Clinical Policy Title:	apomorphine
Policy Number:	RxA.14
Drug(s) Applied:	Apokyn®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

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

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 with carbidopa/levodopa therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
apomorphine (Apokyn®)	Parkinson's disease	Initial dose: 0.2 mL (2mg) SC injection. 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. Doses must be separated by at least 2 hours.	0.6 mL per dose, 2 mL per day

Dosage Forms

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

Clinical Policy

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

I. Initial Approval Criteria

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

1. Diagnosis of Parkinson's disease;
2. Patient is experiencing hypomobility episodes at the end of the dosing interval or is experiencing unpredictable hypomobility ("on/off") episodes with documentation of number and frequency of "off" episodes;
3. Dose initiation was or will be supervised by a healthcare provider;

4. Documentation that at least one other agent has been added to carbidopa/levodopa (e.g. dopamine agonist, COMT inhibitor, or MAO-B inhibitor) to reduce number and frequency of "off" episodes;
5. Treatment with a concomitant antiemetic such as trimethobenzamide (not including 5HT3 antagonists) beginning 3 days prior to initial dose;
6. Member is not concurrently taking a 5HT3 antagonist (e.g. ondansetron);
7. Dose does not exceed 0.6 mL per injection, 5 injections per day, or 2 mL per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Member is not concurrently taking a 5HT3 antagonist (e.g. ondansetron);
4. If request is for a dose increase, new dose does not exceed 0.6 mL per injection, 5 injections per day, or 2 mL per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
SC: subcutaneous
MAO-B: monoamine oxidase type B
COMT: catechol-O-methyltransferase
5HT3: 5-hydroxytryptamine type 3 (serotonin type 3 receptor)

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Kynmobi® (apomorphine HCL)	10 mg to 30 mg sublingually per dose as needed for "off" episodes. Doses should be separated by at least 2 hours.	30 mg per dose and 5 doses per day
Inbrija® (inhaled levodopa)	2 capsules (84 mg) inhaled.	84 mg per dose and 5 doses per day not to exceed 420 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant use of Apokyn® with 5HT3 antagonists, including antiemetics (e.g., ondansetron, granisetron, dolasetron, palonosetron) and alosetron.
  - With hypersensitivity/allergic reaction to apomorphine or to any of the excipients of Apokyn®, 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-HT3 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.

References

1. Apokyn® Prescribing Information. Louisville, KY: US WorldMeds, LLC; April 2020. Available at: www.apokyn.com. Accessed January 25, 2021.
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. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 25, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Updated References.	05/2020	05/21/2020
Policy was reviewed: 1. Policy title table was updated. 2. Background section updated to include use of carbidopa/levodopa. 3. Dosing regimen section was updated for clarity and to include information for dose separation. 4. Initial approval criteria I.A.2 was updated to include documentation for “off” episode specifics. Criteria I.A.3 to I.A.6 were added to reflect additional limitations. 5. Continued therapy criteria II.A.1 was rephrased to	01/25/2021	03/09/2021

"Currently receiving medication that has been authorized by RxAdvance...". Criteria II.A.3 was added to consider contraindication. 6. Approval duration for commercial plans was added for initial and continued approval criteria. 7. Appendix A information was added. 8. Appendix B information was added. 9. Reference reviewed and updated.		