BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

CREXONT® (carbidopa and levodopa) extended-release oral
RYTARY™ (carbidopa and levodopa) extended-release oral
TASMAR® (tolcapone) oral
Tolcapone oral
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 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.

Criteria:

CREXONT (carbidopa and levodopa, extended release)
RYTARY (carbidopa and levodopa, extended release)

➢ **Criteria for initial therapy:** Crexont (carbidopa/levodopa ER) or Rytary (carbidopa/levodopa ER) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is 18 years of age or older

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Parkinson's disease
    b. Post-encephalitic parkinsonism
    c. Carbon monoxide or manganese intoxication parkinsonism
3. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **generic extended-release Carbidopa/Levodopa tablets**
4. **FOR RYTARY ONLY:** Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **extended-release Crexont (carbidopa/levodopa ER)**
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
6. There are **NO** FDA-label contraindications such as use with or within 14 days of stopping nonselective monoamine oxidase (MAO) inhibitors such as isocarboxazid, phenelzine, or tranylcypromine
7. Requested agent will not be used with other levodopa products
8. Crexont (carbidopa/levodopa ER) and Rytary (carbidopa/levodopa ER) will not be used concurrently

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Crexont (carbidopa/levodopa ER) or Rytary (carbidopa/levodopa ER) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual has documentation of positive clinical response to therapy defined as **ONE** of the following:
    a. Able to perform most of activities of daily living
    b. Improvement in symptoms of tremor, bradykinesia, rigidity
    c. Achieved and maintains reduced "off" time during waking hours
    d. Achieved and maintains increased "on" time without troublesome dyskinesia
2. Individual has been adherent with the medication
3. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follow:
    a. Contraindications as listed in the criteria section for initial therapy section
    b. Significant adverse effect such as:
        i. Hallucinations or psychosis
        ii. Impulse control issues or compulsive behavior
        iii. Significant daytime sleepiness or episodes of falling asleep during activities of daily living that require active participation

5. Requested agent will not be used with other levodopa products

6. Crexont (carbidopa/levodopa ER) and Rytary (carbidopa/levodopa ER) will not be used concurrently

Renewal duration: 12 months

- 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**

TASMAR (tolcapone)
Tolcapone (generic)

- **Criteria for initial therapy:** Tasmar (tolcapone) and tolcapone generic are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

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

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of Parkinson's disease, and the individual is experiencing symptom fluctuations

4. Individual must continue use of carbidopa and levodopa

5. Individual is experiencing symptom fluctuations and is not responding satisfactorily to or is not appropriate candidates for other adjunctive therapies (e.g., pramipexole, ropinirole, selegiline)

6. **For brand Tasmar (tolcapone)**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** the following:

a. Generic tolcapone
b. Entacapone (brand or generic)

7. Individual has completed a **baseline** liver function test before initiation of treatment and will have continued monitoring as clinically appropriate

8. There are **NO** FDA-label contraindications such as:
   a. Liver disease
   b. Individual who was withdrawn from Tasmar or tolcapone due to hepatic injury
   c. History of non-traumatic rhabdomyolysis
   d. Hyperpyrexia and confusion related to medication
   e. Individual who has demonstrated hypersensitivity to Tasmar or tolcapone or its ingredients

9. Individual does not have severe dyskinesia or dystonia

10. Individual does not currently exhibit clinical evidence of liver disease or two alanine transaminase (ALT) or aspartate transaminase (AST) values greater than the upper limit of normal or previously developed hepatocellular injury from Tasmar or tolcapone

11. Individual will not use requested agent with non-selective MAO inhibitors (e.g., phenelzine, tranylcypromine)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tasmar (tolcapone) and tolcapone generic are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

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

2. Individual has documentation of positive clinical response to therapy defined as **ONE** of the following:
   a. Able to perform most of activities of daily living
   b. Improvement in symptoms of tremor, bradykinesia, rigidity
   c. Achieved and maintains reduced "off" time during waking hours
   d. Achieved and maintains increased "on" time without troublesome dyskinesia

3. Individual has been adherent with the medication

4. Individual continues use of carbidopa and levodopa

5. **For brand Tasmar (tolcapone)**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **generic tolcapone**

6. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Hepatotoxicity toxicity, exhibited by elevation of ALT and AST that are > 2x ULN or clinical symptoms
        ii. Significant daytime sleepiness or episodes of falling asleep during activities of daily living that require active participation
        iii. Paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium
        iv. Frequent dyskinesias
        v. Impulse control/Compulsive behaviors

7. Individual does not have severe dyskinesia or dystonia

8. Individual does not currently exhibit clinical evidence of liver disease or two alanine transaminase (ALT) or aspartate transaminase (AST) values greater than the upper limit of normal or previously developed hepatocellular injury from Tasmar or tolcapone

9. Individual will not use requested agent with non-selective MAO inhibitors (e.g., phenelzine, tranylcypromine)

Renewal duration: 12 months

- 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**

Description:

Rytary (carbidopa/levodopa) extended-release capsule is indicated for the treatment of Parkinson's disease (PD), post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication. Tasmar (tolcapone) tablet is indicated as an adjunct to carbidopa and levodopa for the treatment of signs and symptoms of idiopathic PD in patients who are experiencing symptom fluctuations and are not responding satisfactorily to or are not appropriate candidates for other adjunctive therapies.

Motor symptoms of PD are caused by a progressive degeneration of Dopamine (DA) containing neurons in the brain. Non-motor manifestations such as cognitive and psychiatric symptoms are thought to be due to degeneration of other neurotransmitter systems within the brain. Degeneration of the DA neurons leads to DA

deficiency and as a result the development of the classic triad of motor symptoms of resting tremor, muscle rigidity and bradykinesia. With the development of DA deficiency, there is also a relative excess of acetylcholine activity.

Drug therapy is targeted at reducing symptoms by enhancing the effects of DA or inhibiting the effects of acetylcholine. Levodopa has been long recognized in clinical practice guidelines and texts as the standard of care for PD. It is a precursor of DA and is able to cross the blood brain barrier where it is converted to DA. Levodopa is thought to be protective against the dopaminergic neuron damage observed in PD. Levodopa is converted to DA in the periphery before it is able to cross the blood brain barrier resulting in gastrointestinal adverse effects and a lower-than-expected concentration of levodopa within the brain. To avoid this, levodopa is combined with carbidopa resulting in a decrease in the peripheral conversion of levodopa to DA and allowing for more levodopa to reach the brain to then be converted to DA. The combination of carbidopa/levodopa is one of the most effective treatments available for symptomatic relief of PD.

In the early stages of levodopa therapy, patients experience a smooth and even response. As PD advances, the effect of levodopa wears off approximately 4 hours after each dose. As many as 50% of patients on levodopa for 5 years, will eventually experience motor fluctuations and dyskinesia. Motor fluctuations are shifts between “on” periods where the patient is responding to levodopa therapy and “off” periods, or end-of-dose effect, where the patient experiences PD symptoms. Dyskinesia consists of a wide range of involuntary movements and typically appears during the patient’s “on” period. These symptoms of motor fluctuations and dyskinesia are commonly seen in patients with early onset (< 50 years of age) PD and are unique to levodopa therapy. For treatment of PD with motor fluctuations and dyskinesia, adjunctive therapy is often necessary to address these complications.

Other treatments for PD include DA receptor agonists, catechol-O-methyltransferase (COMT) inhibitors, selective mono-amine oxidase type-B (MAOI-B) inhibitors, amantadine, and selective use of anticholinergic agents. These agents are effective and safe in controlling motor symptoms in patients with advanced PD when used as adjunctive treatment to Levodopa. 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.

Low-cost generic options are available in immediate and extended-release formulations of carbidopa/levodopa as well as for each class of adjunctive therapy and are sufficient to meet the needs of most patients.

Definitions:

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

Oral Anti-Parkinson’s disease agents	
Carbidopa	Carbidopa generic tabs Lodosyn tabs

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Tolcapone oral
Generic Equivalent (if available)

Carbidopa+Levodopa	Carbidopa+Levodopa – immediate release generic tabs Carbidopa+Levodopa ER – extended-release generic tabs Carbidopa+Levodopa ODT generic tabs Crexont – extended release caps 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 Ongentys (opicapone) caps Tolcapone generic tabs Tasmar (tolcapone) tabs
DA agonists	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
MAO-B inhibitors	Rasagiline generic tabs Azilect (rasagiline) tabs Xadago (safinamide) tabs Selegiline generic tabs and caps Eldepryl (selegiline) caps Zelapar (selegiline) – ODT tab
Anticholinergic agents for PD	Benztropine Diphenhydramine Trihexyphenidyl

The Child-Pugh classification system:

	Score: 1 point	**Score: 2 points**	**Score: 3 points**
Serum Albumin (g/dL)	>3.5	3.0 - 3.5	<3.0
Serum Bilirubin (mg/dL)	<2.0	2.0 - 3.0	>3.0

Prothrombin time (seconds)	1 - 4	4 - 6	>6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:

- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease

Activities of daily living (ADL):

Instrumental ADL:

Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.

Self-care ADL:

Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

Resources:

Crexont (levodopa and carbidopa) extended release capsule product information, revised by Amneal Pharmaceuticals, LLC. 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

Rytary (levodopa and carbidopa) extended release capsule product information, revised by Amneal Pharmaceuticals, LLC. 12-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

Tasmar (tolcapone) product information, revised by Bausch Health US, LLC. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

Tolcapone product information, revised by Oceanside Pharmaceuticals. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

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 May 2025. Topic last updated May 22, 2025. Accessed June 16, 2025.

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 May 2025. Topic last updated June 10, 2025. Accessed June 19, 2025.

Liang TW. 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 May 2025. Topic last updated June 10, 2025. Accessed June 16, 2025.

Chahine L. Management of nonmotor symptoms in Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated May 23, 2024. Accessed June 16, 2025.