Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 08/01/2021**
Policy Number: PA.CP.PMN.42	**Effective Date: 01/2020** **Revision Date: 07/2021**
Policy Name: Sodium Oxybate (Xyrem) and Calcium, Magnesium, Potassium, and Sodium Oxybate (Xywav)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

Allowed members 65 years old or older to bypass redirections to any TCA throughout the policy; for narcolepsy with excessive daytime sleepiness: added trial of Sunosi, and added requirement for combination use of preferred agents if request is for concomitant use.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Sodium Oxybate (Xyrem) and Calcium, Magnesium, Potassium, and Sodium Oxybate (Xywav)

Reference Number: PA.CP.PMN.42
Effective Date: 01/18
Last Review Date: 07/2021

Coding Implications
Revision Log

Description
Sodium oxybate (Xyrem®) and calcium, magnesium, potassium, and sodium oxybate (Xywav™) are central nervous system (CNS) depressants.

FDA approved indication
Xyrem and Xywav are indicated for the treatment of patients 7 years of age and older with:
- Cataplexy in narcolepsy
- Excessive daytime sleepiness (EDS) in narcolepsy

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness ® that Xyrem and Xywav are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Narcolepsy with Cataplexy (must meet all)**:**
1. Prescribed for the treatment of cataplexy in narcolepsy;
2. Age ≥ 7 years;
3. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
4. Documentation of one of the following (a or b):
   a. Excessive daytime sleepiness associated with narcolepsy as confirmed by documented multiple sleep latency test and one of the following:
      i. Mean sleep latency ≤ 8 minutes with evidence of two or more sleep-onset rapid eye movement periods (SOREMPs);
      ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight polysomnography (PSG);
   b. Lumbar puncture shows cerebrospinal fluid (CSF) hypocretin-1 level ≤ 110 pg/mL;
5. Failure of 2 of the following antidepressants, each trialed for ≥ 1 month, unless all are contraindicated, or clinically significant adverse effects are experienced: venlafaxine, fluoxetine, atomoxetine, clomipramine*, or protriptyline*;
   **If member's age is ≥ 65, tricyclic antidepressants are not required for trial.*
6. Dose does not exceed 9 grams (18 mL) per day.

Approval duration: 12 months

B. Narcolepsy with Excessive Daytime Sleepiness (EDS) (must meet all)**:**
1. Diagnosis of narcolepsy with EDS;
2. Age ≥ 7 years;

3. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
4. Documentation of both of the following (a and b):
   a. Excessive daytime sleepiness associated with narcolepsy as confirmed by documented multiple sleep latency test and one of the following:
      i. Mean sleep latency ≤ 8 minutes with evidence of two or more sleep-onset rapid eye movement periods (SOREMPs);
      ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight polysomnography (PSG);
   b. Member has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months;
5. Failure of a 1-month trial of one of the following generic central nervous system stimulant-containing agent at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: amphetamine, dextroamphetamine, or methylphenidate;
   **Prior authorization may be required for CNS stimulants*
6. If member is ≥ 17 years of age, failure of a 1-month trial of armodafinil or modafinil at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for armodafinil and modafinil*
7. Failure of a 1-month trial of Sunosi™ at up to maximally indicated doses, unless contraindicated or clinically significant side effects are experienced;
   **Prior authorization may be required for Sunosi*
8. If request is for concomitant therapy with other antinarcoleptic agents (e.g., Wakix®, Sunosi) for members ≥ 18 years of age, failure of combination therapy with modafinil or armodafinil and Sunosi, unless contraindicated or clinically significant adverse effects are experienced;
9. Dose does not exceed 9 grams (18 mL) per day .

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care Policy, PA.LTSS.PHAR.01, applies;
2. Documentation of positive response to therapy as evidenced by, but not limited to, improvement in <u>any</u> of the following parameters: reduction in frequency of cataplexy attacks, reported daytime improvements in wakefulness;
3. If request is for a dose increase, new dose does not exceed 9 grams (18 mL) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy, PA.LTSS.PHAR.01, applies; or
2. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12 months

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CNS: central nervous system
EDS: excessive daytime sleepiness
FDA: Food and Drug Administration
IR: immediate-release
MSLT: multiple sleep latency test
PSG: polysomnography
SOREMP: sleep-onset rapid eye movement period

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cataplexy		
Venlafaxine (Effexor®)†	75–150 mg PO BID, or 75–150 mg (extended release) PO QAM	375 mg/day* (IR tablets); 225* mg/day (extended release)
Fluoxetine (Prozac®)†	20 to 80 mg PO QAM	80 mg/day
Clomipramine (Anafranil®)†	10 to 150 mg PO as a single dose every morning or in divided doses	250 mg/day*
Protriptyline (Vivactil®)†	5 to 60 mg PO as a single dose every morning or in divided doses	60 mg/day
atomoxetine (Strattera®)†	40–60 mg PO QD	100 mg/day*
Excessive daytime sleepiness		
amphetamine (Evekeo®)	5 to 60 mg/day PO in divided doses	60 mg/day
amphetamine/ dextroamphetamine (Adderall®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
dextroamphetamine ER (Dexedrine® Spansule®)		
dextroamphetamine IR (Zenzedi®, Procentra®)		
methylphenidate (Ritalin® LA or SR, Concerta®, Metadate® CD or ER, Methylin® ER, Daytrana®)	Dosing varies; 10-60 mg PO divided 2 to 3 times daily 30-45 min before meals	60 mg/day
armodafinil (Nuvigil®)	150 mg to 250 mg PO once a day	250 mg/day
modafinil (Provigil®)	200 mg PO QD as a single dose in the morning	400 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Non-indication specific (maximum dose for the drug)*
†Off-label indication

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In combination with sedative hypnotics or alcohol
  - Succinic semialdehyde dehydrogenase deficiency
- Boxed warning(s):
  - Central nervous system depression: In clinical trials at recommended doses, obtundation and clinically significant respiratory depression occurred in adult patients treated with Xyrem and Xywav.
  - Abuse and misuse: Xyrem and Xywav are sodium salts 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cataplexy in narcolepsy	Adults: The recommended starting dose is 4.5 grams (g) per night administered orally in two equal, divided doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later. Increase the dose by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to the effective dose range of 6 g to 9 g per night orally Pediatrics: Dosing is weight-based as follows:	9 g/ per night
EDS in narcolepsy		

Indication	Dosing Regimen	Maximum Dose
	20 to < 30 kg: ≤ 1 g at bedtime and ≤ 1 g taken 2.5 to 4 hours later. Increase the dose by 1 g per night at weekly intervals (additional 0.5 g at bedtime and 0.5 g taken 2.5 to 4 hours later) to a maximum dose of 6 g per night orally *30 to < 45 kg*: ≤ 1.5 g at bedtime and ≤ 1.5 g taken 2.5 to 4 hours later. Increase the dose by 1 g per night at weekly intervals (additional 0.5 g at bedtime and 0.5 g taken 2.5 to 4 hours later) to a maximum dose of 7.5 g per night orally ≥ *45 kg*: ≤ 2.25 g at bedtime and ≤ 2.25 g taken 2.5 to 4 hours later. Increase the dose by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to a maximum dose of 9 g per night orally	

IV. Product Availability

Drug Name	Availability
Xyrem (sodium oxybate)	Oral solution: 0.5 g per mL in 180 mL bottle
Xywav (calcium, magnesium, potassium, and sodium oxybate)	Oral solution: 0.5 g per mL

V. References

1. Xyrem Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; September 2020. Available at: https://www.xyrem.com/. Accessed January 29, 2021.
2. Xywav Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; July 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212690s000lbl.pdf. Accessed January 29, 2021.
3. Morgenthaler TI, Kapur VK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin An American Academy of Sleep Medicine Report: An American Academy of Sleep Medicine Report. Sleep. 2007;30(12):1705-1711.
4. Wise MS, Arand DL, Auger RR, Brooks SN, Watson NF. Treatment of Narcolepsy and other Hypersomnias of Central Origin: An American Academy of Sleep Medicine Review. Sleep. 2007;30(12):1712-1727.
5. Scammell TE. The neurobiology, diagnosis and treatment of narcolepsy. Ann Neurol 2003;53:154 –166.
6. Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. Nat Sci Sleep. 2015; 7:159-169.
7. Billiard M. Narcolepsy: current treatment options and future approaches. Neuropsychiatric Disease and Treatment. 2008;4(3):557-566.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: added age requirement as safety and effectiveness in pediatric patients have not been established	1.23.18	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
per PI; modified initial approval duration from 3 to 6 months; references reviewed and updated.		
2Q 2019 annual review: Updated policy to reflect new pediatric indication expansion for patients aged 7 years and older for both cataplexy and EDS of narcolepsy; references reviewed and updated.	4.17.19	
2Q 2020 annual review: expanded initial approval durations from 6 months to 12 months; added atomoxetine as a potential redirection for narcolepsy with cataplexy; references reviewed and updated.	04.2020	
Updated policy to only require 1 month T/F of armodafinil/modafinil for narcolepsy with EDS if member is ≥ 17 years given lack of evidence supporting use of armodafinil/modafinil in pediatric populations; references reviewed and updated.	09.20	11.20
2Q 2021 annual review: added new salt formulation Xywav to policy; added diagnostic criteria for narcolepsy with cataplexy and narcolepsy associated with excessive daytime sleepiness; added prescriber requirements for neurologist or sleep medicine specialist for all indications; references reviewed and updated.	04/2021	
Allowed members 65 years old or older to bypass redirections to any TCA throughout the policy; for narcolepsy with excessive daytime sleepiness: added trial of Sunosi, and added requirement for combination use of preferred agents if request is for concomitant use.	07/2021	