



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/16/17
LAST REVIEW DATE: 8/15/19
LAST CRITERIA REVISION DATE: 8/15/19
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.

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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)

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864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms or forms without the chart notes will be returned.

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. Individual is 18 years of age or older
 2. A confirmed diagnosis of **ONE** of the following:
 - **For Gocovri:** A diagnosis of dyskinesia in an individual with Parkinson's disease who is receiving levodopa-based therapy, with or without concomitant dopaminergic medications
 - **For Osmolex ER one of the following:**
 - A diagnosis of Parkinson's disease in a patient who is receiving levodopa-based therapy, with or without concomitant dopaminergic medications
 - A diagnosis of drug-induced extrapyramidal reaction while on bztropine or trihexyphenidyl
 3. Individual has failure, contraindication, or intolerance to immediate-release amantadine (capsule, tablet, or oral solution)
 4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
 - Basic metabolic panel
 5. Will not be used with live vaccines
 6. Gocovri and Osmolex ER will not be used simultaneously
 7. There are **NO** contraindications
 - Contraindications include:
 - End stage renal disease (creatinine clearance < 15 mL/min/1.73 m²)

Initial approval duration: 6 months

For Gocovri: Max daily dose of two 137 mg (total of 274 mg)

For Osmolex ER: Max daily dose 129 mg plus 193 mg (total of 322 mg) no other combination of tablet strengths allowed

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➤ **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's condition responded while on therapy
 - Response is defined as:
 - No evidence of disease progression of Parkinson's symptoms or worsening of extrapyramidal reaction
 - Functionality retained in most activities of daily living
 - Documented evidence of efficacy, disease stability and/or improvement
2. Individual has been adherent with the medication
3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
 - Contraindications as listed in the criteria for initial therapy section
 - Significant adverse effect such as:
 - Psychosis
 - Hallucinations
 - Depression
 - Suicidality
 - Compulsive disorders
 - Neuroleptic malignant syndrome
 - Seizure disorder
4. Gocovri and Osmolex ER will not be used simultaneously
5. There are no significant interacting drugs

Renewal duration: 12 months

For Gocovri: Max daily dose of two 137 mg (total of 274 mg)

For Osmolex ER: Max daily dose 129 mg plus 193 mg (total of 322 mg) no other combination of tablet strengths allowed

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.



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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 a 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.

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.



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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., deutetrabenazine, 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 Tasmар (tolcapone) tabs

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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
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. Package Insert. Revised by manufacturer 8/2017. Accessed 10/12/17.

UpToDate: Motor fluctuations and dyskinesia in Parkinson disease. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/motor-fluctuations-and-dyskinesia-in-parkinson-disease?search=dyskinesia%20treatment&source=search_result&selectedTitle=2~150&usage_type=default&disp_lay_rank=2#H869237432

UpToDate: Pharmacologic treatment of Parkinson disease. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacologic-treatment-of-parkinson-disease?search=dyskinesia%20treatment&source=search_result&selectedTitle=9~150&usage_type=default&disp_lay_rank=9#H33



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UpToDate: Pharmacologic treatment of Parkinson disease. Current through Jun 2018. [https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacologic-treatment-of-parkinson-disease?search=parkinson%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1](https://www.uptodate-com.mwu.idm.oclc.org/contents/pharmacologic-treatment-of-parkinson-disease?search=parkinson%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1)

UpToDate: Pharmacotherapy for schizophrenia: Side effect management. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacotherapy-for-schizophrenia-side-effect-management?search=extrapyramidal%20symptoms%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

Osmolex ER (amantadine) product information accessed 07-12-18 at DailyMed:
<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2bced627-51e3-4e5c-a23c-30deb86ff37b>

Gocovri (amantadine) product information accessed 07-12-18 at DailyMed:
<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=82ff865f-78f3-4c94-b6a9-727a54944b28>

Pringsheim T, Doja A, Belanger S, et al.: Treatment recommendations for extrapyramidal side effects associated with second generation antipsychotic use in children and youth. Paediatr Child Health 2011;16 (9):590-598
