Pitolisant

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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 ALL of the following criteria are met:

- Individual is 18 years of age or older
- Diagnosis of Narcolepsy (with or without cataplexy) established by a polysomnogram (PSG) and multiple sleep latency test (MSLT)
- The individual has daily periods of irrepressible need to sleep or lapses into sleep during waking hours, occurring for at least three months.
- A mean sleep latency of ≤8 minutes and two or more sleep-onset rapid eye movement periods (SOREMPs) are found on an MSLT performed according to standard techniques with a preceding nocturnal polysomnogram (PSG) to rule out other causes of excessive daytime sleepiness. A SOREMp (within 15 minutes of sleep onset) on the preceding 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)
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 including the following:
- Combination of stimulant medications (for example, armodafinil, amphetamine, dextroamphetamine/amphetamine, methylphenidate, modafinil, solriamfetol) and Wakix for narcolepsy

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 a histamine-3 (H3) receptor antagonist/inverse agonist indicated for the treatment of excessive daytime sleepiness (EDS) 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**

**Therapeutic Alternatives**
Therapeutic alternatives to Wakix, for excessive daytime sleepiness associated with narcolepsy, include the following drugs: armodafinil (generic for Nuvigil) and modafinil (generic for Provigil).

**Professional Societies/Organizations**
American Academy of Sleep Medicine (AASM) practice parameters for the treatment of narcolepsy and other hypersomnias of central origin (2007) list modafinil as an effective for treatment of daytime sleepiness due to
narcolepsy (Standard) and Xyrem as effective for treatment of cataplexy, daytime sleepiness, and disrupted sleep due to narcolepsy (Standard). Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are considered effective for the treatment of daytime sleepiness due to narcolepsy (Guideline). At the time this practice parameter was written, published studies involving armodafinil were limited. (Morgenthaler, 2007)

AASM Levels of Recommendations

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Standard</td>
<td>This is a generally accepted patient-care strategy that reflects a high degree of clinical certainty. The term standard generally implies the use of level 1 evidence, which directly addresses the clinical issue, or overwhelming level 2 evidence.</td>
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<tr>
<td>Guideline</td>
<td>This is a patient-care strategy that reflects a moderate degree of clinical certainty. The term guideline implies the use of level 2 evidence or a consensus of level 3 evidence.</td>
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<tr>
<td>Option</td>
<td>This is a patient-care strategy that reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.</td>
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Off Label Uses
AHFS Drug Information 2019 Edition does not support any off-label uses of Wakix.

Comparative Studies
The efficacy of Wakix was established in two pivotal studies (HARMONY 1 and HARMONY 1bis) in adults with narcolepsy with or without cataplexy. Both of the pivotal trials used the change in Epworth Sleepiness Scale (ESS) score from baseline to Week 8 as the primary efficacy endpoint. The ESS score is a subjective evaluation which relies on patient estimation of their usual chances of having dozed off or fallen asleep while engaged in eight different activities. The pivotal trials included the active comparator modafinil. Wakix demonstrated modest efficacy vs. placebo on a measure of a patient’s perceived likelihood of falling asleep during usual daily activities and was less effective than modafinil. However, the efficacy results were supported by the secondary efficacy endpoints including maintenance of wakefulness test (MWT) scores. (Dauvilliers, 2013)

References