BlueCross BlueShield of Alabama

Amantadine Extended Release Prior Authorization with Quantity Limit Program Summary

This prior authorization applies to Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE
The intent of the Amantadine Extended Release (ER) Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling.

TARGET AGENTS
Gocovri™ (amantadine)
Osmolex ER™ (amantadine)

QUANTITY LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Limit
Gocovri (amantadine) extended release			
68.5 mg capsule	73200010107020	M, N, O, or Y	1 capsule
137 mg capsule	73200010107040	M, N, O, or Y	2 capsules
Osmolex ER (amantadine) extended release			
129 mg tablet	73200010107520	M, N, O, or Y	1 tablet
193 mg tablet	73200010107530	M, N, O, or Y	1 tablet
258 mg tablet	73200010107540	M, N, O, or Y	1 tablet

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
The targeted agent will be approved when ALL of the following are met:

1. ONE of the following:
   - A. The requested agent is Gocovri AND ALL of the following:
     - i. The patient has a diagnosis of Parkinson's disease
       AND
     - ii. The requested agent will be used for the treatment of dyskinesia
       AND
     - iii. The patient is currently receiving levodopa therapy

   OR
   - B. The requested agent is Oxmolex ER AND ONE of the following:
     - i. The patient has a diagnosis of Parkinson's disease
       OR
     - ii. The patient has a diagnosis of drug-induced extrapyramidal reaction AND the following:
       - a. The prescriber has assessed and adjusted, if applicable, any medications known to cause extrapyramidal symptoms

   OR
   - C. The patient has another FDA approved diagnosis for the requested agent

   AND
2. The prescriber is a specialist (e.g. neurologist) or the prescriber has consulted with a specialist
   AND
3. ONE of the following:
   - A. The patient has tried and failed immediate release amantadine

OR

B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to immediate release amantadine that is not expected to occur with the requested agent

AND

4. The patient does NOT have any FDA labeled contraindication(s) to the requested agent

AND

5. ONE of the following
   A. The requested quantity (dose) is NOT greater than the program quantity limit

      OR

   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit

         AND

      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose

         AND

      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

   OR

   C. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit

         AND

      ii. The requested quantity (dose) is greater than the FDA labeled dose

         AND

      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

FDA APPROVED INDICATION AND DOSAGE[1,6]

Agent	Indications	Dose
Gocovri™ (amantadine) extended-release capsule	Treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications	Initial dose: 137 mg orally daily at bedtime, after one week increase to recommended daily dose Maintenance dose: 274 mg orally daily at bedtime
Osmolex ER™ (amantadine) extended-release tablet	Treatment of Parkinson's disease Treatment of drug-induced extrapyramidal reactions in adult patients	Initial dose: 129 mg orally once daily in the morning Dosage may be increased in weekly intervals to a maximum daily dose of 322 mg once daily in the morning

CLINICAL RATIONALE

Parkinson's disease (PD) is a chronic, progressive movement disorder that affects at least one–half million patients across the United States.[2] PD belongs to a group of conditions called motor system disorders, which are the results of loss of dopamine-producing brain cells. The four primary symptoms of PD are tremor, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination. PD usually affects those over the age of 60. Early symptoms of PD are subtle and occur gradually and may progress more quickly in some people than others. Other symptoms may include depression and other emotional changes; difficulty swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions. Diagnosis is based on medical history and neurological examinations.[3]

There is no cure for PD and management of PD requires consideration of patient's symptoms, age, stage of disease, degree of functional disability, and level of physical activity and production. Treatment options can be divided into pharmacologic, non-pharmacologic, and surgical therapy. Pharmacologic treatment of PD can be further divided into neuroprotective and symptomatic therapy. Treatment of advanced PD, particularly the complications associated with long-term levodopa therapy, and management of the comorbid problems including daytime sleepiness, hallucinations, and psychosis. Agents available for the treatment of PD motor symptoms include levodopa, dopamine agonists, monoamine oxidase (MAO) B inhibitors, anticholinergic agents, amantadine, and catechol-O-methyl transferase (COMT) inhibitors.[4]

Levodopa or a dopamine agonist can be used as initial therapy for patients who require symptomatic therapy for PD. Levodopa is the most effective drug for the symptomatic treatment of PD and is the first choice if symptoms, particularly related to bradykinesia, become intrusive or troublesome. Dopamine agonists may be employed as either monotherapy in early PD or in combination with other antiparkinsonian drugs for the

treatment of more advanced disease. They are ineffective in patients who do not show response to levodopa. Dopamine agonists may be associated with fewer motor fluctuations than levodopa and there is a higher incidence of levodopa related dyskinesia in young-onset PD. Given this, dopamine agonists are reasonable initial therapy for younger patients (age <65 years) and with levodopa in older patients (age >65 years).[4]

Although initially effective, dopaminergic therapies are eventually complicated by motor fluctuations and dyskinesia. Motor fluctuations include off time, where periods of when the medication wears off and the PD symptoms appear. Dyskinesia is defined as drug-induced involuntary movements including chorea and dystonia. The motor complications can impair the quality of life and cause significant disability. Risk factors for motor complications include younger age at onset of PD, disease severity, higher levodopa dosage, and longer disease duration. Motor complications are usually addressed with levodopa adjustments and the addition of adjunctive medications. Motor fluctuations and dyskinesia can be resistant to medical therapy.[5]

Anticholinergic drugs are most useful as monotherapy in patients under 70 years of age with disturbing tremor who do not have significant bradykinesia or gait disturbance. They also may be useful in patients with more advanced disease who have persistent tremor despite treatment with levodopa or dopamine agonists. Their use in older or demented individuals and those without tremor is strongly discouraged.[4]

Amantadine may be considered for patients with PD with motor fluctuations in reducing dyskinesia.[5] Amantadine is a relatively weak antiparkinsonian drug with low toxicity that is most useful in treating younger patients with early or mild PD and perhaps later when dyskinesia becomes problematic. However, toxic side effects are more likely in older patients.[3] Amantadine in divided doses of 200 to 400 mg a day may reduce the intensity of levodopa-related dyskinesia and motor fluctuations in patients with PD. Although the published randomized trials on amantadine in advanced PD are limited by serious methodological flaws and small numbers of patients, experience has shown that individual patients with advanced PD who have motor fluctuations and dyskinesia can benefit dramatically, at least for a while, from the addition of amantadine to a regimen of levodopa. Furthermore, a randomized controlled trial of 56 patients with PD and levodopa-related dyskinesia found that withdrawal compared with continuation of amantadine led to significant worsening of dyskinesia.[4]

Safety[1]
Gocovri
The most common adverse reactions reported in >10% of GOCOVRI-treated patients and more frequently than on placebo were: hallucination, dizziness, dry mouth, peripheral edema, constipation, falls, and orthostatic hypotension.

The overall rate of discontinuation because of adverse reactions for GOCOVRI-treated patients was 20%, compared to 8% for placebo-treated patients. Adverse reactions that led to treatment discontinuation in at least 2% of patients were hallucination (8% GOCOVRI vs. 0% placebo), dry mouth (3% GOCOVRI vs. 0% placebo), peripheral edema (3% GOCOVRI vs. 0% placebo), blurred vision (GOCOVRI 3% vs. 0% placebo), postural dizziness and syncope (GOCOVRI 2% vs. 0% placebo), abnormal dreams (GOCOVRI 2% vs. 1% placebo), dysphagia (GOCOVRI 2% vs. 0% placebo), and gait disturbance (GOCOVRI 2% vs. 0% placebo).

Gocovri is contraindicated in patients with end-stage renal disease (i.e., creatinine clearance below 15 mL/min/1.73 m^2). There are several warning and precautions within FDA approved label including suicidality and depression, hallucinations/psychotic behavior, dizziness,

orthostatic hypotension, withdrawal-emergent hyperpyrexia, compulsive behavior, and somnolence.

Osmolex ER
The most common adverse reactions reported in ≥5% of patients at the recommended dosage of immediate-release amantadine were nausea, dizziness/lightheadedness, and insomnia.

The following serious adverse reactions are described in the Osomolex ER labeling:
- Falling Asleep During Activities of Daily Living and Somnolence
- Suicidality and Depression
- Hallucinations/Psychotic Behavior
- Dizziness and Orthostatic Hypotension
- Withdrawal-Emergent Hyperpyrexia and Confusion
- Impulse Control/Compulsive Behaviors.

Osmolex ER is contraindicated in patients with end-stage renal disease (i.e., creatinine clearance below 15 mL/min/1.73 m^2).

REFERENCES

1. Gocovri prescribing information. Adamas Pharma, Inc. August 2017.
2. National Institute of Neurological Disorders and Stroke. Focus on Parkinson's Disease Research. www.ninds.nih.gov.
3. American Academy of Neurology. Parkinson's Disease. American Academy of Neurology Foundation. 2017. Accessed at: http://patients.aan.com/disorders/?event=view&disorder_id=1029. Accessed on February 21, 2017.
4. Tarsy, Daniel, MD, Hurtig, Howard, MD, Dashe, John, MD, PhD. Pharmacologic Treatment of Parkinson's Disease. UpToDate. Topic 4896, Version 32.0. Last updated August 2017.
5. Pahwa, R, MD, et al. Practice Parameters: Treatment of Parkinson Disease With Motor Fluctuations and Dyskinesia (An Evidenced Based Review). *Neurology*. April 11, 2006: 66 (7); 983-995.
6. Osmolex ER prescribing information. Vertex Pharmaceuticals LLC. February 2018.