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5.60.014

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	May 1, 2009
Subject:	Provigil Nuvigil	**Page:**	1 of 6

Last Review Date: December 8, 2023

Provigil Nuvigil

Description

Provigil (modafinil) / Nuvigil (armodafinil)

Background
Provigil and Nuvigil are central nervous system stimulants and share the well-known potential for abuse of this class of drugs. The Drug Enforcement Administration (DEA) has rated Provigil and Nuvigil as Schedule IV drugs. Provigil and Nuvigil produce psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants. Physicians should follow patients closely, especially those with a history of drug and/or stimulant abuse (1-2).

In obstructive sleep apnea (OSA), Provigil and Nuvigil 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 Provigil. If Provigil is used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is necessary (3).

A 12-week study of patients with excessive sleepiness (ES) associated with treated sleep apnea (OSA), shift work disorder (SWD), or narcolepsy evaluated the tolerability and efficacy of armodafinil for 12 months. The conclusion of the study was that armodafinil remained effective and was generally well tolerated. Armodafinil represents an option for long-term treatment of patients with ES associated with treated OSA, SWD, or narcolepsy (4).

Regulatory Status
FDA-approved indications: Provigil and Nuvigil are central nervous system stimulants that are

indicated for: Improving wakefulness in adult patients with excessive sleepiness associated with narcolepsy, shift work disorder, and obstructive sleep disorder. Provigil and Nuvigil are also used as an adjunct to standard treatments for the underlying obstruction in OSA (1-2).

Off-Label Uses:
Provigil has been found effective in the treatment of multiple sclerosis fatigue (3). Modafinil is a unique wake-promoting agent that is chemically distinct from traditional stimulants. Results of a placebo-controlled study showed it to significantly improve fatigue and sleepiness and to be well tolerated by patients with multiple sclerosis (MS) (5,6). For MS patients who experience significant fatigue there are several medications that have proven effective in this regard. Modafinil is among the most commonly used medications for fatigue associated with MS and according to expert opinion, is currently a first-line drug for MS patients (5).

Idiopathic hypersomnia, a condition similar to narcolepsy, is characterized by constant or recurrent daytime sleepiness with no other cause of sleepiness, prolonged nocturnal sleep, difficulty awakening with sleep drunkenness, and long unrefreshing naps with no history of cataplexy. Modafinil has proven effective in treating idiopathic hypersomnia in one case series and several open-label trials. The practice parameters for the treatment of narcolepsy and other hypersomnias of central origin, updated in 2007, state that modafinil may be effective for the treatment of daytime sleepiness due to idiopathic hypersomnia. As there may be underlying causes/behaviors associated with EDS, a sleep specialist physician has the training to correctly recognize and diagnose this condition. While armodafinil has not been studied for this use, expert opinion considers it to be interchangeable with modafinil for this condition (4).

Related Policies
Sunosi, Wakix

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Nuvigil and Provigil may be considered **medically necessary** if the conditions indicated below are met.

Nuvigil and Provigil may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 16 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Narcolepsy
2. Idiopathic or Primary Hypersomnia
3. Multiple Sclerosis (MS) Fatigue
4. Shift Work Sleep Disorder (SWSD) - Irregular sleep/wake rhythm
5. Excessive sleepiness due to obstructive sleep apnea (OSA) **AND ONE** of the following:
    a. Compliant with other standard OSA treatments (such as CPAP and oral appliances)
    b. CPAP therapy is contraindicated
    c. Standard OSA treatments found to be ineffective after history of compliant use

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Medication	Daily Dosing Limits
Provigil	600 mg per day **OR**
Nuvigil	300 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
Provigil and Nuvigil are central nervous system stimulants used to increase wakefulness in adult patients with narcolepsy, shift work sleep disorder and obstructive sleep apnea. The Drug Enforcement Administration (DEA) has rated Provigil and Nuvigil as Schedule IV drugs. Provigil and Nuvigil produce psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants and share the potential for abuse. Provigil has been found effective in the treatment of multiple sclerosis fatigue, improving wakefulness in adult patients with excessive sleepiness associated with narcolepsy, shift work disorder, and obstructive sleep disorder (3-6).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Provigil and Nuvigil while maintaining optimal therapeutic outcomes.

References

1. Provigil [package insert]. North Wales, PA: Cephalon, Inc; December 2022.
2. Nuvigil [package insert]. North Wales, PA: Cephalon, Inc; December 2022.
3. Black JE, Hull SG, Tiller J, et al. The long-term tolerability and efficacy of armodafinil in patients with excessive sleepiness associated with treated obstructive sleep apnea, shift work disorder, or narcolepsy: an open-label extension study. *J Clin Sleep Med*. 2010 Oct 15;6(5):458-66.
4. Morgenthaler TI, Kapur VK, Brown T, et al.Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin: An American Academy of Sleep Medicine Report. *Sleep*. 2007;30(12):1705-1711.
5. Zifko UA, Rupp M, Schwarz S, et al. Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. *J Neurol*. 2002;249:983-987.
6. Brown JN, Howard CA, Kemp DW. Modafinil for the treatment of multiple sclerosis-related fa*tigue. Ann Pharmacother*. 2010 Jun;44(6):1098-103.

Policy History

Date	Action
May 2009	Addition of Nuvigil (armodafinil), the active ingredient or R-enantiomer of Provigil (modafinil), which is a mixture of the R- and S-enantiomers. Nuvigil shares the same indications as Provigil. The concentration-time profiles of

	the pure R-enantiomer following administration of 50mg Nuvigil or 100mg Provigil are nearly superimposable. The recommended daily dose of Nuvigil is 150mg or 250mg.
May 2009	PA quantity limits of Provigil 600mg or Nuvigil 300mg per day is recommended to safeguard patient health. There is no consistent evidence that there is any additional benefit beyond that of 200mg Provigil or 150mg Nuvigil per day. However, doses up to Provigil 600 mg per day, given as a single dose or in divided dose, have been well tolerated. Doses of Provigil 800mg per day and above were shown to have higher incidence of side effects with no measurable improvement in symptom relief. Side effects include increased blood pressure and pulse rate (tachycardia). Due to the increased incidence of side effects with the increased dose, a change to the criteria is proposed to safeguard patient health.
October 2009	Addition of quantity limits.
August 2011	Documentation of acceptability of 600mg / day (modafinil). Some studies have shown additional benefit in daily doses greater than 400mg, up to 600mg / day (modafinil).
June 2012	Annual editorial review and reference update
June 2013	Annual editorial review Addition of maximum mg per day in limits
February 2014	Reference update Addition of new strength of Nuvigil 200mg
June 2015	Annual editorial review and reference update
September 2016	Annual editorial review and reference update. Policy number changed from 5.07.04 to 5.60.14
December 2017	Annual editorial review and reference update
November 2018	Annual review
March 2019	Annual review and reference update
September 2019	Annual review
December 2019	Annual review and reference update
December 2020	Annual review
March 2021	Annual review
September 2021	Annual review
December 2021	Annual editorial review. Removed “acute or persistent” from hypersomnia indication
March 2022	Annual review
December 2022	Annual review. Changed policy number to 5.60.014

March 2023	Annual review and reference update
July 2023	Revised quantity chart to remove quantities and set Provigil at 600 mg per day and Nuvigil at 300 mg per day
September 2023	Annual review
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.