Clinical Policy: Apomorphine (Apokyn)

Reference Number: ERX.SPA.439
Effective Date: 09.01.21
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Apomorphine (Apokyn®) is a non-ergoline dopamine agonist.

FDA Approved Indication(s)
Apokyn is indicated for acute, intermittent treatment of hypomobility, "off`" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) associated with advanced Parkinson's disease.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Apokyn is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Parkinson's Disease (must meet all)**:**

1. Diagnosis of Parkinson's disease;
2. Prescribed by or in consultation with neurologist;
3. Prescribed concurrently with an anti-Parkinson agent (e.g., levodopa/carbidopa, dopamine agonists [e.g., ropinirole], catechol-O-methyl transferase [COMT] inhibitors [e.g., tolcapone], monoamine oxidase type B [MAO-B] inhibitors [e.g., rasagiline]);
4. Member is experiencing hypomobility episodes at the end of the dosing interval or is experiencing unpredictable hypomobility ("on/off") episodes (*see Appendix D*);
5. Dose does not exceed 0.6 mL per injection, 5 injections per day, or 2 mL per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Parkinson's Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 0.6 mL per injection, 5 injections per day, and 2 mL per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
COMT: catechol-O-methyl transferase
FDA: Food and Drug Administration
MAO-B: monoamine oxidase type B

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant use with $5HT_3$ antagonists, including antiemetics (e.g., ondansetron, granisetron, dolasetron, palonosetron) and alosetron
  - Hypersensitivity/allergic reaction to apomorphine or to any of the excipients, including a sulfite (i.e., sodium metabisulfite); angioedema or anaphylaxis may occur
- Boxed warning(s): none reported

Appendix D: General Information

- Based on reports of profound hypotension and loss of consciousness when apomorphine was given to patients receiving ondansetron, the concomitant use of apomorphine with drugs of the 5-HT_3 antagonist class is contraindicated. These drugs should not be used to prevent or treat apomorphine-induced nausea and vomiting.
- Apomorphine induces nausea and vomiting. Patients should be pretreated with trimethobenzamide 300 mg orally three times a day for three days prior to beginning apomorphine therapy. The manufacturer recommends continuing trimethobenzamide for the first two months of apomorphine therapy. However, the length of concomitant therapy in trials varied
- Off time/episodes represent a return of Parkinson's disease symptoms (bradykinesia, rest tremor or rigidity) when the L-dopa treatment effect wears off after each dosing interval.
- Parkinson's disease symptoms, resulting from too little levodopa (L-dopa), are in contrast with dyskinesia which typically results from too much L-dopa. The alterations between "on" time (the time when Parkinson's disease symptoms are successfully suppressed by L-dopa) and "off" time is known as "motor fluctuations".
- The addition of carbidopa to L-dopa prevents conversion of L-dopa to dopamine in the systemic circulation and liver.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Parkinson's disease	0.2 mL SC initial test dose. If patient tolerates and responds, starting dose should be 0.2 mL used on an as needed basis to treat "off" episodes. If needed, may increase dose by 0.1 mL (1 mg) increments every few days	0.6 mL/dose, max of 2 mL/day

VI. Product Availability

Multi-dose glass cartridge solution for injection: 30 mg/3 mL (10 mg/mL) with a multiple-dose pen injector

VII. References

1. Apokyn Prescribing Information. Louisville, KY: US WorldMeds, LLC.; April 2020. Available at: www.apokyn.com. Accessed March 23, 2021.
2. Kynmobi Prescribing Information. Marlborough, MA: Sunovion Pharmaceuticals Inc.; May 2020. Available at www.kynmobi.com. Accessed March 23, 2021.
3. 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.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thompson Healthcare. Updated periodically. Accessed March 23, 2021.
5. Suchowersky O, Reich S, Perlmutter J, et al. Practice Parameter: diagnosis and prognosis of new onset Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;66: 968-975.
6. Clarke CE, Patel S, Ives N, et al.; Clinical effectiveness and cost-effectiveness of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's disease: a large pragmatic randomized controlled trial (PD REHAB). Southampton (UK): NIHR Journals Library; 2016 Aug. No. 20.63.
7. Fox SH, Katzenschlager R, Lim S, et al. International Parkinson and Movement Disorder Society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Movement Disorders; 2018. Published online in Wiley Online Library. DOI: 10.1002/mds.27372.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.23.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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