



Policy Type: PA/SP

Pharmacy Coverage Policy: EOCCO060

Description

Solriamfetol (Sunosi) is a dopamine and norepinephrine reuptake inhibitor (DNRI).
Pitolisant (Wakix) is a histamine-3 receptor antagonist/reverse agonist.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
solriamfetol (Sunosi)	75 mg tablets	Excessive sleepiness associated with either OSA or narcolepsy	60 tablets/30 days
	150 mg tablets		30 tablets/30 days
pitolisant (Wakix)	4.45 mg tablets	Excessive daytime sleepiness associated with narcolepsy	14 tablets/7 days
	17.8 mg tablets		60 tablets/30 days

Initial Evaluation

- I. Solriamfetol (Sunosi) and 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. A diagnosis of excessive daytime sleepiness; **AND**
 - C. A diagnosis of one of the following:
 1. **Narcolepsy; AND**
 - i. Treatment with the following has been ineffective, contraindicated, or not tolerated:
 - a. Stimulant (e.g., methylphenidate, amphetamine, etc.); **AND**
 - b. Modafinil or armodafinil; **OR**
 2. **Obstructive sleep apnea (OSA) [Only for Sunosi]; AND**
 - i. The member has current or prior use of a primary OSA therapy (e.g., CPAP, mandibular advancement device or surgical intervention); **AND**
 - ii. Treatment with the following has been ineffective, contraindicated, or not tolerated:
 - a. Modafinil or armodafinil



- 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. Clinical documentation of response to treatment, such as symptomatic improvement.

Supporting Evidence

- I. Solriamfetol (Sunosi) is FDA-approved for the treatment of excessive daytime sleepiness associated with OSA and narcolepsy in adults.
- II. The efficacy and safety of solriamfetol (Sunosi) was established in two Phase 3, multi-center, double-blind, placebo-controlled, randomized trials of fair quality that evaluated the use of solriamfetol (Sunosi) in patients with excessive daytime sleepiness associated with OSA (n=459) or either type I or type II narcolepsy (n=231).
- III. In clinical trials, patients with OSA were required to be stable for greater than one month on primary OSA therapy (e.g. CPAP, mandibular advancement device, or surgical intervention) prior to use of solriamfetol (Sunosi).
- IV. Stimulants such as amphetamine have not been studied in OSA.
- V. Current guidelines for patients with excessive sleepiness associated with narcolepsy recommend modafinil or armodafinil as first-line treatment options. Stimulants are recommended as second line therapy.
- VI. The current FDA maximum dose for solriamfetol (Sunosi) is 150 mg per day. Although doses of 300 mg were studied, the 300 mg dose was not approved due to tolerability concerns.
- VII. 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).
- VIII. 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.
 - IX. 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.
 - X. 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.
 - XI. 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).
 - XII. 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.

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.

Policy Implementation/Update:

Date Created	April 26, 2019
Date Effective	August 2019
Last Updated	September 2019
Last Reviewed	09/2019

Action and Summary of Changes	Date
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