Pharmacy Policy Bulletin: J-0210 Wakix (pitolisant) – Commercial and Healthcare Reform	
Number: J-0210	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0210-009	**Original Date:** 11/06/2019
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Wakix (pitolisant)
FDA-Approved Indication(s):	• Treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy • Treatment of EDS in pediatric patients 6 years of age and older with narcolepsy

Background:	• Wakix is a histamine-3 (H3) receptor antagonist/inverse agonist that has been shown in clinical studies to reduce excessive daytime sleepiness and cataplexy in patients with narcolepsy. However, the precise mechanism by which Wakix works is unknown. • Wakix is the first and only treatment approved for patients with narcolepsy that is not scheduled as a controlled substance by the U.S. Drug Enforcement Agency (DEA). • Narcolepsy is a neurological disorder characterized by EDS and abnormal regulation of sleep-wake cycles. EDS is the primary symptom of narcolepsy and is displayed by all patients to some degree. Cataplexy occurs in 70% of patients and is defined as the sudden, often brief (less than 2 minutes) loss of muscle tone with retained consciousness. It is usually triggered by strong emotions. • The American Academy of Sleep Medicine (AASM) 2021 guidelines strongly recommend modafinil, Wakix, Xyrem, and Sunosi in the treatment of narcolepsy in adults. They conditionally recommend armodafinil, dextroamphetamine, and methylphenidate. However, the guidelines note that modafinil does not provide clinically significant improvement in cataplexy. • The AASM 2021 guidelines conditionally recommend modafinil and sodium oxybate for the treatment of narcolepsy in pediatric patients. The guidelines do not include methylphenidate or amphetamines because the literature review did not yield data that met their inclusion criteria. However, a 2007 report by AASM suggests that using methylphenidate for treating hypersomnias of central origin (including narcolepsy) with methylphenidate in children aged 6 to 15 years is relatively safe.

	• Diagnostic Criteria
	  ○ The multiple sleep latency test (MSLT) is a day-time sleep study where patients are instructed to try to fall asleep as they take scheduled naps with breaks in between. The time it takes to fall asleep is sleep latency; 97% of people take more than 8 minutes to fall asleep.
	  ○ Polysomnography is an overnight sleep study that measures the amount of time spent in different phases of sleep, in addition to the number of apneic and hypoapneic episodes.
	  ○ Sleep-onset rapid eye movement periods (SOREMPs) define the number of periods with REM sleep and can be calculated with a polysomnography or MSLT. People with narcolepsy have more frequent and shorter periods of REM sleep.
	  ○ Individuals with narcolepsy may have lower levels of hypocretins, a neurotransmitter involved in the sleep-wake cycle. Patients may undergo a lumbar puncture to quantify the amount of hypocretin-1 in their cerebrospinal fluid; levels under 110 pg/mL are indicative of narcolepsy.
	  ○ The Epworth Sleepiness Scale (ESS) is a subject assessment completed by the patient, generating a rating representative of their level of excessive daytime sleepiness (EDS)
	  ○ The maintenance of wakefulness test (MWT) is very similar to the MSLT, but patients are instructed to stay awake rather than fall asleep. Sleep latency is also generated from the MWT.
	• Prescribing considerations
	  ○ Wakix is contraindicated in patients with severe liver disease; in addition, it is not recommended in patients with end-stage kidney disease. The risk of QT prolongation may be greater in patients with liver or kidney disease.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Wakix may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 6 years of age and older.

B. The member has a diagnosis of narcolepsy (ICD-10: G47.419, G47.21, G47.429).

C. The member meets one (1) of the following criteria **(1., 2., or 3.)**:

1. The prescriber provides a multiple sleep latency test (MSLT) substantiating both of the following **(a. and b.)**:

a. Mean sleep latency ≤ 8 minutes.

b. ≥ 2 sleep-onset rapid eye movement periods (SOREMPs).

2. The prescriber provides a polysomnography and an MSLT substantiating all of the following **(a., b., and c.)**:

a. MSLT demonstrating a mean sleep latency ≤ 8 minutes.

b. MSLT demonstrating ≥ one (1) SOREMP.

c. Polysomnography demonstrating ≥ one (1) SOREMP.

3. The member has a documented hypocretin-1 deficiency defined as one (1) of the following **(a. or b.)**:

a. Cerebrospinal fluid hypocretin-1 < 110 pg/mL.

b. Cerebrospinal fluid hypocretin-1 < one-third of the normal value based on laboratory reference range.

D. The prescriber provides documentation of baseline data of one (1) of the following criteria **(1. or 2.)**:

1. Excessive daytime sleepiness (EDS) via the Epworth Sleepiness Scale (ESS)

2. Maintenance of Wakefulness Test (MWT)

E. The member meets one (1) of the following criteria **(1., 2. or 3.):**

1. If the member is ≥ 18 years of age and has a diagnosis of narcolepsy with cataplexy, the member meets both of the following criteria **(a. and b.)**
   a. There is documentation of baseline number of cataplexy episodes.
   b. The member has experienced therapeutic failure, contraindication, or intolerance to a plan-preferred generic CNS stimulant (e.g. dextroamphetamine).
2. If the member is ≥ 18 years of age and has a diagnosis of narcolepsy without cataplexy, the member has experienced therapeutic failure, contraindication, or intolerance to all of the following plan-preferred products **(a. and b.)**:
   a. generic modafinil
   b. generic CNS stimulant (e.g. methylphenidate, dextroamphetamine)
3. If the member is < 18 years of age and has a diagnosis of narcolepsy, the member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following plan-preferred products (**a. or b.)**:
   a. generic modafinil
   b. generic CNS stimulant (e.g. methylphenidate, dextroamphetamine)

II. Reauthorization

When a benefit, reauthorization of Wakix may be approved when one (1) of the following criteria is met **(A. or B.)**:

A. The prescriber attests that the member experienced a decrease in cataplexy episodes with narcolepsy compared to baseline.

B. The prescribed attests the member experienced a decrease in daytime sleepiness with narcolepsy as proven by improvement on the Epworth Sleepiness Scale (ESS) or Maintenance of Wakefulness Test (MWT) compared to baseline.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of its FDA-approved indications should be denied based on the lack of clinical data to support its effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Wakix [package insert]. Plymouth Meeting, PA: Harmony Biosciences, LLC; May 2025.
2. 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.
3. Morgenthaler TI, Kapur VK, Brown T, et al; Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *SLEEP* 2007;30(12):1705-11.

4. Kushida C, Littner M, Morgenthaler T, et al. Practice Parameters for the Indications for Polysomnography and Related Procedures: An Update for 2005. *SLEEP*, Vol. 28, No. 4, 2005.
5. Littner M, Kushida C, Wise M, et al. Practice Parameters for Clinical Use of the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test. *SLEEP*, Vol. 28, No. 1, 2005.
6. Bidmc – Neurology Fellowship: Sleep Disorders. Available at: https://bidmcneurology.org/education-programs/harvard-bidmc-neurology-fellowship-training-programs/sleep-disorders/. Accessed July 30, 2025.
7. Better breathing, better sleeping. Sleep Apnea Guide. Available at: https://www.sleep-apnea-guide.com/epworth-sleepiness-scale.html. Accessed July 30, 2025.
8. Test ID: ORXNA [Internet]. ORXNA - Clinical: Orexin-A/Hypocretin-1, Spinal Fluid. Available at: https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/604230. Accessed July 30, 2025.