

Policy Type: PA/SP

Pharmacy Coverage Policy: EOCCO060

Description

Pitolisant (Wakix) is a histamine-3 receptor antagonist/reverse agonist.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
pitolisant (Wakix)	Excessive daytime sleepiness associated with narcolepsy or narcolepsy with cataplexy	4.45 mg tablets	14 tablets/7 days
		17.8 mg tablets	60 tablets/30 days

Initial Evaluation

- I. **Pitolisant (Wakix)** may be considered medically necessary when the following criteria below are met:
 - A. Member is 18 years of age or older; **AND**
 - B. Medication is prescribed by, or in consultation with, a sleep specialist, psychiatrist, or neurologist; **AND**
 - C. A diagnosis of one of the following:
 1. **Excessive daytime sleepiness; AND**
 - i. **Narcolepsy without cataplexy; AND**
 - a. Treatment with the following has been ineffective, contraindicated, or not tolerated:
 - i. Stimulant (e.g., methylphenidate, amphetamine, etc.); **AND**
 - ii. Modafinil or armodafinil; **AND**
 - iii. If the request is for pitolisant (Wakix): Treatment with solriamfetol (Sunosi) has been ineffective, contraindicated, or not tolerated; **OR**
 2. **Narcolepsy with cataplexy; AND**
 - i. The request is for pitolisant (Wakix); **AND**
 - ii. Confirmation of cataplexy defined as episodes of sudden loss of muscle tone; **AND**

- iii. Documented impairment/limitation of activities of daily living (e.g. missing school/work, household chores, driving).
- II. Solriamfetol (Sunosi) and pitolisant (Wakix) are considered investigational when used for all other conditions, including but not limited to:
 - 1. Excessive sleepiness associated with Parkinson's Disease or glioblastoma
 - 2. Shift work sleep disorder (SWSD)
 - 3. Attention-deficit/hyperactivity disorder (ADHD)
 - 4. Fatigue not related to narcolepsy or OSA
 - A. Solriamfetol (Sunosi)
 - 1. Major depressive disorder
 - 2. Steinert myotonic dystrophy syndrome
 - B. Pitolisant (Wakix)
 - 1. Excessive daytime sleepiness associated with obstructive sleep apnea

Renewal Evaluation

- I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
- II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
- III. Member has exhibited improvement or stability of disease symptoms [e.g., reduction in cataplexy attacks, improvement in ability to complete activities of daily living, improvement in ability to stay awake)

Supporting Evidence

- I. Pitolisant (Wakix) is FDA-approved for the treatment of excessive daytime sleepiness in adults with narcolepsy. Pitolisant (Wakix) is the only agent for the treatment of narcolepsy that is not scheduled at this time. Pitolisant (Wakix) was studied in three randomized controlled trials, and one open-label, single-arm, long term safety & efficacy trial, in a total of 468 patients with EDS. HARMONY I and I bis included modafinil as an active comparator to pitolisant (Wakix).
- II. HARMONY I (n = 95): The primary efficacy outcome was the change in the Epworth Sleepiness Scale (ESS) score after eight weeks. Pitolisant (Wakix) 35.6 mg demonstrated a statistically greater reduction in the ESS score compared to placebo (change of -3.1 points [-5.73, -0.46]). When compared to modafinil, pitolisant (Wakix) failed to demonstrate non-inferiority for changes in ESS score. The ESS score has been commonly used in standard practice and was originally validated through a study in 1991.
- III. HARMONY I bis (n = 165): The primary efficacy outcome was the change in the ESS score and compared pitolisant (Wakix) 17.4 mg vs. placebo. Pitolisant (Wakix) demonstrated statistically

- significant reduction in the ESS score compared to placebo (change of -2.12 points [-4.10, -0.14]). When compared to modafinil, pitolisant (Wakix) failed to demonstrate non-inferiority for changes in ESS score.
- IV. HARMONY CTP (n = 106): The primary efficacy outcome was the change in the average number of cataplexy attacks per week as documented by patient diaries. The cataplexy ratio rate was 0.51 (0.44-0.60, $p < 0.0001$) for pitolisant (Wakix) compared to placebo.
 - V. HARMONY III (n = 102): Efficacy was a secondary endpoint and was measured by the change in the ESS score from baseline to one year. The mean decrease in ESS scores was -4.6 ± 0.59 (-5.82, -3.44).
 - VI. Pitolisant (Wakix) has a noted contraindication for patients with severe hepatic impairment, as well as a warnings and precaution for QTc prolongation. Common side effects were headache, insomnia, irritability, anxiety, and nausea. Less common side effects of musculoskeletal pain, upper respiratory tract infection, heart rate increase, hallucinations, abdominal pain, sleep disturbance, and decreased appetite were also noted.
 - VII. There are no direct head-to-head studies comparing pitolisant (Wakix) and solriamfetol (Sunosi) to establish superior safety or efficacy of one product over the other; however, pitolisant (Wakix) is significantly more costly than solriamfetol (Sunosi) despite not having any evidence of improved clinical efficacy or safety.
 - VIII. The use of pitolisant (Wakix) in the treatment of narcolepsy with cataplexy was established in HARMONY CTP with supporting evidence in HARMONY I. Primary outcomes of HARMONY CTP evaluated weekly rate of cataplexy (WRC) while HARMONY I, Daily Rate of Cataplexy (DRC) was evaluated as a secondary endpoint to support the use in cataplexy. Secondary outcomes of DRC in HARMONY I showed a significant improvement DRC.

Investigational or Not Medically Necessary Uses

- I. Solriamfetol (Sunosi) and pitolisant (Wakix) currently have no evidence supporting efficacy or safety in the following conditions:
 - A. Shift work sleep disorder (SWSD)
 - B. Attention-deficit/hyperactivity disorder (ADHD)
 - C. Fatigue not related to narcolepsy or OSA
 - D. Excessive sleepiness associated with Parkinson's Disease
- II. Solriamfetol (Sunosi) has not been studied in the following indications:
 - A. Major depressive disorder
 - B. Steinert myotonic dystrophy syndrome
- III. Pitolisant (Wakix) is currently being studied for use in excessive daytime sleepiness in patients with obstructive sleep apnea, however, there is currently a lack of sufficient safety and efficacy information to support use in this condition.

References

1. SUNOSI (solriamfetol) tablets, for oral use. Prescribing Information. Palo Alto, CA. Jazz
2. Thorpy M, Shapiro C, Mayer G, et al. A Randomized Study of Solriamfetol for Excessive Sleepiness in Narcolepsy. *Annals of Neurology*. 2019; 85:359-370.
3. Schweitzer PK, Rosenberg R, Zammit GK, Gotfried M, Chen D, Carter LP et al. Solriamfetol for Excessive Sleepiness in Obstructive Sleep Apnea (TONES 3): A Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2018 Dec 6. doi: 10.1164/rccm.201806-11000C.
4. Wakix (pitolisant) [Prescribing Information]. Harmony Biosciences, LLC: Plymouth Meeting, PA. August 2019.
5. Wakix (pitolisant) [Formulary Dossier]. Harmony Biosciences, LLC: Plymouth Meeting, PA. September 2019.
6. Dauvilliers Y, Bassetti C, Lammers GJ, et al. Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomized trial. *Lancet Neurol*. 2013; 12: 1068–75.
7. Dauvilliers Y, Arnulf I, Szakacs Z, et al. Long-term use of pitolisant to treat patients with narcolepsy: Harmony III Study. *Sleep*. 2019.
8. 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.
9. Dauvilliers Y, Bassetti C, Lammers GJ, et al. Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomised trial. *Lancet Neurol*. 2013;12(11):1068-1075.
1. Zoltan Szakacs, Yves Dauvilliers, et. al. Safety and efficacy of pitolisant on cataplexy in patients with narcolepsy: a randomised, double-blind, placebo-controlled trial (HARMONY CTP). *Lancet Neurol* 2017; 16: 200–07

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed Sunosi from policy due to its designation as 07/11	05/2023
Removed criteria "Use will not be in combination with sodium oxybate (Xyrem) or calcium, magnesium, potassium, sodium oxybates (Xywav)" After going into the different mechanisms of these drugs, clinical trials, and consulting the team, it was decided that these drugs can be used in combination with each other	12/2021
Updated policy to include new indication for Wakix use in patients with narcolepsy with cataplexy.	12/2020
Updated policy to require trial and failure of solriamfetol (Sunosi) prior to approval of pitolisant (Wakix) for narcolepsy.	06/2020
Addition of pitolisant (Wakix) information for coverage including: experimental/investigational, coverage for narcolepsy, quantity limits, and evidence base.	09/2019
New policy for solriamfetol (Sunosi).	08/2019