Effective Date 11/15/2023
Next Review Date… 11/15/2024
Coverage Policy Number IP0292

Pitolisant

Table of Contents

Related Coverage Resources

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.

Overview

This policy supports medical necessity review for pitolisant tablets (**Wakix®**).

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

Medical Necessity Criteria

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

1. **Narcolepsy Type 1 (Narcolepsy with Cataplexy).** Individual meets **ALL** of the following criteria:
   A. Age 18 years or older
   B. Daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months
   C. Cataplexy
   D. Documentation of **ONE** of the following:

i. 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.
ii. A SOREMP (within 15 minutes of sleep onset) on a nocturnal PSG

E. 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
F. Documentation of **ONE** of the following:
    i. Treatment of Cataplexy and failure, contraindication or intolerance to **ONE** of the following:
        1. dextroamphetamine
        2. a tricyclic antidepressant (TCA) [for example, amitriptyline, desipramine, imipramine]
        3. a selective serotonin reuptake inhibitor (SSRI) [for example, fluoxetine, sertraline, paroxetine]
        4. venlafaxine
    ii. Treatment of Excessive Daytime Sleepiness and **ONE** of the following:
        1. Failure, contraindication, or intolerance to modafinil OR armodafinil
        2. Failure, contraindication, or intolerance to dextroamphetamine, dexmethylphenidate OR methylphenidate
        3. History of substance abuse and, according to the prescriber, a wakefulness-promoting agent that is not a controlled substance is necessary
G. Medication is prescribed by, or in consultation with, a neurologist, pulmonologist or sleep specialist

2. **Narcolepsy Type 2 (Narcolepsy without Cataplexy).** Individual meets **ALL** of the following criteria:
    A. Age 18 years or older
    B. Daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months
    C. Documentation of 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.
    A SOREMP (within 15 minutes of sleep onset) on a nocturnal PSG may replace one of the SOREMPs on the MSLT.
    D. 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
    E. Documentation of **ONE** of the following:
        i. Failure, contraindication, or intolerance to modafinil OR armodafinil
        ii. Failure, contraindication, or intolerance to dextroamphetamine, dexmethylphenidate OR methylphenidate
        iii. History of substance abuse and, according to the prescriber, a wakefulness-promoting agent that is not a controlled substance is necessary
    F. Medication is prescribed by, or in consultation with, a neurologist, pulmonologist or sleep specialist

---

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.

Reauthorization Criteria

Continuation of pitolisant (Wakix) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Wakix, an antagonist/inverse agonist of the histamine-3 receptor, is indicated for the following uses:[1]

- **Excessive daytime sleepiness in adults with narcolepsy**.
- **Cataplexy in adults with narcolepsy**.

Wakix is the only wakefulness-promoting agent that is not a controlled substance.[1-4]

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.[2,3] Sunosi® (solriamfetol tablets), a dopamine and norepinephrine reuptake inhibitor, is indicated to improve wakefulness in adults with excessive daytime sleepiness associated with narcolepsy or OSA.[4] 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] Polysomnogram 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 polysomnogram, 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.[5,6]

- Modafinil, Wakix, 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, and serotonin-norepinephrine reuptake inhibitors.
- 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.

References

1. Wakix® tablets [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences; October 2020.
2. Sunosi® tablets [prescribing information]. Palo Alto, CA: Jazz; October 2021.
3. Provigil® tablets [prescribing information]. North Wales, PA: Cephalon; January 2015.
4. Nuvigil® tablets [prescribing information]. North Wales, PA: Cephalon; February 2017.
5. 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.
6. 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.
7. National Institutes of Health. Narcolepsy Fact Sheet. National Institute of Neurological Disorders and Stroke. Date last modified: July 25, 2022. Available at: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet. Accessed on September 6, 2022.
8. Xyrem® oral solution [prescribing information]. Palo Alto, CA: Jazz; March 2022.
9. Xywav® oral solution [prescribing information]. Palo Alto, CA: Jazz; March 2022.

Supplemental References

10. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed, text revision, American Academy of Sleep Medicine, 2023.