Clinical Policy: Modafinil (Provigil)
Reference Number: CP.PMN.39
Effective Date: 05.01.08
Last Review Date: 05.20
Line of Business: HIM, Medicaid

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 Provigil 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;
      3. Age ≥ 17 years;
      4. Failure of a 1-month trial of one of the following central nervous system stimulants at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: amphetamine immediate-release (IR), amphetamine; dextroamphetamine IR, dextroamphetamine, methylphenidate IR, or Metadate® ER; *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. 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 $\geq 17$ 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. 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 $\geq 17$ 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. 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 $\geq 17$ years;
   3. Failure of 200 mg/day of amantadine and $\geq 10$ 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. 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.PHAR.21 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. 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.PHAR.21 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.PHAR.21 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>amphetamine (Evekeo®)</td>
<td>Narcolepsy</td>
<td>5 to 60 mg/day PO in divided doses</td>
</tr>
<tr>
<td>amphetamine/ dextroamphetamine (Adderall®)</td>
<td>Narcolepsy</td>
<td>Dosing varies; 10-60 mg PO divided 2 to 3 times daily 30-45 min before meals</td>
</tr>
<tr>
<td>dextroamphetamine ER (Dexedrine® Spansule®)</td>
<td>Narcolepsy</td>
<td>Usual effective dose: 10-20 mg PO QAM and noon</td>
</tr>
<tr>
<td>dextroamphetamine IR (Zenzedi®, Procentra®)</td>
<td>MS-related fatigue</td>
<td>10-20 mg PO QAM and noon</td>
</tr>
<tr>
<td>methylphenidate (Ritalin® LA or SR, Concerta®, Metadate® CD or ER, Methylin® ER, Daytrana®)</td>
<td>MS-related fatigue</td>
<td>10-20 mg PO QAM and noon</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>amantadine (Symmetrel®)</td>
<td>MS-related fatigue‡: 200 mg PO once daily or 100 mg PO twice daily</td>
<td>200 mg/day</td>
</tr>
<tr>
<td></td>
<td>Narcolepsy and OSA: 150 mg to 250 mg PO once a day</td>
<td>250 mg/day for narcolepsy and OSA/HS; 150 mg/day circadian rhythm disruption.</td>
</tr>
<tr>
<td>armodafinil (Nuvigil®)</td>
<td>Narcolepsy and OSA: 150 mg PO once a day</td>
<td>250 mg/day for narcolepsy and OSA/HS; 150 mg/day circadian rhythm disruption.</td>
</tr>
<tr>
<td></td>
<td>SWD: 150 mg PO once a day as a single dose approximately 1 hour prior to the start of work shift</td>
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</tr>
<tr>
<td></td>
<td>MS-related fatigue‡: 150 mg PO every morning</td>
<td></td>
</tr>
</tbody>
</table>

*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

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

### VI. Product Availability
- Tablets: 100 mg and 200 mg

### VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>02.16</td>
<td>05.16</td>
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<tr>
<td>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)</td>
<td>03.17</td>
<td>05.17</td>
</tr>
</tbody>
</table>
## Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
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<th>P&amp;T Approval Date</th>
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<tr>
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<td>02.26.19</td>
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<td>04.25.19</td>
<td>08.19</td>
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<tr>
<td>02.25.20</td>
<td>05.20</td>
</tr>
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</table>

### 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.
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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.

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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.

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