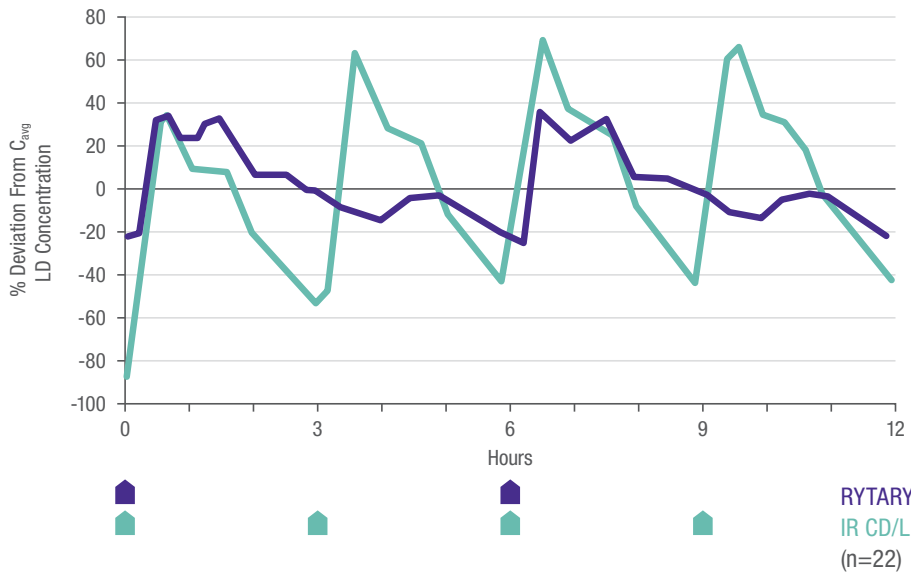
RYTARY can fill in the low troughs and smooth out the high peaks created by IR CD/LD[3,4]

Predicted multiple-dose PK profile of RYTARY and IR CD/LD[5]



The multi-dose curves of levodopa plasma concentration levels were developed based on superposition of observed data from healthy volunteers receiving single doses.[5]

RYTARY q6h*

IR CD/LD q3h*

*Predicted steady state profile based on RYTARY dosed every 6 hours and IR CD/LD dosed every 3 hours.
C_{avg}, average concentration; CD/LD, carbidopa/levodopa; PK, pharmacokinetics.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

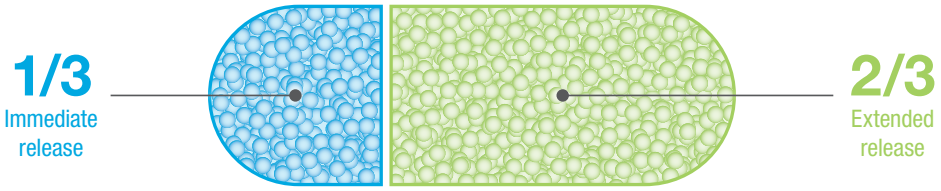
Falling Asleep During Activities of Daily Living and Somnolence (continued): Prescribers should consider discontinuing RYTARY in patients who report significant daytime sleepiness or episodes of falling asleep during activities that require active participation (e.g., conversations, eating). If a decision is made to continue RYTARY, patients should be advised not to drive and to avoid other potentially dangerous activities that might result in harm if the patients become somnolent.

Please see additional Important Safety Information throughout, complete Important Safety Information on pages 12-13, and enclosed Full Prescribing Information.

RYTARY®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
23.75 mg/95 mg • 36.25 mg/145 mg
48.75 mg/195 mg • 61.25 mg/245 mg

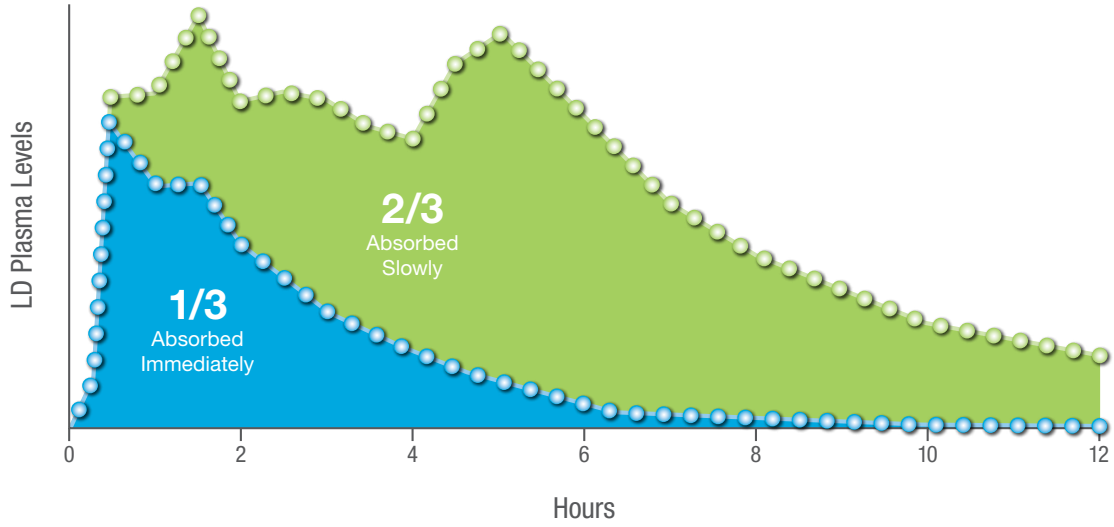
Technology that delivers **predictable levodopa plasma levels**

Each capsule contains multi-beaded technology providing an immediate and extended release of levodopa.[6]



For illustrative purposes only.

RYTARY provides an initial peak of levodopa at about 1 hour and extends plasma levels to 4 or 5 hours, for a predictable delivery of levodopa[7]



Adapted from data on file.[6] For illustrative purposes only. This chart is based on a single dose of RYTARY.

LD, levodopa.

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. If the decision is made to discontinue RYTARY, the dose should be tapered to reduce the risk of hyperpyrexia and confusion.

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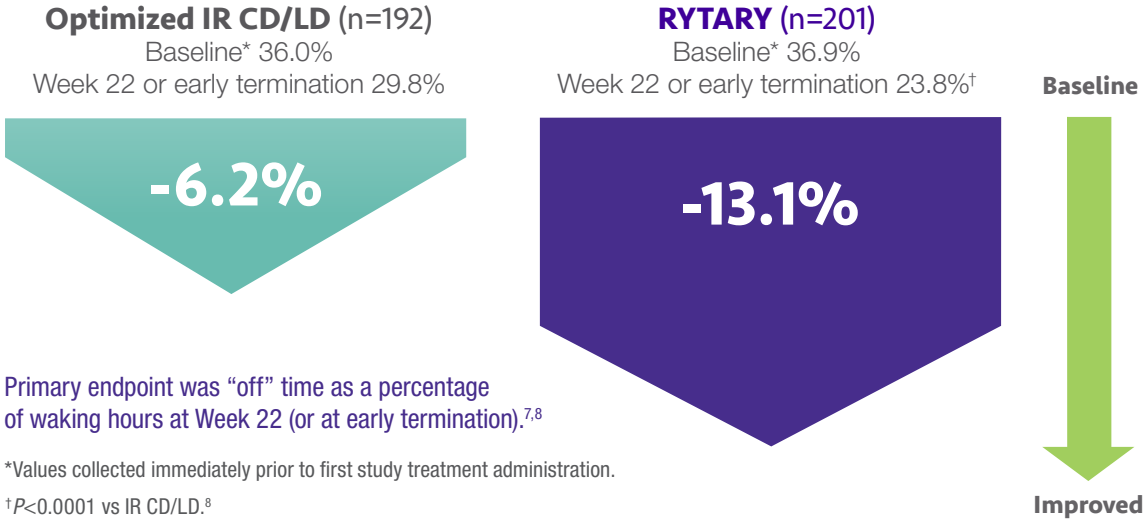
In a **head-to-head study** vs optimized IR CD/LD,

RYTARY demonstrated **2X the reduction** in "off" time[7,8]

PRIMARY ENDPOINT AND RESULTS

Percentage of "off" time during waking hours: head-to-head vs IR CD/LD (N=393)[7,8]



Primary endpoint was "off" time as a percentage of waking hours at Week 22 (or at early termination).[7,8]

*Values collected immediately prior to first study treatment administration.

†*P*<0.0001 vs IR CD/LD.[8]

Pivotal trial 2 study design: Data are from a 22-week clinical trial in patients with advanced Parkinson's disease 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.[7,8]

The term "optimized" refers to the process of adjusting the dose and frequency of IR CD/LD as necessary to achieve optimum motor function.[8]

CD/LD, carbidopa/levodopa; MAO-B, monoamine oxidase-B.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hallucinations/Psychosis: There is an increased risk for hallucinations and psychosis in patients taking RYTARY. Hallucinations present shortly after the initiation of therapy and may be responsive to dose reduction in levodopa. Hallucinations may be accompanied by confusion, insomnia, and excessive dreaming. Abnormal thinking and behavior may present with one or more symptoms, including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium.

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.

SECONDARY ENDPOINT RESULTS

In the same head-to-head study vs optimized IR CD/LD, RYTARY resulted in:

2X REDUCTION IN "OFF" TIME

during waking hours (2.2 hours* vs 1.0 hour with IR CD/LD)[7]

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 hour with IR CD/LD)[7]

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.

Improved ADL and motor functions measured through UPDRS Parts II and III scores§[8]

Secondary endpoints included the total "off" time and the total "on" time without troublesome dyskinesia.[7]

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

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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. In some cases, although not all, these urges were reported to have stopped when the dose was reduced or the medication was discontinued. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, or other urges while being treated with RYTARY. Consider a dose reduction or stopping the medication if a patient develops such urges while taking RYTARY.

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Comparable adverse event rates vs IR CD/LD

Most common adverse reactions in patients with advanced Parkinson's disease in a head-to-head pivotal trial[6]

Adverse reaction*	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[6]
- The most common adverse reactions leading to discontinuation during dose conversion were dyskinesia, anxiety, dizziness, and "on-off" phenomenon[6]

CD/LD, carbidopa/levodopa.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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: RYTARY may cause increased intraocular pressure in patients with glaucoma. Monitor intraocular pressure in patients with glaucoma after starting RYTARY.

Melanoma: Patients with Parkinson's disease have a higher risk of developing melanoma than the general population. Patients and providers are advised to monitor for melanoma frequently and on a regular basis when using RYTARY.

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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.

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, and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1 year after initiation of treatment. Before initiating treatment with RYTARY, advise patients of the potential to develop drowsiness and specifically ask about factors that may increase the risk for somnolence with RYTARY, such as concomitant sedating medications or the presence of a sleep disorder.

Prescribers should consider discontinuing RYTARY in patients who report significant daytime sleepiness or episodes of falling asleep during activities that require active participation (e.g., conversations, eating). If a decision is made to continue RYTARY, patients should be advised not to drive and to avoid other potentially dangerous activities that might result in harm if the patients become somnolent.

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. If the decision is made to discontinue RYTARY, the dose should be tapered to reduce the risk of hyperpyrexia and confusion.

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. Hallucinations present shortly after the initiation of therapy and may be responsive to dose reduction in levodopa. Hallucinations may be accompanied by confusion, insomnia, and excessive dreaming. Abnormal thinking and behavior may present with one or more symptoms, including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium.

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. In some cases, although not all, these urges were reported to have stopped when the dose was reduced or the medication was discontinued. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, or other urges while being treated with RYTARY. 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: RYTARY may cause increased intraocular pressure in patients with glaucoma. Monitor intraocular pressure in patients with glaucoma after starting RYTARY.

Melanoma: Patients with Parkinson's disease have a higher risk of developing melanoma than the general population. Patients and providers are advised to monitor for melanoma frequently and on a regular basis when using RYTARY.

ADVERSE REACTIONS:

Clinical Trials Experience:

Early Parkinson's Disease: Most common adverse reactions (incidence ≥ 5 % and greater than placebo) are nausea, dizziness, headache, insomnia, abnormal dreams, dry mouth, dyskinesia, anxiety, constipation, vomiting, and orthostatic hypotension.

Advanced Parkinson's Disease: Most common adverse reactions (incidence ≥ 5 % and greater than oral immediate-release carbidopa-levodopa) are nausea and headache.

Postmarketing Experience: Reported adverse reactions identified during post approval use of RYTARY include suicide attempt and ideation. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to RYTARY exposure.

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. Monitor patients for worsening Parkinson's symptoms.

USE IN SPECIFIC POPULATIONS:

Pregnancy and nursing mothers: Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. In animal studies, carbidopa-levodopa has been shown to be developmentally toxic (including teratogenic effects) at clinically relevant doses. RYTARY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Carbidopa is excreted in rat milk. Excretion of levodopa in human milk was reported in one nursing mother. Caution should be exercised when RYTARY is administered to a nursing woman.

Pediatrics: Safety and effectiveness in pediatric populations have not been established.

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

RYTARY should not be chewed, divided, or crushed. Swallow RYTARY whole with or without food. A high-fat, high-calorie meal may delay the absorption of levodopa by about 2 hours.

For patients who have difficulty swallowing capsules, administer RYTARY by carefully twisting apart both halves of the capsule. Sprinkle the entire contents of both halves of the capsule on a small amount of applesauce (1 to 2 tablespoons) and consume the mixture immediately. Do not store the drug/food mixture for future use.

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 enclosed Full Prescribing Information.

References: 1. Olanow CW, Obeso JA, Stocchi F. Continuous dopamine-receptor treatment of Parkinson's disease: scientific rationale and clinical implications. *Lancet Neurol.* 2006;5(8):677-687. **2.** Jankovic J. Motor fluctuations and dyskinesias in Parkinson's disease: clinical manifestations. *Mov Disord.* 2005;20(suppl 11):S11-S16. **3.** Espay AJ, Pagan FL, Walter BL, et al. Optimizing extended-release carbidopa/levodopa in Parkinson disease: consensus on conversion from standard therapy. *Neurol Clin Pract.* 2017;7(1):86-93. **4.** Nausieda PA, Hsu A, Elmer L, et al. Conversion to IPX066 from standard levodopa formulations in advanced Parkinson's disease: experience in clinical trials. *J Parkinsons Dis.* 2015;5(4):837-845. **5.** Hsu A, Yao HM, Gupta S, Modi NB. Comparison of the pharmacokinetics of an oral extended-release capsule formulation of carbidopa-levodopa (IPX066) with immediate-release carbidopa-levodopa (Sinemet®), sustained-release carbidopa-levodopa (Sinemet® CR), and carbidopa-levodopa-entacapone (Stalevo®). *J Clin Pharmacol.* 2015;55(9):995-1003. **6.** Data on file, MA-2016-2005-DOF, Impax Laboratories, LLC. **7.** RYTARY [package insert]. Hayward, CA: Impax Laboratories, LLC; 2016. **8.** 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. **9.** Data on file, Appendix Q IPX066-B09-02. Impax Laboratories, LLC. **10.** Morgan JC, Dhall R, Rubens R, Khanna S, Gupta S. Dosing patterns during conversion to IPX066, extended-release carbidopa-levodopa (ER CD-LD), in Parkinson's disease with motor fluctuations. *Parkinsons Dis.* 2018. doi: 10.1155/2018/9763057. **11.** Pahwa R, Lyons KE, Hauser RA, et al; APEX-PD Investigators. Randomized trial of IPX066, carbidopa/levodopa extended release, in early Parkinson's disease. *Parkinsonism Relat Disord.* 2014;20(2):142-148.

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EXTENDED-RELEASE CAPSULES
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48.75 mg/195 mg • 61.25 mg/245 mg

INFORMATION

Starting IR CD/LD patients on the **appropriate RYTARY dose**

Although RYTARY is CD/LD, its patented technology combining immediate-release and extended-release beads means that the dosages of other carbidopa and levodopa products are not interchangeable on a 1:1 basis with the dosages of RYTARY.[7]

Starting on RYTARY[7]

Step 1	Step 2	Maintenance
Calculate the current total daily dose of levodopa in IR CD/LD	**Determine the recommended daily starting dose of RYTARY** (23.75 mg carbidopa / **95 mg** levodopa)	Doses can be administered **3, 4, or 5 times a day** if more frequent dosing is needed and if tolerated.
100 mg x 4 (400 mg total)	 **3 capsules TID*** (855 mg LD total)	
100 mg x 5 (500 mg total)	 **3 capsules TID*** (855 mg LD total)	
100 mg x 6 (600 mg total)	 **4 capsules TID*** (1140 mg LD total)	
100 mg x 7 (700 mg total)	 **4 capsules TID*** (1140 mg LD total)	

Capsules may not be representative of actual size.

*Dosing for RYTARY is TID with 4- to 6-hour intervals between doses.[9]

The above chart is based on data listed in Table 1 of the enclosed Prescribing Information (PI). For complete dosing and conversion information, please see Table 1.

The maximum recommended daily dose of RYTARY is 612.5 mg / 2450 mg.[7]

For patients currently treated with CD/LD plus a COMT inhibitor, the initial total daily dose of levodopa in RYTARY described in Table 1 of the enclosed PI may need to be increased.[7]

CD/LD, carbidopa/levodopa; COMT, catechol-O-methyl transferase; TID, three times a day.

IMPORTANT SAFETY INFORMATION (continued)

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

Available in 4 strengths

*carbidopa/levodopa	23.75 mg / **95 mg***	36.25 mg / **145 mg***	48.75 mg / **195 mg***	61.25 mg / **245 mg***

Capsules may not be representative of actual size.

Adjust the dose and dosing frequency as necessary to maintain patient tolerance and sufficient symptomatic control[7]

Adjust dose[9]	If your patient requires more "on" time per individual dose...	+	23.75 mg / **95 mg** per dose
	If your patient is experiencing dyskinesia...	−	23.75 mg / **95 mg** per dose

When dosing RYTARY, **remember:**

- RYTARY doses can be administered 3, 4, or 5 times a day if more frequent dosing is needed and if tolerated[7]
- Consider following up with patients at least every 3 days during the initial weeks of dose initiation. Dose adjustments may be required[9]
- Managing patient and care partner expectations regarding future dose adjustments may help the transition to RYTARY, as approximately 76% of patients required dose titration to optimize "on" time[7,10]
- A meal high in fat or calories may delay the absorption of levodopa by about 2 hours. A high-protein meal may decrease levodopa absorption. Advise patients to take their first dose of RYTARY about 1 to 2 hours before eating[7]
- Patients can take RYTARY either by swallowing the capsule whole or sprinkling the contents on 1 to 2 tablespoons of applesauce[7]

IMPORTANT SAFETY INFORMATION (continued)

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). 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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Why it's time to MOVE ON with RYTARY

PREDICTABLE PLASMA LEVELS

Can fill in the low troughs and smooth out the high peaks created by IR CD/LD[3,4]

PROVEN HEAD-TO-HEAD EFFICACY VS OPTIMIZED IR CD/LD

- Provided 2X the reduction in "off" time compared to optimized IR CD/LD (13.1% vs 6.2%, respectively)[7,8]
- Resulted in 2X increase in "on" time without troublesome dyskinesia[7]

DEMONSTRATED SAFETY PROFILE

In a head-to-head pivotal trial in patients with advanced Parkinson's disease, the most common adverse reactions (incidence ≥ 5% and greater than optimized IR CD/LD) were nausea and headache[7]

CD/LD, carbidopa/levodopa.

IMPORTANT SAFETY INFORMATION (continued)

GENERAL DOSING AND ADMINISTRATION INFORMATION (continued):

RYTARY should not be chewed, divided, or crushed. Swallow RYTARY whole with or without food. A high-fat, high-calorie meal may delay the absorption of levodopa by about 2 hours.

For patients who have difficulty swallowing capsules, administer RYTARY by carefully twisting apart both halves of the capsule. Sprinkle the entire contents of both halves of the capsule on a small amount of applesauce (1 to 2 tablespoons) and consume the mixture immediately. Do not store the drug/food mixture for future use.

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 throughout, complete Important Safety Information on pages 12-13, and enclosed Full Prescribing Information.

The MyRYTARY® Patient Support Program helps eligible patients start on RYTARY, connect to access and affordability support, and find educational resources to allow them to stay on the medication you prescribed.

Call 1.844.467.2928, Monday-Friday, 8AM-8PM EST or visit **MyRYTARY.com** to enroll!

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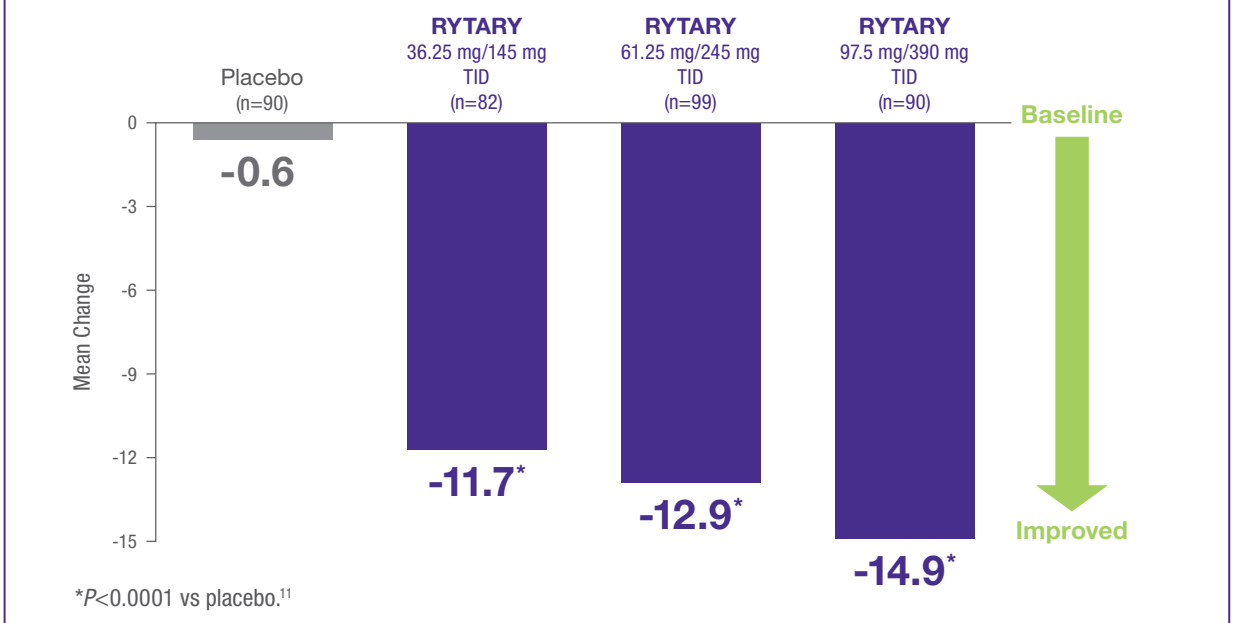
PIVOTAL TRIAL 1

Treatment with RYTARY resulted in a nearly **20- to 25-fold improvement** in UPDRS II (ADL) and III (motor function) scores vs placebo[7,11]

PRIMARY ENDPOINT AND RESULTS

Mean change from baseline in combined UPDRS Parts II and III scores at Week 30 or early termination[7,11]



*$P<0.0001$ vs placebo.[11]

Pivotal trial 1 study design: Data are from a 30-week, randomized, double-blind, placebo-controlled, fixed-dose, parallel-group clinical trial. Patients (n=381) were Hoehn and Yahr Stage I-III with a median disease duration of 1 year, and naïve to levodopa (not exposed for >30 days and not within 4 weeks of enrollment) and dopamine agonists (not exposed within 30 days of screening). Concomitant Parkinson's medications (anticholinergics, amantadine, and MAO-B inhibitors) were continued, provided the doses were stable for ≥4 weeks prior to screening. Primary endpoint was the mean change from baseline in the sum of UPDRS II and III for RYTARY compared to placebo at Week 30 or early termination.[7,11]

ADL, activities of daily living; MAO-B, monoamine oxidase-B; UPDRS, Unified Parkinson's Disease Rating Scale.

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.

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Most common adverse reactions in levodopa-naïve patients in pivotal trial 1[7]

Adverse reaction*	Placebo	RYTARY		
	(n=92)	36.25 mg/145 mg TID (n=87)	61.25 mg/245 mg TID (n=104)	97.5 mg/390 mg TID (n=98)
Nausea	9%	14%	19%	20%
Dizziness	5%	9%	19%	12%
Headache	11%	7%	13%	17%
Insomnia	3%	2%	9%	6%
Abnormal dreams	0%	2%	6%	5%
Dry mouth	1%	3%	2%	7%
Dyskinesia	0%	2%	4%	5%
Anxiety	0%	2%	3%	5%
Constipation	1%	2%	6%	2%
Vomiting	3%	2%	2%	5%
Orthostatic hypotension	1%	1%	1%	5%

*Adverse reactions occurring in at least 5% of patients treated with RYTARY and at a higher rate than placebo.

- 12% of patients discontinued RYTARY early due to adverse reactions[7]
- 14% of patients in the 61.25 mg/245 mg RYTARY-treated group and 15% in the 97.5 mg/390 mg RYTARY-treated group experienced adverse reactions leading to early discontinuation compared to 4% in the placebo group[7]
- The most common adverse reactions resulting in early discontinuation were nausea, dizziness, and vomiting[7]

TID, three times a day.

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, and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1 year after initiation of treatment. Before initiating treatment with RYTARY, advise patients of the potential to develop drowsiness and specifically ask about factors that may increase the risk for somnolence with RYTARY, such as concomitant sedating medications or the presence of a sleep disorder.

Please see additional Important Safety Information throughout, complete Important Safety Information on pages 12-13, and enclosed Full Prescribing Information.

RYTARY (carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
23.75 mg/95 mg • 36.25 mg/145 mg
48.75 mg/195 mg • 61.25 mg/245 mg

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NAÏVE DOSING

Levodopa-Naïve[7]		
RYTARY		**Dosing schedule**
	23.75 mg / **95 mg TID**	First 3 days
	36.25 mg / **145 mg TID**	Increase on Day 4 if needed

Capsules may not be representative of actual size.

TID, three times a day.

- Maximum recommended dose for levodopa-naïve patients is 97.5 mg / 390 mg TID[7]
- Dosing frequency may be changed from TID to 4 or 5 times a day if more frequent dosing is needed and if tolerated[7]

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.

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RYTARY (carbidopa and levodopa)
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MyRYTARY
PATIENT SUPPORT PROGRAM

Help appropriate patients

get on RYTARY and stay on RYTARY

The **MyRYTARY Patient Support Program** helps eligible patients start on RYTARY, connect to access and affordability support, and find educational resources to help them along the treatment journey.

The MyRYTARY Patient Support Program provides patients with the resources they need to:

GET ON RYTARY*

- Starter Rx Program may give eligible patients access to RYTARY at no cost during the patient's initial dose adjustment and coverage determination processes

GET ACCESS TO RYTARY*

- RYTARY Co-Pay Savings Card for commercially insured patients
- A comprehensive list of alternative foundation support resources that patients may contact for additional financial support†
- Amneal Patient Assistance Program for eligible patients with low income or no insurance

GET SUPPORT WITH RYTARY

- Dedicated patient case managers
- Benefits investigation
- Educational resources

*Eligibility restrictions apply. See MyRYTARY.com for full terms and conditions.

†Charitable foundations and other third-party patient support organizations are independent from Amneal. Each third-party organization has its own eligibility criteria and evaluation process, and Amneal cannot guarantee that a patient will qualify for assistance.

The accurate completion and submission of reimbursement or coverage-related documentation is the responsibility of the patient and healthcare provider. Amneal and its agents make no guarantee regarding coverage or reimbursement for any service.

Call 1.844.467.2928 Monday-Friday, 8AM-8PM EST, or visit MyRYTARY.com

- **Get information** on access support for patients (full terms, conditions, and eligibility criteria)
- **Access** a downloadable patient enrollment form for the MyRYTARY Patient Support Program
- **Learn more** about the RYTARY Co-Pay Savings Card

NOW AVAILABLE
MyRYTARY Provider Portal
Visit hcp.MyRYTARY.com

The MyRYTARY Provider Portal provides healthcare professionals and office staff the ability to enroll and manage their patients into the MyRYTARY Patient Support Program. You may access the online provider portal 24 hours a day, 7 days a week from any location to track the current status of patient cases.

Please see Important Safety Information throughout, complete Important Safety Information on pages 12-13, and enclosed Full Prescribing Information.

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