



**BlueCross BlueShield
of Alabama**

**Nuvigil® /armodafinil,
Provigil®/modafinil
Prior Authorization
with Quantity Limit
Program Summary**

This program applies to Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Nuvigil/armodafinil, Provigil/modafinil Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling (one tablet per day). The PA criteria will approve modafinil or armodafinil when prescribed according to product labeling for patients 17 years and over. Requests for modafinil or armodafinil will be reviewed when patient-specific documentation has been provided. The PA criteria will approve only one of these agents at a time. Brand and generic products are included in this program.

TARGET AGENTS

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

Nuvigil/armodafinil, Provigil/modafinil 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, or shift work disorder
AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
4. The patient is receiving only one of the listed agents – Nuvigil/armodafinil OR Provigil/modafinil - in the past 90 days
AND
5. ONE of the following:
 - a. The quantity requested is less than or equal to the program quantity limit

OR

- b. The quantity (dose) requested is above the program limit, less than or equal to the maximum dose recommended in FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength

OR

- c. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of Approval: 12 months

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FDA APPROVED INDICATIONS AND DOSAGE^{1,2}

Agent	FDA Approved Indications	Dosing and Administration
Nuvigil®* (armodafinil)**	Improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD)	OSA/Narcolepsy: 150-250 mg/day; in OSA, there is no consistent evidence that doses >150 mg/day provide greater benefit SWD: 150 mg/day
Provigil®* (modafinil)**	Improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD)	200 mg/day Doses up to 400 mg/day have been well tolerated but there is no consistent evidence that this dose provides benefit beyond that of the 200 mg dose

*Safety and effectiveness in pediatric patients below age 17 have not been established. Serious skin rashes, including erythema multiforme major and Stevens-Johnson Syndrome have been associated with modafinil use in pediatric patients.

** generic available

CLINICAL RATIONALE

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.³ There is limited evidence to advise on treatment of special populations such as children, pregnant women, and breastfeeding mothers.⁷

The American Family Physician recommends referral to a sleep clinic if narcolepsy is suspected.⁴ Treatment goal for narcolepsy is to obtain normal alertness during conventional waking hours or to maximize alertness at important times of the day (e.g. during work, school, or while driving). Non-pharmacological treatments include avoidance of medications that can cause drowsiness, such as benzodiazepines, opiates, antipsychotics, napping, and improved sleep hygiene.⁵

Excessive Daytime Sleepiness (EDS)

EDS is characterized by persistent sleepiness regardless of how much sleep an individual gets at night. However, sleepiness in narcolepsy is more like a "sleep attack", where an overwhelming sense of sleepiness comes on quickly. In between sleep attacks, individuals have normal levels of alertness, particularly if doing activities that keep their attention. All patients with narcolepsy have EDS, and it is often the most obvious symptom.³

Pharmacological agents that may be used for treatment of EDS include stimulants such as modafinil, amphetamine, methamphetamine, methylphenidate, dextroamphetamine. These agents have shown benefit for treatment of EDS however, they are typically ineffective for cataplexy.^{3,5,6} Modafinil is considered first-line agent.⁵

Obstructive Sleep Apnea (OSA)

Recommendations for treatment of OSA include behavioral measures (e.g., weight loss, altered sleeping position, avoidance of alcohol and sedatives). The mainstay of therapy for OSA is administration of continuous positive airway pressure (CPAP). Oral appliances may benefit patients who are unable or unwilling to use CPAP or other forms of positive air pressure therapy.⁸

Guidelines from the American College of Physicians (ACP, 2013) 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.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. CPAP is the primary therapy for the breathing. Excessive sleepiness can persist despite effective CPAP therapy. 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.⁹

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.^{11,12}

A systematic review (2014) evaluated pharmacologic interventions for sleepiness and sleep disturbances due to SWD: Analysis included 15 RCTs (N=715) using melatonin, modafinil, armodafinil, or caffeine. Armodafinil taken before the night shift probably reduces sleepiness by one point on the Karolinska Sleepiness Scale (KSS) and increases alertness by 50 ms in a simple reaction time test at three months' follow-up in shift work disorder patients. Modafinil probably has similar effects on sleepiness (KSS) and alertness in the psychomotor vigilance test in the same patient group. Post-marketing, severe skin reactions have been reported. Adverse effects reported by trial participants were headache, nausea and a rise in blood pressure. Authors concluded modafinil and armodafinil increase alertness and reduce sleepiness to some extent in SWD but are associated with adverse events.¹³

Another systematic review (JAMA, 2015) also evaluated pharmacological interventions for sleepiness and sleep disturbances caused by shift work (15 RCTs; N=1240). Modafinil was associated with small benefit and frequent adverse outcomes.¹⁴

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

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