BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/16/2017
LAST REVIEW DATE: 5/20/2021
LAST CRITERIA REVISION DATE: 5/20/2021
ARCHIVE DATE:

GOCOVRI™ (amantadine) extended release oral capsule
OSMOLEX ER™ (amantadine) extended release oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Gocovri (amantadine) ER and Osmolex ER (amantadine) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist or Psychiatrist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:

     a. **For Gocovri one of the following:**
        i. Parkinson's disease in an individual who is experiencing dyskinesia while receiving levodopa-based therapy, with or without concomitant dopaminergic medications

        ii. Parkinson's disease in an individual who is experiencing "off" episodes while receiving levodopa-based therapy, to be used as adjunctive therapy

     b. **For Osmolex ER one of the following:**
        i. Parkinson's disease in an individual who is receiving levodopa-based therapy, with or without concomitant dopaminergic medications

        ii. Drug-induced extrapyramidal reaction despite use of benztropine or trihexyphenidyl

  4. Documented failure, contraindication per FDA label, intolerance to immediate-release amantadine (capsule, tablet, or oral solution)

  5. Gocovri and Osmolex ER will not be used simultaneously and will not be used simultaneously with generic amantadine

  6. There are **NO** FDA-label contraindications, such as:
     a. End stage renal disease (creatinine clearance < 15 mL/min/1.73 m^2)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Gocovri (amantadine) ER and Osmolex ER (amantadine) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist or Psychiatrist

  2. Individual's condition responded while on therapy

a. Response is defined as:
   i. **When used for Parkinson's disease**, at least **TWO** of the following:
      - At least a 30% reduction in Parkinson's disease symptoms of tremor, rigidity, bradykinesia, and postural instability using MDS-USDRS part III motor score from baseline
      - No evidence of disease progression of Parkinson's symptoms
      - Functionality retained in most activities of daily living

   ii. **When used for Parkinson's disease dyskinesia**, at least **TWO** of the following:
      - Increase in number of hours of "on" time per day without troublesome dyskinesia
      - No evidence of disease progression of Parkinson's symptoms or dyskinesia
      - Functionality retained in most activities of daily living

   iii. **When used for Parkinson's disease "off" episodes**, at least **TWO** of the following:
      - Reduction in number of hours of "off" time per day
      - No evidence of disease progression of Parkinson's symptoms or "off" episodes
      - Functionality retained in most activities of daily living

   iv. **When used for drug-induced extrapyramidal reactions**, at least **TWO** of the following:
      - No evidence of worsening of extrapyramidal reaction
      - Functionality retained in most activities of daily living
      - Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as:
      i. Psychosis
      ii. Hallucinations
      iii. Depression
      iv. Suicidality
      v. Compulsive disorders
      vi. Neuroleptic malignant syndrome

5. Gocovri and Osmolex ER will not be used simultaneously and will not be used simultaneously with generic amantadine

6. There are no significant interacting drugs

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of a Non-Cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

Description:

Parkinson disease (PD) is a debilitating neurodegenerative disease affecting about 1% of the population that manifests itself as dopamine (DA) levels in the brain decrease. The result of this dopamine deficiency is seen as motor symptoms of rest tremor, rigidity and bradykinesia. These symptoms can severely limit activities of daily living. Non-motor cognitive and psychiatric symptoms, are thought to be due to degeneration of other neurotransmitter systems within the brain.

The pharmacologic treatment of PD can be categorized into neuroprotective and symptomatic therapy. Nearly all of the available treatments treat the symptoms of PD and do not appear to slow or reverse the natural course of the disease. The decision to initiate symptomatic medical therapy in patients with PD is determined by the degree to which the patient is functionally impaired.

Available drugs for the treatment of PD include: levodopa (with or without carbidopa), dopamine agonists (DAs), monoamine oxidase type B (MAO-B) inhibitors, anticholinergic agents, amantadine, & catechol-O-methyl transferase (COMT) inhibitors.

Levodopa is the most effective drug for the symptomatic treatment of PD and is the drug of first choice if symptoms related to bradykinesia become intrusive or troublesome. Either levodopa or a DAs can be used initially for patients who require symptomatic therapy for PD. Levodopa should be given when akinetic symptoms become disabling. The DAs (e.g., bromocriptine, pramipexole, ropinirole, & others) can be used either as monotherapy in early PD or in combination with other antiparkinsonian drugs for treatment of more advanced disease. The MAO B inhibitors (e.g., selegiline, rasagiline, & others) may be useful in early PD but have only modest benefit as monotherapy. COMT inhibitors (e.g., tolcapone, entacapone) are not effective when used as monotherapy, they are useful as levodopa extenders. Anticholinergic drugs (e.g., benztropine, trihexyphenidyl) are most useful as monotherapy in patients with disturbing tremor who do not have significant bradykinesia or gait disturbance. They also may be useful in patients with more advanced disease who have persistent tremor despite treatment with levodopa or DAs. Amantadine is a weak antiparkinsonian drug that is useful in treating younger patients with early or mild PD and later when dyskinesia becomes problematic.

Patients with PD who take levodopa chronically are likely to develop motor fluctuations and dyskinesia as the disease progresses. Dyskinesia involves levodopa-related abnormal, involuntary movements and can occur at a dose that is considered therapeutic. Dyskinesias are sometimes mistaken for manifestations of progressive PD or confused with tremor, rather than recognized as reversible consequences of levodopa treatment. Approaches to

managing dyskinesia often begins with adjusting the levodopa regimen or use of adjunctive medications such as DAs.

Early in the course of PD, peak-dose dyskinesia can be managed by lowering levodopa dose, use of more frequent dosing of levodopa dose if associated with "wearing off," changing to a controlled-release preparation of levodopa, or reducing adjunctive drugs such as dopamine agonists, MAO inhibitors, or anticholinergic drugs.

After some time, some individuals start experiencing motor fluctuations where there are alterations between periods of being "on," during which the patient experiences a positive response to medication, and being "off," during which the patient experiences a reemergence of the Parkinson symptoms. “Off” episodes may be characterized by muscle stiffness, slow movements, or difficulty starting movements. “Off” episodes are common in PD and can happen at any time.

Patients with PD often begin to be aware of a "wearing off" or “end-of-dose” effect less than four hours following a dose of levodopa. In some cases, "wearing off" can be managed initially by increasing the dose of levodopa if the patient is taking a relatively low dose and is not having side effects. For patients with more advanced PD, reducing the interval between doses is often an effective strategy and may require the addition of an extra levodopa dose at the end of the day. Some patients may benefit from alternative levodopa formulations.

Other treatments include DA receptor agonists, catechol-O-methyl-transferase (COMT) inhibitors, selective mono-amine oxidase type-B (MAOI-B) inhibitors, and amantadine. These agents are effective and safe in controlling motor symptoms in patients with advanced PD. There is insufficient evidence to conclude that any one of these medications is clinically superior to another and there is insufficient evidence that shows one PD medication as superior to another in terms of improvement in functional outcomes.

Amantadine may be useful for treating dyskinesia in advanced PD. Several studies have shown short-term benefit, and a few suggest long-term benefit. It was not associated with worsening of parkinsonian symptoms in these studies. The starting dose of amantadine for dyskinesia is one tablet (100 mg) a day, titrating to as much as four times a day, as needed. Side effects may include peripheral edema, psychosis, livedo reticularis (mottled skin), and hallucinations, all reversible when the drug is stopped.

Drug-induced extrapyramidal symptoms (EPS) are mainly seen with use of antipsychotic drugs and other drugs that block dopamine receptors. Reactions include akathisia, Parkinsonism, and acute dystonias. Chronic EPS includes, tardive akathisia, tardice dystonia, and tardive dyskinesia.

Akathisia is described a subjective feeling of restlessness accompanied in more severe presentations with motor movements such as fidgeting, pacing, or difficulty sitting still. Akathisia can be treated with a benzodiazepine or a beta blocker.

For patients with drug-induced Parkinsonism that is uncomfortable or disabling, benztropine is considered first-line treatment. Amantadine, a non-anticholinergic antiparkinsonian medication, is a reasonable alternative and may be preferable for patients already experiencing anticholinergic side effects.

Acute dystonias are involuntary contractions of major muscle groups and are characterized by symptoms such as torticollis, retrocollis, oculogyric crisis, and opisthotonos. Severe dystonias can be treated with intramuscular or

intravenous benztropine or diphenhydramine. Milder dystonias can be treated with lower, less frequent doses of benztropine.

Tardive dyskinesia (TD), a syndrome of characteristic involuntary movements of the lips, tongue, face, jaw, extremities, or trunk, occurs after chronic use of antipsychotic medications. TD seldom occurs prior to three months of antipsychotic use and usually after years of treatment. TD appears to be more common with first-generation antipsychotics rather than second-generation antipsychotics. When patients develop TD, clinicians should re-evaluate the current treatment strategy. Changing patients to an antipsychotic with a low risk for TD or use of inhibitors of the vesicular monoamine transporter II (e.g., deutetrabenaziene, valbenazine) may be effective for treating the abnormal movements of TD.

Definitions:

Drugs used in the treatment of Parkinson Disease:

Carbidopa	Carbidopa generic tabs Lodosyn tab
Carbidopa/Levodopa	Carbidopa+Levodopa – immediate release generic tabs Carbidopa+Levodopa ER – extended release generic tabs Carbidopa+Levodopa – ODT generic tabs Rytary – extended release caps Sinemet – immediate release tabs Sinemet CR – extended release tabs
Carbidopa+Levodopa+Entacapone	Carbidopa+Levodopa+Entacapone generic tabs Stalevo tabs
COMT inhibitors	Entacapone generic tabs Comtan (entacapone) tabs Tolcapone generic tabs Tasmar (tolcapone) tabs
DA agonists	Apomorphine injection Bromocriptine generic tabs Parlodel (bromocriptine) tabs Pramipexole – immediate release generic tabs Pramipexole ER – extended release generic tabs Mirapex (pramipexole) – immediate release tabs Mirapex ER (pramipexole) – extended release tabs Ropinirole – immediate release generic tabs Ropinirole ER – extended release generic tabs Requip (ropinirole) – immediate release tabs Requip XL (ropinirole) – extended release tabs Neupro (rotigotine) patch

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MAO-B inhibitors	Rasagiline generic tabs Azilect (rasagiline) tabs Eldepryl (selegiline) caps Emsam (selegiline) patch Selegiline generic tabs and caps Xadago (safinamide) tabs Zelapar (selegiline) – ODT tab
Anticholinergic agents for PD	Benztropine Diphenhydramine Trihexyphenidyl
Other	Gocovri (amantadine, extended release) caps Osmolex ER (amantadine extended release) tabs

Resources:

Gocovri (amantadine) extended release capsule product information, revised by Adamas Pharma, LLC 01-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 27, 2021.

Osmolex ER (amantadine) extended release tablet product information, revised by Vertical Pharmaceuticals, LLC. 10-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 27, 2021.

Amantadine capsule product information, revised by Sandoz Inc. 05-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 28, 2021.

Amantadine liquid-filled capsule product information, revised by Banner Life Sciences LLC. 02-2015. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 28, 2021.

Amantadine solution product information, revised by Morton Grove Pharmaceuticals, Inc. 07-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 28, 2021.

Amantadine tablet product information, revised by Upsher-Smith Laboratories, LLC 05-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 28, 2021.

Amantadine syrup product information, revised by Mikart, LLC 03-2013. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 28, 2021.

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