BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

KYNMOBI™ (apomorphine) sublingual Generic Equivalent (if available)

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 prior authorization 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:** Kynmobi (apomorphine) sublingual and/or generic equivalent (if available) 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 acute, intermittent "off" episodes while receiving stable dose of concurrent levodopa-based therapy that is to be continued

4. Individual has at least one (and up to a maximum of 5) well-defined early morning "OFF" episode per day with a total daily "OFF" time duration of 2-hours or more during the waking day

5. Individual has Stage III or less on the modified Hoehn and Yahr scale in the "ON" state

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **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

7. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. Individual does not have severe and end-stage renal disease (CrCl < 30 mL/min)

9. Individual does not have severe hepatic impairment (Child-Pugh Class C)

10. There are **NO** FDA-label contraindications such as:
    a. Concurrent use with 5HT3 antagonists (such as Lotronex (alosetron), Anzemet (dolasetron), granisetron, ondansetron, Aloxi (palonosetron))
    b. Hypersensitivity to sodium metabisulfite

Initial approval duration: 6 months
Maximum of 5 doses per day (verify number of OFF episodes per week)
Maximum single dose of 30 mg (verify the dosage required per episode)

- **Criteria for continuation of coverage (renewal request):** Kynmobi (apomorphine) sublingual and/or generic equivalent (if available) 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 **TWO** of the following:
    a. Achieved and maintains reduced "off" time of at least 1 hour during waking hours
    b. Achieved and maintains increased "on" time of at least 1 hour without troublesome dyskinesia
    c. Able to perform most of activities of daily living

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. 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 effect such as:
        i. Falling asleep during activities of daily living and daytime somnolence
        ii. Severe oral mucosal irritation, ulceration, or stomatitis
        iii. Impulse control issues or compulsive behavior
        iv. Falling
        v. Hallucinations, delusions, disorientation, aggression, agitation, delirium, or confusion
        vi. Hemolytic anemia
        vii. Prolonged QTc and torsades de pointes

6. Individual does not have severe and end-stage renal disease (CrCl < 30 mL/min)

7. Individual does not have severe hepatic impairment (Child-Pugh Class C)

Renewal duration: 12 months
Maximum of 5 doses per day (verify number of OFF episodes per week)
Maximum single dose of 30 mg (verify the dosage required per episode)

- 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:

Kynmobi (apomorphine) sublingual is indicated for the acute, intermittent treatment of “off” episodes (“end-of-dose wearing off” and unpredictable “on/off” episodes) in patients advanced with Parkinson's disease (PD). Apomorphine has been studied in patients with PD who were Hoehn and Yahr Stage III or less in the “on” state, and who were all receiving stable dose of concurrent levodopa.

Motor fluctuations of PD are alterations between periods of being "on," during which the patient experiences a positive response to medication, and being "off," during which the patient experiences a reemergence of the Parkinson symptoms suppressed during the "on" state. There are several types of motor fluctuations, including the following: "wearing off" phenomenon, characterized by the re-emergence of parkinsonian motor problems as the effect of levodopa diminishes near the end of the dose interval; unpredictable "off" periods, with no obvious relationship between the time of levodopa administration and the appearance of "off" episodes; freezing of gait; failure of the "on" response, with lack of an "on" response following a dose of levodopa; and acute akinesia, which manifests as a sudden severe exacerbation of PD including an akinetic state that lasts for several days and does not respond to treatment with antiparkinson medication.

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Apomorphine is a non-ergoline dopamine agonist with high *in vitro* binding affinity for the dopamine D4 receptor, and moderate affinity for the dopamine D2, D3, and D5, and adrenergic α1D, α2B, α2C receptors. The precise mechanism of action of apomorphine as a treatment for "off" episode associated with PD is unknown, although it is believed to be due to stimulation of post-synaptic dopamine D2-type receptors within the caudate-putamen in the brain.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Hoehn and Yahr Scale and the Modified Hoehn and Yahr Scale:

Stage	Hoehn and Yahr Scale	Modified Hoehn and Yahr Scale
0	No signs of disease	No signs of disease
1	Unilateral involvement only, usually minimal or no functional disability	Unilateral involvement only
1.5	--	Unilateral and axial involvement
2	Bilateral or midline involvement without impairment of balance	Bilateral involvement without impairment of balance
2.5	--	Mild bilateral disease with recovery on pull test
3	Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent	Mild to moderate bilateral disease; some postural instability; physically independent
4	Severely disabling disease; still able to walk or stand unassisted	Severely disability; still able to walk or stand unassisted
5	Confined to bed or wheelchair unless aided	Wheelchair bound or bedridden unless aided
Hoehn M, Yahr M: Parkinsonism: onset, progression and mortality. Neurology 1967; 17 (5):427-442		

Resources:

Kynmobi (apomorphine) sublingual product information, revised by Sunovion Pharmaceuticals, Inc. 05-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 18, 2022. **Discontinued 07-03-2023**

Liang TW. 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. Literature current through June 2024. Topic last updated February 26, 2024. Accessed July 11, 2024.

Spindler MA. Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated April 05, 2024. Accessed July 11, 2024.

Chou KL. Clinical manifestations of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated March 14, 2024. Accessed July 11, 2024.