



Nuvigil (armodafinil), Provigil (modafinil) Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid only.

Quantity limits apply to all products. Prior Authorization only applies to the MN Medicaid Preferred Drug List (PDL) non-preferred drugs: generic armodafinil and generic modafinil.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE^{1,2}

Agent	FDA Approved Indications	Dosing and Administration
Nuvigil®* (armodafinil)	<p>Improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD)</p> <p>Safety and effectiveness in pediatric patients below age 17 have not been established.</p> <p>Limitation of use: Nuvigil is indicated to treat excessive daytime sleepiness in OSA 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 Nuvigil for excessive sleepiness.</p>	<p>OSA/Narcolepsy: 150-250 mg orally once daily. In OSA, there is no consistent evidence that doses >150 mg/day provide greater benefit</p> <p>SWD: 150 mg orally once daily, 1 hour prior to the start of the work shift.</p>
Provigil®* (modafinil)	<p>Improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD)</p> <p>Safety and effectiveness in pediatric patients below age 17 have not been established.</p> <p>Limitation of use: Provigil is indicated to treat excessive daytime sleepiness in OSA and not as</p>	<p>Narcolepsy/OSA: 200 mg orally once daily. Doses up to 400 mg/day as a single dose have been well tolerated but there is no consistent evidence that this dose provides benefit beyond that of the 200 mg dose.</p> <p>SWD: 200 mg orally once daily, 1 hour prior to the start of the work shift.</p>

Agent	FDA Approved Indications	Dosing and Administration
	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 Provigil for excessive sleepiness.	

* generic available

CLINICAL RATIONALE

Excessive daytime sleepiness (EDS) is characterized by persistent sleepiness regardless of how much sleep an individual gets at night. In between sleep attacks, individuals have normal levels of alertness, particularly if doing activities that keep their attention.³ The most common causes of EDS include narcolepsy, obstructive sleep apnea, shift work disorder, sleep deprivation, medication effects, and other medical and psychiatric conditions.⁶

Narcolepsy

Narcolepsy is a chronic neurological disorder caused by the inability to regulate sleep-wake cycles. At various times throughout the day, patients with narcolepsy experience irresistible bouts of sleep and could fall asleep. If left undiagnosed or untreated, narcolepsy can interfere with psychological, social, and cognitive function and development and can inhibit academic, work, and social activities. Symptoms may include excessive daytime sleepiness, cataplexy, sleep paralysis, and hallucinations. All patients diagnosed with narcolepsy will have excessive daytime sleepiness. However, sleepiness in narcolepsy is more like a “sleep attack”, where an overwhelming sense of sleepiness comes on quickly.³ There is limited evidence to advise on treatment of special populations such as children, pregnant women, and breastfeeding mothers.⁵

The American Family Physician recommends referral to a sleep clinic if narcolepsy is suspected.⁴ The American Academy of Sleep Medicine indicates treatment goals should be to alleviate daytime sleepiness and produce the fullest possible return of normal function for patients at work, school, home, and socially. Modafinil is effective treatment for EDS associated with narcolepsy.⁵

Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea (OSA) is a prevalent condition with serious health consequences, including EDS, cognitive disturbances, depression, hypertension, and cardiovascular and cerebrovascular disease.¹⁰

Guidelines from the American College of Physicians (ACP) on management of OSA do not include modafinil/armodafinil in their recommendations for treatment. ACP guidelines state that pharmacologic therapy is not currently supported by evidence and should not be prescribed for OSA treatment.⁷ The American Academy of Sleep Medicine (AASM) practice parameters recommend modafinil in patients with OSA for the treatment of residual excessive daytime sleepiness despite effective positive airway pressure treatment and who are lacking any other identifiable cause for their sleepiness.¹⁰ Both guidelines recommend weight loss for obese and overweight patients and continuous positive airway pressure treatment as initial therapy.^{7,10}

A review on the treatment of OSA suggested pharmacologic agents play a minimal role in the treatment of breathing itself in patients with a sleep disorder. Modafinil and armodafinil are considered adjunctive therapies to improve wakefulness in these patients. These agents are

recommended for patients who experience residual sleepiness despite optimal CPAP therapy, provided CPAP compliance is closely monitored. Modafinil or armodafinil do not treat the OSA itself but only the associated symptoms of sleepiness. The majority of patients (75%) with severe sleepiness at baseline still had mean multiple sleep latency times of less than 10 minutes despite the addition of modafinil to effective therapy with CPAP. This suggests that these drugs do not necessarily eliminate the risk of motor vehicle and other accidents in the OSA population. Concern also exists that the use of pharmacotherapy to treat excessive sleepiness associated with OSA may lead to subsequent reduction in CPAP compliance.⁶

Shift Work Disorder (SWD)

Shift work disorder refers to non-standard work schedules (e.g., night work, early morning work, and rotating schedules). Recommended AASM treatments for SWD disorders include: planned sleep schedules, timed light exposure, timed melatonin administration, hypnotics, stimulants [e.g., caffeine], and alerting agents [e.g., modafinil]. Studies using psychostimulants (modafinil, caffeine, and methamphetamine) for SWD have shown efficacy in countering sleepiness and improving psychomotor performance during the night shift compared with placebo. Modafinil and caffeine in medical doses have established safety records so in most cases when enhanced alertness is necessary, the benefits are considered to outweigh the risks for this application. Stimulants have not been shown to be a safe substitute for adequate sleep.⁸

A systematic review evaluated pharmacologic interventions for sleepiness and sleep disturbances due to SWD showed that armodafinil/modafinil taken before the night shift probably reduces sleepiness using the Karolinska Sleepiness Scale (KSS), and increases night shift alertness. The review also found that both agents caused severe adverse effects, including headache, nausea, anxiety, and nervousness.⁹

Off-Label Use

There are many reports and ongoing studies of off-label use (jet lag, fatigue, depression, schizophrenia, etc.) for modafinil and armodafinil. Although there may be potential clinical benefits for some of these uses in certain patients, current data is generally limited and conflicting, and the benefit-risk profile of these agents for off-label use is unclear.

Safety

Armodafinil and modafinil are contraindicated in patients with known hypersensitivity to armodafinil or modafinil. Armodafinil and modafinil are Schedule IV controlled substances.^{1,2}

For additional clinical information see Prime Therapeutics Formulary Chapter 9.5A: Stimulants.

REFERENCES

1. Nuvigil prescribing information. Cephalon, Inc. February 2017.
2. Provigil prescribing information. Cephalon, Inc. November 2018.
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7. Qaseem A, Holty J, Owens D, et al. Management of obstructive sleep apnea in adults: A clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2013;159:471–483.
8. Morgenthaler T, Lee-Chiong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine Report. *Sleep.*2007;30(11):1445-1459.
9. Liira J, Verbeek J, Costa G, et al. Pharmacological interventions for sleepiness and sleep disturbances caused by shift work. *Cochrane Data Syst Rev.* 2014;8: CD009776.
10. Morgenthaler TI, Kapen S, Lee-Chiong T, Alessi C, Boehlecke B, Brown T, et al. Practice parameters for the medical therapy of obstructive sleep apnea. *Sleep* (2006) 29:1031–5.

Nuvigil (armodafinil), Provigil (modafinil) Prior Authorization with Quantity Limit

TARGET AGENTS - Quantity limits apply to all products. Prior Authorization only applies to the MN Medicaid Preferred Drug List (PDL) non-preferred drugs: generic armodafinil and generic modafinil.

Nuvigil® (armodafinil)^a

Provigil® (modafinil)^a

a – generic available, subject to prior authorization program

PROGRAM QUANTITY LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Per Day Limit
Nuvigil (armodafinil)^a			
50 mg tablet	61400010000310	M, N, O, or Y	1 tablet
150 mg tablet	61400010000330	M, N, O, or Y	1 tablet
200 mg tablet	61400010000335	M, N, O, or Y	1 tablet
250 mg tablet	61400010000340	M, N, O, or Y	1 tablet
Provigil (modafinil)^a			
100 mg tablet	61400024000310	M, N, O, or Y	1 tablet
200 mg tablet	61400024000320	M, N, O, or Y	1 tablet

a – generic available, subject to quantity limit

PRIOR AUTHORIZATION WITH QUANTITY LIMIT CRITERIA FOR APPROVAL

Target Agent will be approved when ALL of the following are met:

1. The patient is 17 years of age or over
AND
2. The patient has a diagnosis of narcolepsy, obstructive sleep apnea (OSA), shift work disorder (SWD), or fatigue related to multiple sclerosis
AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
4. ONE of the following:
 - a. The patient is NOT currently being treated with another agent in this program
OR
 - b. The patient is currently being treated with another agent in this program AND will discontinue prior to starting the requested agent**AND**
5. ONE of the following:
 - a. The patient has tried and had an inadequate response to the preferred agent, brand name Provigil
OR
 - b. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to brand name Provigil that is not expected to occur with the requested agent
OR
 - c. The prescriber has submitted documentation in support of the use of the requested non-preferred agent, for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist**AND**
6. ONE of the following:
 - a. The requested quantity (dose) does NOT exceed the program quantity limit
OR
 - b. ALL of the following:

- i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
AND
 - iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
- OR**
- c. ALL of the following:
 - i. The requested quantity (dose) is greater than the program quantity limit
AND
 - ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
AND
 - iii. The prescriber has submitted documentation in support of therapy with a higher dose for the requested indication

Length of Approval: 12 months



Step Therapy Supplement Program Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
 - a. A statement by the prescriber that the patient is currently taking the requested agent
AND
 - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
AND
 - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
- OR**
2. BOTH of the following
 - a. The patient's medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
 - i. Evidence of a paid claim(s) within the past 999 days
OR
 - ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days**AND**
 - b. ONE of the following:
 - i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
OR
 - ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)
- OR**
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria