Pharmacy Policy

Dopamine Agonists/Antiparkinsonian Agents

Policy Number: 9.119
Version Number: 10
Version Effective Date: 05/02/2017

Product Applicability  □ All Plan* Products

Well Sense Health Plan
☑ New Hampshire Medicaid
☑ NH Health Protection Program
☐ ______________________

Boston Medical Center HealthNet Plan
☑ MassHealth
☑ Qualified Health Plans/ConnectorCare/Employer Choice Direct
☑ Senior Care Options
☐ ______________________

Note: Disclaimer and audit information is located at the end of this document.

Policy Summary

The Plan will authorize coverage of specific Dopamine Agonists/Antiparkinsonian Agents when appropriate criteria are met.

Description of Item or Service

Parkinson’s Disease (PD) is a degenerative, progressive disorder of the central nervous system in which mainly effecting the motor system resulting in significant disability. Medication, caregiver as well as societal costs infer a significant financial burden to this disease. The underlying etiology of Parkinson’s disease involves the progressive loss of dopamine producing cells in the substantia nigra, which results in a decrease in dopamine in the corpus striatum. There is no cure for Parkinson’s disease, but medications, surgery and multidisciplinary management can provide relief from the symptoms. Drug therapy is initially aimed at preventing long-term therapeutic complications and possibly slowing disease progression while later in the course of the disease symptomatic relief dictates therapy. Agents commonly used in the treatment of PD include, anticholinergics (benztropine and trihexyphenidyl), dopamine agonists or analogues, levodopa and MAO-B inhibitors. The selection of which agent to use is patient dependent and should take into account such features as the patient’s symptoms and signs, age, stage of disease, degree of functional disability, and level of physical activity and productivity.

In PD, dopamine depletion produces a state of cholinergic sensitivity so that cholinergic drugs exacerbate and anticholinergic drugs improve parkinsonian symptoms. Anticholinergic drugs should be reserved for younger patients in

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whom tremor is the predominant problem. Their use in older or demented individuals and those without tremor is strongly discouraged. Adverse effects of anticholinergic drugs are common and often limit their use. Older adults and cognitively impaired patients are particularly susceptible to memory impairment, confusion, and hallucinations and should not receive these drugs.

Dopamine agonists are synthetic agents that directly stimulate dopamine receptors, bypassing the requirement of metabolic conversion and neuronal uptake and release. Dopamine agonists tend to cause fewer dyskinesias and on-off fluctuations than levodopa and allow for later introduction to levodopa. FDA approved dopamine agonists include bromocriptine, pramipexole (Mirapex® and Mirapex® ER), ropinirole, rotigotine (Neupro®) and injectable apomorphine. Extended release formulations of pramipexole and ropinirole and transdermal continuous delivery rotigotine patches are currently available; these may contribute to the stability of plasma levels and continuous dopaminergic stimulation. Extended release formulations have proved to be non-inferior to the immediate release formulations (generally three times per day), and even better tolerated (ropinirole vs. ropinirole ER). Despite a generally good safety profile, serious adverse events, such as impulse control disorder and sleep attacks need to be routinely monitored, with higher doses more likely to result in impulse control disorder. Unlike carbidopa-levodopa (Sinemet), these drugs are direct agonists that do not require metabolic conversion, do not compete with amino acids for transport across the gut or into the brain, and do not depend upon neuronal uptake and release. An additional advantage over immediate-release forms of levodopa is the longer duration of action of most of these agents.

Ropinirole immediate-release, pramipexole immediate-release and rotigotine are indicated for treatment of restless leg syndrome, as well as Parkinson’s disease.

Levodopa is the most effective symptomatic therapy for PD and should be introduced when the patient and physician jointly decide that quality of life is substantially compromised. However, levodopa is associated with a higher risk of dyskinesia than the dopamine agonists. There does not appear to be a benefit of initiating treatment with controlled release levodopa compared with the immediate release preparation, and the former may limit the ability to follow the initial response to therapy. As a result, it is recommended that therapy be initiated with an immediate release preparation with a subsequent switch to controlled release if indicated.

Dopamine Analogues formulations include carbidopa (Lodosyn), carbidopa/levodopa controlled release#, carbidopa/levodopa extended release (Rytary®), carbidopa/levodopa ODT and carbidopa/levodopa (Sinemat) and carbidopa/levodopa (Stalevo®). Levodopa circulates in the plasma to the blood brain barrier, where it crosses, to be converted by striatal enzymes to dopamine. Carbidopa inhibits the peripheral plasma breakdown of levodopa by inhibiting its decarboxylation, and thereby increases available levodopa at the blood brain barrier. In the ADVANCE-PD and ASCEND-PD trials the newest extended release formulation, Rytary®, was shown to be effective at reducing off time in advanced PD compared with carbidopa/levodopa immediate release formulation and to carbidopa/levodopa with entacapone. Patients had more ‘on’ time while taking fewer doses, in Rytary® compared to the immediate release and entacapone products. The adverse effects in these extended release capsules were comparable to the immediate release formulation. The most common adverse events include nausea, headache, dizziness and insomnia. This formulation can decrease daily pill burden for these patients as well as decrease the use of rescue medications as it is composed of both immediate release and extended release forms.

Based on literature review, potential off-label uses of carbidopa/levodopa include the treatment of restless leg syndrome, Cerebral palsy spasticity and chronic alcohol remission. Rytary® will only be authorized for FDA approved indications.

Selegiline, a selective monoamine oxidase (MAO) type B inhibitor, is modestly effective as symptomatic treatment for PD and may have neuroprotective properties. In many individuals, selegiline monotherapy does not produce a functionally significant benefit. However, the use of selegiline in early PD is a reasonable option as long as the patient understands its limitations.

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Dopamine Agonist/Antiparkinsonian Agents
Initially marketed as adjunct therapy in advanced Parkinson’s disease, the dopamine agonists have become effective treatments in early stages of Parkinson’s disease. Although there have been limited head to head studies of rotigotine to older dopamine agonists, results confirm similar efficacy for rotigotine and ropinirole, and for rotigotine and pramipexole. There is no universal first choice in the treatment of Parkinson’s disease. Clinical and lifestyle characteristics of the patient should be taken into account. Most patients will develop motor complications over time and will require levodopa therapy. Adjuvant medications may help to reduce motor complications and raise quality of life in late stage Parkinson’s disease. Anticholinergics are poorly tolerated in the elderly and should be avoided.

**Policy**

The Plan may authorize coverage of specific Dopamine Agonists/Antiparkinsonian Agents for members meeting the following criteria:

**Policy Applicability by Product**

<table>
<thead>
<tr>
<th>Medication</th>
<th>BMC HealthNet Plan</th>
<th>Well Sense Health Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MassHealth</td>
<td>QHP</td>
</tr>
<tr>
<td>pramipexole ER (Mirapex ER®)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ropinirole ER (Requip XL®)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Neupro® (rotigotine transdermal system)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Stalevo® (carbidopa/levodopa/entacapone)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>carbidopa/levodopa ODT</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rytary® (carbidopa/levodopa ER)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Zelapar® (selegiline ODT)</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

**Prior Authorization** – *(Approval Duration – Maximum of 2 years)*

A prior authorization request will be required for all prescriptions for the Dopamine Agonists/Antiparkinsonian Agents listed below. These requests will be approved when the following criteria are met:

**ropinirole extended-release tablet (Requip XL®)**

Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An inadequate response, intolerance to ropinirole immediate release tablet.

**pramipexole ER (Mirapex® ER)**

Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An inadequate response, intolerance to pramipexole immediate release tablet.

**Neupro® (rotigotine transdermal system)**

Documentation of the following:
1. A diagnosis of Parkinson’s disease or Restless Leg Syndrome; **AND**
2. An inadequate response, intolerance to ropinirole and pramipexole; **OR**
   A topical dosage form is required due to swallowing difficulties.

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**Stalevo® (carbidopa/levodopa/entacapone)**
Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An allergy or intolerance to one of the inactive ingredient(s) found in the generic tablet formulation of carbidopa/levodopa/entacapone.

**carbidopa/levodopa orally disintegrating tablet**
Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An inadequate response or intolerance to carbidopa/levodopa tablet; **OR**
3. Member is experiencing swallowing difficulties due to a clinical condition.

**Rytary® (carbidopa / levodopa ER)**
Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An allergy or intolerance to one of the inactive ingredient(s) found in the generic tablet formulation of carbidopa/levodopa ER.

**Zelapar® (selegiline ODT)**
Documentation of the following:
1. A diagnosis of Parkinson’s disease; **AND**
2. An inadequate response or intolerance to selegiline tablet; **OR** swallowing difficulties due to a clinical condition

**Quantity Limitations Apply – See appendix A**

**Limitations**
The Plan will not approve coverage of Dopamine Agonists/Antiparkinsonian Agents in the following instances:

- When the above criteria is not met.
- For the treatment of Restless Leg Syndrome (for ropinirole extended-release and Mirapex® ER).

**Clinical Background Information and References**

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Dopamine Agonist/Antiparkinsonian Agents

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10. Rytary (carbidopa and levodopa) [prescribing information]. Hayward, CA: Impax Pharmaceuticals; January 2015

**Appendix A: Quantity Limitations**

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Quantity Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirapex ER (pramiprexole ER)</td>
<td>1 per day</td>
</tr>
<tr>
<td>Requip XL (Ropinirole ER)</td>
<td>1 per day</td>
</tr>
<tr>
<td>Neupro (rotigotine transdermal system)</td>
<td>1 per day</td>
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</table>

<table>
<thead>
<tr>
<th>Original Approval Date</th>
<th>Original Effective Date</th>
<th>Policy Owner</th>
<th>Approved by</th>
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<tbody>
<tr>
<td>11/01/2008</td>
<td>03/12/2009</td>
<td>Pharmacy Services</td>
<td>Pharmacy &amp; Therapeutics (P&amp;T) Committee</td>
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**Policy Revisions History**

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
<th>Revision Effective Date</th>
<th>Approved by</th>
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<tbody>
<tr>
<td>01/14/2010</td>
<td>P&amp;T annual review, no changes required</td>
<td>05/01/2010</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/13/2011</td>
<td>P&amp;T annual review, renamed policy “Antiparkison agents”, Mirapex ER added to criteria, add QL to Requip XR</td>
<td>05/01/2011</td>
<td>P&amp;T Committee</td>
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<tr>
<td>01/12/2012</td>
<td>P&amp;T annual review, no changes required</td>
<td>05/01/2012</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/10/2013</td>
<td>P&amp;T annual review, reflected availability of generic ropinirole ER, added criteria for Neupro® to policy</td>
<td>05/01/2013</td>
<td>P&amp;T Committee</td>
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<tr>
<td>12/13/2013</td>
<td>Policy applied to ConnectorCare/Qualified Health Plan (QHP)</td>
<td>01/01/2014</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/08/2015</td>
<td>P&amp;T annual review, no criteria changes required</td>
<td>05/05/2015</td>
<td>P&amp;T Committee</td>
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<tr>
<td>05/29/2015</td>
<td>Policy applied to NH Medicaid</td>
<td>10/01/2015</td>
<td>P&amp;T Committee NH DHHS</td>
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<tr>
<td>01/14/2016</td>
<td>P&amp;T annual review, changed title to include other antiparkinsonian agents, reflected generic availability of Mirapex ER, added step therapy with trial of IR</td>
<td>05/03/2016</td>
<td>P&amp;T Committee NH DHHS</td>
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</tbody>
</table>

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### Dopamine Agonist/Antiparkinsonian Agents

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Reviewer</th>
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<tbody>
<tr>
<td>1/12/2017</td>
<td>Added in allergy or intolerance to brand products, Rytary and Stalevo, where generic products are available.</td>
<td>P&amp;T Committee</td>
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<td></td>
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<td>NH DHHS</td>
</tr>
</tbody>
</table>

### Next Review Date

01/11/2018

### Other Applicable Policies

- 9.002 Mandatory Generic Substitution Program
- 9.015 Quantity Limitation Program

### Reference to Applicable Laws and Regulations, If Any

N/A

### Disclaimer Information

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.

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**Dopamine Agonist/Antiparkinsonian Agents**

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