Extended Release Amantadine Products

Policy # 00610
Original Effective Date: 03/21/2018
Current Effective Date: 12/14/2020

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 Gocovri™‡ (amantadine extended release) capsules or Osmolex ER™‡ (amantadine extended release) tablets for the treatment of dyskinesia to be **eligible for coverage**** when the patient selection criteria are met**.**

Patient Selection Criteria

Coverage eligibility for Gocovri (amantadine extended release) capsules or Osmolex ER (amantadine extended release) tablets will be considered when the following criteria are met for the requested drug:

- The requested drug is Gocovri; AND
    - Patient has a diagnosis of Parkinson disease; AND
    - Patient is currently being treated with levodopa/carbidopa and is experiencing dyskinesia; AND
    - Patient has failed (e.g. intolerance or inadequate response) generic amantadine immediate release (IR) for at least 2 weeks unless there is clinical evidence or patient history that suggests the use of generic amantadine IR will be ineffective or cause an adverse reaction to the patient; AND
    - Patient has failed (e.g. intolerance or inadequate response) ONE of the following alternatives: generic entacapone, generic rasagiline, generic pramipexole, generic ropinirole, generic selegiline, or generic bromocriptine for at least 2 weeks unless there is clinical evidence or patient history that suggests the use of the alternatives will be ineffective or cause an adverse reaction to the patient.

*(Note: The patient criteria requiring the patient to try and fail another agent are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*

- The requested drug is Osmolex ER; AND
  - Patient is greater than or equal to 18 years of age; AND
  - Patient has a diagnosis of Parkinson disease or drug-induced, extrapyramidal reactions; AND
  - Patient has tried and failed (e.g. intolerance or inadequate response) GENERIC amantadine IR for at least 2 weeks unless there is clinical evidence or patient history that suggests the use of a GENERIC amantadine IR product for at least 2 weeks will be ineffective or cause an adverse reaction to the patient; AND
  - Patient has tried and failed (e.g. intolerance or inadequate response) ONE of the following alternative agents: generic entacapone, generic rasagiline, generic pramipexole, generic ropinirole, generic selegiline, or generic bromocriptine for at least 2 weeks unless there is clinical evidence or patient history that suggests the use of the alternative agents listed will be ineffective or cause an adverse reaction to the patient.

    *(Note: The patient criteria requiring the patient to try and fail another agent are additional Company requirements 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 Gocovri (amantadine extended release) or Osmolex ER (amantadine extended release) when the patient has not tried and failed generic amantadine IR and one additional agent 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 the use of Gocovri (amantadine extended release) or Osmolex ER (amantadine extended release) when patient selection criteria are not met (except those noted to be not medically necessary**) to be **investigational.***

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Background/Overview

Amantadine is a weak uncompetitive antagonist of the NMDA receptor that treats dyskinesia in patients with Parkinson disease through an unknown mechanism. Immediate release amantadine was originally approved as an antiviral agent to treat or prevent influenza A, but is now primarily used in the treatment of Parkinson disease and drug-induced motor symptoms. Gocovri is an extended release formulation of amantadine indicated only for the treatment of dyskinesia in patients with Parkinson disease receiving levodopa-based therapy. The initial daily dosage of Gocovri is 137 mg once daily at bedtime. After one week, the dose may be increased to 274 mg once daily at bedtime. Osmolex ER is another extended release formulation of amantadine that is indicated for the treatment of Parkinson disease and drug-induced extrapyramidal reactions in adult patients. The initial daily dosage of Osmolex ER is 129 mg once daily in the morning. The dose may be increased in weekly intervals to a maximum daily dose of 322 mg. Neither Gocovri nor Osmolex ER is interchangeable with each other or with amantadine immediate release products.

Parkinson 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. However, when higher doses of levodopa are required the patient may experience dyskinesia— levodopa-related, abnormal, involuntary movements. While these movements are caused by a relative excess amount of levodopa, dyskinesia can occur at a dose that is otherwise therapeutic and does not necessarily represent an overdose. Because levodopa is more likely than other antiparkinson drugs to cause dyskinesia, approaches to managing troublesome dyskinesia often begin with adjusting the levodopa regimen or the use of adjunctive medications such as dopamine agonists. Another option with some evidence is the addition of amantadine to the patient's current levodopa regimen. The 2006 American Academy of Neurology guidelines for the treatment of Parkinson disease with motor fluctuations and dyskinesia recommend considering the use of amantadine in patients with Parkinson disease and motor fluctuations to reduce dyskinesia (Level C). The authors concluded that amantadine IR (given as 100 mg BID) is possibly effective in reducing dyskinesia based on one Class II study. The guidelines have not been updated to include Gocovri or Osmolex ER.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Gocovri was approved by the FDA in September 2017 for the treatment of dyskinesia in patients with Parkinson disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications.

Osmolex ER was approved by the FDA in February 2018 for the treatment of Parkinson disease and for the treatment of drug-induced extrapyramidal reactions in adult patients.

Rationale/Source

Gocovri was assessed in two randomized, double-blind, placebo-controlled efficacy trials, EASE LID (n=121) and EASE LID 3 (n=75), in patients with Parkinson disease and dyskinesia. In both studies, the primary efficacy endpoint was the change in total score of the Unified Dyskinesia Rating Scale (UDysRS) between baseline and Week 12. Patients in EASE LID and EASE LID 3 were treated with a stable dose of levodopa, with 32% of patients on levodopa monotherapy; 54% of patients and 44% of patients were treated with concomitant dopamine agonists and/or MAO-B inhibitors, respectively. In EASE LID and EASE LID 3, a significant decrease in mean UDysRS total score (reduction in dyskinesia) was observed at Week 12 in patients treated with Gocovri compared with placebo (EASE LID treatment difference: -7.9; P=0.0009 and EASE LID 3 treatment difference: -14.4; P<0.0001). Gocovri has not been compared with amantadine IR or other active treatments in clinical trials.

No clinical efficacy studies were undertaken for approval of Osmolex ER. The efficacy of Osmolex ER is based upon bioavailability studies comparing Osmolex ER with IR amantadine.

References

1. Gocovri [package insert]. Adamas Pharma, LLC. Emeryville, CA. September, 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.
3. UpToDate. Motor Fluctuations and dyskinesia in Parkinson disease.
4. Express Scripts Prior Authorization policy on Amantadine Extended-Release Drugs. 06/2018

5. Osmolex ER [package insert]. Vertical Pharmaceuticals. Bridgewater, NJ. July 2018

Policy History

Original Effective Date: 03/21/2018
Current Effective Date: 12/14/2020

03/01/2018	Medical Policy Committee review
03/21/2018	Medical Policy Implementation Committee approval. New policy.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Changed policy name to "Extended release amantadine products" and added new drug, Osmolex ER.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. No change to coverage.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 11/2021

*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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.