Clinical Policy: Safinamide (Xadago)
Reference Number: ERX.NPA.45
Effective Date: 09.01.17
Last Review Date: 05.18

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

**Description**
Safinamide (Xadago®) is monoamine oxidase type B (MAO-B) inhibitor.

**FDA Approved Indication(s)**
Xadago is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson’s disease (PD) experiencing “off” episodes.

Limitation(s) of use: Xadago has not been shown to be effective as monotherapy for the treatment of PD.

**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 Envolve Pharmacy Solutions™ that Xadago is medically necessary when the following criteria are met:

I. **Initial Approval Criteria**
   A. **Parkinson’s Disease** (must meet all):
      1. Diagnosis of idiopathic PD;
      2. Member is experiencing “off” time (see Appendix C) on levodopa/carbidopa therapy;
      3. Failure of two drugs*, as specified below, unless contraindicated or clinically significant adverse effects are experienced (a and b):
         a. Rasagiline (Azilect®);
         b. One of the following drugs: entacapone (Comtan®/Stalevo®), ropinirole/ropinirole ER (Requip®/Requip ER®, pramipexole/promipexole ER (Mirapex®/Mirapex ER®), Neupro® (ritigotine);
      *Prior authorization is (or may be) required.
      4. Xadago is prescribed in combination with levodopa/carbidopa;
      5. Dose does not exceed 100 mg once daily.

   Approval duration: 12 months

   B. **Other diagnoses/indications**
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. **Continued Therapy**
   A. **Parkinson’s Disease** (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 100 mg once daily.

   Approval duration: 12 months

   B. **Other diagnoses/indications** (must meet 1 or 2):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

   Appendix A: Abbreviation/Acronym Key
   COMP: catechol-O-methyl transferase
   FDA: Food and Drug Administration
   MAO-B: monoamine oxidase inhibitor
   PD: Parkinson’s disease

   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 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>entacapone (Comtan)</td>
<td>COMP inhibitor Oral: 200 mg with each dose of levodopa/carbidopa.</td>
<td>1600 mg daily (divided doses).</td>
</tr>
<tr>
<td>carbadopa/levodopa/</td>
<td>COMP inhibitor Oral: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.</td>
<td>1200 mg daily (divided doses).</td>
</tr>
<tr>
<td>entacapone (Stalevo)</td>
<td>COMP inhibitor Oral: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.</td>
<td>1200 mg daily (divided doses).</td>
</tr>
<tr>
<td>rasagiline (Azilect)</td>
<td>MAO B inhibitor Oral: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5 mg once daily; may increase to 1 mg once daily based on response and tolerability.</td>
<td>1 mg once daily.</td>
</tr>
<tr>
<td>ropinirole (Requip)</td>
<td>Dopamine agonist Oral: Recommended starting dose: 0.25 mg 3 times/day. Based on individual patient response, the dosage should be titrated with weekly increments: Week 1: 0.25 mg 3 times/day; total daily dose: 0.75 mg; week 2: 0.5 mg 3 times/day; total daily dose: 1.5 mg; week 3: 0.75 mg 3 times/day; total daily dose: 2.25 mg; week 4: 1 mg 3 times/day; total daily dose: 3 mg. After week 4, if necessary, daily dosage may be increased by 1.5 mg/day on a weekly basis up to a dose of 9 mg/day, and then by up to 3 mg/day weekly to a total of 24 mg/day.</td>
<td>24 mg daily (divided doses).</td>
</tr>
<tr>
<td>ropinirole ER (Requip ER)</td>
<td>Dopamine agonist Oral: Initial dose: 2 mg once daily for 1 to 2 weeks, followed by increases of 2 mg/day at weekly or longer intervals based on therapeutic response and tolerability.</td>
<td>24 mg once daily.</td>
</tr>
<tr>
<td>pramipexole (Mirapex)</td>
<td>Dopamine agonist Oral: Initial dose: 0.125 mg 3 times daily, increase gradually every 5 to 7 days; maintenance (usual): 0.5 to 1.5 mg 3 times daily.</td>
<td>4.5 mg daily (divided doses).</td>
</tr>
</tbody>
</table>
## CLINICAL POLICY
#### Safinamide

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<th>Drug Name</th>
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<tr>
<td>pramipexole ER (Mirapex ER)</td>
<td>Oral: Initial dose: 0.375 mg once daily; increase gradually not more frequently than every 5 to 7 days to 0.75 mg once daily and then, if necessary, by 0.75 mg per dose.</td>
<td>4.5 mg once daily.</td>
</tr>
<tr>
<td>Dopamine agonist</td>
<td></td>
<td></td>
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<tr>
<td>Neupro (rotigotine)</td>
<td>Transdermal: Initial dose: 2 mg/24 hours for early-stage disease or 4 mg/24 hours for advanced-stage disease.</td>
<td>6 mg/24 hours for early-stage disease; 8 mg/24 hours for advanced-stage disease.</td>
</tr>
<tr>
<td>Dopamine agonist</td>
<td></td>
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</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.

### Appendix C: Definition of Wearing Off Time

Off time/episodes represent a return of PD symptoms (bradykinesia, rest tremor or rigidity) when the levodopa (L-dopa) treatment effect wears off after each dosing interval.

### Appendix D: General Information

- PD symptoms, resulting from too little L-dopa, are in contrast with dyskinesia which typically results from too much L-dopa.
- The alterations between "on" time (the time when PD symptoms are successfully suppressed by L-dopa) and "off" time is known as "motor fluctuations".
- The addition of carbidopa to L-dopa prevents conversion of L-dopa to dopamine in the systemic circulation and liver.

### V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjunctive treatment to levodopa/carbidopa in patients with PD experiencing “off” episodes</td>
<td>50 mg orally once daily; 100 mg once daily after 2 weeks if needed</td>
<td>100 mg once daily</td>
</tr>
</tbody>
</table>

### VI. Product Availability

Tablets: 50 mg, 100 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>Policy created</td>
<td>06.17</td>
<td>08.17</td>
</tr>
<tr>
<td>Q 2018 annual review: no significant changes; added preferencing for generic drugs based on current clinical guidance; removed COC; references reviewed and updated.</td>
<td>03.23.18</td>
<td>05.18</td>
</tr>
</tbody>
</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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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