Clinical Policy: Modafinil (Provigil)

Reference Number: CP.PMN.39
Effective Date: 05.01.08
Last Review Date: 05.22
Line of Business: HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Modafinil (Provigil®) is a wakefulness-promoting agent.

FDA Approved Indication(s)
Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD).

Limitation(s) 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that modafinil is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Narcolepsy (must meet all)**:**

1. Diagnosis of narcolepsy;
2. Prescribed by or in consultation with a neurologist or sleep medicine specialist;
3. Age ≥ 17 years;
4. Failure of a 1-month trial of one of the following generic central nervous system stimulant-containing agent at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: amphetamine, dextroamphetamine, or methylphenidate;
   **Prior authorization may be required for CNS stimulants*
5. Failure of a 1-month trial of armodafinil at up to maximally indicated doses, unless clinically significant side effects are experienced;
   **Prior authorization may be required for armodafinil*
6. Member must use generic modafinil, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 400 mg (2 tablets) per day.

Approval duration: 12 months

B. Obstructive Sleep Apnea/Hypopnea Syndrome (must meet all)**:**
1. Diagnosis of OSA;
2. Age ≥ 17 years;
3. Documented evidence of residual sleepiness despite compliant CPAP use as monotherapy;
4. Failure of a 1-month trial of armodafinil at up to maximally indicated doses, unless clinically significant side effects are experienced;
   **Prior authorization may be required for armodafinil*
5. Member must use generic modafinil, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 400 mg (2 tablets) per day.

Approval duration: 12 months

C. Shift Work Disorder (SWD) (must meet all)**:**
1. Diagnosis of SWD;
2. Age ≥ 17 years;
3. Failure of a 1-month trial of armodafinil at up to maximally indicated doses, unless clinically significant side effects are experienced;
   **Prior authorization may be required for armodafinil*
4. Member must use generic modafinil, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 200 mg (1 tablet) per day.

Approval duration: 12 months

D. Fatigue Associated with Multiple Sclerosis (MS) (off-label) (must meet all)**:**
1. Diagnosis of MS-associated fatigue;
2. Age ≥ 17 years;
3. Failure of 200 mg/day of amantadine and ≥ 10 mg/day of methylphenidate, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 1-month trial of armodafinil at up to maximally indicated doses, unless clinically significant side effects are experienced;
   **Prior authorization may be required for armodafinil*
5. Member must use generic modafinil, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 400 mg (2 tablets) per day.

Approval duration: 12 months

E. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

2. Member is responding positively to therapy;
3. Member must use generic modafinil, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed:
   a. Narcolepsy, OSA, and MS-associated fatigue: 400 mg (2 tablets) day;
   b. SWD: 200 mg (1 tablet) day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CPAP: continuous positive airway pressure
FDA: Food and Drug Administration
IR: immediate-release
MS: multiple sclerosis
OSA: obstructive sleep apnea
SWD: shift work disorder

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
amphetamine (Evekeo®)	**Narcolepsy** 5 to 60 mg/day PO in divided doses	60 mg/day
amphetamine/ dextroamphetamine (Adderall®)		
dextroamphetamine ER (Dexedrine® Spansule®)		
dextroamphetamine IR (Zenzedi®, Procentra®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methylphenidate (Ritalin® LA or SR, Concerta®, Metadate® CD or ER, Methylin® ER, Daytrana®)	**Narcolepsy** Dosing varies; 10-60 mg PO divided 2 to 3 times daily 30-45 min before meals **MS-related fatigue†** Usual effective dose: 10-20 mg PO QAM and noon	60 mg/day
amantadine (Symmetrel®)	**MS-related fatigue†** 200 mg PO once daily or 100 mg PO twice daily	200 mg/day
armodafinil (Nuvigil®)	**Narcolepsy and OSA** 150 mg to 250 mg PO once a day **SWD** 150 mg PO once a day as a single dose approximately 1 hour prior to the start of work shift **MS-related fatigue†** 150 mg PO every morning	250 mg/day for narcolepsy and OSA/HS; 150 mg/day circadian rhythm disruption.

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
†Off-label indication

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): known hypersensitivity to modafinil or armodafinil
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Narcolepsy	200 mg PO QD as a single dose in the morning	400 mg/day
OSA		
SWD	200 mg orally once a day as a single dose approximately 1 hour prior to the start of work shift	200 mg/day
MS-associated fatigue (off-label)	200 mg PO once daily in the morning	400 mg/day

VI. Product Availability
Tablets: 100 mg and 200 mg

VII. References

1. Provigil Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; January 2015. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/020717s037s038lbl.pdf. Accessed January 29, 2022.
2. 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: An American Academy of Sleep Medicine Report. *Sleep*. 2007;30(12):1705-1711.
3. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*. 2009; 15;5(3):263-76.
4. Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Practice Parameters for the Clinical Evaluation and Treatment of Circadian Rhythm Sleep Disorders: An American Academy of Sleep Medicine Report. *Sleep*. 2007;30(11):1445-1459.
5. Bassetti CL, Kallweit U, Vignatelli, et al. European guideline and expert statements on the management of narcolepsy in adults and children. J Sleep Res. 2021;00:e13387. DOI: 10.1111/jsr.13387.
6. Management of MS-Related Fatigue. Expert Opinion Paper. National Multiple Sclerosis Society; 2006. Available at: http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Opinion-Paper-Management-of-MS-Related-Fatigue.pdf.
7. Braley TJ; Chervin RD. Fatigue in multiple sclerosis: mechanisms, evaluation, and treatment. *Sleep*. 2010;33(8):1061-1067.
8. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed January 29, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes from previously approved corporate policy; policies combined for commercial, HIM, and Medicaid lines of business: Commercial: split from CP.CPA.105 armodafinil (Nuvigil), modafinil (Provigil); commercial: added age; Narcolepsy: added criterion related to stimulant trial; OSA: added documented evidence of residual sleepiness despite compliant CPAP use; MS-related fatigue: added requirement related to trial and failure of amantadine and methylphenidate; HIM: added the preferred use of armodafinil because of market pricing; Medicaid: modified initial approval duration from 6 months to 12 months; Narcolepsy and MS-related fatigue: removed timeframe of trial within the last 6 months; references reviewed and updated.	01.16.18	05.18
2Q 2019 annual review: no significant changes; removed commercial line of business and moved to CP.CPA.83; references reviewed and updated.	02.26.19	05.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Per specialist feedback, updated the initial approval criteria for narcolepsy to require a prescription/consultation by a neurologist.	04.25.19	08.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.25.20	05.20
For narcolepsy indication added sleep medicine specialist as optional prescriber.	06.11.20	11.20
2Q 2021 annual review: added redirection to generic modafinil if request is for brand; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.29.21	05.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.31.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.