



Nuvigil™/ Provigil® Prior Authorization Criteria

| Brand | Generic | Dosage Form |
|-----------|-------------|-------------|
| Nuvigil™ | armodafinil | tablet |
| Provigil® | modafinil | tablet |

FDA APPROVED INDICATIONS^{1,2}

The following information is taken from individual drug prescribing information and is provided here as background information only. Not all FDA-approved indications may be considered medically necessary. All criteria are found in the section "Prior Authorization (PA) Criteria for Approval."

Nuvigil/Provigil^{1,2}

Nuvigil (armodafinil) and Provigil (modafinil) are indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder.

In OSAHS, Nuvigil and Provigil are indicated as an adjunct to standard treatment(s) for the underlying obstructions. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximum effort to treat with CPAP for an adequate period of time should be made prior to initiating Nuvigil or Provigil. If Nuvigil or Provigil is used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is necessary.

In all cases, careful attention to the diagnosis and treatment of the underlying sleep disorder(s) is of utmost importance. Prescribers should be aware that some patients may have more than one sleep disorder contributing to their excessive sleepiness.

Provigil: Safety and effectiveness in individuals below sixteen years of age have not been established. Leukopenia has been reported in pediatric patients taking Provigil.

Nuvigil: The effectiveness of Nuvigil in long-term use (greater than 12 weeks) has not been systematically evaluated in placebo-controlled trials. The physician who elects to prescribe Nuvigil for an extended time in patients should periodically re-evaluate long-term usefulness for the individual patient.

RECOMMENDED QUANTITY LIMITS ^{1,2}

Table 1: Summary of Recommended Doses and Quantity Limits

| Agent | Recommended Dosage | Quantity per Day Limit |
|-----------------|--|------------------------|
| Provigil 100 mg | The recommended dose of Provigil is 200 mg given once a day, in the a.m. for narcolepsy and OSAHS, and one hour before work for SWSD | 1 tablet |
| Provigil 200 mg | | 1 tablet |
| Nuvigil 50 mg | The recommended dose of Nuvigil is 150 mg or 250 mg given once a day, in the a.m. for narcolepsy and OSAHS, and 150 mg one hour before work for SWSD | 1 tablet |
| Nuvigil 150 mg | | 1 tablet |
| Nuvigil 250 mg | | 1 tablet |

OSAHS = Obstructive sleep apnea/hypopnea syndrome, SWSD = Shift work sleep disorder

RATIONALE FOR PRIOR AUTHORIZATION

The intent of the Nuvigil/Provigil Prior Authorization Criteria is to appropriately select patients for therapy and approve dosing according to indications in product labeling and/or clinical guidelines and/or clinical studies. Modafinil and armodafinil are indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder.^{1,2} Armodafinil is the R-enantiomer of modafinil (mixture of R- and S- enantiomers).^{1,2}

Modafinil has been used to treat other indications not approved by the Food and Drug Administration (FDA) including attention deficit/hyperactivity disorder (ADHD),³⁻⁶ as an adjunct to antidepressants in treatment of depression,⁷⁻⁹ and to combat general fatigue unrelated to lack of sleep such as in Parkinson's disease,¹⁰⁻¹² multiple sclerosis (MS),¹³⁻¹⁵ and chronic fatigue syndrome.¹⁶ Modafinil has also been studied for the treatment of cocaine addiction¹⁷, relief of acute pain¹⁸, myotonic dystrophy^{19,20}, post-polio²¹, and schizophrenia.^{22,23} The compendium Clinical Pharmacology includes adjunctive treatment of fatigue secondary to MS as an accepted unlabeled use of modafinil for patients 16 years of age and older at a dose of 200 mg to 400 mg daily.²⁴ The compendium Micromedex also indicates modafinil as effective in fatigue in MS.²⁵

Micromedex suggests, from one small single dose crossover trial comparing 200 mg modafinil and placebo (N=20), treatment of adult ADHD with modafinil may be effective.²⁵ However, Clinical Pharmacology reports on the use of Provigil for the treatment of ADHD in adults and indicates that, according to a phase III trial (N=113), modafinil, compared to placebo, showed no benefit in reducing the symptoms of ADHD in adults, as measured by the DSM-IV ADHD Rating Scale.²⁴ Based on this information, it appears modafinil is not effective for ADHD in adults.²⁴

Information included in Micromedex indicates modafinil may be effective for treatment of pediatric ADHD.²⁵ However, Cephalon, the manufacturer of modafinil, had submitted a supplemental new drug application to market modafinil under the trade name, Sparlon, in doses of 85 mg, 170 mg, 255 mg, 340 mg and 425 mg tablets for the treatment of ADHD in children and adolescents six through seventeen years of age.²⁶ FDA approval was denied after the FDA advisory committee voted 12-to-1 against Sparlon due to concerns about a number of reported cases of skin rash reactions in a patient trial involving 1,000 patients.²⁶ One skin rash report was thought to be Stevens-Johnson syndrome.²⁶ Cephalon decided to discontinue development of Sparlon for pediatric use.

Other diagnoses for which there is information in Micromedex indicating modafinil favors efficacy include treatment of daytime sleepiness in patients receiving levodopa and/or dopamine agonist therapy for Parkinson's disease (PD), use in restoring cognitive function performance during sleep deprivation, and reduction of daytime sleepiness in patients with myotonic dystrophy.²⁵ Diagnoses for which Micromedex considers evidence inconclusive are delirium resulting from alcohol withdrawal, depression, fatigue due to fibromyalgia, and as adjunct therapy in schizophrenia.²⁵

There are on-going clinical studies evaluating modafinil for the treatment of fatigue in cancer, HIV/AIDS, PD, amyotrophic lateral sclerosis (ALS), and MS as well as studies for use in cocaine, methamphetamine, and nicotine addiction and use in traumatic brain injury, effects on brain function in schizophrenia, and effects on memory and attention in Lupus patients.²⁷ There are also on-going clinical trials evaluating armodafinil for the following conditions; treatment of fatigue in patients with malignant gliomas, sarcoidosis, HIV/AIDS, fibromyalgia, and patients on chemotherapy; treatment of excessive sleepiness in patients with closed traumatic brain injury, and jet lag disorder; adjunctive treatment of schizophrenia in

patients with and without cognitive deficits, depression associated with bipolar disorder, and OSAHS with comorbid depression or dysthymic disorder.²⁷ There are currently insufficient published data supporting the use of armodafinil for any of these off-label uses. No accepted off-label uses are cited in American Hospital Formulary Service (AHFS), Micromedex DrugDex, or Clinical Pharmacology compendia.^{24,25,27}

The World Anti-Doping Agency (WADA) added modafinil to the list of prohibited substances in August 2004 after a runner in the 2003 World Track and Field Championships tested positive for the agent.²⁸ It is unknown how widely modafinil is used for enhancing athletic performance and there no studies are available indicating if there is a positive impact.

The PA criteria will approve modafinil or armodafinil when prescribed according to product labeling or for MS-related fatigue for patients sixteen years and older. Safety and effectiveness in individuals below sixteen years of age have not been established.^{1,2} Serious skin rashes, including erythema multiforme major and Stevens-Johnson Syndrome have been associated with modafinil use in pediatric patients. In controlled and open-label clinical studies of modafinil in pediatric patients, treatment emergent adverse events of the psychiatric and nervous system included Tourette's syndrome, insomnia, hostility, increased cataplexy, increased hallucinations and suicidal ideation. Transient leucopenia, which resolved without medical intervention, was also observed.^{1,2}

Approvals will be indefinite for the diagnosis of narcolepsy and twelve months for all other indications. Indefinite approvals may be subject to reevaluation if selection criteria change or safety issues become apparent.

The PA criteria for Provigil and Nuvigil will also limit dispensed quantities to one tablet per day. Prescribing information for modafinil recommends a dose of 200 mg given once a day in the morning for narcolepsy and OSAHS.¹ When prescribed for shift work sleep disorder the dose should be taken approximately one hour prior to the start of the work shift.¹ Single doses of modafinil up to 400 mg per day have been well tolerated, but there is no consistent evidence that this dose is more efficacious than a 200 mg per day dose.¹ For armodafinil, prescribing information recommends single daily doses of 150 mg or 250 mg for OSAHS or narcolepsy. The recommended dose of armodafinil for SWSD is 150 mg given daily approximately 1 hour prior to the start of their work shift.² Requests for higher doses will be evaluated if the prescriber submits documentation for use of increased quantities in the patient.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Nuvigil (armodafinil), Provigil (modafinil)

Initial and Renewal Evaluation

1. Is the patient 16 years of age or older?
If yes, continue to 2. If no, deny.
2. Is the patient's diagnosis an FDA-approved labeled indication (narcolepsy, obstructive sleep apnea/hypopnea syndrome [OSAHS], shift work sleep disorder)?
If yes, continue to 4. If no, continue to 3.
3. Is the patient's diagnosis fatigue related to multiple sclerosis (MS)?
If yes, continue to 4. If no, deny.
4. Can the prescribed dose be accomplished with a quantity of one tablet per day?
If yes, approve indefinitely for one tablet per day if prescribed for narcolepsy,
approve for 12 months for one tablet per day for OSAHS or shift work sleep disorder.
If no (quantities requested are greater than one tablet per day), continue to 5.
5. Has the prescriber provided and pharmacist reviewed evidence supporting a dose exceeding one tablet per day?
If yes, pharmacist must review and may approve for 12 months for requested quantity based on review of information provided.
If no, deny higher quantity (may approve for one tablet per day, duration as indicated above).

SUMMARY

The intent of the prior authorization criteria for modafinil and armodafinil are to appropriately select patients for therapy according to labeled indications and recommended dosing. Due to lack of safety and efficacy data in patients under the age of sixteen, modafinil and armodafinil will not be approved for this age group. Modafinil and armodafinil are indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder. They will also be approved in these criteria for fatigue related to MS. The use of modafinil for attention deficit/hyperactivity disorder has been reviewed but not approved by the Food and Drug Administration. There are insufficient data supporting efficacy for the use of modafinil for improving wakefulness or decreasing fatigue in other diagnoses such as depression, Parkinson Disease, chronic fatigue syndrome or for treatment of cocaine addiction. There are also insufficient data supporting efficacy for use of armodafinil for any off-label uses.

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Document History

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