Xadago® (safinamide)

Policy # 00603
Original Effective Date: 01/17/2018
Current Effective Date: 01/17/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Xadago®‡ (safinamide) for to be **eligible for coverage** when the patient selection criteria are met**.**

Patient Selection Criteria
Coverage eligibility for Xadago (safinamide) will be considered when the following criteria are met:

- The patient has a diagnosis of Parkinson's disease; AND
- The patient is currently being treated with levodopa/carbidopa and is experiencing "off" episodes; AND
- The patient has failed (e.g. intolerance or inadequate response) TWO of the following alternatives: generic pramipexole, generic ropinirole, generic entacapone, generic selegiline, or generic rasagiline
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of Xadago (safinamide) when the patient has not tried and failed at least two alternative products listed in the patient selection criteria to be **not medically necessary.****

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers Xadago (safinamide) for the treatment of any indication other than "off" episodes with levodopa/carbidopa treatment in Parkinson's disease to be **investigational.***

Background/Overview

Xadago is a reversible inhibitor of monoamine oxidase B (MAO-B) that is used to prevent the degradation of dopamine and prevent "off" episodes in patients with Parkinson's disease managed by levodopa/carbidopa. It is available as a 50 mg and 100 mg tablet and dosed 50 or 100mg once daily. Unlike the other MAO-B inhibitors, selegiline and rasagiline, Xadago inhibits MAO-B reversibly. It is contraindicated in severe

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hepatic impairment and when administered concomitantly with any other MAO inhibitor (including linezolid), opioid drugs, serotonin-norepinephrine receptor inhibitors (SNRIs), tricyclic, tetracyclic, or triazolopyridine antidepressants, cyclobenzaprine, methylphenidate, amphetamine derivatives, St. John's Wort, and dextromethorphan.

Parkinson's disease is a progressive neurodegenerative disease in which dopamine depletion from the basal ganglia results in disruptions in the connections to the thalamus and motor cortex. For most patients, first line therapy involves supplementation of dopamine via levodopa/carbidopa. As the disease progresses, periods of increased symptoms known as "off" episodes can occur when levodopa/carbidopa begins to wear off between doses. Initially, these episodes may be managed by adjusting the levodopa/carbidopa dose and schedule, but this may not be sufficient if the patient is experiencing adverse effects of the levodopa/carbidopa (such as dyskinesia). There are three classes of drugs indicated as adjunctive therapy to manage "off" episodes with levodopa/carbidopa: dopamine agonists, catecholamine-O-methyltransferase (COMT) inhibitors, and MAO-B inhibitors. Dopamine agonists such as pramipexole or ropinirole can be effective at prolonging symptom-free periods, but patients must be monitored for excessive dopaminergic effects (hallucinations, confusion, somnolence). The COMT inhibitors entacapone and tolcapone prolong and potentiate the levodopa effect by preventing its degradation. MAO-B inhibitors also prevent the degradation of levodopa by blocking its catabolism. There are three available MAO-B inhibitors: rasagiline, safinamide, and selegiline. Both rasagiline and safinamide have demonstrated consistent efficacy in reducing motor complications in combination with levodopa/carbidopa, but the clinical benefit of selegiline appears to be relatively mild.

The American Academy of Neurology guidelines for the treatment of Parkinson's disease with motor fluctuations and dyskinesia were published in 2006, prior to the approval of Xadago. These guidelines recommend that rasagiline, pramipexole, ropinirole, and tolcapone should be considered to reduce "off" time. It should be noted that tolcapone is associated with liver injury and is therefore rarely used.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xadago is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes.

Rationale/Source

Xadago was approved based on two double-blind, placebo-controlled, 24-week studies in patients with Parkinson's disease experiencing "off" time during treatment with levodopa/carbidopa. The primary efficacy endpoint in both studies was the change from baseline in total daily "on" time without troublesome dyskinesia.

Study 1 included 669 patients randomized equally to receive Xadago 50 mg/day, Xadago 100 mg/day, or placebo. Patients taking both doses of Xadago had significantly increased "on" time compared to placebo

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with an increase of 1.37 hours for the 50 mg dose, 1.36 hours for the 100 mg dose and 0.97 hours for the placebo.

Study 2 included 549 patients randomized equally to receive Xadago 100 mg/day or placebo. Patients taking Xadago had significantly increased "on" time compared to placebo with an increase of 1.42 hours for Xadago and 0.57 hours for placebo.

References

1. Xadago [package insert]. US WorldMeds. Louisville, KY. May 2017
2. Pahwa R, Factor SA, Lyons KE, et al. Practice parameter: treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review). Report of the quality standards subcommittee of the American Academy of Neurology. Neurology. 2006;66:983-995.

Policy History

Original Effective Date: 01/17/2018
Current Effective Date: 01/17/2018
01/04/2018 Medical Policy Committee review
01/17/2018 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 01/2019

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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