Clinical Policy: Modafinil (Provigil)
Reference Number: CP.PMN.39
Effective Date: 05/08
Last Review Date: 05/17
Line of Business: Medicaid

Coding Implications
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
Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with:

- Narcolepsy
- Obstructive sleep apnea (OSA)
- Shift work disorder (SWD)

Limitation 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 (including office chart notes and lab results) supporting that member has met all approval criteria

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

I. Initial Approval Criteria

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

1. Diagnosis of narcolepsy;
2. Age ≥ 17 years;
3. Failure of a 1 month trial of one of the following central nervous system (CNS) stimulants: amphetamine immediate release (IR), amphetamine; dextroamphetamine IR, dextroamphetamine, or methylphenidate IR, at up to maximally indicated doses within the last 6 months, unless contraindicated or clinically significant adverse effects are experienced;
3. ~~Documented failure of a 2 month course of methylphenidate or amphetamine derivative at up to maximally indicated doses at the maximum recommended dose of 60mg daily within the last 6 months, unless contraindicated;~~
4. Failure of ≥ 1 month trial of armodafinil (Nuvigil) at up to maximally indicated doses, unless clinically significant side effects are experienced (*Note: Armodafinil requires prior authorization)*;~~Modafinil will not be approved for concurrent use with benzodiazepines;~~

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5. No documentation of hypersensitivity to armodafinil or modafinil;
5.6. ~~Requested d~~Dose does not exceed 400 mg/day.~~;~~
6. ~~Preferred use of Nuvigil® (which also requires meeting all criteria stated above).~~

Approval duration: 6 months

B. Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS) (must meet all)**:**
1. Diagnosis of obstructive sleep apnea;
2. Age ≥ 17 years;
3. Documented evidence of residual sleepiness despite compliant CPAP use as monotherapy;
4. Failure of ≥ 1 month trial of armodafinil (Nuvigil) at up to maximally indicated doses, unless clinically significant side effects are experienced (*Note: Armodafinil requires prior authorization*);
3.5. No documentation of hypersensitivity to armodafinil or modafinil;
4. ~~Modafinil will not be approved for concurrent use with benzodiazepines;~~
5. ~~Requested d~~Dose does not exceed 400 mg/day.
6. ~~Preferred use of Nuvigil® (which also requires meeting all criteria stated above).~~

Approval duration: 6 months

C. Shift Work Disorder (SWD) (must meet all)**:**
1. Diagnosis of shift work disorder;
2. Age ≥ 17~~8~~ years;
3. Failure of ≥ 1 month trial of armodafinil (Nuvigil) at up to maximally indicated doses, unless clinically significant side effects are experienced (*Note: Armodafinil requires prior authorization*);
4. No documentation of hypersensitivity to armodafinil or modafinil;
2. ~~Modafinil will not be approved for concurrent use with benzodiazepines;~~
3. ~~Requested d~~Dose does not exceed 200 mg/day.~~;~~
4.5. ~~Preferred use of Nuvigil® (which also requires meeting all criteria stated above).~~

Approval duration: 6 months

D. Fatigue Associated with Multiple Sclerosis (MS) (must meet all)**:**
1. Diagnosis of MS-related fatigue;
2. Age ≥ 17~~8~~ years;
3. Failure of 200 mg/day of amantadine and ≥ 10 mg/day of methylphenidate, one of which must be within the last 6 months, ~~Trial and failure of the following (a and b), one of which must be within the last 6 months:~~unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of ≥ 1 month trial of armodafinil (Nuvigil) at up to maximally indicated doses, unless clinically significant side effects are experienced *(Note: Armodafinil requires prior authorization)*;
5. No documentation of hypersensitivity to armodafinil or modafinil;
3. ~~a. Amantadine 100 mg bid, unless contraindicated;~~

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~~b. Methylphenidate 10 to 60 mg per day, in two to three divided doses, unless contraindicated;~~
~~4. Modafinil will not be approved for concurrent use with benzodiazepines;~~
~~5.~~6. D~~Requested d~~ose does not exceed 400 mg/day.~~;~~
~~6. Preferred use of Nuvigil® (which also requires meeting all criteria stated above).~~
Approval duration: 6 months

E. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications (must meet all)**:**
1. ~~Claims history shows member is currently receiving this medication via Centene benefit and adherent to treatment regimen.~~ Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
~~2.~~3. If request is for a dose increase, ~~request must not~~new dose does not ~~exceed~~ the FDA approved ~~limit per indication~~maximum recommended dose for the relevant indication. For MS-related fatigue, ~~requested~~ dose does not exceed 400 mg/day.~~;~~
~~3. Modafinil will not be approved for concurrent use with benzodiazepines.~~

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; or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12 months

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 policy – CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CNS: central nervous system
CPAP: continuous positive airway pressure
FDA: Food and Drug Administration
MS: multiple sclerosis
OSA: obstructive sleep apnea
OSAHS: obstructive sleep apnea/hypopnea syndrome
SWD: shift work disorder

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V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Narcolepsy	200 mg orally once a day as a single dose in the morning	400 mg/day
Obstructive sleep apnea		
Shift work disorder	200 mg orally once a day as a single dose approximately 1 hour prior to the start of work shift	200 mg/day
MS-related fatigue†	200 mg orally once daily in the morning	400 mg/day

†*Off-label indication*

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VI. Product Availability

Tablets: 100 mg and 200 mg

VII. Workflow Document

CP.PMN.39.modafinil (Provigil)workflow

Field Code Changed

VIII. References

1. Provigil® Pprescribing Iinformation. North Wales, PA: Teva Pharmaceuticals USA, Inc.; January 2015. Available at: http://www.provigil.com/PDFs/prescribing_info.pdf. Accessed ~~February~~ January 10, 2017~~6~~. ~~Available at: http://www.provigil.com/~~
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 Jun 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. Billiard M, Dauvilliers Y, Dolenc-Groselj L, Lammers GJ, Mayer G, Sonka K. Management of narcolepsy in adults. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 513-28. [118 references]
6. Management of MS-Related Fatigue. Expert Opinion Paper. National Multiple Sclerosis Society; 2006. 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.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.
~~2. Clinical Pharmacology Modafinil monograph. Accessed February 2016. http://www.clinicalpharmacology-ip.com/~~
~~3. Clinical Pharmacology Amphetamine; Dextroamphetamine monograph. Accessed February 2016. http://www.clinicalpharmacology-ip.com~~
~~4. Clinical Pharmacology Methylphenidate monograph. Accessed February 2016. http://www.clinicalpharmacology-ip.com~~
~~5. Billiard M, Dauvilliers Y, Dolenc-Groselj L, Lammers GJ, Mayer G, Sonka K. Management of narcolepsy in adults. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 513-28. [118 references]~~
~~6. Management of MS-Related Fatigue. Expert Opinion Paper. National Multiple Sclerosis Society. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical_Bulletin_MS-Related-Fatigue.pdf. Accessed February 8, 2016.~~
~~7. Olek MJ. Symptom management of multiple sclerosis in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed February 4, 2016.~~

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised Criteria for Approval from "Documented failure of 2 month course of methylphenidate or amphetamine derivatives" to "Documented failure of 2 month course of methylphenidate or amphetamine derivatives, unless contraindicated" Added the following to Criteria for Approval: "MS fatigue, where patient has failed the standard of care options including both amantadine and methylphenidate"	08/08	08/08
References updated to reflect current literature search.	04/10	04/10
Criteria for approval revised to exclude concomitant use with benzodiazepines. Indicated the preferred use of Nuvigil® because of market pricing. Updated the Special Instructions section with warnings on abuse potential. References updated to reflect current literature search.	05/11	05/11
Added the following language to the diagnosis requirement: "consistent with DSM-IV criteria and evidenced in the progress notes". Added dosing qualifiers to prior trials and failures.	05/12	05/12

Reviews, Revisions, and Approvals	Date	P&T Approval Date
References updated.		
Updated the Special Instructions section with geriatric dosing caution and impaired hepatic function dosing. References updated.	05/13	05/13
References updated.	05/14	05/14
Updated approval age and references.	03/15	03/15
Converted into new policy template; Criteria: updated age to ≥17 years of age (≥18 years for SWD and MS-related fatigue per Clinical Pharmacology); added max dose per indication, trial must be within the last 6 months (narcolepsy and MS related fatigue); re-auth: removed reported daytime improvements or use of the Epworth Sleepiness Scale requirement as they are subjective information; added member is receiving medication via Centene benefit and adherent as evidenced in claims history and max dosage per indication; added no concurrent use with benzodiazepines requirement. Updated reference section to reflect current literature search.	02/16	05/16
~~No clinical changes to criteria:~~ -Converted to new template -Modified duration of stimulant trial for narcolepsy from ≥ 2 months to ≥ 1 month so that it is consistent with Xyrem policy; -Added duration of trial to requirement related to failure of armodafinil for clarity -Removed "Modafinil will not be approved for concurrent use with benzodiazepines" per template update, and since this requirement cannot be enforced post-approval without an edit -Added "No documentation of hypersensitivity to armodafinil or modafinil" per PI -Modified age requirement for SWD and MS-related fatigue from ≥18 years to ≥17 years of age per PI (pediatric patients defined as less than 17 years of age) -Updated references to reflect current literature search	03~~1~~/17	05/17

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.