Clinical Policy: Apomorphine (Apokyn Apokyn NXT, Onapgo)

Reference Number: PA.CP.PHAR.488
Effective Date: 07/2020
Last Review Date: 04/2025

Description
Apomorphine (Apokyn ®, Apokyn® NXT, Onapgo™) is a non-ergoline dopamine agonist.

FDA Approved Indication(s)
Apokyn and Apokyn NXT are 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.

Onapgo is indicated for the treatment of motor fluctuations in adults 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

It is the policy of PA Health & Wellness® that apomorphine, Apokyn, Apokyn NXT, and Onapgo are **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. Member is experiencing hypomobility episodes at the end of the dosing interval or is experiencing unpredictable hypomobility ("on/off") episodes (*see Appendix D*);
4. Failure of at least two anti-Parkinson agents from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated:*
   a. MAO-B inhibitor: rasagiline;
   b. COMT inhibitor: entacapone Comtan®/Stalevo®), tolcapone;
   c. Dopamine agonist: ropinirole/ropinirole ER, pramipexole/pramipexole ER;
   **Prior authorization may be required for the above agents*
5. Prescribed in combination with levodopa/carbidopa;
6. For Apokyn or Apokyn NXT requests, member must use generic apomorphine, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed the following (a or b):
   a. Apokyn, Apokyn NXT (i, ii, and iii):
      i. 0.6 mL (6 mg) per injection;
      ii. 5 injections per day;
      iii. 2 mL (20 mg) per day;
   b. Onapgo: 98 mg (1 cartridge) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. For Apokyn or Apokyn NXT requests, member must use generic apomorphine, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Apokyn, Apokyn NXT (i, ii, and iii):
      i. 0.6 mL (6 mg) per injection;
      ii. 5 injections per day;
      iii. 2 mL (20 mg) per day;
   b. Onapgo: 98 mg (1 cartridge) per day.

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 policies – PA.CP.PMN.53

IV. Appendices/General Information

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

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
COMT Inhibitors		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
carbidopa/ levodopa/ entacapone (Stalevo®)	PO: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.	1,200 mg/day of levodopa (divided doses)
entacapone (Comtan®)	PO: 200 mg with each dose of levodopa/carbidopa	1,600 mg/day (divided doses)
tolcapone (Tasmar®)	PO: 100 mg 3 times daily, as adjunct to levodopa/carbidopa	600 mg/day
MAO-B Inhibitors		
rasagiline (Azilect®)	PO: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5 mg once daily; may increase to 1 mg once daily based on response and tolerability.	1 mg/day
Dopamine Agonists		
pramipexole (Mirapex®)	PO: Initial dose: 0.125 mg 3 times daily, increase gradually every 5 to 7 days; maintenance (usual): 0.5 to 1.5 mg 3 times daily	4.5 mg/day (divided doses)
pramipexole ER (Mirapex® ER)	PO: Initial dose: 0.375 mg once daily; increase gradually not more frequently than every 5 to 7 days to 0.75 mg once daily and then, if necessary, by 0.75 mg per dose	4.5 mg/day
ropinirole (Requip®)	PO: Recommended starting dose: 0.25 mg 3 times/day. Based on individual patient response, the dosage should be titrated with weekly increments: Week 1: 0.25 mg 3 times/day; total daily dose: 0.75 mg; week 2: 0.5 mg 3 times/day; total daily dose: 1.5 mg; week 3: 0.75 mg 3 times/day; total daily dose: 2.25 mg; week 4: 1 mg 3 times/day; total daily dose: 3 mg. After week 4, if necessary, daily dosage may be increased by 1.5 mg/day on a weekly basis up to a dose of 9 mg/day, and then by up to 3 mg/day weekly to a total of 24 mg/day.	24 mg/day (divided doses)
ropinirole ER (Requip® ER)	PO: Initial dose: 2 mg once daily for 1 to 2 weeks, followed by increases of 2 mg/day at weekly or longer intervals based on therapeutic response and tolerability	24 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 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 as long as necessary to control nausea and vomiting, and generally no longer than two months.. 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

Drug Name	Dosing Regimen	Maximum Dose
Apomorphine (Apokyn, Apokyn NXT)	The initial test dose should be 0.1 mL (1 mg) or 0.2 mL (2 mg) SC. If patient tolerates the initial test dose, and responds adequately, the starting dose should be the same as the test dose 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 (6 mg)/dose, 5 injections/day, max of 2 mL (20 mg)/day
Apomorphine (Onapgo)	Onapgo is administered as a SC infusion with the Onapgo pump. The daily dosage is determined by individualized patient titration and is composed of a continuous dosage and as needed extra dose(s). Continuous dosage: The recommended initial continuous dosage is 1 mg/hr. Titrate the continuous dosage, as needed, in 0.5 mg/hr to 1 mg/hr increments. Dose adjustments may be made	Continuous dosage: 6 mg/hour for up to 16 hours/day Total daily dosage, including extra doses: 98 mg/day

Drug Name	Dosing Regimen	Maximum Dose
	daily, or at longer intervals, through the titration process. The maximum continuous dosage is 6 mg/hr administered over the waking day (e.g., 16 hours). Extra dose: The extra dose may be titrated to clinical response and tolerability with adjustments in increments of 0.5 mg or 1 mg. Subsequent extra doses may be between 0.5 mg and 2 mg. Administer no more than 3 extra doses per day over 16 hours with at least 3 hours between extra doses. If 3 extra doses are routinely required during daily infusion, consider further adjustment of the continuous dosage. The maximum recommended total daily dosage, including extra doses, is 98 mg during the waking day (e.g., 16 hours).	

VI. Product Availability

Drug Name	Availability
Apomorphine (Apokyn)	Single-patient-use cartridge: 30 mg/3 mL (10 mg/mL) with a multiple-dose pen injector
Apomorphine (Apokyn NXT)	Single-patient-use disposable prefilled pen: 30 mg/3 mL (10 mg/mL)
Apomorphine (Onapgo)	Single-dose cartridge: 98 mg/20 mL (4.9 mg/mL)

VII. References

1. Apokyn Prescribing Information. Rockville, MD: MDD US Operations.; January 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/021264s025lbl.pdf. Accessed February 13, 2025.
2. Onapgo Prescribing Information. Rockville, MD: MDD US Operations; February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/214056s000lbl.pdf. Accessed February 13, 2025.
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 February 13, 2025.
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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.
8. Pringsheim T, Day GS, Smith DB, et al. Dopaminergic therapy for motor symptoms in early Parkinson disease practice guideline summary: a report of the AAN guideline subcommittee. Neurology 2021;97:942-957.
9. Trenkwalder C, Chaudhuri KR, Garcia Ruiz PJ, et al. Expert consensus group report on the use of apomorphine in the treatment of Parkinson's disease – Clinical practice recommendations. Parkinsonism & Related Disorders 2015;21(9):1023-1030.
10. Katzenschlager R, Poewe W, Rascol O, et al. Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicenter, double-blind, randomized, placebo-controlled trial. The Lancet Neurology 2018;17(9):749-759.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0364	Injection, apomorphine hydrochloride, 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	07/2020
3Q 2021 annual review: added criteria for new formulation Kynmobi; references reviewed and updated.	07/2021
3Q 2022 annual review: no significant changes; updated language in section I from "or" to "and" for dose limits; references reviewed and updated.	07/2022
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
Remove Kynmobi since on PA Statewide PDL	01/2024
3Q 2024 annual review: no significant changes; references reviewed and updated.	07/2024
RT4: added new formulations Apokyn NXT and Onapgo to policy; added generic apomorphine to policy requiring PA; for Apokyn or Apokyn NXT, added must use generic apomorphine language; revised "prescribed concurrently with an anti-Parkinson agent" to "prescribed concurrently with levodopa/carbidopa"; added requirement for trial and failure of at least two anti-Parkinson agents from different therapeutic classes, unless clinically significant adverse events are experienced or all are contraindicated.	04/2025