

## Clinical Policy: Pitolisant (Wakix)

Reference Number: MDN.CP.PMN.221

Effective Date: 04.01.22

Last Review Date: 4.24.23

Line of Business: Meridian IL Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Wakix<sup>®</sup> (pitolisant) is a selective histamine 3 (H<sub>3</sub>) receptor antagonist/inverse agonist.

### FDA Approved Indication(s)

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

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Wakix is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Narcolepsy with Cataplexy (must meet all):

1. Diagnosis of narcolepsy with cataplexy;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age  $\geq$  18 years;
4. Documentation of one of the following (a or b):
  - a. EDS associated with narcolepsy as confirmed by documented multiple sleep latency test (MSLT) and one of the following (i or ii):
    - i. Mean sleep latency  $\leq$  8 minutes with evidence of two or more sleep-onset rapid eye movement periods (SOREMPs);
    - ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight polysomnography (PSG);
  - b. Lumbar puncture shows cerebrospinal fluid (CSF) hypocretin-1 level  $\leq$  110 pg/mL;
5. Failure of 2 of the following antidepressants, each used for  $\geq$  1 month, unless member's age is  $\geq$  65, clinically significant adverse effects are experienced, or all are contraindicated: venlafaxine, fluoxetine, atomoxetine, clomipramine, protriptyline;
6. Dose does not exceed 35.6 mg (two 17.8 mg tablets) per day.

**Approval duration: 6 months**

##### B. Narcolepsy with Excessive Daytime Sleepiness (must meet all):

1. Diagnosis of narcolepsy with EDS;

2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;

3. Age  $\geq$  18 years;
4. Documentation of both of the following (a and b):
  - a. Excessive daytime sleepiness associated with narcolepsy as confirmed by documented MSLT and one of the following (i or ii):
    - i. Mean sleep latency  $\leq$  8 minutes with evidence of two or more SOREMPs;
    - ii. At least one SOREMP on MSLT and a SOREMP (less than 15 minutes) on the preceding overnight PSG;
  - b. Member has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months;
5. Failure of a 1-month trial of one of the following generic central nervous system stimulant-containing agent at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: amphetamine, dextroamphetamine, or methylphenidate;  
*\*Prior authorization may be required for CNS stimulants*
6. Failure of a 1-month trial of or modafinil (Provigil<sup>®</sup>), generic preferred at up to maximally indicated doses, unless clinically significant side effects are experienced or both are contraindicated;  
*\*Prior authorization may be required for modafinil*
7. Dose does not exceed 35.6 mg (two 17.8 mg tablets) per day.

**Approval duration: 6 months**

**C. Other diagnoses/indications (must meet 1 or 2):**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.  
;
3. Member is responding positively to therapy as evidenced by, but not limited to, improvement in any of the following parameters: reduction in frequency of cataplexy attacks, reported daytime improvements in wakefulness;
4. If request is for a dose increase, new dose does not exceed 35.6 mg (two 17.8 mg tablets) per day.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CNS: central nervous system	MSLT: multiple sleep latency test
EDS: excessive daytime sleepiness	PSG: polysomnography
FDA: Food and Drug Administration	SOREMP: sleep-onset rapid eye movement period
IR: immediate-release	

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Cataplexy</b>		
venlafaxine (Effexor®)†	75–150 mg PO BID, or 75–150 mg (extended release) PO QAM	375 mg/day* (IR tablets); 225* mg/day (extended release)
fluoxetine (Prozac®)†	20 to 80 mg PO QAM	80 mg/day
clomipramine (Anafranil®)†	10 to 150 mg PO as a single dose every morning or in divided doses	250 mg/day*
protriptyline (Vivactil®)†	5 to 60 mg PO as a single dose every morning or in divided doses	60 mg/day
atomoxetine (Strattera®)†	40–60 mg PO QD	100 mg/day*
<b>Excessive Daytime Sleepiness</b>		
amphetamine/ dextroamphetamine (Adderall®)	5 to 60 mg PO QD in divided doses	60 mg/day
dextroamphetamine (Dexedrine®, ProCentra®, Spansule®, Zenzedi®)		
amphetamine (Evekeo®)		
methylphenidate (Ritalin® (LA, SR), Concerta®, Metadate® (CD, ER), Methylin® (ER), Daytrana®)	Dosing varies; 10 to 60 mg PO divided 2 to 3 times daily 30 to 45 min before meals	60 mg/day
armodafinil (Nuvigil®)	150 mg PO QD in the morning	250 mg/day
modafinil (Provigil®)	200 mg PO QD in the morning	400 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sunosi™ (solriamfetol)	Initiate at 75 mg PO once a day; dose may be doubled at intervals of at least 3 days	150 mg/day

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*\*Non-indication specific (maximum dose for the drug)*

*†Off-label indication*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): hypersensitivity, severe hepatic impairment
- Boxed warning(s): none reported

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Narcolepsy	Dose range is 17.8 to 35.6 mg PO once daily in the morning upon waking. Titrate dosage as follows: <ul style="list-style-type: none"> <li>• Week 1: Initiate with a dosage of 8.9 mg once daily</li> <li>• Week 2: Increase dosage to 17.8 mg once daily</li> <li>• Week 3: May increase to the maximum recommended dosage of 35.6 mg once daily</li> </ul>	35.6 mg/day

**VI. Product Availability**

Tablets: 4.45 mg, 17.8 mg

**VII. References**

1. Wakix Prescribing Information. Plymouth Meeting, PA: Harmony Biosciences, LLC; December 2022. Available at: [www.wakix.com](http://www.wakix.com). Accessed February 7, 2023.
2. Morgenthaler TI, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin: an American Academy of Sleep Medicine report. *Sleep*. 2007;30(12):1705-1711.
3. Szakacs Z, Dauvilliers Y, Mikhaylov V, et al. Safety and efficacy of pitolisant on cataplexy in patients with narcolepsy: a randomized, double-blind, placebo-controlled trial. *Lancet Neurol*. 2017; 16:200-07.
4. Krahn LE, Hershner S, Loeding L, et al. Quality measures for the care of patients with narcolepsy. *J Clin Sleep Med* 2015;11(3):335– 355.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created, adapted from CP.PMN.221	04.1.22	04.22

2Q 2023 Annual review: Updated criteria for narcolpsy with EDDS; updated criteria for narcolepsy with cataplexy section, template changes applied to diagnoses/indications and continued review sections, references reviewed and updated.	4.23.24	
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**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited.

**CLINICAL POLICY**  
Pitolisant



Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.



**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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