BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

XADAGO™ (safinamide) 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:

- **Criteria for initial therapy:** Xadago (safinamide) is 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 in an individual who is having "off" episodes
  4. Xadago will only be used as adjunctive treatment to levodopa and carbidopa
  5. Documented failure, contraindication per FDA label, intolerance, or not a candidate to **ALL** the following:
     a. One trial of dopamine agonist: pramipexole, **or** ropinirole

b. One trial of monoamine oxidase inhibitor (MAO) B inhibitor: Selegiline (capsule or tablet) **or** rasagiline mesylate tablet
c. One trial of catechol O-methylase inhibitor (COMT): entacapone **or** tolcapone

6. There are **NO** FDA-label contraindications, such as:
   a. 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
   b. 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
   c. Simultaneous use with dextromethorphan
   d. History of hypersensitivity to safinamide
   e. Severe hepatic impairment (Child-Pugh Class C)

Initial approval duration: 6 months

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

3. Individual has been adherent with the medication.

4. 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 effects such as:
      i. Serotonin syndrome
      ii. Severe hypertension or hypertensive crisis
      iii. Severe liver impairment (Child-Pugh Class C)
      iv. Neuroleptic malignant syndrome
      v. Falling asleep during activities of daily living
      vi. Hallucinations or psychosis
      vii. Impulse control issues or compulsive behavior

Renewal duration: 12 months

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- 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:

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 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) product information, revised by MDD US Operations, LLC, a subsidiary of Supernus Pharmaceutical, Inc. 08-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 18, 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.