BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

GOCOVRI™ (amantadine) extended release oral capsule
OSMOLEX ER™ (amantadine) extended release oral tablet
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for GOCOVRI (amantadine extended-release oral capsule)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a neurologist or psychiatrist or in consultation with a neurologist or psychiatrist

Indication
- Dyskinesia in Parkinson's disease while receiving levodopa-based therapy (with or without dopaminergic medications)

- Parkinson's disease experiencing "off" episodes while on levodopa-based therapy

Age Requirement
- 18 years or older

Alternative Therapies
- Failure, contraindication, intolerance to immediate-release amantadine (capsule, tablet, or oral solution)

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the Food and Drug Administration (FDA)

Safety
- Will not be used simultaneously with Osmolex ER or generic amantadine
- Does not have ESRD (creatinine clearance less than 15 mL/min/1.73 m²)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with a neurologist

Clinical Response
- **For Parkinson's disease dyskinesia indication, 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
- **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 dyskinesia
  - Functionality retained in most activities of daily living

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Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- Will not be used simultaneously with Osmolex ER or generic amantadine
- No contraindications or significant adverse effects such as:
  - ESRD (creatinine clearance less than 15 mL/min/1.73 m²)
  - Psychosis
  - Hallucinations
  - Depression
  - Suicidality
  - Compulsive disorders
  - Neuroleptic malignant syndrome
  - Seizure disorder

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration:
- 12 months OR end of plan year

Medical Necessity Requirements for OSMOLEX ER (amantadine extended-release oral tablet)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a neurologist or psychiatrist or in consultation with a neurologist or psychiatrist

Indication
- Parkinson's disease
- Drug-induced extrapyramidal reaction while on benztropine or trihexyphenidyl

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GOCOVRI™ (amantadine) extended release oral capsule
OSMOLEX ER™ (amantadine) extended release oral tablet
Generic Equivalent (if available)

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Confirmed diagnosis of Parkinson's disease or drug-induced extrapyramidal reaction

Alternative Therapies
- Failure, contraindication, intolerance to immediate-release amantadine (capsule, tablet, or oral solution)

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the Food and Drug Administration (FDA)

Safety
- Will not be used simultaneously with Osmolex ER or generic amantadine
- Does not have ESRD (creatinine clearance less than 15 mL/min/1.73 m²)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (basic metabolic panel)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with a neurologist or psychiatrist

Clinical Response
- **For Parkinson's disease, 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
- **For drug-induced extrapyramidal reactions, TWO** of the following:
  - No evidence of worsening of extrapyramidal reactions

- Functionality retained in most activities of daily living
- Documented evidence of efficacy, disease stability and/or improvement

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Will not be used simultaneously with Osmolex ER or generic amantadine
- No contraindications or significant adverse effects such as:
  - ESRD (creatinine clearance less than 15 mL/min/1.73 m²)
  - Psychosis
  - Hallucinations
  - Depression
  - Suicidality
  - Compulsive disorders
  - Neuroleptic malignant syndrome
  - Seizure disorder

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration:

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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 Non-Cancer Medications

2. Off-Label Use of Cancer Medications

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OSMOLEX ER™ (amantadine) extended release oral tablet
Generic Equivalent (if available)

Description:

Gocovri (amantadine) extended-release capsule is indicated for the treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications and as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes. Osmolex ER (amantadine) extended-release tablet is indicated for the treatment of Parkinson's disease and for the treatment of drug-induced extrapyramidal reactions in adult patients
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, tardive 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., deutetrabenazine, valbenazine) may be effective for treating the abnormal movements of TD.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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
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

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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 February 18, 2025. **O**

Osmolex ER (amantadine) extended release tablet product information, revised by Adamas Pharma, LLC. 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025. **O**

Spindler MA. Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025.Topic last updated January 21, 2025. Accessed February 26, 2025. **E**

Chou KL. Clinical manifestations of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated May 14, 2024. Accessed February 26, 2025. **E**

Liang TW, Tarsy D. Medical management of motor fluctuations and dyskinesia in Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated February 06, 2025. Accessed on February 26, 2025. **E**

Chou KL. Device-assisted and lesioning procedures for Parkinson disease. In: UpToDate, Hurtig HI, Tung GA, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated January 21, 2025. Accessed February 26, 2025. **E**