Clinical Policy: Apomorphine (Apokyn, Kynmobi)

Reference Number: CP.PHAR.488
Effective Date: 09.01.20
Last Review Date: 08.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Apomorphine (Apokyn®, Kynmobi®) 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.

Kynmobi is indicated for the acute, intermittent treatment of "off" episodes in patients with 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 health plans affiliated with Centene Corporation® that Apokyn and Kynmobi 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. 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 the following (a or b):
   a. Apokyn (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. Kynmobi (i and ii):
      i. 30 mg (1 film) per dose;
      ii. 5 films per day.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months (Kynmobi), 6 months or to the member's renewal date, whichever is longer (Apokyn)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Parkinson's Disease (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations *(refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Apokyn (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. Kynmobi (i and ii):
      i. 30 mg (1 film) per dose;
      ii. 5 films per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months (Kynmobi), 6 months or to the member's renewal date, whichever is longer (Apokyn)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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 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)	0.2 mL (2 mg) SC initial test dose. If patient tolerates and responds, starting dose should be 0.2 mL (2 mg) 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 (Kynmobi)	10 to 30 mg per dose sublingually as needed; separated by at least 2 hours	30 mg/dose, max of 5 doses/day

VI. Product Availability

Drug Name	Availability
Apomorphine (Apokyn)	Multi-dose glass cartridge solution for injection: 30 mg/3 mL (10 mg/mL) with a multiple-dose pen injector
Apomorphine (Kynmobi)	Sublingual film: 10 mg, 15 mg, 20 mg, 25 mg, 30 mg

VII. References

1. Apokyn Prescribing Information. Louisville, KY: US WorldMeds, LLC.; June 2022. Available at: www.apokyn.com. Accessed April 20, 2023.
2. Kynmobi Prescribing Information. Marlborough, MA: Sunovion Pharmaceuticals Inc.; September 2022. Available at: www.kynmobi.com. Accessed April 20, 2023.
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 May 17, 2023.
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.
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.

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
J8499	Kynmobi Film (all strengths); Prescription drug, oral, non chemotherapeutic, nos

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy CP.PCH.14 (to be retired); removed Commercial line of business and added Medicaid; added criteria for new formulation Kynmobi; added neurologist prescriber requirement; added requirement that Apokyn is prescribed concurrently with an anti-Parkinson agent; references reviewed and updated.	06.02.20	08.20
3Q 2021 annual review: no significant changes; added HCPCS codes; references revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	03.23.21	08.21
Added Commercial line of business	12.17.21	02.22
3Q 2022 annual review: no significant changes; updated language in section I from "or" to "and" for dose limits; separated approval duration for Apokyn and Kynmobi for Commercial line of business; references reviewed and updated.	04.06.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.20.23	08.23

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.