BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 9/15/17**
SECTION: DRUGS	**LAST REVIEW DATE: 8/15/19**
	LAST CRITERIA REVISION DATE: 8/15/19
	ARCHIVE DATE:

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

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

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

Rytary (carbidopa and levodopa, extended release)

Criteria:

- **Criteria for initial therapy:** Rytary (carbidopa/levodopa ER) is 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 Parkinson's disease
  3. Tried, failed, or has contraindication to use of generic extended-release **Carbidopa/Levodopa** tablets
  4. There are no contraindications such as use with or within 14 days of stopping isocarboxazid, phenelzine, or tranycypromine

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Rytary (carbidopa/levodopa ER) is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

  1. Individual's condition responded while on therapy
     - Response is defined as **ONE** of the following:
       - Achieved and maintains improvement in motor ability
       - Able to perform most of activities of daily living
       - Achieved and maintains reduced "off" time
       - Achieved and maintains increased "on" time
  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
  4. There are no significant interacting drugs

  Renewal duration: 12 months

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

- Rytary (carbidopa/levodopa ER) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - Treatment with dosing or frequency outside the FDA-approved dosing and frequency

Tasmar (tolcapone)

Criteria:

- **Criteria for initial therapy:** Tasmar (tolcapone) is 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 Parkinson's disease
  3. Requires continued use of carbidopa and levodopa
  4. Individual experiencing symptom fluctuations
  5. Individual is not responding to or not a candidate for other adjunctive therapy for Parkinson's disease
  6. Tried, failed, or has contraindication to use of generic tolcapone **and** entacapone (brand and generic)
  7. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Liver function tests
  8. There are no contraindications such as liver disease, individuals who were withdrawn from Tasmar or tolcapone due to hepatic injury, history of non-traumatic rhabdomyolysis, or hyperpyrexia and confusion related to medication

  Initial approval duration: 2 months

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

- **Criteria for continuation of coverage (renewal request):** Tasmar (tolcapone) is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

  1. Individual's condition responded while on therapy
     - Response is defined as **ONE** of the following:
       - Achieved and maintains a reduction in symptom fluctuations
       - Achieved and maintains at least 1.5-2 hours more of relatively good functioning
       - Achieved and maintains at least 1 hour less of relatively poor functioning

  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, such as:
     - Any of the contraindication listed above
     - Hepatotoxicity toxicity, exhibited by elevation of ALT and AST that are > 2x ULN or clinical symptoms

  4. There are no significant interacting drugs

  Renewal duration: 12 months

- Tasmar (tolcapone) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - Treatment with dosing or frequency outside the FDA-approved dosing and frequency

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.

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

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(ropinirile) – extended release tabs
MAO-B inhibitors	Rasagiline generic tabs Azilect (rasagiline) tabs Xadago (safinamide) tabs Selegiline generic tabs and caps Eldedryl (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. Package Insert. Revised by manufacturer 11/2016, accessed 7/19/18; revised 04/2016, accessed 8/09/16; Reference ID 3680199 revised 01/2015, accessed 7/22/15, 7/22/16.

Tasmar. Package Insert. Revised by manufacturer 1/2017, accessed 7/19/18; revised 11/2013; accessed 7/22/15; revised 8/2015, accessed 7/22/16.

Zelapar. Package Insert. Revised by manufacturer 8/2016, accessed 07-19-2018; revised 07/2014, accessed 7/22/15, 7/22/16.

UpToDate: Motor fluctuations and dyskinesia in Parkinson disease. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/motor-fluctuations-and-dyskinesia-in-parkinson-disease?source=search_result&search=parkinsons%20disease%20adult&selectedTitle=13~150#H3

UpToDate: Pharmacologic treatment of Parkinson disease. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacologic-treatment-of-parkinson-disease?source=search_result&search=parkinsons%20disease%20adult&selectedTitle=2~150