



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

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Coverage Policy Number ..... 5001

Subject **Apomorphine (Apokyn™)**

## Table of Contents

Coverage Policy .....	1
General Background .....	2
Coding/Billing Information .....	2
References .....	3
Policy History.....	4

## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

CIGNA covers apomorphine (Apokyn™) as medically necessary for the treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) associated with Parkinson disease.

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to apomorphine (Apokyn™) therapy.

## FDA Approved Indications

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 disease. Apokyn has been studied as an adjunct to other Parkinson disease medications.

## FDA Recommended Dosing

The dose of Apokyn must be titrated on the basis of effectiveness and tolerance, starting at 0.2 mL and up to a maximum recommended dose of 0.6 mL. In the apomorphine development program, most patients studied responded to 0.3 to 0.6 mL. Apokyn is used prn 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.

## Drug Availability

Apokyn (10 mg/mL) containing apomorphine hydrochloride (as apomorphine hydrochloride hemihydrate), USP is supplied as a clear, colorless, sterile, solution in 3 mL cartridges. The 3 mL glass cartridges are used with a manual reusable, multiple dose injector pen. The pen can deliver doses up to 1.0 mL in 0.02 mL increments. The pen is provided in a package with six needles and a carrying case.

## General Background

### Pharmacology

Apomorphine is a non-ergoline dopamine agonist labeled for the acute treatment of “off” episodes associated with Parkinson Disease (PD). Apomorphine is also used as an alternative to levodopa to substantiate the diagnosis of PD. Apomorphine is thought to stimulate post-synaptic dopamine-2 (D<sub>2</sub>) receptors in the caudate-putamen of the brain. Apomorphine is rapidly and completely absorbed following subcutaneous administration. The mean volume of distribution of apomorphine is 218 L. Apomorphine is extensively metabolized via multiple pathways with only 0.3 % excreted renally unchanged. The average terminal elimination half-life is 40 minutes.

### Clinical Efficacy

Five clinical trials have established the clinical efficacy of apomorphine for rescue treatment of “off” episodes. The Unified Parkinson Disease Rating Scale (UPDRS) motor score improve significantly more from baseline with apomorphine (20–24.2 points) than placebo (0.1–7.4 points) and significantly more “off” episodes are aborted with apomorphine (95%) than placebo (23%). The amount of daily “off” time is significantly lower with apomorphine (303 minutes/day) compared with placebo (616 minutes/day). Apomorphine also reduces the severity of “off” periods compared to placebo. For the diagnosis of PD, levodopa/carbidopa may be preferred over apomorphine, since levodopa/carbidopa has a higher sensitivity and specificity.

A study to assess the efficacy of intermittent subcutaneous apomorphine (APO) as acute therapy for off episodes in advanced Parkinson disease (PD) patients who had previously received APO for 3 months was published in 2007. Patients (n=62) were randomized to receive double-blind treatment with APO at their typically effective dose (TED; APO), APO at their TED+0.2mL (2.0mg; APO+2), placebo at volume equal to their TED (PL), or placebo at volume equal to their TED+0.2mL (PL+2), for a single off episode. Significantly greater improvement in mean Unified PD rating scale motor scores was seen with pooled APO versus pooled placebo 20min after administration (-24.2 vs. -7.4; p<0.0001); the difference was also significant at 10min (p<0.0001). Overall adverse event incidence did not significantly differ between pooled APO and pooled PL. This study supports the long-term use of intermittent APO as effective acute therapy for off episodes in advanced PD patients.

### Adverse Reactions

The most common adverse events seen in controlled trials were yawning, dyskinesias, nausea and/or vomiting, somnolence, dizziness, rhinorrhea, hallucinations, edema, chest pain, increased sweating, flushing, and pallor.

The risk of profound hypotension and other serious adverse effects increases with concomitant use of apomorphine with serotonin type 3 receptor (5HT<sub>3</sub>) antagonists, antihypertensives, vasodilators, nitrates, or alcohol. Additive QT prolongation may occur if apomorphine is given with other drugs that prolong the QT interval. Concomitant therapy with dopamine antagonists may decrease apomorphine’s effectiveness. Levodopa’s duration of effect is increased when administered with apomorphine, although maximal effects are unchanged. Oral contraceptives may decrease the sedative effects of apomorphine.

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## Coding/Billing Information

**Note:** This section is not in use.

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## Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	2/15/2008	5001	Apomorphine (Apokyn™)

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