PRIOR AUTHORIZATION POLICY WITH STEP THERAPY

POLICY: Wakefulness-Promoting Agents – Wakix Prior Authorization Policy with Step Therapy
- Wakix® (pitolisant tablets – Harmony)

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OVERVIEW

Wakix is indicated for the treatment of:[1]
- **Excessive daytime sleepiness in adults with narcolepsy**.
- **Cataplexy in adults with narcolepsy**.

Wakix is an antagonist/inverse agonist of the histamine-3 (H_3) receptor.[1] Wakix should be titrated up to the recommended dosage range of 17.8 mg to 35.6 mg once daily (QD) in the morning upon wakening. The dose may be adjusted based on patient tolerability. For some patients, it may take up to 8 weeks to achieve a clinical response. Wakix is the only wakefulness-promoting agent that is not a controlled substance.

Armodafinil and modafinil are wakefulness-promoting agents with actions similar to sympathomimetic agents (e.g., amphetamine and methylphenidate). They are indicated to improve wakefulness in adults with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD).[2,3] For narcolepsy and OSA, they are dosed QD in the morning. For SWD, they are dosed QD as a single dose approximately 1 hour prior to the start of their work shift. Sunosi™ (solriamfetol tablets), a dopamine and norepinephrine reuptake inhibitor (DNRI), is indicated to improve wakefulness in adults with excessive daytime sleepiness associated with narcolepsy or OSA.[4] Sunosi whould be titrated to the recommended dose range of 37.5 mg to 150 mg QD, taken upon awakening with or without food. Sunosi should be avoided within 9 hours of planned bedtime because of the potential to interfere with sleep if taken too late in the day. Armodafinil, modafinil, and Sunosi are Schedule IV controlled substances.[2-4] Armodafinil, modafinil, and Sunosi are not indicated for the treatment of cataplexy.

Two specialized tests, which can be performed in a sleep disorders clinic, are required to establish a diagnosis of narcolepsy.[7] Polysomnography is an overnight recording of brain and muscle activity, breathing, and eye movements. The multiple sleep latency test (MSLT) assesses daytime sleepiness by measuring how quickly a person falls asleep and whether they enter rapid eye movement (REM) sleep. Polysomnography is routinely indicated for the diagnosis of sleep-related breathing disorders; for continuous positive airway pressure titration in patients with sleep-related breathing disorders; with a MSLT in the evaluation of suspected narcolepsy; and in certain atypical or unusual parasomnias.[8] The MSLT is indicated as part of the evaluation of patients with suspected narcolepsy to confirm the diagnosis. Most patients with narcolepsy have objective evidence of hypersomnia as determined by a mean sleep latency < 5 minutes. In studies, the presence of two or more sleep-onset REM episodes (SOREMPs) was associated with a sensitivity of 0.78 and a specificity of 0.93 for the diagnosis of narcolepsy. SOREMPs do not occur exclusively in patients with narcolepsy, and thus it is important to rule out or treat other sleep disorders before evaluating SOREMPs in the diagnosis of narcolepsy. For this reason, polysomnography and a MSLT performed on the day after the polysomnographic evaluation are routinely indicated in the evaluation of suspected narcolepsy.

Guidelines

The American Academy of Sleep Medicine (AASM) published practice parameters in 2007 for the treatment of narcolepsy with and without cataplexy and other hypersomnias of central origin.[5,6] It should

be noted that the guidelines are dated and do not include more recently-approved medications. Modafinil is listed as an effective for treatment of daytime sleepiness due to narcolepsy and Xyrem as effective for treatment of cataplexy, daytime sleepiness, and disrupted sleep due to narcolepsy. Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are considered effective for the treatment of daytime sleepiness due to narcolepsy. Tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and venlafaxine may be effective for the treatment of cataplexy. Selegiline may be an effective treatment for cataplexy and daytime sleepiness.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Wakix. This Prior Authorization Policy also contains a Step Therapy component. When clinically appropriate, patients are directed to try one Step 1 agent (modafinil or armodafinil for excessive daytime sleepiness in narcolepsy; a tricyclic antidepressant, an SSRI, or venlafaxine for cataplexy in narcolepsy) prior to Wakix (Step 2). All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Wakix is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Excessive Daytime Sleepiness Associated with Narcolepsy.** Approve for 1 year if the patient meets one of the following criterion (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has been evaluated using polysomnography and a multiple sleep latency test (MSLT); AND
   - **C)** Diagnosis of narcolepsy has been confirmed, according to the prescriber; AND
   - **D)** Patient meets one of the following criteria (i or ii):
     - **i.** Patient has tried generic modafinil or generic armodafinil; OR
       Note: An exception to this requirement is allowed if the patient has previously tried brand Provigil or Nuvigil.
     - **ii.** Patient has a history of misuse or abuse of controlled substances and a wakefulness-promoting agent that is not a controlled substance is necessary, per the prescriber.

2. **Cataplexy Treatment in Patients with Narcolepsy**. Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has tried one of the following treatments: a tricyclic antidepressant, a selective serotonin reuptake inhibitor (SSRI), or venlafaxine; AND
     Note: Examples of tricyclic antidepressants include amitriptyline, desipramine, and imipramine. Examples of SSRIs include fluoxetine, sertraline, and paroxetine.
   - **C)** Patient has been evaluated using polysomnography and a multiple sleep latency test (MSLT); AND
   - **D)** Diagnosis of narcolepsy has been confirmed, according to the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Wakix is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Wakix® tablets [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences, LLC; October 2020.
2. Sunosi™ tablets [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; June 2019.
3. Provigil® tablets [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.
4. Nuvigil® tablets [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2019.
5. Morgenthaler TI, Kapur VK, Brown TM, et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin: An American Academy of Sleep Medicine Report. Available at: http://www.aasmnet.org/Resources/PracticeParameters/PP_Narcolepsy.pdf. Accessed on September 4, 2020.
6. Wise MS, Arand DL, Auger R, et al. Treatment of narcolepsy and other hypersomnias of central origin: An American Academy of Sleep Medicine Review. *Sleep*. 2007;30(12):1712-27. Available at: http://www.aasmnet.org/Resources/PracticeParameters/Review_Narcolepsy.pdf. Accessed on September 4, 2020.
7. National Institutes of Health. Narcolepsy Fact Sheet. National Institute of Neurological Disorders and Stroke. Date last modified: March 16, 2020. Available at: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet. Accessed on September 4, 2020.
8. Kushida CA, Littner MR, Morgenthaler T, et al. Practice Parameters for the Indications for Polysomnography and Related Procedures: An Update for 2005. *SLEEP*. 2005;28(4):499-521.