BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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KYNMOBI™ (apomorphine) sublingual

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Kynmobi (apomorphine) sublingual is considered ***medically necessary*** and will be approved when **ALL** of 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. 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. Documented failure, contraindication per FDA label, intolerance, to **ALL** of 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. Individual does not have severe and end-stage renal disease (CrCl < 30 mL/min)
  8. Individual does not have severe hepatic impairment (Child-Pugh Class C)
  9. 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
  10. There are no significant interacting drugs

  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 is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

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2. Individual's condition responded while on therapy
    a. Response is defined as **BOTH** of the following:
        i. Achieved and maintains a reduction in "off" time of at least 1 hour
        ii. 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
    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

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

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

7. There are no significant interacting drugs

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 a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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

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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.

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:

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. 05-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on July 28, 2021.

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 Accessed on July 26, 2021.

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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. Accessed on July 26, 2021.
Olanow CW, Factor SA, Espay AJ, Hauser RA, Shill HA, Isaacson S, et al.: Apomorphine sublingual film for off episodes in Parkinson's disease: a randomized, double-blind, placebo-controlled phase 3 study. Lancet Neurol 2020; 19: 135–144. Accessed July 16, 2020. Re-reviewed July 28, 2021.

ClinicalTrials,gov. NCT02469090. Efficacy, safety, and tolerability study of APL-130277 for acute treatment of OFF episodes in patients with Parkinson's disease. Last updated November 20, 2018. Bethesda (MD): National Library of Medicine (US). Accessed 07-16-20. Available from: http://clinicaltrials.gov. Accessed July 16, 2020. Re-reviewed July 28, 2021.