MEDICAL MUTUAL®

Drug Policy

Policy:	Nuvigil (armodafinil) and Provigil (modafinil) Prior Approval Criteria	Annual Review Date: 06/22/2023 Last Revised Date: 07/20/2023

OVERVIEW

Nuvigil (armodafinil) and Provigil (modafinil), agents with wake-promoting actions that are similar to sympathomimetic agents (e.g., amphetamine and methylphenidate), are indicated to improve wakefulness in patients with excessive daytime sleepiness (EDS) associated with narcolepsy; obstructive sleep apnea/hypoapnea syndrome (OSAHS) [approved as adjunctive therapy]; and shift work sleep disorder (SWSD). Armodafinil and modafinil are Schedule IV controlled substances. Review of the medical literature notes many other uses of modafinil that are considered off-label or investigational. While armodafinil has not been studied off-label to the same extent as modafinil, it is expected that armodafinil will have similar clinical efficacy for these uses.

POLICY STATEMENT

This policy involves the use of Nuvigil (brand and generic) and Provigil (brand and generic). Prior authorization is recommended for pharmacy benefit coverage of Nuvigil or Provigil. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. Approval will only be granted for those over 18 years of age as the safety and efficacy of Nuvigil and Provigil have not been established in pediatric patients. Patients continuing Nuvigil or Provigil drug therapy are subject to all criteria below, with the exception that they are NOT required to have a history of a sleep study. Quantity limits may apply.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of armodafinil or modafinil is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Narcolepsy.** Approve if criteria below are met (a, b, c, AND d):
    a. Patient is ≥ 18 years of age; AND
    b. Narcolepsy has been confirmed with two sleep studies: a polysomnogram (PSG) and a multiple sleep latency test (MSLT); AND
    c. The medication is prescribed by or in consultation with a sleep specialist physician or a neurologist; AND
    d. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):

i. The patient has tried generic modafinil or generic armodafinil; AND
ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

2. **Excessive Sleepiness Due to Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS).** Approve if criteria below are met (a, b cAND d):
   a. Patient is ≥ 18 years of age; AND
   b. Patient must meet one of the following criteria (i OR ii):
      i. The requested drug is being used along with continuous positive airway pressure (CPAP) therapy; OR
      ii. The patient is not a candidate for CPAP therapy; AND
   c. Sleep apnea has been confirmed by a sleep study (most commonly a polysomnogram)
   d. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
      i. The patient has tried generic modafinil or generic armodafinil; AND
      ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

3. **Excessive Sleepiness Due to Shift Work Sleep Disorder (SWSD).** Approve if criteria below are met (a, b, c, d AND e):
   a. Patient is ≥ 18 years of age; AND
   b. Request for the treatment of shift-work sleep disorder is provided in situations where the patient is a night shift worker; AND
   c. The patient has complaints of persistent and frequent excessive sleepiness and/or falling asleep while at work; AND
   d. The patient is working at least five overnight shifts per month.
   e. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
      i. The patient has tried generic modafinil or generic armodafinil; AND
      ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 365 days (1 year)
B) *Extended Approval:* 365 days (1 year)

Other Uses with Supportive Evidence

1. **Idiopathic Hypersomnolence.** Approve if criteria below are met (a, b, c AND d):
    a. Patient is ≥ 18 years of age; AND
    b. The patient has a diagnosis of idiopathic hypersomnolence that has been confirmed by sleep studies (polysomnography) in order to rule out disorders such as narcolepsy, obstructive sleep apnea or posttraumatic hypersomnia; AND
    c. Coverage is provided when the diagnosis has been confirmed by a sleep specialist physician.
    d. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
        i. The patient has tried generic modafinil or generic armodafinil; AND
        ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

2. **Depression Associated with Fatigue and/or Sleepiness.** Approve if criteria below are met (a, b AND c)**:**
    a. Patient is ≥ 18 years of age; AND

    b. Patient is concurrently receiving other medication therapy for depression; AND
    Note: Examples of other medications for the treatment of depression include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs).
    c. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
        i. The patient has tried generic modafinil or generic armodafinil; AND
        ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

3. **Fatigue Associated with Multiple Sclerosis (MS).** Approve if criteria below are met (a, b AND c):
    a. Patient is ≥ 18 years of age; AND
    b. Other causes of fatigue, tiredness or decreased energy have been evaluated and treated if necessary (examples include but are not limited to: depression and sleep disorders).
    c. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
        i. The patient has tried generic modafinil or generic armodafinil; AND
        ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

4. **Excessive daytime sleepiness (EDS) due to myotonic dystrophy.** Approve if criteria below are met (a, AND b):
    a. Patient is ≥ 18 years of age; AND
    b. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
        i. The patient has tried generic modafinil or generic armodafinil; AND

ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

5. **Excessive daytime sleepiness (EDS) in Parkinson's disease (PD).** Approve if criteria below are met (a, AND b):
   a. Patient is ≥ 18 years of age; AND
   b. If brand Provigil or Nuvigil is being requested, the patient meets both of the following criteria (i and ii):
      i. The patient has tried generic modafinil or generic armodafinil; AND
      ii. The brand product (Nuvigil or Provigil) is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 365 days (1 year)
B) *Extended Approval:* 365 days (1 year)

QUANTITY LIMIT

Nuvigil and Provigil will approve at point of sale for the following maximum quantities:

- Nuvigil to be dispensed at a max quantity of 7500 mg in 30 days
- Provigil to be dispensed at a max quantity of 6000 mg in 30 days

Additional quantities require a coverage review request.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Nuvigil and Provigil (brand and generic) have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Attention Deficit/Hyperactivity Disorder (ADD/ADHD).** The American Academy of Pediatrics (AAP) clinical practice guidelines for the treatment of ADHD in children and adolescents (2011 and 2019) do not address the use of modafinil/armodafinil. These guidelines note that with the greater availability of approved medications for children/adolescents with ADHD, it has become increasingly unlikely that clinicians need to consider the off-label use of other medications. Two published studies, both of which involved approximately 20 adults with ADHD, preliminarily suggested that modafinil may be useful for this condition. However, a 9-week, randomized, double-blind, placebo-controlled, parallel-group, dose-finding study in adults with ADHD (n = 338) evaluated modafinil doses of 255 mg to 510 mg and did not find significant benefit in reducing ADHD symptoms, as measured by the change from baseline at

final visit in the Adult ADHD Investigator Symptom Rating Scale (AISRS) total score. Many options exist for the treatment of ADHD in adults (e.g., methylphenidate, dextroamphetamine) and further large scale trials that demonstrate benefit for modafinil in adults with ADHD are needed.

2. **Bipolar Disorder, including Bipolar Depression.** Limited data (one small study [n = 85] and case reports [n = 2]) are available that describe the use of modafinil for bipolar disorder and bipolar depression. In one study (n = 257) armodafinil was not more effective than placebo in treating bipolar depression.[28] Only limited data supports modafinil for this condition and more data are needed.

3. **Cancer-Related Fatigue.** The National Comprehensive Cancer Network (NCCN) guidelines on cancer-related fatigue (version 2.2020 – May 4, 2020) no longer consider modafinil to be effective for the treatment of cancer-related fatigue and recommend against its use. A randomized, double-blind, placebo-controlled trial involving 631 patients with cancer receiving chemotherapy found modafinil useful in the control of severe cancer-related fatigue only. Other studies do not support the use of modafinil or armodafinil for cancer-related fatigue.

4. **Chronic Fatigue Syndrome.** Limited data characterize modafinil therapy in those with chronic fatigue syndrome. In a randomized, double-blind, crossover study in 14 patients with chronic fatigue syndrome, use of modafinil for 20 days had minimal effects on cognitive function and no significant effects on fatigue, health-related quality of life, or mood. More data are required to assess efficacy in this patient population.

5. **Excessive Daytime Sleepiness (EDS) Associated with Primary Insomnia.** One randomized, placebo-controlled study found that neither combination therapy with modafinil and cognitive behavioral therapy nor modafinil as monotherapy significantly decreased daytime sleepiness associated with primary insomnia.

6. **Enhancement of Performance in Situations of Induced Sleep Deprivation.** Studies are needed to define the role/appropriateness of modafinil in these situations for the general population (as opposed to military personnel, etc.). Studies have shown that modafinil may enhance performance and sustain alertness in individuals subjected to situations that deprive sleep (e.g., military aviation, emergency physicians). Further studies are needed before its use in the general population in these types of situations can be promoted.

7. **Fibromyalgia.** Limited data are available regarding the use of modafinil in fibromyalgia with most of the data being observational. Larger-sized, randomized, placebo-controlled trials are required to better assess and validate the efficacy of modafinil in patients with fibromyalgia before it can be recommended as a therapeutic modality.

8. **Hypersomnia, Fatigue or Sleepiness Due to Other Conditions (not Idiopathic Hypersomnia, see Other Uses with Supportive Evidence).** More data are needed in specific conditions to define the role of modafinil and armodafinil.

9. **Post-Stroke Sleep-Wake Disorders or Sleep Disorders.** Sleep-wake disorders occur in approximately 20% to 40% of patients that have experienced a stroke, which includes hypersomnia and excessive daytime sleepiness. Very limited data (i.e., case reports and one small study) have explored the use of modafinil in these patients to improve alertness. More data are needed to determine effectiveness in this condition.

10. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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