Drug Coverage Policy

Effective Date.....3/1/2025
Coverage Policy Number.....IP0102
Policy Title.....Sunosi

Wakefulness-Promoting Agents – Sunosi

- Sunosi® (solriamfetol tablets – Jazz)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Sunosi, a dopamine and norepinephrine reuptake inhibitor, is indicated to improve wakefulness in adults with **excessive daytime sleepiness** associated with the following conditions:[1]

- **Narcolepsy**.
- **Obstructive sleep apnea** (OSA).
  Limitations of Use: Sunosi is not indicated to treat the underlying airway obstruction in OSA.[1] The underlying airway obstruction should be treated (e.g., with continuous positive airway pressure [CPAP]) for at least 1 month prior to initiating Sunosi for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi.

Sunosi is a Schedule IV controlled substance.[1]

Armodafinil and modafinil are wakefulness-promoting agents with actions similar to sympathomimetic agents (e.g., amphetamine and methylphenidate).[2,3] They are indicated to improve wakefulness in adults with excessive sleepiness associated with narcolepsy, OSA, or shift work disorder. Armodafinil and modafinil are Schedule IV controlled substances. Wakix® (pitolisant tablets), an antagonist/inverse agonist of the histamine-3 receptor, is indicated for the treatment of excessive daytime sleepiness or cataplexy in adult patients with narcolepsy and for the treatment of excessive daytime sleepiness in pediatric patients ≥ 6 years of age with narcolepsy.[13] Wakix is the only wakefulness-promoting agent that is not a controlled substance. Stimulant medications (e.g., amphetamine, methamphetamine, dextroamphetamine, and methylphenidate) are used off-label for the treatment of daytime sleepiness due to narcolepsy and OSA and are mentioned in guidelines.[4-7]

Two specialized tests, which can be performed in a sleep disorders clinic, are required to establish a diagnosis of narcolepsy.[8] Polysomnogram (PSG) is an overnight recording of brain and muscle activity, breathing, and eye movements. The multiple sleep latency test assesses daytime sleepiness by measuring how quickly a person falls asleep and whether they enter rapid eye movement (REM) sleep. On the day after PSG, the patient is asked to take five short naps separated by two hours over the course of a day. If an individual falls asleep in < 8 minutes on average over the five naps, this indicates excessive daytime sleepiness. However, patients with narcolepsy also have an abnormally quick start to REM sleep. If REM sleep happens within 15 minutes at least two times out of the five naps and the sleep study the night before, this is likely an abnormality caused by narcolepsy.

Guidelines

Narcolepsy and Cataplexy

The American Academy of Sleep Medicine (AASM) practice parameters for the treatment of central disorders of hypersomnolence were updated in 2021.[4,5]

- Modafinil, Wakix (pitolisant tablet), Xyrem® (sodium oxybate oral solution), and Sunosi are recommended as effective treatments for daytime sleepiness due to narcolepsy and reducing disease severity in adults (Strong Recommendation for each).
- Wakix and Xyrem have also demonstrated efficacy for the treatment of cataplexy in patients with narcolepsy (Strong Recommendation for each).
- Xyrem and armodafinil have Conditional Recommendations for the treatment of narcolepsy, showing efficacy for daytime sleepiness due to narcolepsy and reducing disease severity.
- Dextroamphetamine has a Conditional Recommendation for the treatment of narcolepsy, showing efficacy for excessive daytime sleepiness and cataplexy.
- Methylphenidate has a Conditional Recommendation for the treatment of narcolepsy, showing efficacy in reducing disease severity.
- There was insufficient and inconclusive evidence to make recommendations for l-carnitine, scheduled naps, selegiline, triazolam, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs).
- Modafinil and Xyrem have Conditional Recommendations for the treatment of narcolepsy in pediatric patients.
- A Strong Recommendation should be followed by clinicians under most circumstances. A Conditional Recommendation requires that the clinician use clinical knowledge and experience and strongly consider the individual patient's values and preferences to determine the best course of action.

Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea/Hypoapnea Syndrome

- According to the AASM guideline on medical therapy for OSA (2006), CPAP is the most uniformly effective therapy, and, to date, this is the only intervention for OSA shown to have favorable impacts on both cardiovascular and neurobehavioral morbidities.[6,7]
- Modafinil, in patients compliant with nasal CPAP, consistently improved subjective and objective sleepiness, quality of life, and vigilance compared with placebo.
- Sunosi is not addressed in these guidelines.

Medical Necessity Criteria

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information.

Sunosi is considered medically necessary when ONE of the following is met:

FDA-Approved Indications

1. **Excessive Daytime Sleepiness Associated with Narcolepsy.** Approve for 1 year if the patient meets the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Documentation that the patient has been evaluated using polysomnography and a multiple sleep latency test; AND
   - **C)** Documented diagnosis of narcolepsy has been confirmed ; AND
   - **D)** The medication is prescribed by or in consultation with a sleep specialist physician or a neurologist; AND
   - **E)** Documentation that the patient has tried at least ONE of the following treatments: a central nervous system (CNS) stimulant, generic modafinil or generic armodafinil.
     Note: Examples of CNS stimulants include methylphenidate, dexmethylphenidate, and dextroamphetamine. An exception to this requirement is allowed if the patient has previously tried brand Provigil or brand Nuvigil.

2. **Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i or ii):
     - **i.** Sunosi will be used in conjunction with continuous positive airway pressure (CPAP) therapy; OR
     - **ii.** Documentation that the patient is unable to initiate or tolerate CPAP therapy; AND
   - **C)** Documentation that the patient has tried generic modafinil or generic armodafinil.
     Note: An exception to this requirement is allowed if the patient has previously tried brand Provigil or brand Nuvigil.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concomitant Use of Sunosi with an Oxybate Product and/or Wakix (pitolisant tablets).** Sunosi, a dopamine and norepinephrine reuptake inhibitor, is indicated to improve wakefulness in adults with excessive daytime sleepiness due to narcolepsy or obstructive sleep apnea.[1] Oxybate products include Xyrem (sodium oxybate oral solution), Lumryz (sodium oxybate extended-release oral suspension), and Xywav (calcium, magnesium, potassium, and sodium oxybates oral solution).[10-12] These have the same active ingredient (oxybate, a central nervous system depressant) and have not been studied for use in combination or as alternating treatments. Wakix, an antagonist/inverse agonist of the histamine-3 receptor, is indicated for excessive daytime sleepiness and cataplexy in adults with narcolepsy.[13] Currently, there are no published studies evaluating combination use of these medications.

References

1. Sunosi® tablets [prescribing information]. New York, NY: Axsome Therapeutics; June 2023.
2. Provigil® tablets [prescribing information]. Parsippany, NJ: Teva; December 2022.
3. Nuvigil® tablets [prescribing information]. Parsippany, NJ: Teva; December 2022.
4. 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.
5. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med*. 2021;17(9):1895-1945.
6. Veasey SC, Guilleminault C, Strohl KP, et al. Medical therapy for obstructive sleep apnea: a review by the medical therapy for obstructive sleep apnea task force of the standards of practice committee of the American Academy of Sleep Medicine. *Sleep*. 2006;29(8):1036-1044.
7. Morgenthaler TI, Kapen S, Lee-Chiong T, et al. Practice parameters for the medical therapy of obstructive sleep apnea. *Sleep*. 2006;29(8):1031-1035.
8. National Institutes of Health. Narcolepsy. National Institute of Neurological Disorders and Stroke. Last reviewed on July 19, 2024. Available at: Narcolepsy | National Institute of Neurological Disorders and Stroke (nih.gov). Accessed on September 2, 2024.
9. Mayo Clinic. Obstructive sleep apnea. Available at: https://www.mayoclinic.org/diseases-conditions/obstructive-sleep-apnea/symptoms-causes/syc-20352090?p=1. Accessed on September 2, 2024.
10. Xyrem® oral solution [prescribing information]. Palo Alto, CA: Jazz; April 2023.
11. Lumryz™ extended-release oral suspension [prescribing information]. Chesterfield, MO: Avadel; May 2023.
12. Xywav® oral solution [prescribing information]. Palo Alto, CA: Jazz; April 2023.
13. Wakix® tablets [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences; June 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Updated** title from 'Solriamfetol' to 'Wakefulness-Promoting Agents – Sunosi' **Excessive Daytime Sleepiness Associated with Narcolepsy.** **Updated** 'Treatment of Excessive Daytime Sleepiness Associated with Narcolepsy (Type 1 or 2)' TO	10/15/2024

	'Excessive Daytime Sleepiness Associated with Narcolepsy.' **Added** 'Diagnosis of narcolepsy has been confirmed, according to the prescriber' **Removed '**Daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months' **Updated** 'Documentation of **ONE** of the following: (i) Diagnosis of **narcolepsy type 1** and **ONE** of the following: (a) Mean Sleep Latency Test (MSLT) performed according to standard techniques, showing a mean sleep latency of less than or equal to 8 minutes and two or more sleep-onset rapid eye movement periods (SOREMPs) following a nocturnal polysomnogram (PSG) that rules out other causes of excessive daytime sleepiness, (b) A SOREMP (within 15 minutes of sleep onset) on a nocturnal PSG, (2) Diagnosis of **narcolepsy type 2** and Mean Sleep Latency Test (MSLT) performed according to standard techniques, showing a mean sleep latency of less than or equal to 8 minutes and two or more sleep-onset rapid eye movement periods (SOREMPs) following a nocturnal polysomnogram (PSG) that rules out other causes of excessive daytime sleepiness. A SOREMP (within 15 minutes of sleep onset) on a nocturnal PSG may replace one of the SOREMPs on the MSLT' 'TO 'Patient has been evaluated using polysomnography and a multiple sleep latency test' **Removed** 'The hypersomnolence and/or MSLT findings are not better explained by other causes such as insufficient sleep, delayed sleep phase disorder, or the effect of medication or substances or their withdrawal' **Updated** 'Documentation of failure, contraindication, or intolerance to **ONE** of the following: (i) modafinil OR armodafinil, (ii) dextroamphetamine, dexmethylphenidate OR methylphenidate' TO 'Patient has tried generic modafinil or generic armodafinil. Note: An exception to this requirement is allowed if the patient has previously tried brand Provigil or brand Nuvigil.' **Removed** pulmonologist from 'Medication is prescribed by, or in consultation with' bullet **Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea.** **Removed** 'Daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months' **Removed** 'Documentation of diagnosis of Obstructive Sleep Apnea (OSA) is confirmed by sleep study' **Removed** 'The hypersomnolence and/or sleep study findings are not better explained by other causes such	

	as insufficient sleep, delayed sleep phase disorder, or the effect of medication or substances or their withdrawal' **Removed** 'Sunosi will be used in combination with non-pharmacologic treatment for obstructive sleep apnea (OSA), unless contraindicated or intolerant' **Updated '**Documentation of inadequate response to at least 1 month of non-pharmacologic treatment for OSA (for example, continuous positive airway pressure [CPAP])' TO 'Patient meets one of the following (i or ii): (i) Sunosi will be used in conjunction with continuous positive airway pressure (CPAP) therapy; OR (ii) Patient is unable to initiate or tolerate CPAP therapy' **Updated** 'Documentation of failure, contraindication, or intolerance to **ONE** of the following: (i) armodafinil, (ii) modafinil' TO 'Patient has tried generic modafinil or generic armodafinil. Note: An exception to this requirement is allowed if the patient has previously tried brand Provigil or brand Nuvigil.' **Conditions Not Covered.** **Added** 'Concomitant Use of Sunosi with an Oxybate Product and/or Wakix (pitolisant tablets).'	
Selected Revision	**Excessive Daytime Sleepiness Associated with Narcolepsy.** The criteria were updated to include central nervous system (CNS) stimulants as an option for patients to have tried prior to approval of Sunosi. Now a patient needs to have tried a central nervous system (CNS) stimulant, generic modafinil, or generic armodafinil prior to approval of Sunosi. Previously, a patient had to have tried one of generic modafinil or generic armodafinil. Additionally, examples CNS stimulants were added to the Note.	11/01/2024
Selected Revision	**Added "Documentation**: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information." **Excessive Daytime Sleepiness Associated with Narcolepsy.** **Updated** criteria **from** "Patient has been evaluated using polysomnography and a multiple sleep latency test" **to** "Documentation that the patient has been evaluated using polysomnography and a multiple sleep latency test." **Updated** criteria **from** " Diagnosis of narcolepsy has been confirmed, according to the prescriber" **to** "Documented diagnosis of narcolepsy has been confirmed." **Updated** criteria **from** "Patient has tried at least ONE of the following treatments: a central nervous system	3/1/2025

	(CNS) stimulant, generic modafinil or generic armodafinil" **to** "Documentation that the patient has tried at least ONE of the following treatments: a central nervous system (CNS) stimulant, generic modafinil or generic armodafinil." **Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea.** **Updated** criteria **from** "Patient is unable to initiate or tolerate CPAP therapy" **to** "Documentation that the patient is unable to initiate or tolerate CPAP therapy." **Updated** criteria **from** "Patient has tried generic modafinil or generic armodafinil" **to** "Documentation that the patient has tried generic modafinil or generic armodafinil."	

The policy effective date is in force until updated or retired.