Clinical Policy: Pitolisant (Wakix)

Reference Number: IL.ERX.NPA.132
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Illinois Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Wakix® (pitolisant) is a selective histamine 3 (H_3) 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 18 years;
4. Documentation of one of the following (a or b):
   a. Excessive daytime sleepiness associated with narcolepsy as confirmed by documented multiple sleep latency test (MSLT) and one of the following (i or ii):
      i. Mean sleep latency ≤ 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 ≤ 110 pg/mL;
5. Failure of 2 of the following antidepressants, each used for ≥ 1 month, unless member's age is ≥ 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: 12 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 ≥ 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 ≤ 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;

7. 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, methylphenidate, or dexmethylphenidate;
   **Prior authorization may be required for CNS stimulants*
5. Failure of a 1-month trial of modafinil (Provigil®) at up to maximally indicated doses, unless clinically significant side effects are experienced or both are contraindicated;
   **Prior authorization may be required for modafinil*
6. Dose does not exceed 35.6 mg (two 17.8 mg tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. 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;
3. 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CNS: central nervous system
EDS: excessive daytime sleepiness
FDA: Food and Drug Administration
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cataplexy		
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)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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*
Narcolepsy		
amphetamine/ dextroamphetamine	5 to 60 mg PO QD in divided doses	60 mg/day
amphetamine		
methylphenidate	Dosing varies; 10 to 60 mg PO divided 2 to 3 times daily 30 to 45 min before meals	60 mg/day
dexmethylphenidate	Dosing varies; 2.5 mg PO twice daily to 10 mg PO twice daily	20 mg/day
modafinil (Provigil®)	200 mg PO QD in the morning	400 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 dosing 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 wakening. Titrate dosage as follows: • Week 1: Initiate with a dosage of 8.9 mg once daily • Week 2: Increase dosage to 17.8 mg once daily • Week 3: May increase to the maximum recommended dosage of 35.6 mg once daily	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; October 2020. Available at: www.wakix.com. Accessed February 26, 2021.
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	04.22.21	05.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.