BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 4/08/10**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
	LAST CRITERIA REVISION DATE: 11/16/17
	ARCHIVE DATE:

NUVIGIL™ (armodafinil) oral tablet
ARMODAFINIL oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

NUVIGIL™ (armodafinil) oral tablet
ARMODAFINIL oral tablet (cont.)

Description:

Nuvigil (armodafinil) and generic armodafinil are non-amphetamine wake-promoting agents for oral administration. Nuvigil (armodafinil) and generic armodafinil are approved by the Food and Drug Administration (FDA) to improve wakefulness in individuals with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA) and shift work sleep disorder (SWSD).

Narcolepsy is a chronic neurologic disorder of the central nervous system characterized by the brain's inability to control sleep-wake cycles, resulting in excessive daytime sleepiness (EDS) and intermittent bouts of rapid eye movement (REM) sleep during wakefulness. At various times throughout the day, individuals with narcolepsy experience irresistible and sudden bouts of sleep, which can last from a few seconds to several minutes. In addition to EDS, other major symptoms of narcolepsy include cataplexy (an emotionally triggered transient sudden loss of voluntary muscle tone), hypnagogic hallucinations (vivid dream-like images often frightening tactile, or auditory hallucinations during sleep onset or upon waking), and sleep paralysis (brief episodes of total paralysis, also during sleep onset or upon waking). Most individuals experience poor sleep quality that can involve frequent awakenings during nighttime sleep, and other sleep disorders. Sleep may be disrupted by insomnia, vivid dreaming, sleep talking, acting out while dreaming, and periodic leg movements. Patients with sleepiness severe enough to require medication can be treated with stimulant medications, such as armodafinil, modafinil, methylphenidate, or amphetamines.

SWSD is a persistent or recurrent pattern of sleep disruption in which late night or rotating shift work disrupts normal sleep patterns; leading to misalignment with the individual’s endogenous circadian sleep-wake cycle and exogenous demands in regards to timing and duration of sleep. This misalignment causes disturbed sleep, which is associated with symptoms of excessive sleepiness during shift work hours and insomnia during sleep hours. The diagnosis should be reserved for those patients in whom there is clinically significant distress or impairment in social, occupational, or other important areas of functioning related to the sleep disorder and in whom the sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance abuse disorder. Criteria for SWSD often includes documentation of symptoms for at least 3 months, excessive sleepiness at the time of their night shifts, work a minimum 5 night shifts per month, and have documented daytime insomnia. Management of SWSD includes use of short-acting hypnotic agents and melatonin for insomnia or initiating sleep during the desired time, caffeine for alertness, modafinil or armodafinil for excessive sleepiness during work shift.

In OSA, Nuvigil (armodafinil) or generic armodafinil are indicated as an adjunct to standard treatment(s) for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating Nuvigil (armodafinil) or generic armodafinil. If Nuvigil (armodafinil) or generic armodafinil are used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is strongly recommended. Certain medications with inhibitory effects on the central nervous system should be avoided if reasonable alternatives exist. Medications that may exacerbate OSA and worsen daytime sleepiness include benzodiazepine receptor agonists, barbiturates, other antiepileptic drugs, sedating antidepressants, antihistamines, and opiates. When such medications are felt to be necessary, their use in a patient with OSA should be monitored closely and the dose carefully titrated if possible.

Multiple sclerosis (MS) is a disease of the central nervous system whose symptoms wax and wane. Symptoms of MS are numerous, but fatigue is a common and potentially disabling complaint. The mechanism of fatigue is poorly understood. Recommendations on management of MS related fatigue include identification of reversible or manageable causes such as side effects of other medications, untreated co-existing medical illnesses, poor sleep hygiene, etc. Medications known to result in fatigue or sleepiness include certain anticonvulsants, sedative-hypnotics, antihistamines, some antidepressants, antispasmodics, opioids, certain antihypertensive medications, and others. A critical evaluation of their use and/or dose reduction should be undertaken to minimize their impact as a cause of fatigue.

Pharmacologic management of fatigue of MS includes off-label use of amantadine, methylphenidate, amphetamines and aspirin. Amantadine is the most extensively studied agent and has been shown to significantly reduce fatigue. Methylphenidate and amphetamines have been used and have shown positive results. Modafanil (Provigil and generics), Nuvigil (armodafinil), and generic armodafinil are suggested as off-label alternative to these agents.

The mechanism(s) through which armodafinil promotes wakefulness is unknown. Armodafinil (R-modafinil) has pharmacological properties similar to those of modafinil (a mixture of R- and S-modafinil), to the extent tested in animal and in vitro studies. The R- and S-enantiomers have similar pharmacological actions in animals. 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. Armodafinil is also an indirect dopamine receptor agonist; both armodafinil and modafinil bind *in vitro* to the dopamine transporter and inhibit dopamine reuptake.

Nuvigil (armodafinil)
Armodafinil

Medication class:
Central nervous system stimulant

FDA-approved indication(s):
- To improve wakefulness in patients with excessive sleepiness associated with narcolepsy
- To improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea (OSA)
- To improve wakefulness in patients with excessive sleepiness associated with shift-work sleep disorder (SWD)
- Off-label: To improve fatigue related to Multiple Sclerosis (MS)

Recommended Dose:
- Narcolepsy: 150 or 250 mg once daily in the morning
- OSA: 150 or 250 mg once daily in the morning, doses > 150 mg have not been shown to have an increased benefit
- SWSD: 150 mg once daily approximately 1 hour prior to the start of the work shift

Maximum dosage

NUVIGIL™ (armodafinil) oral tablet
ARMODAFINIL oral tablet (cont.)

- 250 mg once daily

Available Dosage Forms:
- 50 mg, 150 mg, 200 mg, and 250 mg tablets

Limitations of use:
- In OSA, armodafinil is indicated to treat excessive sleepiness and not as treatment for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating armodafinil for excessive sleepiness

Warnings and Precautions:
- Should not be used in patients with a history of left ventricular hypertrophy or mitral valve prolapse
- Discontinue at first sign of serious drug-related rash, skin or mouth sores, blistering or ulceration (Stevens-Johnson syndrome, toxic epidermal necrolysis)
- Discontinue if drug rash with eosinophilia and systemic symptoms (DRESS)/Multi-organ hypersensitivity is suspected
- Discontinue if angioedema or anaphylaxis is suspected
- Consider stopping if psychiatric symptoms develop such as depression, anxiety, mania, hallucinations, thoughts of suicide, aggressive behavior, or other significant psychiatric symptoms
- Woman of reproductive potential using hormonal contraception should use additional methods of contraception such as barrier method or non-hormonal methods

NUVIGIL™ (armodafinil) oral tablet
ARMODAFINIL oral tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Nuvigil (armodafinil) and armodafinil is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is 17 years of age and older

2. A confirmed diagnosis of **ONE** of the following:
    - A patient with excessive sleepiness associated with **narcolepsy** with **ALL** of the following:
        - Diagnosis confirmed by polysomnography followed by a multiple sleep latency test (MSLT) indicating sleep onset of less than 8 minutes and ≥ 2 sleep onset REM periods
        - Failure, contraindication or intolerance to **ALL**:
            - Modafinil
            - Methylphenidate
            - An amphetamine

    - A patient with excessive sleepiness associated with **obstructive sleep apnea (OSA)** on continuous positive airway pressure (CPAP) therapy with **ALL** of the following:
        - Diagnosis confirmed by polysomnography showing ≥ 5 respiratory events/hour (apneas, hypopneas, respiratory effort-related arousals) with respiratory effort during each
        - Failure, contraindication or intolerance to **Modafinil**

    - A patient with persistent and frequent excessive sleepiness and/or falling asleep while at work associated with shift work sleep disorder (SWSD) with **ALL** of the following:
        - Diagnosis confirmed by **ALL** of the following:
            - Must frequently (5 or more times per month) work night shifts
            - Works at least 6 hours of the night shift between 10 PM and 8 AM
            - Experiences sleepiness and impaired performance while at work
        - Failure, contraindication or intolerance to **Modafinil**

    - A patient with fatigue related to multiple sclerosis (MS) not receiving other drugs known to cause or contribute to sleepiness or fatigue **and** has failure, contraindication or intolerance to **ALL**:
        - Modafinil
        - Amantadine
        - Methylphenidate
        - An amphetamine

3. There are **NO** contraindications:
    - Contraindications include:
        - Known hypersensitivity to Modafinil

Initial approval duration: 12 months

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- **Criteria for continuation of coverage (renewal request):** Nuvigil (armodafinil) and armodafinil is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined by improvement in quantifying sleepiness tests:
       - Multiple sleep latency test (MSLT) for SWSD
       - Maintenance of wakefulness test (MWT) for OSA, Narcolepsy,
       - Or other measure of improvement as measured by other tests such as:
         - Epworth sleepiness scale
         - Stanford sleepiness scale
         - Osler test

  2. Individual has been adherent with the medication

  3. There are no significant interacting drugs

  Renewal duration: 12 months

Resources:

Nuvigil. Package Insert, October 2010. Reviewed on 01/02/2013

Nuvigil. Package Insert, revised by manufacturer on 04-2015. Reviewed on 10/12/2015

Nuvigil. Package Insert, revised by manufacturer on 04-2015. Reviewed on 10/17/2016

Armodafinil by Actavis Pharma, Inc. Package insert, revised by manufacturer on 05-2016. Reviewed on 10/17/16

UpToDate: Treatment of narcolepsy in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-narcolepsy-in-adults?source=search_result&search=narcolepsy&selectedTitle=2~113

UpToDate: Clinical features and diagnosis of narcolepsy in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-features-and-diagnosis-of-narcolepsy-in-adults?source=search_result&search=narcolepsy&selectedTitle=1~113#H17

UpToDate: Quantifying sleepiness. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/quantifying-sleepiness?source=see_link#H21

UpToDate: Management of obstructive sleep apnea in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/management-of-obstructive-sleep-apnea-in-adults?source=search_result&search=obstructive%20sleep%20apnea&selectedTitle=5~150

UpToDate: Overview of obstructive sleep apnea in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-obstructive-sleep-apnea-in-adults?source=search_result&search=obstructive%20sleep%20apnea&selectedTitle=1~150

UpToDate: Clinical presentation and diagnosis of obstructive sleep apnea in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-presentation-and-diagnosis-of-obstructive-sleep-apnea-in-adults?source=search_result&search=obstructive%20sleep%20apnea&selectedTitle=4~150

UpToDate: Sleep-wake disturbances in shift workers. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/sleep-wake-disturbances-in-shift-workers?source=search_result&search=shift%20work%20sleep%20disorder&selectedTitle=1~38#H1304329353

UpToDate: Symptom management of multiple sclerosis in adults. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/symptom-management-of-multiple-sclerosis-in-adults?source=search_result&search=fatigue%20from%20multiple%20sclerosis&selectedTitle=1~150

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.