcolepsy Type 1) with **both** of the following:

(a) The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.

-AND-

(b) A mean sleep latency of ≤ 8 minutes and two or more sleep onset REM periods (SOREMPs) on an MSLT performed according to standard techniques following a normal overnight polysomnogram. A SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.

-AND-

(2) Physician attestation to **both** of the following:

(a) Patient has experienced cataplexy defined as more than one episode of sudden loss of muscle tone with retained consciousness

-AND-

(b) Other causes of sleepiness have been ruled out or treated (including but not limited to obstructive sleep apnea, insufficient sleep syndrome, shift work, the effects of substances or medications, or other sleep disorders).

–AND–

(3) Prescribed by **one** of the following:

(a) Neurologist
(b) Psychiatrist
(c) Pulmonologist
(d) Sleep Medicine Specialist

–AND–

(4) For **sodium oxybate [Xyrem authorized generic (manufactured by Amneal)]* and brand Xyrem***: A trial, failure or intolerance to **THREE** of the following:

(a) Lumryz
(b) sodium oxybate [Xyrem authorized generic (manufactured by Hikma)]
(c) Xywav
(d) Wakix

Authorization will be issued for 3 months.

2. **Reauthorization**

a. The requested medication will be approved for continuation of therapy based on **one** of the following criteria:

(1) Documentation demonstrating a reduction in frequency of cataplexy attacks associated with therapy

–OR–

(2) Documentation demonstrating reduction in symptoms of excessive daytime sleepiness associated with therapy

Authorization will be issued for 12 months.

B. Narcolepsy without Cataplexy (i.e., Narcolepsy Type 2)

1. **Initial Authorization**

a. **Lumryz, sodium oxybate [Xyrem authorized generic (manufactured by Amneal)]*, sodium oxybate [Xyrem authorized generic (manufactured by Hikma)], Xyrem*** or **Xywav** will be approved based on **all** of the following criteria:

(1) Submission of medical records (e.g. chart notes, lab values) documenting a diagnosis of narcolepsy *without* cataplexy (i.e., Narcolepsy Type 2) with **both** of the following:

(a) The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.

(b) A mean sleep latency of ≤ 8 minutes and two or more sleep onset REM periods (SOREMPs) are found on a MSLT performed according to standard techniques following a normal overnight polysomnogram. A

SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.

(2) Physician attestation to the following:

(a) Other causes of sleepiness have been ruled out or treated (including but not limited to obstructive sleep apnea, insufficient sleep syndrome, shift work, the effects of substances or medications or their withdrawal, sleep phase disorder, or other sleep disorders).

–AND–

(3) History of failure, contraindication, or intolerance of **all** of the following:

(a) **One** of the following:

i. Amphetamine based stimulant (e.g., amphetamine, dextroamphetamine)
ii. Methylphenidate based stimulant

–AND–

(b) **One** of the following:

i. modafanil (Provigil)
ii. armodafanil (Nuvigil)

–AND–

(c) Sunosi

–AND–

(4) Prescribed by **one** of the following:

(a) Neurologist
(b) Psychiatrist
(c) Pulmonologist
(d) Sleep Medicine Specialist

–AND–

(5) For **sodium oxybate [Xyrem authorized generic (manufactured by Amneal)]* and brand Xyrem***: A trial, failure or intolerance to **THREE** of the following:

(a) Lumryz
(b) sodium oxybate [Xyrem authorized generic (manufactured by Hikma)]
(c) Xywav
(d) Wakix

Authorization will be issued for 3 months.

2. **Reauthorization**

a. The requested medication will be approved for continuation of therapy based on the following criteria:

(1) Documentation demonstrating reduction in symptoms of excessive daytime sleepiness associated with therapy

Authorization will be issued for 12 months.

C. Idiopathic Hypersomnia

1. **Initial Authorization**

a. **Xywav** will be approved based on **all** of the following criteria:

(1) Submission of medical records (e.g. chart notes, lab values) documenting a diagnosis of idiopathic hypersomnia with **both** of the following:

(a) The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.

(b) A mean sleep latency of ≤ 8 minutes and fewer than two REM periods (SOREMPs) are found on a MSLT performed according to standard techniques following a normal overnight polysomnogram, or no SOREMPs if the REM sleep latency on the preceding polysomnogram was ≤ 15 minutes.

(2) Physician attestation to the following:

(a) Other causes of sleepiness have been ruled out or treated (including but not limited to obstructive sleep apnea, insufficient sleep syndrome, shift work, the effects of substances or medications or their withdrawal, sleep phase disorder, or other sleep disorders).

–AND–

(3) History of failure, contraindication, or intolerance of **all** of the following:

(a) **One** of the following:

i. Amphetamine based stimulant (e.g., amphetamine, dextroamphetamine)
ii. Methylphenidate based stimulant

–AND–

(b) **One** of the following:

i. modafanil (Provigil)
ii. armodafanil (Nuvigil)

(4) Prescribed by **one** of the following:

(a) Neurologist
(b) Psychiatrist
(c) Pulmonologist
(d) Sleep Medicine Specialist

Authorization will be issued for 3 months.

2. **Reauthorization**

a. **Xywav** will be approved for continuation of therapy based on the following criteria:

(1) Documentation demonstrating reduction in symptoms of excessive daytime sleepiness associated with therapy

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

*Sodium oxybate [Xyrem authorized generic (manufactured by Amneal)] and brand Xyrem are typically excluded from coverage.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc; March 2022.
2. American Academy of Sleep Medicine. International Classification of Sleep Disorders: Diagnostic and Coding Manual [online]. 3rd ed. Westchester, IL: American Academy of Sleep Medicine; 2014.
3. Morgenthaler TI1, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. Sleep. 2007 Dec;30(12):1705-11.
4. Wise MS1, Arand DL, Auger RR, et al. Treatment of narcolepsy and other hypersomnias of central origin. Sleep. 2007 Dec;30(12):1712-27.
5. Sunsoi [package insert]. New York, NY: Axsome Therapeutics, Inc;. June 2022.
6. Xywav [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc; March 2022.
7. Lumryz [package insert]. Chesterfield, MO: Avadel CNS Pharmaceuticals, LLC; May 2023.

8. Sodium Oxybate [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals NY LLC; April 2023.
9. Sodium Oxybate [package insert]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc.; April 2023.

Program	Prior Authorization/Medical Necessity - Sodium oxybates
Change Control	
4/2014	New medical necessity criteria.
8/2014	Added NJ language. Updated Background and References.
11/2014	Administrative change - Tried/Failed exemption for State of New Jersey removed.
4/2015	Removed antidepressant requirement and added additional criteria for confirmation of diagnosis.
2/2016	Annual review with no change to clinical criteria. Indicate initial authorization of 3 months. Updated references.
4/2016	Removed 'reduction in cataplexy attacks' from reauthorization criteria for Narcolepsy Type 2.
7/2016	No change to clinical criteria. Update background to change Xyrem Success program to the Xyrem REMS program. Updated formatting. Added Maryland Continuation of Care. Added Indiana and West Virginia coverage information.
11/2016	Administrative change. Added California coverage information.
7/2017	Annual review with no changes to coverage criteria. Updated references. State mandate reference language updated.
7/2018	Annual review with no changes to coverage criteria. Updated references.
8/2019	Annual review with reorganization of criteria requiring documentation vs. provider attestation.
1/2020	Added requirement for trial of Sunosi for narcolepsy without cataplexy.
4/2020	Removed physician attestation that cataplexy is absent for type 2 narcolepsy.
12/2020	Added Xywav to criteria.
11/2021	Added criteria for idiopathic hypersomnia for Xywav due to new labeling. Added pulmonologist to specialists.
11/2022	Annual review. Updated references.
11/2023	Added Lumryz to criteria. Noted sodium oxybate (manufactured by Amneal) and brand Xyrem are typically excluded.