PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME* **(generic)**	**PROVIGIL (modafinil)**
Status: CVS Caremark Criteria	***Ref # 178-C***
Type: Initial Prior Authorization with Quantity Limit	***REG Ref # 2814-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, or shift work disorder.

Limitations of Use

In OSA, Provigil is indicated to treat excessive sleepiness and not as treatment 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 and during treatment with Provigil for excessive sleepiness.

Compendial Uses/ Limited Treatment Option

Fatigue related to multiple sclerosis[8,9]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of narcolepsy AND the diagnosis is confirmed by sleep lab evaluation

OR

- The patient has a diagnosis of Shift Work Disorder (SWD)

OR

- The patient has a diagnosis of obstructive sleep apnea (OSA) AND the diagnosis is confirmed by polysomnography

  AND

- The patient has been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month

OR

- The requested drug is being prescribed for multiple sclerosis-related fatigue

Quantity Limits Apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Provigil is a Schedule IV controlled substance, and has been shown to produce psychoactive and euphoric effects consistent with other scheduled central nervous system (CNS) stimulants. Patients should be observed for signs of misuse or abuse. Provigil is indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), and shift

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work disorder (SWD). Provigil should be used only in patients who have had a complete evaluation of their excessive sleepiness, and in whom a diagnosis of narcolepsy, OSA, or SWD has been made in accordance with International Classification of Sleep Disorders (ICSD) or DSM-5 diagnostic criteria.[1-3]

Provigil is used to improve wakefulness in adults with excessive sleepiness associated with narcolepsy. According to the American Academy of Sleep Medicine (AASM), successful treatment of hypersomnia of central origin requires an accurate diagnosis, individual tailoring of therapy to produce the fullest possible return of normal function, and regular follow-up to monitor response to treatment. The evaluation should include a thorough evaluation of other possible contributing causes of excessive daytime sleepiness. The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies necessary diagnostic tests and criteria for each disorder of central origin. For narcolepsy, a sleep lab evaluation consisting of an overnight polysomnography (PSG) and mean sleep latency tests (MSLT) is recommended to confirm the diagnosis. Many other conditions produce such sleepiness and can mimic or coexist with a hypersomnia of central origin.[4,5]

In OSA, Provigil is indicated to treat excessive sleepiness and not as a treatment 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. OSA should be confirmed by polysomnography with respiratory monitoring. Oral appliances are indicated for use in patients with mild to moderate OSA who prefer them to CPAP therapy, or who do not respond to, are not appropriate candidates for, or who fail treatment attempts with CPAP.[6]

The presence or absence of obstructive sleep apnea (OSA) must be determined before initiating treatment. Diagnostic criteria for OSA are based on clinical signs and symptoms determined during a comprehensive sleep evaluation, which includes a sleep oriented history and physical examination, and findings defined by sleep testing.[6] Following the history and physical examination, patients can be stratified according to their OSA disease risk. Those patients deemed high risk should have the diagnosis confirmed and severity determined with objective testing such as polysomnography with respiratory monitoring.[5] OSA should be approached as a chronic disease requiring long-term, multidisciplinary management. The patient should be an active participant in the decision on treatment type and taught to contribute to the management of his or her own disease. Positive airway pressure (PAP) is the treatment of choice for mild, moderate, and severe OSA and should be offered as an option to all patients. Alternative therapies may be offered depending on the severity of the OSA and the patient's anatomy, risk factors, and preferences.[6] Oral appliances (OA) may improve upper airway patency during sleep by enlarging the upper airway and/or by decreasing upper airway collapsibility (e.g., improving upper airway muscle tone). Although not as efficacious as PAP, OAs are indicated for use in patients with mild to moderate OSA who prefer OAs to CPAP or who do not respond to CPAP, are not appropriate candidates for CPAP, or who fail CPAP or other measures.[6] Patients should be established on effective treatment of the underlying airway obstruction associated with OSA before considering pharmacologic therapy for excessive sleepiness associated with OSA.[6] Patients should be continued on their treatment for the underlying airway obstruction while using pharmacologic treatment for excessive sleepiness due to OSA.[1-3,6] Therefore, patients with OSA must be established on therapy to treat the underlying obstruction for approval of Provigil.

The effectiveness of Provigil to improve wakefulness in adults with excessive sleepiness associated with SWD was demonstrated in a 12-week placebo-controlled clinical trial. Enrolled patients were required to work a minimum of 5 night shifts per month (each shift ≤12 hours, with ≥6 hours worked between 10pm and 8am) and have excessive sleepiness at the time of their night shifts.[7]

The Levels of Evidence policy states coverage will be provided for a disease or condition that has limited treatment options, including disorders that have no FDA-approved drugs available and those for which the existing FDA-approved drugs have limited effectiveness and/or significant toxicity concerns. Fatigue is one of the most common and disabling symptoms of people with Multiple Sclerosis (MS) with negative impacts extending from general functioning to quality of life. Although a number of strategies have been devised for reducing fatigue, treatment recommendations are based on a limited amount of scientific evidence. Clinical practice guidelines suggest medication (e.g., Amantadine and Modafinil) and rehabilitation (e.g., exercise, energy or fatigue self-management education, and cognitive behavioral therapy) for managing fatigue.[8]

Based on systematic review of 2 randomized placebo-controlled trials, 1 nonrandomized placebo-controlled crossover trial, and 3 uncontrolled trials evaluating modafinil for fatigue in 308 patients with multiple sclerosis, Modafinil is a

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reasonable therapeutic option in this patient population. Treatment with modafinil significantly improves fatigue and sleepiness and is well tolerated by patients with MS.[9]

Provigil is available as 100mg and 200mg tablets. The recommended dosage of Provigil for narcolepsy, OSA, and SWD is 200 mg daily. For narcolepsy and OSA, doses up to 400mg daily have been tolerated, but there is no consistent evidence that this dose confers additional benefit beyond that of the 200mg/day dose. In patients with severe hepatic impairment, the dosage of Provigil should be reduced to one-half of that recommended for patients with normal hepatic function.[1-3] For fatigue associated with multiple sclerosis, study doses did not exceed the recommended maximum daily dosage of 400 mg per day.[3] Therefore, the approval will be limited to 60 tablets per month of Provigil 100mg and 200mg tablets.

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CRITERIA FOR APPROVAL

1	Does the patient have a diagnosis of narcolepsy? [If no, then skip to question 3.]	Yes	No
2	Has the diagnosis been confirmed by sleep lab evaluation? [If yes, then skip to question 8.]	Yes	No
3	Does the patient have a diagnosis of Shift Work Disorder (SWD)? [If yes, then skip to question 8.]	Yes	No

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4	Does the patient have a diagnosis of obstructive sleep apnea (OSA)? [If no, then skip to question 7.]	Yes	No
5	Has the diagnosis been confirmed by polysomnography? [If no, then no further questions.]	Yes	No
6	Has the patient been receiving treatment for the underlying airway obstruction (e.g., continuous positive airway pressure [CPAP]) for at least one month? [If yes, then skip to question 8.] [If no, then no further questions.]	Yes	No
7	Is the requested drug being prescribed for multiple sclerosis-related fatigue? [If no, then no further questions.]	Yes	No
8	Does the patient require MORE than the plan allowance of 60 tablets per month? [RPh Note: If yes, then deny and enter a partial approval for 60 tablets / 25 days or 180 tablets / 75 days of Provigil.]	Yes	No

Mapping Instructions (178-C, REG 2814-C)			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Go to 3	
2.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a sleep lab test to confirm your diagnosis. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
3.	Go to 8	Go to 4	
4.	Go to 5	Go to 7	
5.	Go to 6	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have had a test to confirm your diagnosis. Your request has been denied based on the information we have. [Short Description: No confirmation of diagnosis (tests, labs, etc.)]
6.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have been on treatment for airway problems due to obstructive sleep apnea for at least one month. Your request has been denied based on the information we have. [Short Description: No underlying treatment for OSA]
7.	Go to 8	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet one of these conditions: - You have narcolepsy confirmed by sleep lab testing - You have shift work disorder - You have obstructive sleep apnea confirmed by testing - You have Multiple Sclerosis-related fatigue Your request has been denied based on the information we have. [Short Description: No approvable diagnosis.]
8.	Deny	Approve, 12	You have requested more than the maximum quantity allowed by your

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		months, 60 tablets/25 days* or 180 tablets/75 days*	plan. Current plan approved criteria cover up to 60 tablets/month of the requested drug and strength. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*

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