

5.60.014

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

Last Review Date: September 6, 2024

Provigil Nuvigil

Description

Provigil (modafinil) / Nuvigil (armodafinil)

Background

Provigil and Nuvigil are central nervous system stimulants. The Drug Enforcement Administration (DEA) has listed Provigil and Nuvigil as Schedule IV drugs. The mechanism through which Provigil and Nuvigil promote wakefulness is unknown. They have wake-promoting actions similar to sympathomimetic agents including amphetamine and methamphetamine, but the pharmacologic profile is not identical to that of the sympathomimetic amines (1-2).

Regulatory Status

FDA-approved indications: (1-2)

- Provigil is indicated for improving wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder.
- Nuvigil is indicated for improving wakefulness in adult patients with excessive sleepiness associated with obstructive sleep apnea (OSA), narcolepsy, or shift work disorder.

Limitations of Use: (1-2)

In OSA, Provigil and Nuvigil are indicated to treat excessive sleepiness and not as treatment for the underlying obstruction.

Off-Label Uses:

- Provigil and Nuvigil are used as adjuncts to standard treatments for OSA (3-4)
- Provigil has been found effective in the treatment of multiple sclerosis fatigue. Provigil is

| | | | |
|--------------------|------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | October 1, 2024 |
| Subsection: | Central Nervous System Drugs | Original Policy Date: | May 1, 2009 |
| Subject: | Provigil Nuvigil | Page: | 2 of 6 |

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). For MS patients who experience significant fatigue there are several medications that have proven effective in this regard. Provigil 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 (5-6).

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. Provigil 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 state that Provigil 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 Nuvigil has not been studied for this use, expert opinion considers it to be interchangeable with Provigil 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

| | | | |
|--------------------|------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | October 1, 2024 |
| Subsection: | Central Nervous System Drugs | Original Policy Date: | May 1, 2009 |
| Subject: | Provigil Nuvigil | Page: | 3 of 6 |

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

| | | | |
|--------------------|------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | October 1, 2024 |
| Subsection: | Central Nervous System Drugs | Original Policy Date: | May 1, 2009 |
| Subject: | Provigil Nuvigil | Page: | 4 of 6 |

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 listed Provigil and Nuvigil as Schedule IV drugs. They are also used off-label to treat MS fatigue (1-6).

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 fatigue. *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 |

5.60.014

| | | | |
|--------------------|------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | October 1, 2024 |
| Subsection: | Central Nervous System Drugs | Original Policy Date: | May 1, 2009 |
| Subject: | Provigil Nuvigil | Page: | 5 of 6 |

| | |
|----------------|---|
| | 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 |
| September 2024 | Annual review. Revised background and regulatory status sections |

Keywords

5.60.014

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

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.