

# PRIOR AUTHORIZATION CRITERIA

**BRAND NAME\***  
(generic)

**XYREM**  
(sodium oxybate)

**Status: CVS Caremark Criteria**

**Type: Initial Prior Authorization with Quantity Limit**

**Ref # 254-C**

\* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

## **FDA-APPROVED INDICATIONS**

Xyrem is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

## **COVERAGE CRITERIA**

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for continuation of Xyrem (sodium oxybate) AND the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy

**OR**

- The requested drug is being prescribed for the treatment of cataplexy in narcolepsy in a patient 7 years of age or older AND the diagnosis is confirmed by sleep lab evaluation

**OR**

- The requested drug is being prescribed for the treatment of excessive daytime sleepiness in a patient 7 years of age or older with narcolepsy AND the diagnosis is confirmed by sleep lab evaluation

**AND**

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate)

**AND**

- If the patient is 18 years of age or older, the patient experienced an inadequate treatment response, intolerance, or contraindication to at least one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)

Quantity Limits Apply.

## **RATIONALE**

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Xyrem is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

Because of the risks of central nervous system depression and abuse/misuse, Xyrem is available only through a restricted distribution program called the Xyrem REMS (Risk Evaluation and Mitigation Strategy) Program. The Xyrem REMS Program required components are: medication is dispensed by a certified centralized pharmacy, prescribers must complete the enrollment forms and comply with the requirements, and patients must understand the risks and benefits of Xyrem.

According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and

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regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.<sup>4,5</sup>

According to AASM guidelines, modafinil is effective for treatment of daytime sleepiness due to narcolepsy. One additional study of 196 subjects involved assessment of armodafinil (the longer half-life enantiomer of modafinil) for treatment of excessive sleepiness in patients with narcolepsy.<sup>4</sup> Subjects receiving armodafinil experienced significant improvement in sleepiness as measured by the Mean Wakefulness Test (MWT) mean sleep latency, and in the Clinical Global Impression of Change.<sup>4</sup> The guidelines also state that amphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy.<sup>4</sup> Since Xyrem has risks associated with therapy and there are effective alternatives available, a trial of one central nervous system (CNS) promoting wakefulness drug (e.g., modafinil, armodafinil) and one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) will be required unless the patient has a contraindication to these drugs.

Central Nervous System (CNS) stimulants (e.g., amphetamine, dextroamphetamine, or methylphenidate) are indicated for pediatric patients in the treatment of narcolepsy.<sup>2,3</sup> Provigil (modafinil) and Nuvigil (armodafinil) safety and effectiveness have not been studied in pediatric patients, and are not approved in this population for any indication.<sup>7,8</sup> For pediatric patients 17 years of age and younger, only a trial with one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) will be required unless the patient has a contraindication to these drugs.

The guidelines state that the goal of therapy should be to produce the fullest possible return of normal function for patients.<sup>4,6</sup> Therefore, if the request is for the continuation of Xyrem, it should be determined that the patient has experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy.

The recommended starting dose of Xyrem 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. The dose can be increased 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. For pediatric patients, the initial starting dose is based on body weight (ranging from 2 g per night to the adult dose of 4.5 g per night in equally divided doses) and increases at weekly intervals to an effective dose range of 6 g to 9 g per night. Doses higher than 9 g per night have not been studied and should not ordinarily be administered. Xyrem is available as an oral solution at a concentration of 0.5 grams per milliliter (g/mL). The maximum daily dose of 9 grams equals 18 milliliters. Therefore, the approval will be limited to a maximum of three 180 milliliter (mL) bottles (540 mL) per month.

## **REFERENCES**

1. Xyrem [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; October 2018.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. <http://online.lexi.com/>. Accessed October 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. <http://www.micromedexsolutions.com/>. Accessed October 2018.
4. Morgenthaler TI, Vishesh KK, Brown T, et al. Practice Parameters for the Treatment of Narcolepsy and Other Hypersomnias of Central Origin. *Sleep* 2007; 30(12):1705-11.
5. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 3<sup>rd</sup> edition. Westchester, IL: American Academy of Sleep Medicine; 2014.
6. Krahn, L, Hershner S, et al. Quality Measures for the Care of Patients with Narcolepsy; *Journal of Clinical Sleep Medicine*; 2015; 11(3): 335-55.
7. Nuvigil [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2018.
8. Provigil [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; April 2018.

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 Reviewed: CRC 09/2002; Medical Affairs (MM) 01/2005, 11/2005, 02/2006; (WF) 02/2007, 11/2007, 11/2008, 09/2009; (KP) 11/2010, 11/2011; (LMS) 11/2012; (DNC) 11/2013, (DC) 11/2014; (LMS) 11/2016, 05/2017; (TP) 11/2017; (GAD) 11/2018  
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**CRITERIA FOR APPROVAL**

- |   |   |     |    |
|---|---|-----|----|
| 1 | Is this request for the continuation of Xyrem (sodium oxybate)?<br>[If no, then skip to question 3.]  | Yes | No |
| 2 | Has the patient experienced a decrease in daytime sleepiness with narcolepsy or a decrease in cataplexy episodes with narcolepsy?<br>[If yes, then skip to question 9.]   | Yes | No |
| 3 | Is the requested drug being prescribed for the treatment of cataplexy in narcolepsy in a patient 7 years of age or older?<br>[If yes, then skip to question 8.]   | Yes | No |
| 4 | Is the requested drug being prescribed for the treatment of excessive daytime sleepiness in a patient 7 years of age or older with narcolepsy?  | Yes | No |
| 5 | Is the patient 18 years of age or older?<br>[If no, then skip to question 7.]   | Yes | No |
| 6 | Did the patient experience an inadequate treatment response, intolerance or contraindication to at least one central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil)?                  | Yes | No |
| 7 | Did the patient experience an inadequate treatment response, intolerance, or contraindication to at least one central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate)? | Yes | No |
| 8 | Has the diagnosis been confirmed by sleep lab evaluation?   | Yes | No |
| 9 | Does the patient require the use of more than the plan allowance of 540 milliliters (mL) per month (270 grams per month)?   | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval for 540 mL per 25 days or 1620 mL per 75 days.]

**Mapping Instructions**

**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**

	Yes	No	
1.	Go to 2	Go to 3	
2.	Go to 9	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You are using Xyrem and have a decrease in daytime sleepiness with narcolepsy - You are using Xyrem and have a decrease in cataplexy episodes with

			narcolepsy Your request has been denied based on the information we have. [Short Description: Continuation of therapy, No response to treatment]
3.	Go to 8	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You are 7 years of age or older and you have cataplexy with narcolepsy - You are 7 years of age or older and you have excessive daytime sleepiness with narcolepsy Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
5.	Go to 6	Go to 7	
6.	Go to 7	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You tried a central nervous system (CNS) wakefulness promoting drug (e.g., modafinil, armodafinil) - These drugs did not work for you or you cannot take them Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to CNS wakefulness promoting drugs]
7.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet all of these conditions: - You tried a central nervous system (CNS) stimulant drug (e.g., amphetamine, dextroamphetamine, or methylphenidate) - These drugs did not work for you or you cannot take them Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to CNS stimulants]
8.	Go to 9	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a sleep lab test to confirm your diagnosis. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
9.	Deny	Approve, 12 months, 540 milliliters /month*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to: - 540 milliliters/month of Xyrem. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

\*The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.