
When your patients taking IR CD/LD begin to experience motor fluctuations

# It's time to **MOVE ON** with RYTARY

The patient appearing in this piece was compensated for his services.

## Learn how Phil moved on with the proven efficacy of RYTARY.

Individual results may vary.

### INDICATION

RYTARY is a combination of carbidopa and levodopa indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.

### IMPORTANT SAFETY INFORMATION

**CONTRAINDICATIONS**

RYTARY is contraindicated in patients who are currently taking or have recently (within 2 weeks) taken a nonselective monoamine oxidase (MAO) inhibitor (e.g., phenelzine, tranylcypromine). Hypertension can occur if these drugs are used concurrently.

IR CD/LD, immediate-release carbidopa/levodopa.

**Please see additional Important Safety Information on adjacent pages and accompanying Full Prescribing Information.**

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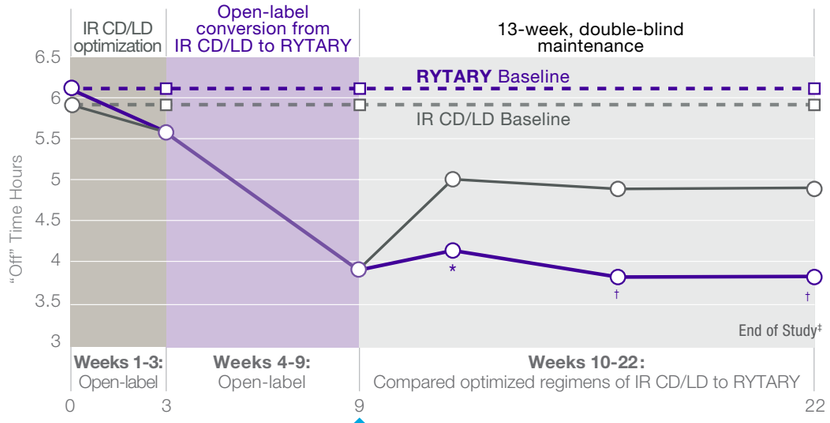
48.75 mg/195 mg • 61.25 mg/245 mg

In a **head-to-head** study vs optimized IR CD/LD in patients with motor fluctuations,

# RYTARY provided a significant reduction in "off" time with less dosing frequency[1,2]

**STUDY DESIGN** **Phase 3, double-blind study of RYTARY vs optimized IR CD/LD[1,2]**




**End of Week 9:** Patients were randomized either back to the optimized dose of IR CD/LD from the end of Week 3 or kept on RYTARY.

**"Off" time reduction was achieved with less dosing frequency[2]**

| | Mean reduction in "off" time from baseline | Average dosing frequency |
|---|---|---|
| Optimized IR CD/LD (n=192) | 1.0 hour | 5 times a day |
| RYTARY (n=201) | 2.2 hours | 3.6 times a day |

## Patient inclusion criteria

| | | |
|---|---|---|
| On a stable LD regimen of ≥400 mg/day for ≥4 weeks | Experienced a 3-day average of ≥2.5 hours "off" time per day | Allowed concomitant medications: dopamine agonists, selective MAO-B inhibitors, amantadine, anticholinergics |

*$P$=0.0004.
†$P$<0.0001.
‡Week 22 or early termination.

**Trial 2 study design:** Data are from a 22-week clinical trial consisting of a 3-week dose adjustment of current levodopa treatment prior to a 6-week conversion to RYTARY, which was followed by a 13-week, randomized, multicenter, double-blind, levodopa-containing active control, double-dummy, parallel-group trial. RYTARY and optimized IR CD/LD were compared in patients (N=471 enrolled; 393 randomized) on a stable regimen of ≥400 mg of levodopa per day for ≥4 weeks with a 3-day average of ≥2.5 hours of "off" time per day. Concomitant Parkinson's medications (dopamine agonists, selective MAO-B inhibitors, amantadine, and anticholinergics) were continued, provided the doses were stable for ≥4 weeks prior to screening.[1,2]

### Phil's treatment history:

- Initially, Phil was treated with **IR CD/LD**, plus pramipexole. The dosage started at 25/100 mg, 1 tablet 3 times a day, but was then increased to 1.5 tablets 4 times a day due to partial "on" and wearing "off"
- Despite the increasing IR CD/LD dose, he still experienced "off" time
- He switched to **RYTARY**, initially at 48.75/195 mg, 2 capsules 4 times a day, and needed a subsequent dose adjustment to 5 times a day, resulting in a reduction of "off" time

Individual results may vary.

**Please see additional Important Safety Information on adjacent pages and accompanying Full Prescribing Information.**



In the same **head-to-head** study vs optimized IR CD/LD,

# RYTARY demonstrated **2X the reduction** in "off" time[1,2]

**PRIMARY ENDPOINT** **Percentage of "off" time during waking hours: head-to-head vs optimized IR CD/LD (N=393)[1,2]**

**Optimized IR CD/LD**
(n=192)
Baseline* 36.0%
Week 22 or early termination 29.8%

**-6.2%**

**RYTARY**
(n=201)
Baseline* 36.9%
Week 22 or early termination 23.8%†

**-13.1%**

**Baseline**

**Improved**

Primary endpoint was "off" time as a percentage of waking hours at Week 22 (or at early termination).[2]

*Values collected immediately prior to first study treatment administration.
†$P$<0.0001 vs IR CD/LD.

The term "optimized" refers to the process of adjusting the dose and frequency of IR CD/LD as necessary to achieve optimum motor function.[2]

### Phil's current treatment status:

- Following the dose optimization on **RYTARY**, Phil had a reduction in "off" time with no morning or end-of-dose wearing "off"
- Currently, Phil experiences good days with **RYTARY**. He reports improvement in motor function with no dyskinesia
- Phil does experience additional symptoms at times, including tremors, stiffness, and feeling stuck and rigid

Individual results may vary.

## IMPORTANT SAFETY INFORMATION (continued)

### WARNINGS AND PRECAUTIONS

**Falling Asleep During Activities of Daily Living and Somnolence:** Patients treated with levodopa (a component of RYTARY) have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes resulted in accidents. Although many of these patients reported somnolence while on levodopa, some perceived that they had no warning signs (sleep attack), such as excessive drowsiness. Some of these events have been reported more than 1 year after initiation of treatment.

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In the same **head-to-head** study vs optimized IR CD/LD,

# RYTARY demonstrated significant improvements in motor symptoms[1,2]

**SECONDARY ENDPOINTS** | **Total "off" time during waking hours and total "on" time without troublesome dyskinesia**

## 2X REDUCTION IN "OFF" TIME

**during waking hours**
(2.2 hours* vs 1.0 hour with optimized IR CD/LD)[2]

**Baseline:** 6.1 hours with RYTARY vs 5.9 hours with IR CD/LD.
**Week 22‡:** 3.9 hours with RYTARY vs 4.9 hours with IR CD/LD.

## 2X INCREASE IN "ON" TIME

**without troublesome dyskinesia**
(1.8 hours† vs 0.8 hours with optimized IR CD/LD)[2]

**Baseline:** 10 hours with RYTARY vs 10.1 hours with IR CD/LD.
**Week 22‡:** 11.8 hours with RYTARY vs 10.9 hours with IR CD/LD.

**Patients also experienced improved ADL and motor functions measured through UPDRS Parts II and III scores§[2]**

ADL, activities of daily living; UPDRS, Unified Parkinson's Disease Rating Scale.
*$P$<0.0001 vs IR CD/LD; †$P$=0.0002 vs IR CD/LD; ‡Or early termination; §$P$<0.0001 vs IR CD/LD.

**Phil began to experience motor fluctuations with IR CD/LD. Switching to RYTARY gave him less "off" time and more "on" time without troublesome dyskinesia.**

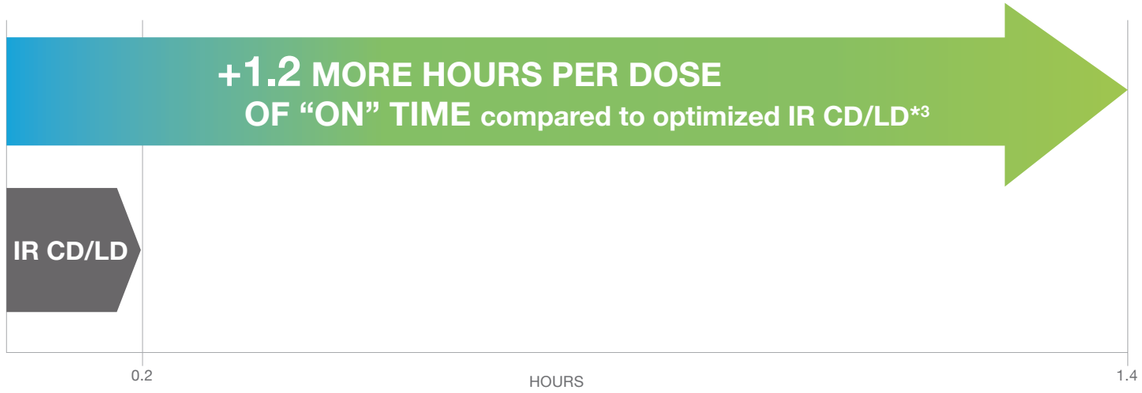




In a **post hoc analysis** from the same **head-to-head** study vs optimized IR CD/LD,

# RYTARY provided an increase in "on" time per ~~day~~ dose[3]

**POST HOC ANALYSIS** | **After dose optimization of RYTARY, patients experienced an increase of:**




**Baseline:** 2.17 hours per dose with RYTARY vs 2.24 hours per dose with IR CD/LD.
**End of study:** 3.55 hours per dose with RYTARY vs 2.38 hours per dose with IR CD/LD.

## RYTARY also demonstrated:

**+1.2 MORE HOURS PER DOSE OF "ON" TIME WITHOUT TROUBLESOME DYSKINESIA compared to optimized IR CD/LD*[3]**

**Baseline:** 2.10 hours per dose with RYTARY and 2.17 hours per dose with IR CD/LD.
**End of study:** 3.41 hours per dose with RYTARY and 2.29 hours per dose with IR CD/LD.

***"As my doctor and I had hoped, the timed-release features of RYTARY do afford me more effective coverage and more "on" time where my tremor is controlled. That's really important to me, especially when I'm giving presentations or playing sports with my friends."***

**—Phil, on RYTARY since 2015**

"On" time per dose was calculated as the number of hours per day spent in the "on" state (regardless of dyskinesia state) divided by the number of LD doses per day. "On" time without troublesome dyskinesia per dose was calculated as the number of hours "on" without troublesome dyskinesia (either "on" without dyskinesia or "on" with non-troublesome dyskinesia) per day divided by the number of LD doses per day.[3]

*The adjusted least square mean difference in increase (from baseline to end of study) in hours of "on" time and "on" time without troublesome dyskinesia was calculated using an ANCOVA model. $P$<0.0001 vs IR CD/LD.[3]

Data based on a post hoc analysis; study was not powered to evaluate duration of "on" time per dose, or "on" time without troublesome dyskinesia per dose, as a primary endpoint.

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# Comparable adverse reactions vs IR CD/LD[1]

**SAFETY** Most common adverse reactions in patients with advanced Parkinson's disease*

| | IR CD/LD (n=192) | | RYTARY (n=201) | |
|---|---|---|---|---|
| | Dose Conversion to RYTARY* | IR CD/LD Maintenance | Dose Conversion to RYTARY* | RYTARY Maintenance |
| Nausea | 6% | 2% | 4% | 3% |
| Headache | 3% | 2% | 5% | 1% |

*Adverse reactions occurring in at least 5% of patients treated with RYTARY and at a higher rate than optimized IR CD/LD.

- 5% of patients discontinued treatment due to adverse reactions during conversion to RYTARY[1]
- The most common adverse reactions leading to discontinuation during dose conversion were dyskinesia, anxiety, dizziness, and "on-off" phenomenon[1]

IMPORTANT SAFETY INFORMATION (continued)

**WARNINGS AND PRECAUTIONS (continued)**

**Withdrawal-Emergent Hyperpyrexia and Confusion:** A symptom complex that resembles neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction of, withdrawal of, or changes in dopaminergic therapy. Avoid sudden discontinuation or rapid dose reduction in patients taking RYTARY.

**Please see additional Important Safety Information on adjacent pages and accompanying Full Prescribing Information.**



# Important Safety Information

IMPORTANT SAFETY INFORMATION (continued)

**WARNINGS AND PRECAUTIONS (continued)**

**Cardiovascular Ischemic Events:** Cardiovascular ischemic events have occurred in patients taking RYTARY. In patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmias, cardiac function should be monitored in an intensive cardiac care facility during the period of initial dosage adjustment.

**Hallucinations/Psychosis:** There is an increased risk for hallucinations and psychosis in patients taking RYTARY. Because of the risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with RYTARY. In addition, medications that antagonize the effects of dopamine used to treat psychosis may exacerbate the symptoms of Parkinson's disease and may decrease the effectiveness of RYTARY.

**Impulse Control/Compulsive Behaviors:** Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking one or more of the medications, including RYTARY, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson's disease. Because patients may not recognize these behaviors as abnormal, specifically ask patients or their caregivers about the development of new or increased urges and consider a dose reduction or stopping the medication if a patient develops such urges while taking RYTARY.

**Dyskinesia:** RYTARY can cause dyskinesias that may require a dosage reduction of RYTARY or other medications used for the treatment of Parkinson's disease.

**Peptic Ulcer Disease:** Treatment with RYTARY may increase the possibility of upper gastrointestinal hemorrhage in patients with a history of peptic ulcer.

**Glaucoma:** Monitor intraocular pressure in patients with glaucoma after starting RYTARY.

**Drug Interactions:** Monitor patients taking selective MAO-B inhibitors and RYTARY. The combination may be associated with orthostatic hypotension. Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone, metoclopramide), isoniazid, and iron salts or multivitamins containing iron salts may reduce the effectiveness of RYTARY.

The most common adverse reactions (incidence ≥ 5% and greater than placebo) in early Parkinson's disease are nausea, dizziness, headache, insomnia, abnormal dreams, dry mouth, dyskinesia, anxiety, constipation, vomiting, and orthostatic hypotension; and in advanced Parkinson's disease are nausea and headache. Reported adverse reactions identified during post approval use of RYTARY include suicide attempt and ideation.

**OVERDOSAGE:**

The acute symptoms of levodopa/dopa decarboxylase inhibitor overdosage can be expected to arise from dopaminergic overstimulation. Doses of a few grams may result in CNS disturbances, with an increasing likelihood of cardiovascular disturbance (e.g., hypotension, tachycardia) and more severe psychiatric problems at higher doses.

**GENERAL DOSING AND ADMINISTRATION INFORMATION:**

See Full Prescribing Information for instructions for starting levodopa-naïve patients on RYTARY and converting patients from immediate-release carbidopa and levodopa to RYTARY (Table 1).

Avoid sudden discontinuation or rapid dose reduction of RYTARY.

The dosages of other carbidopa and levodopa products are not interchangeable on a 1:1 basis with the dosages of RYTARY.

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# It's time to **MOVE ON** with RYTARY

## Proven head-to-head efficacy vs optimized IR CD/LD

- **2X reduction in "off" time as a percentage of waking hours**
  Primary endpoint: 13.1% vs 6.2% reduction; *P*<0.0001 vs IR CD/LD[1,2]
- **2X increase in "on" time without troublesome dyskinesia**
  Secondary endpoint: 1.8 hours vs 0.8 hours; *P*=0.0002 vs IR CD/LD[1,2]
- **1.2 more hours of "on" time per ~~day~~ dose**
  Post hoc analysis: baseline: 2.17 hours vs 2.24 hours; end of study: 3.55 hours vs 2.38 hours; *P*<0.0001 vs IR CD/LD[3]

## Demonstrated safety profile

- Most common adverse reactions in clinical trials were nausea (3%) and headache (1%)[1]

**TO LEARN MORE ABOUT RYTARY:**
Scan this QR code or visit
**RYTARYhcp.com**

**TO CALCULATE STARTING DOSE:**
Scan this QR code or visit
**dosingRYTARY.com**

### IMPORTANT SAFETY INFORMATION (continued)

**GENERAL DOSING AND ADMINISTRATION INFORMATION (continued)**

RYTARY should not be chewed, divided, or crushed and should be swallowed whole with or without food. For patients who have difficulty swallowing, the capsule can be opened and the entire contents can be sprinkled on a small amount of applesauce and consumed immediately.

***To report SUSPECTED ADVERSE REACTIONS, contact Amneal Specialty, a division of Amneal Pharmaceuticals LLC at 1-877-835-5472 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.***

**Please see additional Important Safety Information on adjacent pages and accompanying Full Prescribing Information.**

**References: 1.** RYTARY [package insert]. Bridgewater, NJ: Amneal Specialty, a division of Amneal Pharmaceuticals LLC; 2019. **2.** Hauser RA, Hsu A, Kell S, et al; IPX066 ADVANCE-PD Investigators. Extended-release carbidopa-levodopa (IPX066) compared with immediate-release carbidopa-levodopa in patients with Parkinson's disease and motor fluctuations: a phase 3 randomised, double-blind trial. *Lancet Neurol.* 2013;12(4):346-356. **3.** Hauser RA, Zeitlin L, Fisher S, D'Souza R. Duration of benefit per dose: carbidopa-levodopa immediate release vs extended release capsules (Rytary®). *Parkinsonism Relat Disord*. 2021;82(1):133-137.

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