WHY APOKYN?

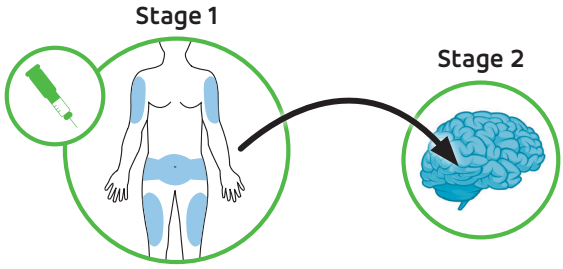
APOKYN®
apomorphine hydrochloride injection

Oral levodopa is unpredictable and unreliable[1,2]

- GI dysfunction affects more than 70% of PD patients[3,4]

APOKYN offers a rapid and reliable subcutaneous delivery system[5,6]

- Subcutaneous apomorphine is nearly 100% bioavailable[7,8]
- Bypasses GI issues and provides robust, levodopa-like effects[6]
- Patients don't need to worry about meal times



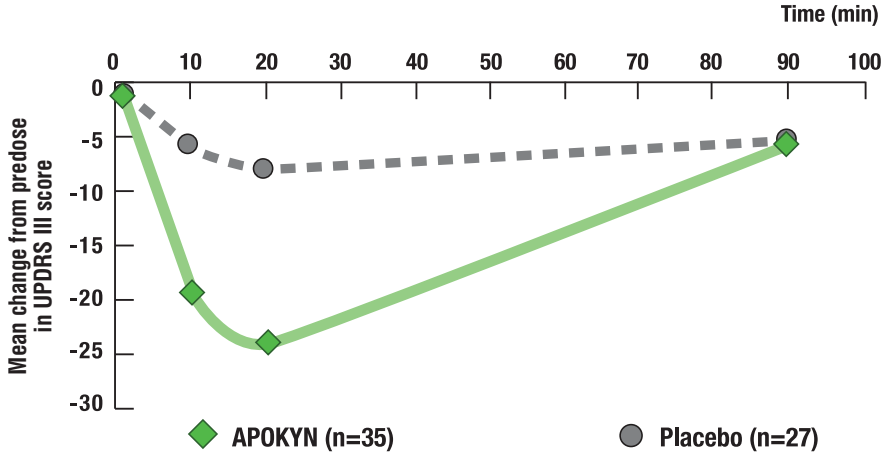
RAPID AND RELIABLE *ON*

APOKYN reverses 95% of *off* episodes[6]

APOKYN significantly improved motor function[5]

- 10 minutes after dosing: mean change of -19.9 points (p<.0001 vs placebo)
- 20 minutes after dosing: mean change of -24.2 points (p<.0001 vs placebo)

MEAN REDUCTION IN UPDRS* III MOTOR SCORES[5]



*UPDRS: Unified Parkinson's Disease Rating Scale

Study design: A prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter study in patients with advanced PD who experienced *off* episodes despite optimal oral therapy. Patients used APOKYN as acute, intermittent therapy on average for 14.5 months before the study. Patients were randomized to receive a single dose of APOKYN or placebo at the typically effective dose, or 0.2 mL higher than that dose, in response to an *off* episode that occurred ≥1 hour after a typical morning dose of oral PD therapy. Mean dose for the APOKYN-treated group was 0.45 mL.[5]

APOKYN 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's disease. APOKYN has been studied as an adjunct to other medications.

Please see Important Safety Information on reverse side and accompanying full Prescribing Information and Pen Instructions for Use/Patient Information.

Important Safety Information for Healthcare Providers

Contraindication: Concomitant use of APOKYN with $5HT_3$ antagonists is contraindicated based on reports of profound hypotension and loss of consciousness when apomorphine was administered with ondansetron.

Contraindication: APOKYN is contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients (notably sodium metabisulfite).

SC Injection: APOKYN should be administered by subcutaneous injection, NOT intravenously, because serious adverse events like thrombus formation and pulmonary embolism may occur. Patients and care partners must receive detailed instructions in the preparation and injection of doses, with particular attention paid to the correct use of the dosing pen.

Nausea and Vomiting: At recommended doses of apomorphine, severe nausea and vomiting can be expected. Therefore, trimethobenzamide hydrochloride should be started 3 days prior to the initial dose of APOKYN and continued as long as necessary to control nausea and vomiting, and generally no longer than two months. In clinical trials, 50% of patients (262/522) discontinued trimethobenzamide hydrochloride after 2 months of APOKYN.

Falling Asleep During Activities of Daily Living (ADL): There have been reports of patients treated with apomorphine subcutaneous injections who suddenly fell asleep while engaged in ADL. Patients should be advised not to drive or participate in potentially dangerous activities until it is known how APOKYN affects them. Patients should be continually reassessed for daytime drowsiness or sleepiness.

Symptomatic Hypotension: Dopamine agonists, including APOKYN, can cause hypotension, orthostatic hypotension, and syncope. Alcohol, antihypertensive medications, and vasodilating medications may potentiate the hypotensive effect of apomorphine. These adverse events occurred with initial dosing and long-term treatment. Whether hypotension contributes to other significant events seen (e.g., falls) is unknown.

Falls: Patients with Parkinson's disease (PD) are at risk of falling due to the underlying postural instability and concomitant autonomic instability seen in some patients with PD, and from syncope caused by the blood pressure lowering effects of the drugs used to treat PD.

Hallucinations / Psychotic-Like Behavior: APOKYN has been associated with new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior. This abnormal thinking and behavior can consist of paranoid ideation, delusions, hallucinations, confusion, disorientation, aggressive behavior, agitation and delirium.

Dyskinesias: APOKYN may cause dyskinesia or exacerbate pre-existing dyskinesia.

Intense Urges: Some people with PD have reported new or increased gambling urges, increased sexual urges, and other intense urges, while taking PD medicines, including APOKYN. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their care partners about the development of new or increased gambling urges, sexual urges, uncontrolled spending or other urges while being treated with APOKYN. Physicians should consider dose reduction or stopping the medication if a patient develops such urges while taking APOKYN.

Cardiac Events: *Coronary Events*—APOKYN reduces resting systolic and diastolic blood pressure and has the potential to exacerbate coronary (and cerebral) ischemia. Therefore, exercise caution when prescribing APOKYN for patients with known cardiovascular and cerebrovascular disease.

QT Prolongation—Caution is recommended when administering APOKYN to patients with increased risk of QT prolongation, such as those with hypokalemia, hypomagnesemia, bradycardia, or a genetic predisposition, or who use other drugs that prolong the QT/QTc interval.

Melanoma: Patients with Parkinson's disease have a higher risk of developing melanoma than the general population. Patients should be monitored for melanomas frequently when using APOKYN.

Adverse Events: The most common adverse events seen in controlled trials were yawning, drowsiness/somnolence, dyskinesias, dizziness/postural hypotension, rhinorrhea, nausea and/or vomiting, hallucinations/confusion and edema/swelling of extremities. Injection-site reactions, including bruising, granuloma, and pruritus, have been reported.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact US WorldMeds at 1-877-727-6596 (1-877-7APOKYN). You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the accompanying full Prescribing Information and Pen Instructions for Use/Patient Information.

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References: 1. Aquino CC, Fox SH. Clinical spectrum of levodopa-induced complications. *Mov Disord.* 2015;30(1):80–89. **2.** Stocchi F. The levodopa wearing off phenomenon in Parkinson's disease: pharmacokinetic considerations. *Expert Opin Pharmacother.* 2006;7(10):1399–1407. **3.** Heetun Z, Quigley EMM. Gastroparesis and Parkinson's disease: A systematic review. *Parkinsonism Relat Disord.* 2012;18:433–440. **4.** Marrinan S, Emmanuel AV, Burn DJ. Delayed gastric emptying in Parkinson's disease. *Mov Disord.* 2014;29(1):23–32. **5.** Pfeiffer RF, Gutmann L, Hull KL Jr, Bottini PB, Sherry JH; APO302 Study Investigators. Continued efficacy and safety of subcutaneous apomorphine in patients with advanced Parkinson's disease. *Parkinsonism Relat Disord.* 2007;13(2):93–100. **6.** Dewey RB, 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(9):1385–1392. **7.** APOKYN® (apomorphine hydrochloride, USP) [Prescribing Information]. Louisville, KY: US WorldMeds, LLC; 2017. **8.** Chaudhuri, KR, Clough C. Subcutaneous apomorphine in Parkinson's disease. *BMJ.* 1998;316:641.

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