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. 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.

Coverage Policy

Pitolisant (Wakix®) is considered medically necessary when ONE of the following are met:

I. Cataplexy associated with Narcolepsy and ALL of the following criteria:
   - Individual is 18 years of age or older
   - The individual has daily periods of irrepresible need to sleep or lapses into sleep during waking hours, occurring for at least three months.
   - Cataplexy
   - Mean Sleep Latency Test (MSLT) performed according to standard techniques, showing a mean sleep latency of ≤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.

   Note: A SOREMP (within 15 minutes of sleep onset) on a nocturnal PSG may replace one of the SOREMPs on the MSLT
   - 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.
   - Prescribed by or in consultation with a neurologist or sleep specialist
• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for one of the following treatments: a tricyclic antidepressant (for example, amitriptyline, desipramine, imipramine), a selective serotonin reuptake inhibitor (SSRI) (for example fluoxetine, sertraline, and paroxetine), or venlafaxine

II. Excessive Daytime Sleepiness associated with Narcolepsy and ALL of the following criteria:
  • Individual is 18 years of age or older
  • The individual has daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months.
  • Mean Sleep Latency Test (MSLT) performed according to standard techniques, showing a mean sleep latency of ≤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.
    Note: A SOREMXP (within 15 minutes of sleep onset) on a nocturnal PSG may replace one of the SOREMPs on the MSLT
  • 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.
  • Prescribed by or in consultation with a neurologist or sleep specialist
  • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate (for example, individual has a history of misuse or abuse of controlled substances) for armodafinil* (generic for Nuvigil) OR modafinil* (generic for Provigil)

*May require prior authorization

Initial authorization is up to 12 months.

Pitolisant (Wakix) is considered medically necessary for continued use when the following are met:
  • Initial criteria are met
  • Attestation of a positive clinical response

Reauthorization for up to 12 months.

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.

Pitolisant (Wakix) is considered experimental, investigational or unproven for ANY other use.

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

*If you're a Cigna provider, please log in to the Cigna for Health Care Professionals website and search for specific patients to view their covered medications.

FDA Approved Indications

FDA Approved Indication
WAKIX is indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy.

Recommended Dosing

FDA Recommended Dosing
The recommended dosage range for Wakix is 17.8 mg to 35.6 mg administered orally once daily in the morning upon wakening. Titrate dosage as follows:

Week 1: Initiate with a dosage of 8.9 mg (two 4.45 mg tablets) once daily
Week 2: Increase dosage to 17.8 mg (one 17.8 mg tablet) once daily
Week 3: May increase to the maximum recommended dosage of 35.6 mg (two 17.8 mg tablets) once daily

Dose may be adjusted based on tolerability.
If a dose is missed, patients should take the next dose the following day in the morning upon wakening.
It may take up to 8 weeks for some patients to achieve a clinical response.

**Drug Availability**
Wakix is available as oral film-coated tablets containing 4.45 or 17.8 mg of pitolisant.

**General Background**

**Overview**
Wakix is an antagonist/inverse agonist of the histamine-3 (H₃) receptor.¹ Wakix should be titrated up to the recommended dosage range of 17.8 mg to 35.6 mg once daily (QD) in the morning upon wakening. The dose may be adjusted based on patient tolerability. For some patients, it may take up to 8 weeks to achieve a clinical response. Wakix is the only wakefulness-prompting agent that is not a controlled substance.

Armodafinil and modafinil are wakefulness-promoting agents with actions similar to sympathomimetic agents (e.g., amphetamine and methylphenidate). They are indicated to improve wakefulness in adults with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD).²,³ For narcolepsy and OSA, they are dosed QD in the morning. For SWD, they are dosed QD as a single dose approximately 1 hour prior to the start of their work shift. Sunosi™ (solriamfetol tablets), a dopamine and norepinephrine reuptake inhibitor (DNRI), is indicated to improve wakefulness in adults with excessive daytime sleepiness associated with narcolepsy or OSA.⁴ Sunosi should be titrated to the recommended dose range of 37.5 mg to 150 mg QD, taken upon awakening with or without food. Sunosi should be avoided within 9 hours of planned bedtime because of the potential to interfere with sleep if taken too late in the day. Armodafinil, modafinil, and Sunosi are Schedule IV controlled substances.²,⁴ Armodafinil, modafinil, and Sunosi are not indicated for the treatment of cataplexy.

Two specialized tests, which can be performed in a sleep disorders clinic, are required to establish a diagnosis of narcolepsy.⁷ Polysomnography is an overnight recording of brain and muscle activity, breathing, and eye movements. The multiple sleep latency test (MSLT) assesses daytime sleepiness by measuring how quickly a person falls asleep and whether they enter rapid eye movement (REM) sleep. Polysomnography is routinely indicated for the diagnosis of sleep-related breathing disorders; for continuous positive airway pressure titration in patients with sleep-related breathing disorders; with a MSLT in the evaluation of suspected narcolepsy; and in certain atypical or unusual parasomnias.⁸ The MSLT is indicated as part of the evaluation of patients with suspected narcolepsy to confirm the diagnosis. Most patients with narcolepsy have objective evidence of hypersonemia as determined by a mean sleep latency < 5 minutes. In studies, the presence of two or more sleep-onset REM episodes (SOREMPs) was associated with a sensitivity of 0.78 and a specificity of 0.93 for the diagnosis of narcolepsy. SOREMPs do not occur exclusively in patients with narcolepsy, and thus it is important to rule out or treat other sleep disorders before evaluating SOREMPs in the diagnosis of narcolepsy. For this reason, polysomnography and a MSLT performed on the day after the polysomnographic evaluation are routinely indicated in the evaluation of suspected narcolepsy.

**Professional Societies/Organizations**
The American Academy of Sleep Medicine (AASM) published practice parameters in 2007 for the treatment of narcolepsy with and without cataplexy and other hypersomnias of central origin.⁵,⁶ It should be noted that the guidelines are dated and do not include more recently-approved medications. Modafinil is listed as an effective for treatment of daytime sleepiness due to narcolepsy and Xyrem as effective for treatment of cataplexy, daytime sleepiness, and disrupted sleep due to narcolepsy. Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are considered effective for the treatment of daytime sleepiness due to narcolepsy. Tricyclic
antidepressants, selective serotonin reuptake inhibitors (SSRIs), and venlafaxine may be effective for the
treatment of cataplexy. Selegiline may be an effective treatment for cataplexy and daytime sleepiness.

**Off Label Uses**

AHFS Drug Information 2019 Edition does not support any off-label uses of Wakix.

**References**

   Hypersomnias of Central Origin: An American Academy of Sleep Medicine Report. Available at:
   http://www.aasmnet.org/Resources/PracticeParameters/PP_Narcolepsy.pdf. Accessed on September 4,
   2020.
   American Academy of Sleep Medicine Review. Sleep. 2007;30(12):1712-27. Available at:
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