RXADVANCE
2 Park Central Drive
Southborough, MA 01772

# NEW DRUG APPROVAL

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| **Brand Name** | KYNMOBI™ |
| **Generic Name** | apomorphine hydrochloride |
| **Drug Manufacturer** | Sunovion Pharmaceuticals Inc. |

## New Drug Approval

KYNMOBI™ is a non-ergoline dopamine agonist indicated for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease.

FDA Approval Date: May 21, 2020

## Place in Therapy

### DISEASE DESCRIPTION & EPIDEMIOLOGY

Parkinson's disease is a condition that affects the brain, resulting in a progressive loss of coordination and movement. It is a progressive disease, which means symptoms get worse over time. This progression is very slow, and symptoms usually are visible after about 70 to 80 percent of the nerve cells have been lost.

Approximately 1.2 million people in the United States are predicted to have Parkinson's disease by the year 2030, according to the results of a large-scale study.

Overall estimated prevalence of Parkinson's disease in the U.S. population, according to the 2010 census, was 572 per 100,000. These estimates were higher in men than in women (667 versus 488), and values rose with age in both genders.

Data indicated that in 2010 about 680,000 individuals in the U.S. ages 45 and older had been diagnosed with the disease. Given the projected future growth of the population, the researchers predicted this number will rise to 930,000 cases in 2020, and to 1,238,000 by 2030.

Geographical analysis of the data showed that, for all regions except Olmsted County, Minnesota, and Northern California, the estimated numbers were in accordance with those retrieved from the Medicare database. For Olmsted County, 14-27% more cases of Parkinson's were identified in the study than in the Medicare data. In Northern California, the study indicated 30% more Parkinson's cases than in the Medicare data.

## Efficacy

The efficacy of KYNMOBI™ for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease was established in one randomized, double-blind, placebo-controlled, parallel-group study (Study 1; NCT02469090).

During the trial, patients were given either KYNMOBI™ or a placebo for 12 weeks, and could take the medication up to five times each day. The KYNMOBI™ treatment group showed a least-square mean improvement (i.e., reduction in score) of -11.1 points (95% CI: -14.0, -8.2), versus -3.5 points for the placebo group (95% CI: -6.1, -0.9).

## Safety

### ADVERSE EVENTS

Most common adverse reactions (incidence at least 10% in patients treated with KYNMOBI™ and with an incidence greater than placebo) were nausea, oral/pharyngeal soft tissue swelling, oral/pharyngeal soft tissue pain and paraesthesia, dizziness, and somnolence.

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## WARNINGS & PRECAUTIONS

- Nausea and vomiting may occur
- Falling asleep during activities of daily living and daytime somnolence may occur, discontinue KYNMOBI™ if occurs
- Syncope and hypotension/orthostatic hypotension may occur, monitor blood pressure
- Oral mucosal irritation may occur, which may require pausing or discontinuing treatment
- Falls may occur or increase
- May cause hallucinations and psychotic-like behavior
- May cause impulse control and impulsive behaviors; consider dose reduction or discontinuing KYNMOBI™ if occurs
- Withdrawal-emergent hyperpyrexia and confusion may occur with rapid dose reduction or withdrawal
- May prolong QTc and cause torsades de pointes or sudden death; consider risk factors prior to initiation

## CONTRAINDICATIONS

- KYNMOBI™ is contraindicated in patients with
  - Hypersensitivity to apomorphine or any of its ingredients including sodium metabisulfite
  - Concomitant use with 5-HT3 antagonists

# Clinical Pharmacology

## MECHANISMS OF ACTION

KYNMOBI™ is a non-ergoline dopamine agonist with high in vitro binding affinity for the dopamine D4 receptor, and moderate affinity for the dopamine D2, D3, and D5, and adrenergic α1D, α2B, α2C receptors. The precise mechanism of action of KYNMOBI™ as a treatment for “off” episodes associated with Parkinson's disease is unknown, although it is believed to be due to stimulation of post-synaptic dopamine D2-type receptors within the caudate-putamen in the brain.

# Dose & Administration

## ADULTS

10 mg to 30 mg per dose, administered sublingually, as needed, for the acute, intermittent treatment of “off” episodes. Doses should be separated by at least 2 hours. If a single dose of KYNMOBI™ is ineffective for a particular “off” episode, a second dose should not be given for that “off” episode; MAX single dose is 30 mg/dose and 5 doses/day.

## PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

## GERIATRICS

Clinical studies of KYNMOBI™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

## RENAL IMPAIRMENT

Mild-to-moderate impairment: No Dose adjustment required for Mild to moderate patient. Dosages adjustment. Avoid use of KYNMOBI™ in patients with severe and end-stage renal disease.

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### HEPATIC IMPAIRMENT

Severe Hepatic Impairment: Avoid use of KYNMOBI™ in patients with severe hepatic impairment.
Mild to moderate Hepatic Impairment: No dosage adjustment is required.

## Product Availability

### DOSAGE FORM(S) & STRENGTH(S)

Sublingual film: 10 mg, 15 mg, 20 mg, 25 mg, and 30 mg.