BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**7/20/17**
LAST REVIEW DATE:	**8/02/18**
LAST CRITERIA REVISION DATE:	**8/02/18**
ARCHIVE DATE:	

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

XADAGO™ (safinamide) oral tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Xadago (safinamide) 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 in an individual who is having "off" episodes

  3. Xadago will only be used as adjunctive treatment to levodopa and carbidopa

  4. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **ALL** of the following due to failure, adverse drug event, or contraindication:
     - One trial of dopamine agonist: pramipexole,**or** ropinirole
     - One trial of monoamine oxidase inhibitor (MAO) B inhibitor: Selegiline (capsule or tablet) **or** rasagiline mesylate tablet
     - One trial of catechol O-methylase inhibitor (COMT): entacapone **or** tolcapone

  5. Absence of **ALL** of the following contraindications:
     - Simultaneous use or use within 14 days, of another monoamine oxidase inhibitor or other drugs that are potent inhibitors of monoamine oxidase such as linezolid
     - Simultaneous use or use within 14 days of opioid drugs (such as tramadol, meperidine and related derivatives); selective norepinephrine reuptake inhibitors; tricyclic or tetracyclic or triazolopyridine antidepressants; cyclobenzaprine; methylphenidate, amphetamine, and their derivatives; St. John's Wort
     - Simultaneous use with dextromethorphan
     - History of hypersensitivity to safinamide
     - Severe hepatic impairment (Child-Pugh Class C)

  6. Woman who is breast feeding an infant or child should stop breast feeding

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Xadago (safinamide) is 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 **BOTH** of the following:
       - Achieved and maintains a reduction in "off" time of at least 1 hour
       - Achieved and maintains an improvement in "on" time of at least 1 hour

  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

XADAGO™ (safinamide) oral tablet (cont.)

- Significant adverse effect such as:
  - Serotonin syndrome
  - Severe hypertension or hypertensive crisis
  - Severe liver impairment (Child-Pugh Class C)
  - Neuroleptic malignant syndrome

4. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Xadago (safinamide) is a monoamine oxidase type B (MAO-B) inhibitor indicated as adjunctive treatment to levodopa and carbidopa to treat adults with Parkinson's disease (PD) who are having "off" episodes. It has not been shown to be effective as monotherapy for the treatment of PD.

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.

Motor symptoms of PD are caused by a progressive degeneration of DA containing neurons located in the substantia nigra. 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. Non-motor cognitive and psychiatric symptoms, are thought to be due to degeneration of other neurotransmitter systems within the brain.

Drug therapy is targeted at reducing symptoms. Oral DA is not used in the treatment of PD because it does not cross the blood brain barrier. On the other hand, oral levodopa does cross the blood brain barrier and it use has been long recognized in clinical practice guidelines and texts as the standard of care for PD. Levodopa is a precursor of DA, after crossing the blood brain barrier it is converted to DA. Levodopa is thought to be protective against the dopaminergic neuron damage observed in PD.

When used alone, some oral levodopa is converted to DA in the periphery before it is able to cross the blood brain barrier resulting in GI adverse effects. Also as a result of this peripheral conversion to DA, there is a lower than expected concentration of levodopa within the brain. To circumvent this, levodopa is combined with carbidopa. Carbidopa decreases peripheral conversion of levodopa to DA and allows for more levodopa to pass into the brain to then be converted to DA. The combination levodopa/carbidopa 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

XADAGO™ (safinamide) oral tablet (cont.)

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 use of other 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. When used as adjunctive treatment to levodopa, 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.

The precise mechanism by which Xadago (safinamide) exerts its effect in PD is unknown. Xadago (safinamide) is an inhibitor of MAO-B. Inhibition of MAO-B activity blocks the catabolism of DA, and is thought to result in an increase in DA levels and a subsequent increase in dopaminergic activity in the brain.

Xadago (safinamide) is selective for inhibition of MAO-B at the recommended dosages of 50 mg or 100 mg daily. This selectivity for inhibiting MAO-B decreases above the recommended daily dosages. Xadago (safinamide) should not be used at daily dosages exceeding those recommended. Dietary tyramine restriction is not required during treatment with recommended doses of Xadago (safinamide). However, use with certain foods that contain very high amounts (i.e., more than 150 mg) of tyramine could cause severe hypertension, resulting from an increased sensitivity to tyramine in patients taking recommended dosages of Xadago (safinamide), and patients should be advised to avoid such foods.

Resources:

Xadago (safinamide). Package Insert. Revised by manufacturer 03-2017. Accessed 05-26-2017.

Xadago (safinamide). Package Insert. Revised by manufacturer 05-2017. Accessed 07-10-2018

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=parkinsons%20disease%20adult%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Motor fluctuations and dyskinesia in Parkinson disease. Current through Jun 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/motor-fluctuations-and-dyskinesia-in-parkinson-disease?topicRef=4899&source=related_link

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.