Subject: Apokyn (apomorphine)	Original Effective Date: 02/27/15
Policy Number: MCP-241	Revision Date(s): 12/15/2016; 6/22/2017

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP document and provide the directive for all Medicare members.

SUMMARY

This policy addresses the coverage of **Apokyn (apomorphine)** for the acute, intermittent treatment of hypomobility, off episodes associated with **advanced Parkinson's disease** when appropriate criteria are met.

Summary of Disease

Parkinson's disease (PD) is a neurologic disease characterized by tremor, rigidity, and bradykinesia.[B,C] PD is a neurodegenerative disorder caused by a loss of dopaminergic neurons in the substantia nigra, as well as other dopaminergic and non-dopaminergic areas of the brain.[1] PD is a common disorder with an estimated prevalence of up to 329 per 100,000.[1] Because PD is progressive and results in significant disability 10 to 15 years after onset, the financial and social burden of PD is substantial, particularly with the aging population.

The cardinal motor features of PD are tremor, bradykinesia, and rigidity.[3] Several types of medications are used in the symptomatic treatment of PD, such as levodopa/carbidopa, dopamine agonists, monoamine oxidase type B (MAO-B) inhibitors (e.g., selegiline), amantadine, and anticholinergic agents.[B,3] Initial dopaminergic therapy usually provides good control of motor symptoms, but is eventually complicated by motor fluctuations including "off" time (return of PD symptoms when medication effect wears off) and dyskinesia (drug-induced involuntary movements).[3] Medications that may be used to reduce off time include entacapone (catechol-O-methyltransferase inhibitor), MAO-B inhibitors, dopamine agonists, and apomorphine.[3]

Parkinson's disease is a progressive neurodegenerative disorder associated with the loss of dopaminergic cells (cells which produce dopamine) in the substantia nigra region of the brain. Dopamine is a neurotransmitter that the brain uses to help direct and control movement. In Parkinson's disease, these dopamine producing nerve cells break down, dopamine levels drop, and brain signals directing movement become abnormal. The incidence and prevalence of PD increases with age. The average age of onset is approximately 60 years. Onset in persons younger than 40 years is relatively uncommon. Patients notice symptoms related to progressive bradykinesia (slow movements and reflexes), rigidity, and gait difficulty eventually leading to dementia.

Treatment Goals
There is no cure for Parkinson's disease, however pharmacological agents, physical therapy, and surgical interventions can help control symptoms and improve quality of life. The central objective of using Parkinson's disease medication is to control or manage motor symptoms.

There are no established disease-modifying or neuroprotective therapies.[9]

Pharmacologic Agents/Conventional Therapy
There are a wide number of symptomatic treatments that are available for PD, including pharmacological therapy, surgical procedures, physiotherapy, occupational therapy and other support services. All of these treatments can have a significant impact on improving an affected individual's quality of life and should be available. However, despite the increase in non-pharmacological treatments, an individual with Parkinson's becomes more reliant on their medication to maintain their ability to function as the disease progresses. A balance between the side effects of the medication and the benefit often becomes more challenging with time.

The current pharmacological treatment options for Parkinson's disease include levodopa/carbidopa, dopamine agonists (bromocriptine, pramipexole, ropinirole), or cathechol-O-methyltransferace (COMT) inhibitors (entacapone, tolcapone). Initial treatments often include low doses of carbidopa/levodopa or a dopamine agonist.[B] Levodopa is still the most effective medication available for treatment of motor symptoms in PD.[D] Patients will eventually need levodopa in their therapeutic regimen as their PD progresses. Levodopa is a first-line medication for PD.[B,D] The combination of carbidopa and levodopa (Sinemet, Sinemet CR, Parcopa, etc) is the most effective agent available for the treatment of motor symptoms. However, its early use is associated with earlier development of dyskinesias (abnormal involuntary movements). Levodopa-carbidopa (*Sinemet*, *Sinemet CR*, *Parcopa*, etc) can be used first-line, especially in elderly patients.[B,D]

This period of good control lasts approximately five years with levodopa, after which motor fluctuations (e.g., wearing off, on-off phenomenon) and dyskinesias develop.[4,5] Eventually the drugs are not as effective in many patients since Parkinson's is a progressive disease. Suboptimal control can be managed by increasing the dose of the dopamine agonist or levodopa; however this approach increases the chance of dopamine agonist side effects (e.g., neuropsychiatric side effects, sedation, sleep attacks).[4] It can also cause or worsen dopamine-associated dyskinesias.[4,5]

As the disease progresses, however, therapy becomes more complex, requiring dosage adjustments, incorporation of multiple medications, and the use of rescue treatments. Initial therapy generally becomes less effective and additional motor complications develop, including dyskinesias and motor fluctuations.[3] "On time" refers to the time when medication is effectively controlling the disease's symptoms, and "off time" occurs when disease symptoms recur gradually or abruptly. As PD progresses, on time becomes shorter, causing complications that can impair quality of life.[6] Within 4 to 5 years of treatment with standard Parkinson's drug treatments, many patients experience episodes of hypomobility (e.g., inability to rise from a chair, to speak, or to walk). The episodes can occur toward the end of a dosing interval with standard medications (so-called "end-of-dose wearing off") or at unpredictable times (spontaneous "on/off" periods). The intensity, duration and frequency of "off" episodes vary for each patient. Therefore most clinicians prefer to use a combination of agents rather than increase the dose of a single agent after the initial "honeymoon."[4]

Dopamine agonists are another option for the treatment of PD. These agents act directly on dopamine receptors and are associated with a lower incidence of dyskinesias.[8] There are 2 subclasses of dopamine agonists: Non-ergot-derived agonists (pramipexole and ropinirole); the ergot-derived drugs (bromocriptine, cabergoline, lisuride and pergolide). Apomorphine is not used first-line and is considered in the section 'Adjuvant therapy for more advanced Parkinson's disease', below.

Apokyn (apomorphine) is a non-ergot dopamine agonist indicated for the acute treatment of "off '' episodes associated with advanced PD.[a-e]

CLASSIFICATION: Neurological Agents; Antiparkinsonian Agents; Dopamine Receptor Agonists, Non-Ergot

FDA INDICATIONS

Apokyn (apomorphine) is indicated for the acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing-off" and unpredictable "on-off" episodes) associated with advanced Parkinson disease. Apokyn has been studied as an adjunct to other Parkinson disease medications.

Available as: 10 mg/mL (3-mL cartridges, 5 cartridges per carton).

FDA Approved: April 20, 2004

Black Box Warnings: *None at the time of this writing*

RECOMMENDATIONS/COVERAGE CRITERIA

Apokyn (apomorphine) may be authorized for members who meet **ALL** of the following criteria **[ALL]**

1. Prescriber specialty [ONE]

- ❒ Prescribed by, or in consultation with, a board-certified neurologist, or physician who has expertise in movement disorders. Submit consultation notes if applicable.

2. Diagnosis/Indication [ONE]

Clinical documentation required (includes clinical notes from the member's medical records including any applicable labs and/or tests, supporting the diagnosis**):**

- ❒ Diagnosis of **advanced** Parkinson's disease (defined as Stages II to IV of the 5-stage Hoehn and Yahr scale in clinical trials)
  - ➢ *In Apokyn clinical trials, 75% of patients were classified as Hoehn and Yahr Stage II or III, and approximately 22% as Stage IV.*[a-e]
- ❒ Member is experiencing acute intermittent hypomobility (defined as "off" episodes characterized by muscle stiffness, slow movements, or difficulty starting movements) despite optimized oral PD therapy. Clinical documentation required (includes clinical notes from the member's medical records including any applicable labs and/or tests, supporting the diagnosis).

3. Age/Gender/Other restrictions [ALL]

N/A

4. Step/Conservative Therapy/Other condition Requirements [ALL: A, B]

- ❒ Currently receiving therapy with anti-Parkinson's agents [e.g., levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa, etc); dopamine agonists (pramipexole [Mirapex, generics, Mirapex ER], ropinirole [Requip, generics, Requip XL]); MAO-B inhibitors, anticholinergic agents)]
  - ➢ *Apomorphine is intended to be used as adjunctive therapy with other anti-Parkinson agents.*[a]

- ❒ Documented failure, intolerance or contraindication to the following agents:
    - ❍ Dopamine agonist: i.e. pramipexole [Mirapex, generics, Mirapex ER], ropinirole [Requip, generics, Requip XL]
    - ❍ Catechol-O-methyl transferase (COMT) inhibitor: i.e. entacapone [Comtan], tolcapone ; Tasmar
    - ❍ Monoamine oxidase type B (MAO-B) inhibitors: i.e. selegiline, generics, Eldepryl, Zelapar, rasagiline [Azilect]

- ❒ Member is **NOT** concurrently taking a 5-HT3 antagonist [i.e., Zofran® (ondansetron), Kytril® (granisetron), Anzemet® (dolasetron), Aloxi® (palonosetron), and Lotronex® (alosetron)]. This is an absolute contraindication to the use of Apokyn.
  NOTE: Molina Staff: Verify pharmacy claims data within the last 30 days, OR for new members to Molina Healthcare, confirm in medical chart history
    - ➢ *Apokyn must not be administered with the 5HT3 antagonists [i.e., Zofran® (ondansetron), Kytril® (granisetron), Anzemet® (dolasetron), Aloxi® (palonosetron), and Lotronex® (alosetron)] since the combination may result in profound hypotension and altered consciousness.*[a-e]

- ❒ Trimethobenzamide will be started 3 days *prior* to beginning treatment.
  NOTE: Trimethobenzamide is the only antiemetic that has been studied and can be used with Apokyn.
    - ➢ *Apokyn should not be initiated without concomitant antiemetic since it 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.*

5. Contraindications/Exclusions/Discontinuations

Authorization will <u>not</u> be granted if ANY of the following conditions apply [ANY]

- ❒ Non-FDA approved indications
- ❒ Hypersensitivity to apomorphine or components of its formulation (notably sodium metabisulfite)
- ❒ Concomitant use with a serotonin 5-HT3-type receptor antagonists (such as ondansetron, granisetron, solasetron, palonosetron or alosetron) which could result in profound hypotension and loss of conciousness

<u>Exclusions</u> [ANY]

- ❒ Test dose of Apokyn (apomorphine) caused clinically significant orthostatic hypotension
    - ➢ *Initiation of apomorphine treatment requires a test dose procedure to determine dosage titration. If the patient has not received an apomorphine injection in more than 1 week, re-institute by implementing the initial test dosage and titration instructions recommended by the manufacturer.*
- ❒ Prescribed as monotherapy as a first-line agent

6. Labs/Reports/Documentation required [ALL]

All documentation for determination of medical necessity must be submitted for review. Prescriber to submit medical records and specific labs, chart notes, and documentation as indicated in the criteria above. Letters of support and/or explanation are often useful, but are not sufficient documentation unless ALL specific information required by this MCP is included.

CONTINUATION OF THERAPY

Apokyn (apomorphine) may be authorized for continuation of therapy if meet **ALL** of the following criteria are met: **[ALL]**

1. Initial Coverage Criteria

- ❑ Member currently meets ALL initial coverage criteria

2. Compliance

- ❑ Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance) [MOLINA MEDICAL/PHARMACY REVIEWER TO VERIFY]

  NOTE: Therapy may be discontinued due to poor adherence upon recommendation of the Molina Medical Director when adherence < 85% has been demonstrated in at least two months during the course of therapy

3. Labs/Reports/Documentation required [ALL APPLICABLE]

- ❒ Documentation of **stabilization or improvement** from Apokyn (apomorphine) therapy as evaluated by a **neurologist** (e.g., an improvement in motor function)

- ❒ Member is **NOT** concurrently taking a 5-HT3 antagonist [i.e., Zofran® (ondansetron), Kytril® (granisetron), Anzemet® (dolasetron), Aloxi® (palonosetron), and Lotronex® (alosetron)]. This is an absolute contraindication to the use of Apokyn.
  NOTE: Molina Staff: Verify pharmacy claims data within the last 30 days, OR for new members to Molina Healthcare, confirm in medical chart history
  - ➢ *Apokyn must not be administered with the 5HT3 antagonists [i.e., Zofran® (ondansetron), Kytril® (granisetron), Anzemet® (dolasetron), Aloxi® (palonosetron), and Lotronex® (alosetron)] since the combination may result in profound hypotension and altered consciousness.*[a-e]

4. Discontinuation of Treatment [ANY]

Discontinue treatment if ANY of the following conditions applies: [ANY]

- ❑ Intolerable adverse effects or drug toxicity
- ❑ Persistent and uncorrectable problems with adherence to treatment
- ❑ Poor response to treatment as evidenced by physical findings and/or clinical symptoms
- ❑ Contraindications/Exclusions to therapy
  - ❍ Non-FDA approved indications
  - ❍ Hypersensitivity to apomorphine or components of its formulation (notably sodium metabisulfite)
  - ❍ Concomitant use with a serotonin 5-HT3-type receptor antagonists (i.e. ondansetron, granisetron, solasetron, palonosetron or alosetron) which could result in profound hypotension and loss of conciousness

<u>Exclusions</u> [ANY]

- ❒ Test dose of Apokyn (apomorphine) caused clinically significant orthostatic hypotension
  - ➢ *Initiation of apomorphine treatment requires a test dose procedure to determine dosage titration. If the patient has not received an apomorphine injection in more than 1 week, re-institute by implementing the initial test dosage and titration instructions recommended by the manufacturer.*
- ❒ Prescribed as monotherapy as a first-line agent

ADMINISTRATION, QUANTITY LIMITATIONS, AND AUTHORIZATION PERIOD

1. Recommended Dosage [ALL]

- ❒ The recommended starting dose of Apokyn (apomorphine hydrochloride) is 0.2 mL (2 mg) for subcutaneous use only.
  - ➢ *Do not inject intramuscularly or intravenously. May lead to crystallization and thrombus formation.*

- ❒ The recommended maximum dose of Apokyn (apomorphine hydrochloride) is 0.6 mL (6 mg)
  - ➢ *In the apomorphine development program, most patients studied responded to 0.3 to 0.6 mL. Apokyn should be administered in response to an off episode, up to 5 times per day.*
  - ➢ *In clinical studies, Apokyn was used on average 3 times per day.*
  - ➢ *Apokyn should be titrated to a levodopa-equivalent efficacy level. In clinical studies, levodopa dosage was not predictive of apomorphine dose requirements.*
  - ➢ *Apokyn should not be initiated without use of the concomitant antiemetic Tigan (trimethobenzamide HCl). In the apomorphine development program, 50% of patients were able to discontinue trimethobenzamide on average 2 months after starting Apokyn.*

2. Authorization Limit [ALL]

- ❒ Quantity limit: 6 mg as a single dose according to the prescribing information.

- ❒ Dispensing limit: 4 cartons of 3-mL cartridges, 5 cartridges per carton (60mL per month). Only a 1-month supply may be dispensed at a time[a-e]

- ❒ Duration of initial authorization: 3 months

- ❒ Continuation of treatment: Re-authorization for continuation of treatment is required every 6 months to determine continued need based on documented positive clinical response

3. Route of Administration [ALL]

- ❒ Apokyn is considered a **self-administered agent** for subcutaneous administration only.

- ❒ If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare. Self-administered medications may not be dispensed for self-administration and billed through the medical benefit by a provider; they must be dispensed through a participating pharmacy.

COVERAGE EXCLUSIONS

Apokyn (apomorphine hydrochloride) is considered **experimental and investigational** for all other diagnosis that is not an FDA-approved indication or included in 'Coverage Criteria' section above and is not a covered benefit.

SUMMARY OF EVIDENCE/POSITION STATEMENTS

- Parkinson disease symptoms are due to a deficiency of the brain chemical dopamine, the main drug treatments help increase dopamine levels in the brain.[4,5] Levodopa, which has been the cornerstone of parkinson disease treatment for many years, is metabolized by neurons to dopamine; however these neurons degenerate over time and thus disease progression results in decreased predictability of dopamine levels. However, many patients receiving long-term levodopa therapy experience dyskinesia and motor fluctuations, such as "wearing-off" and "on-off" episodes.[8,9] Several other classes of medications are also used for the treatment of PD, including monoamine oxidase inhibitors (MAOIs) and catechol-O-methyltransferase (COMT) inhibitors.

- The prevalence of "off" episodes is significant and increases with the length of time the patient is on levodopa therapy. A meta-analysis by Ahlskog and Muenter found that up to 50% of PD patients treated with levodopa for 5 years or more experienced off episodes.[10] Ahlskog and Muenter further found that approximately 70% of PD patients treated with levodopa for 9 years or more experienced off episodes.[10]

- Dopamine agonists, nonergot dopamine agonists, MAO-B inhibitors, and catechol O-methyltransferase (COMT) inhibitors may be used as adjunctive therapy to decrease off time. COMT inhibitors tolocapone (Tasmar) and entacapone (Comtan) are administered with levodopa and prolong symptom relief. The COMT inhibitor tolcapone (Tasmar) is rarely prescribed because it is associated with fatal hepatotoxicity.[6]

- Carbidopa/levodopa (Sinemet), nonergot dopamine agonists, or monoamine oxidase-B inhibitors should be used for initial treatment of Parkinson disease. Evidence Rating A (consistent, good-quality patient-oriented evidence)[6,E,B]

- Nonergot dopamine agonists, catechol O-methyltransferase inhibitors, or monoamine oxidase-B inhibitors should be added to levodopa to treat motor complications in advanced Parkinson disease. Evidence Rating A (consistent, good-quality patient-oriented evidence) [6,E,B,3,2]

- A Cochrane review that indirectly compared these drugs concluded that dopamine agonists were most effective at reducing off time.[2]

- In clinical studies, Apokyn has been studied as an adjunct to other medications, not in place of them. Patients who use Apokyn should continue to receive their appropriate daily dose of oral PD medications.[a]

Pivotal Trials

The approval of subcutaneous apomorphine was based on data from 3 short-term, randomized, controlled clinical trials. These trials enrolled patients with Parkinson disease for an average of 11.3 years who were being treated with levodopa and at least 1 other agent, usually a dopamine agonist.[a]

FDA approval of Apokyn (apomorphine hydrochloride) for the treatment of acute Parkinsonian hypomobility was based on three randomized, controlled studies, enrolling a total of 108 subjects, all of whom had advanced Parkinson's disease (mean disease duration = 11.3 years) and were being treated with L-dopa and at least one other agent, usually a dopamine agonist. Improvement in motor function on the Unified Parkinson's Disease Rating Scale (UPDRS) was the primary endpoint of all three studies. The trials enrolled a combined total of 108 subjects, including 29 (one trial) who had never received apomorphine products (the remaining 79 subjects had experience internationally with apomorphine).

Results showed that Apokyn was significantly efficacious in ending hypomotor episodes and markedly improving UPDRS motor scores (> 20 points mean improvement for all trials) 20 minutes after dosing, compared with placebo ($p<0.0001$ for all trials). 98% of all trial subjects began antiemetic treatment with Tigan (trimethobenzamide) 3 days prior to treatment; roughly 50% were able to eventually discontinue Tigan while continuing Apokyn treatment (mean time to discontinuation = 2 months).

- One parallel, double-blind, placebo-controlled study randomized 29 patients with advanced Parkinson disease to subcutaneous apomorphine or placebo. All patients had 2 or more hours of "off" time (mean, 5.9 hours) despite oral therapy. Patients in this study had no prior exposure to apomorphine, and therefore received an antiemetic (trimethobenzamide) for 3 days prior to beginning apomorphine. The antiemetic was eventually discontinued in 50% of apomorphine-treated patients, on average 2 months after initiating apomorphine. Hypomobility was assessed in an office setting after Parkinson disease medications were withheld overnight. Patients in a hypomobile state received either pH-matched vehicle placebo or 2 mg apomorphine. At 2-hour intervals, patients were redosed with increasing doses (4, 6, 8, or 10 mg), until a therapeutic response approximately equivalent to the patient's response to their usual levodopa dose was observed (or until 10 mg apomorphine or placebo equivalent was given). At 20 minutes, a therapeutic response equivalent to their usual response to levodopa was achieved in 18 of 20 apomorphine recipients. The average apomorphine dose was 5.4 mg. None of the 9 placebo-treated patients achieved a therapeutic response. The mean reduction from baseline for Unified Parkinson Disease Rating Scale (UPDRS) part III (motor examination) scores at the best dose was 23.9 points (62%) for apomorphine and 0.1 points(1%) for placebo ($P < 0.0001$).[a,7] During 1 month of outpatient therapy, patients elected to administer an average of 2.5 doses per day. The mean percentage of outpatient injections resulting in abortion of an "off" episode was 95% for apomorphine and 23%for placebo ($P < 0.001$). "Off" time per day was reduced by 2 hours in the apomorphine-treated patients ($P =0.02$).[7]

- Another trial was a crossover study randomizing 17 patients who had been treated with apomorphine for at least 3 months. Patients received their usual morning doses of Parkinson disease medications and were followed until hypomobility occurred. When hypomobility occurred they received a single dose of subcutaneous apomorphine (at their usual dose) or placebo. The average apomorphine dose was 4 mg. The mean change from baseline in UPDRS part III score at 20 minutes was 20 points for apomorphine and 3 points for placebo ($P < 0.0001$).[a]

- A third study was a single-dose, parallel study enrolling 62 patients who had been receiving apomorphine for at least 3 months. Patients were randomized to receive apomorphine or placebo. Patients received apomorphine at their usual dose, placebo at a volume matching their usual apomorphine dose, apomorphine at their usual dose plus 2 mg (0.2 mL), or placebo at a volume matching their usual apomorphine dose plus 0.2 mL. All patients received their usual morning Parkinson disease medications and were followed until hypomobility occurred, at which time they received the randomly assigned medication. The mean change from baseline in UPDRS part III score at 20 minutes was 24.2 points in the combined apomorphine groups and 7.4 points in the combined placebo groups ($P < 0.0001$). Mean change in UPDRS part III scores did not differ between the patients treated with their usual apomorphine dose (24 points) and those receiving a higher dose (25 points); however, adverse effects occurred more frequently in the group receiving the higher dose.[a]

References:

- *Data on file, Clinical Study Report APO401. Ipsen Pharma, Boulogne-Billancourt, France.*
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- *Data on file, Clinical Study Report APO302. Ipsen Pharma, Boulogne-Billancourt, France.*
- *Dewey RB Jr, Hutton JT, LeWitt PA, Factor SA. A randomized, double-blind, placebo-controlled trial of subcutaneously injected apomorphine for parkinsonian off-state events. Arch Neurol. 2001;58:1385-1392.*

DEFINITIONS

- "On" period: Periods when the patient experiences a good response to medication
- "Off" period: Periods when benefit from Parkinson disease medications wears off and symptoms reemerge (wearing-off–type motor fluctuations)

APPENDIX 1: Hoehn and Yahr Scale

Two rating scales are commonly used to stage PD. The Hoehn and Yahr staging scale[a] was developed and was published in 1967 as a method of designating the severity of Parkinsonism to assess progression and severity of the disease, and is still is a widely used clinical rating scale.[c] Among its advantages are that it is simple and easily applied. It captures typical patterns of progressive motor impairment which can be applied whether or not patients are receiving dopaminergic therapy. Progression in HY stages has been found to correlate with motor decline, deterioration in quality of life, and neuroimaging studies of dopaminergic loss. However, because of its simplicity and lack of detail, the scale is not comprehensive. It is also limited by its focus on issues of unilateral versus bilateral disease and the presence or absence of postural reflex impairment, thereby leaving other specific aspects of motor deficit unassessed. Also it does not provide any information concerning non-motor aspects of PD. A modified version of HY is sometimes used.

It has five stages: from I (unilateral signs are present) to V (patient confined to a bed or chair unless assisted). The Unified Parkinson's Disease Rating Scale (UPDRS) is a more comprehensive and complex PD assessment tool. The three main sections of the UPDRS (Mentation, Behavior, and Mood; Activities of Daily Living; and Motor Examination) contain 42 patient interview questions in broad categories, with a higher total score representing worse overall disability (a score of 0 = no disability).[c]

There are other scales for grading the severity of Parkinsonism: The Unified Parkinson's Disease Rating Scale (UPDRS), the modified Columbia Scale, The Webster Scale, The Schwab and England Disability Scale, the Northwestern University Disability Scale and numerous others, each having its own proponents and usefulness.

The purpose of both the UPDRS and Hoehn and Yahr scale is to provide a snapshot of the patient's condition at the time point at which they are used, and are not meant to suggest a timeframe of disease progression.[d] Importantly, the score of the UPDRS can vary within the same patient hour to hour dependent on correlation of medication schedule with the assessment interval.

In Apokyn (apomorphine)clinical trials, 75% of patients were classified as Stage II or III on the Hoehn and Yahr scale, and 22% of the patients were Stage IV.

Hoehn & Yahr Stage	% (n)[1]	Description[3]
II	26.2 (142)	Bilateral involvement but no postural abnormalities
III	49.0 (266)	Bilateral involvement with mild postural imbalance; patient leads independent life
IV	21.9 (119)	Bilateral involvement with postural instability; patient requires substantial help

References:

a. *Hoehn MM, Yahr MD. Parkinsonism: onset, progression, and mortality. Neurology. 1967; 17:427–42.*
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CODING INFORMATION: THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS A COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

CPT	Description
NA	

HCPCS	Description
J0364	Apokyn (apomorphine)

ICD-9	Description [For dates of service prior to 10/01/2015]
332	Parkinson's disease

ICD-10	Description [For dates of service on or after 10/01/2015]
G20	Parkinson's disease

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Package Insert, FDA, Drug Compendia

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Clinical Trials, Definitions, Peer-Reviewed Publications

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