

Title: Wakefulness Promoting Agents

Policy #: Rx.01.5

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **armodafinil, modafinil, pitolisant (Wakix®), and solriamfetol (Sunosi™)** as provided under the member's prescription drug benefit.

Description:

Obstructive sleep apnea (OSA) is characterized by recurrent, functional collapse during sleep of the velopharyngeal and/or oropharyngeal airway, causing substantially reduced or complete cessation of airflow despite ongoing breathing efforts. This leads to intermittent disturbances in gas exchange and fragmented sleep. Snoring and wake-time sleepiness are common complaints of OSA.

Narcolepsy is a disorder of sleep-wake control in which elements of sleep intrude into wakefulness and elements of wakefulness intrude into sleep. The result is the classic tetrad of chronic daytime sleepiness with varying amounts of cataplexy, hypnagogic hallucinations, and sleep paralysis. Patients with narcolepsy type 1 (narcolepsy with cataplexy) typically present with moderate to severe daytime sleepiness, transient facial weakness or falls triggered by joking or laughter (partial or complete cataplexy), or the inability to move for one or two minutes immediately after awakening or just before falling asleep. Patients with narcolepsy type 2 have excessive daytime sleepiness without cataplexy.

Shift work disorder is a form of circadian sleep-wake rhythm disorders characterized by difficulty with sleep or wakefulness at times that are imposed by shifts running counter to the light-dark cycle. As a result, patients accumulate sleep debt and have increased risk of accidents, errors and other adverse health outcomes.

Multiple sclerosis (MS) is an immune-mediated, inflammatory, neurodegenerative disease of the central nervous system. Fatigue is a characteristic finding in patients with MS. It is usually described as physical exhaustion that is unrelated to the amount of activity performed.

Armodafinil is the R-enantiomer of modafinil with the longer half-life. Its precise mechanism of action is unknown. Both armodafinil and modafinil have wake-promoting actions similar to sympathomimetic agents including amphetamine and methylphenidate, although their pharmacologic profile is not identical to that of the sympathomimetic amines.

Modafinil is a wakefulness-promoting agent. Modafinil promotes actions similar to the traditional central nervous system (CNS) stimulants amphetamine and methylphenidate, but has a pharmacologic profile different from that of sympathomimetic amines. Although the precise mechanism of action is unknown, modafinil promotes wakefulness by selectively increasing neuronal activation in discrete regions of the brain (e.g., anterior hypothalamus) that are believed to be involved in mediating normal wakefulness.

Armodafinil and modafinil are indicated to improve wakefulness in adult patients with excessive sleepiness associated with obstructive sleep apnea (OSA), narcolepsy, or shift work disorder (SWD). Modafinil has been shown to

be beneficial for the treatment of MS fatigue in clinical studies. Neither medication is a treatment for the underlying cause of obstruction in those with OSA.

Pitolisant (Wakix®) indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy. The mechanism of action of pitolisant in excessive daytime sleepiness (EDS) in adult patients with narcolepsy is unclear. However, its efficacy could be mediated through its activity as an antagonist/inverse agonist at histamine-3 (H3) receptors.

Solriamfetol (Sunosi™) is indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy and obstructive sleep apnea (OSA). The mechanism of action of solriamfetol is unclear but it could be attributed to its activity as a dopamine and norepinephrine reuptake inhibitor (DNRI)

Policy:

INITIAL CRITERIA Generic **armodafinil** or **modafinil** is approved when ONE the following is met:

1. Diagnosis of narcolepsy and both of the following:
 - a. Prescribed by or in consultation with a neurologist or sleep specialist; and
 - b. Confirmed by one of the following tests:
 - i. Polysomnography (PSG); or
 - ii. Multiple sleep latency test (MSLT); or
2. Diagnosis of obstructive sleep apnea/hypopnea syndrome (OSAHS) and both of the following:
 - a. Prescribed by or in consultation with a sleep specialist; and
 - b. Used as adjunct to standard therapy; or
3. Diagnosis of Shift Work Sleep Disorder (SWSD) with documentation of ALL of the following
 - a. Documentation of one of the following:
 - i. Prescribed by or in consultation with a neurologist or sleep specialist; or
 - ii. Polysomnography and the multiple sleep latency test (MSLT) demonstrate loss of a normal sleep-wake pattern; and
 - b. Symptoms cannot be attributed to a medical condition; and
 - c. The symptoms do not meet criteria for any other sleep disorder producing insomnia or excessive sleepiness (e.g., time-zone change [jet lag] syndrome)

INITIAL CRITERIA Modafinil is approved when ALL of the following are met:

1. Diagnosis of Multiple Sclerosis (MS) related fatigue; and
2. Prescribed by or in consultation with a neurologist; and
3. Used in combination with standard educational therapies (e.g. psychoeducation, behavioral programs, scheduled naps, additional non-pharmacological therapies, etc.)

INITIAL CRITERIA Pitolisant (Wakix®) is approved when ALL of the following are met:

1. Diagnosis of narcolepsy; and
2. Prescribed by or in consultation with a neurologist or sleep specialist; and
3. Confirmed by one of the following tests:
 - a. Polysomnography (PSG); or
 - b. Multiple sleep latency test (MSLT); and
4. Inadequate response or inability to tolerate ALL of the following:
 - a. Modafinil or armodafinil; and
 - b. One stimulant product (e.g. amphetamine, methylphenidate); and
 - c. Sunosi®

INITIAL CRITERIA Solriamfetol (Sunosi™) is approved when ONE the following is met:

1. Diagnosis of narcolepsy and ALL of the following:
 - a. Prescribed by or in consultation with a neurologist or sleep specialist; and
 - b. Confirmed by one of the following tests:
 - i. Polysomnography (PSG); or

- ii. Multiple sleep latency test (MSLT); and
 - c. Inadequate response or inability to tolerate BOTH of the following:
 - i. Modafinil or armodafinil; and
 - ii. One stimulant product (e.g. amphetamine, methylphenidate); or
- 2. Diagnosis of obstructive sleep apnea/hypopnea syndrome (OSAHS) and ALL of the following:
 - a. Prescribed by or in consultation with a sleep specialist; and
 - b. Used as adjunct to standard therapy; and
 - c. Inadequate response or inability to tolerate BOTH of the following:
 - i. Modafinil or armodafinil; and
 - ii. One stimulant product (e.g. amphetamine, methylphenidate)

Initial authorization: 2 years

REAUTHORIZATION CRITERIA: The requested product is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization: 2 years

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Armodafinil. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com>. Accessed March 31,2021.

Lange R, Volkmer M, Heesen C, et al: Modafinil effects in multiple sclerosis patients with fatigue. J Neurol 2009 Apr;256(4):645-650. Accessed March 31,2021.

Modafinil. Micromedex 2.0. Truven Health Analytics, Inc. Greenwood Village, CO. Available at: <http://www.micromedexsolutions.com>. Accessed March 31,2021.

Nuvigil® (armodafinil) [prescribing information]. North Wales, PA: Teva Pharmaceutical USA, Inc. November 2018. Available at: <https://www.nuvigil.com/globalassets/nuvigil-consumer/prescribinginformation.pdf>. Accessed March 31,2021.

Olek M, Narayan R, Frohman E, Frohman T. Symptom management of multiple sclerosis in adults. UpToDate website. Last updated November 2019. Available at: www.uptodate.com. Accessed March 31,2021.

Provigil® (modafinil) [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc. July 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e16c26ad-7bc2-d155-3a5d-da83ad6492c8>. Accessed March 31,2021.

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obstructive sleep apnea in adults. UpToDate website. Last updated April 03, 2018. Available at: www.uptodate.com. Accessed March 31,2021.

Sunosi™ (solriamfetol) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. June 2019. Available at: <https://pp.jazzpharma.com/pi/sunosi.en.USPI.pdf>. Accessed March 31,2021.

Thorpy MJ, Shapiro C, Mayer G, et al: A randomized study of solriamfetol for excessive sleepiness in narcolepsy. Ann Neurol 2019; 85(3):359-370.Wyatt J. Overview of circadian sleep-wake rhythm disorders. UpToDate website. Last updated January 09, 2019. Available at www.uptodate.com. Accessed March 31,2021.

Wakix® (pitolisant hydrochloride) [prescribing information]. Plymouth Meeting, PA: Harmony Biosciences, LLC. October 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8daa5562-824e-476c-9652-26ceef3d4b0e>. Accessed March 31,2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Generic Name	Brand Name
Armodafinil	Nuvigil®
Modafinil	Provigil®
Pitolisant	Wakix®
Solriamfetol	Sunosi™

Cross References:

Rx.01.33 Off-Label Use

Rx.01.76 Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.