PHARMACY COVERAGE GUIDELINE

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

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 precertification 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:

RYTARY (carbidopa and levodopa, extended release)

➢ **Criteria for initial therapy:** Rytary (carbidopa/levodopa ER) 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 Parkinson's disease.

3. Documented failure, contraindication per FDA label, intolerance, or not a candidate to generic extended-release **Carbidopa/Levodopa** tablets.

4. There are **NO** FDA-label contraindications, such as use with or within 14 days of stopping isocarboxazid, phenelzine, or tranylcypromine.

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Rytary (carbidopa/levodopa ER) 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's condition has responded while on therapy with response defined as **ONE** of the following:
    a. Achieved and maintains improvement in motor ability
    b. Able to perform most of activities of daily living
    c. Achieved and maintains reduced "off" time
    d. Achieved and maintains increased "on" time

2. Individual has been adherent with the medication.

3. 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. Falling asleep during activities of daily living

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. The Individual is 18 years of age or older.

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

4. The Individual is not responding to or not a candidate for other adjunctive therapy for Parkinson's disease.

5. The Individual requires continued use of carbidopa and levodopa.

6. The individual has received and completed a **baseline** Liver function test before initiation of treatment and with continued monitoring of the individual as clinically appropriate.

7. 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

8. Documented failure, contraindication per FDA label, intolerance, or not a candidate to **ALL** the following:
    a. generic tolcapone
    b. entacapone (brand and generic)

Initial approval duration: 2 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's condition has responded while on therapy with response defined as **ONE** of the following:
    a. Achieved and maintains a reduction in symptom fluctuations
    b. Achieved and maintains at least 1.5-2 hours more of relatively good functioning
    c. Achieved and maintains at least 1 hour less of relatively poor functioning

3. Individual has been adherent with the medication.

4. Individual continues use of carbidopa and levodopa.

5. 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 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. Falling asleep during activities of daily living and somnolence
iii. Paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium
iv. Impulse control/Compulsive behaviors

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. Zelapar (selegiline) oral disintegrating tablet is indicated as an adjunct in the management of patients with PD being treated with carbidopa/levodopa who exhibit deterioration in the quality of their response to this therapy.

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 include DA receptor agonists, catechol-O-methyl-transferase (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:

Oral Anti-Parkinson's disease agents	
Carbidopa	Carbidopa generic tabs Lodosyn tabs
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	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:

Rytary (levodopa & carbidopa extended release) capsule product information, revised by Amneal Pharmaceuticals, LLC. 12-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 12, 2022.

Tasmar (tolcapone) product information, revised by Bausch Health US, LLC. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 12, 2022.

Tolcapone product information, revised by Ingenus Pharmaceuticals, LLC. 08-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 12, 2022.

Spindler MA, Tarsy D. Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on April 27, 2021. Accessed July 12, 2022.

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. Topic last updated on May 13, 2022. Accessed July 12, 2022.