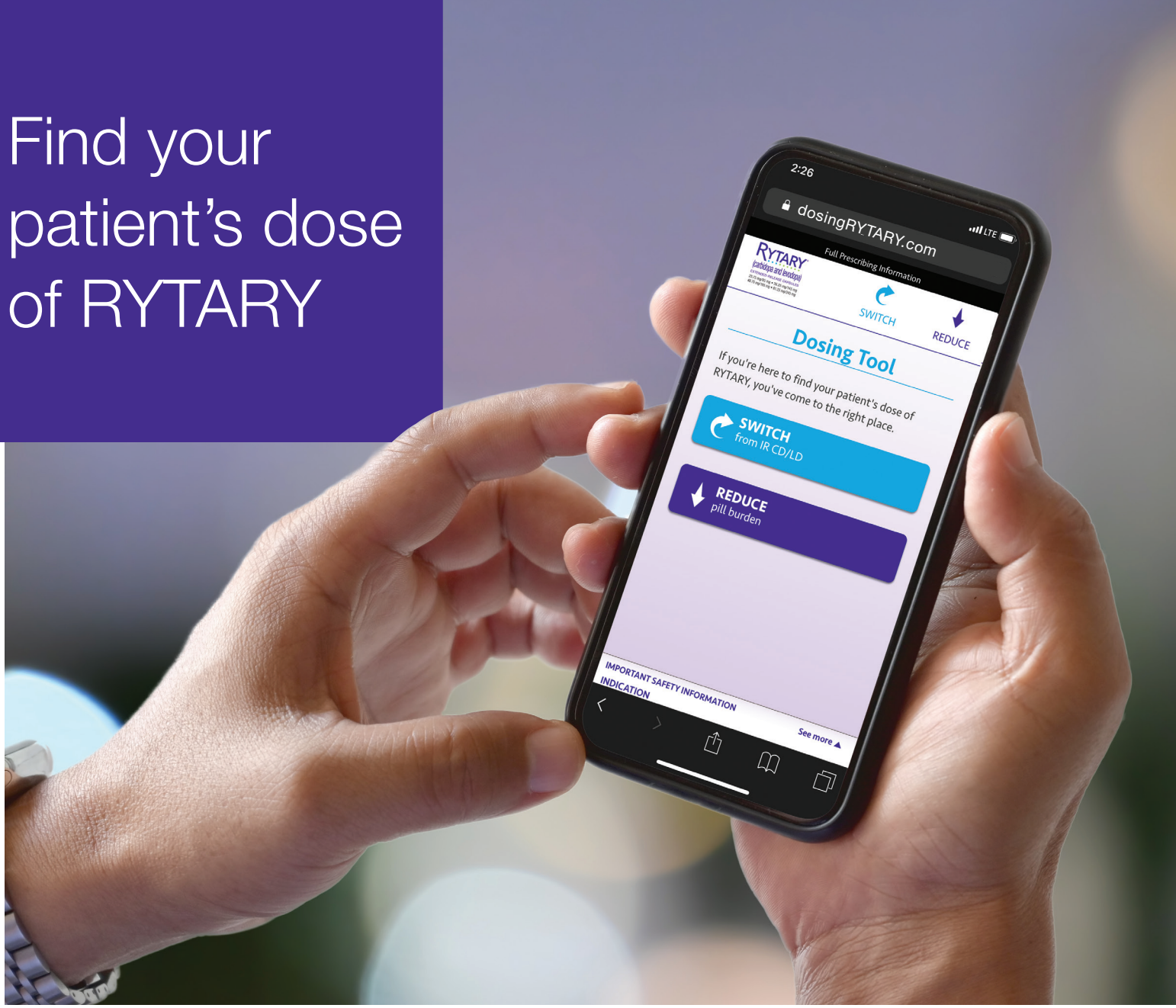
Find your patient's dose of RYTARY



Visit dosingRYTARY.com or point your smartphone camera here to help with your dosing decisions.

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.

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

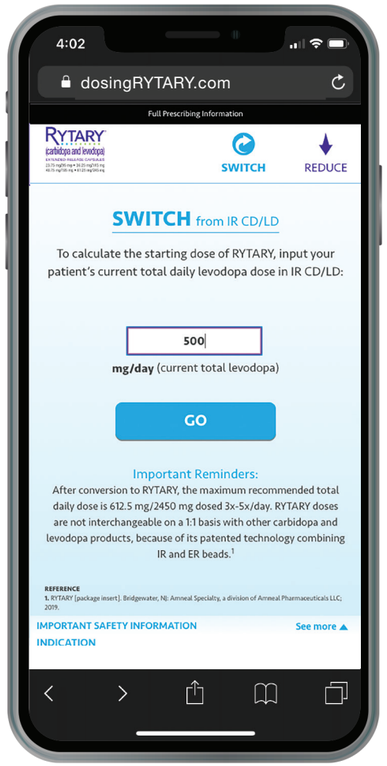
RYTARY®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
23.75 mg/95 mg • 36.25 mg/145 mg
48.75 mg/195 mg • 61.25 mg/245 mg

Switch the IR carbidopa-levodopa dose to RYTARY

When converting your patients from IR CD/LD, the RYTARY Dosing Tool can help you determine their starting dose.

Example:
If your patient is taking 1 tablet 25 mg/100 mg of IR CD/LD 5 times per day (500 mg total daily LD):

1. Enter “500”
2. Tap “Go”



CD/LD, carbidopa/levodopa; ER, extended release; IR, immediate release.

Important Reminder: Because of its patented technology combining IR and ER beads, RYTARY dosages are not interchangeable on a 1:1 basis with other carbidopa and levodopa products. At the initiation of conversion to RYTARY, the maximum starting total daily dose is 585 mg/2340 mg dosed no more than 3x/day. After conversion to RYTARY, the maximum recommended total daily dose is 612.5 mg/2450 mg dosed 3x-5x/day.[1]

See the suggested daily dose of RYTARY

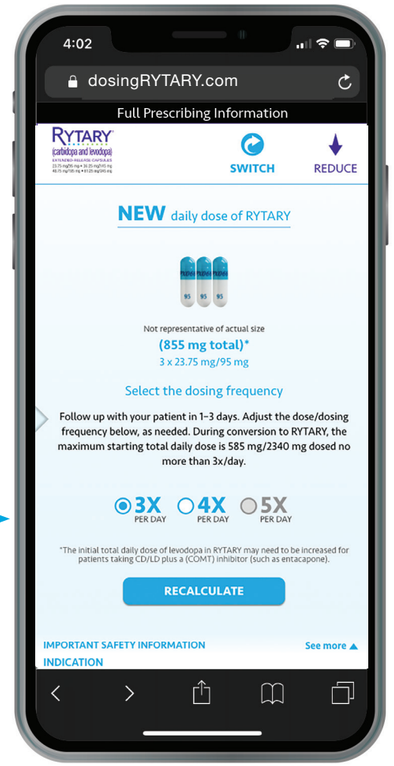
The RYTARY Dosing Tool will use the IR levodopa dose you entered to calculate the corresponding starting dose of RYTARY. Keep in mind, your patient will still likely require a dose adjustment to optimize symptom control and maintain tolerance. In a clinical study, compared with the suggested starting dose, 76% of patients required a dose adjustment.[2,3]

Example continued:
Based on the total daily LD dose you entered, your patient’s suggested daily dose of RYTARY will initially be:
855 mg total (3 capsules of RYTARY 23.75 mg/95 mg, 3 times per day).

If you wish to adjust the dose to 4 times per day:

1. Tap “4x per day”

Your patient’s new total daily dose of RYTARY will be:
1140 mg total (3 capsules of RYTARY 23.75 mg/95 mg, 4 times per day).



Important Reminder:
In order to make sure your patients are taking the optimal dose of RYTARY, follow up in 1 to 3 days to determine whether their dose needs to be adjusted. At the initiation of conversion to RYTARY, the maximum starting total daily dose is 585 mg/2340 mg dosed no more than 3x/day. After conversion to RYTARY, the maximum recommended total daily dose is 612.5 mg/2450 mg dosed 3x-5x/day.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS & 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.

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Help your patients reduce their pill burden

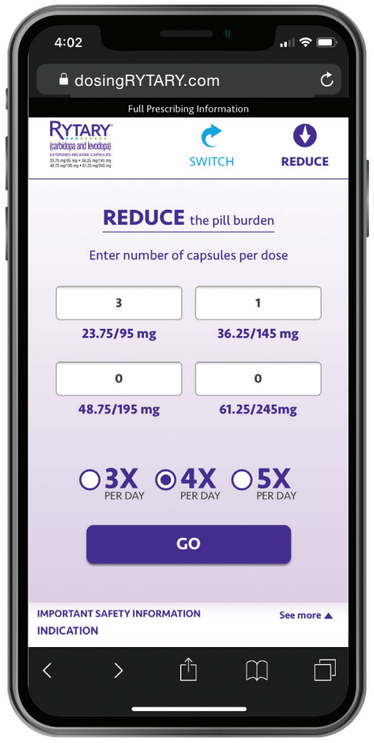
RYTARY is available in 4 different dosage strengths. The various dosage strengths may be combined to customize a dosing regimen for each patient with the lowest pill burden possible, while keeping patients at their prescribed dose.

Example:
If your patient is currently taking 3 capsules of RYTARY 23.75 mg/95 mg and 1 capsule of RTYARY 36.25 mg/145 mg 4 times daily (1720 mg total daily LD):

1. Enter “3” in the “23.75 mg/95 mg” field and “1” in the “36.25 mg/145 mg” field

2. Tap “4x per day”

3. Tap “Go”

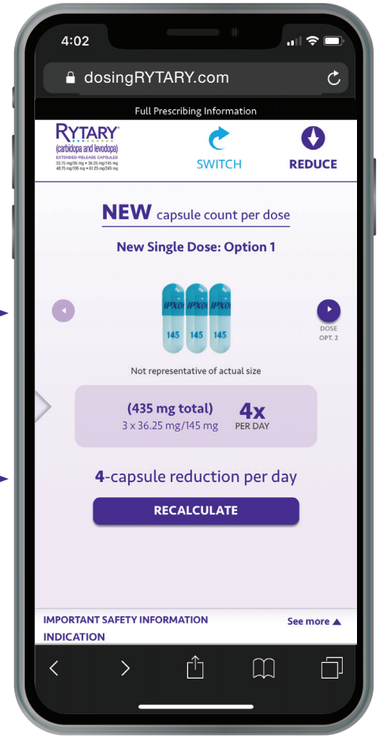


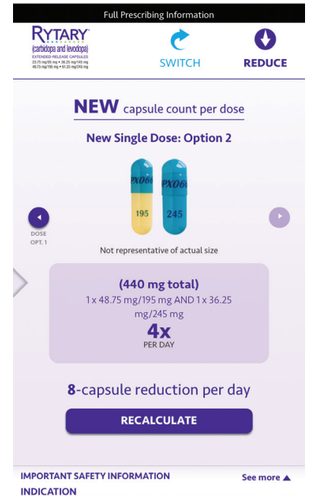
See the suggested daily capsule reduction of RYTARY

The RYTARY Dosing Tool will use the capsule strengths and frequency you enter to calculate the corresponding capsule reduction plan.

Example continued:
Your patient’s new single dose of RYTARY will be:
435 mg (3 capsules of RYTARY 36.25 mg/145 mg).
This is how many capsules your patient will take per dose.

Total capsule number reduction per day is here, based on new capsule count per dose above. This represents a reduction of 4 capsules per day.





Another dose reduction option will be provided in cases with more than one result.

Depending on the information you entered, you may see a message that:

- The number of capsules cannot be reduced. This means your patient’s dose is already optimized
- A suggested capsule reduction is not available for your entry. This means your entry is outside of the dosage range for which we are able to provide a suggestion

→ Number of capsules cannot be reduced.

→ A suggested capsule reduction is not available for your entry.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS & PRECAUTIONS (continued)

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.

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IMPORTANT SAFETY INFORMATION

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.

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.

IMPORTANT SAFETY INFORMATION (continued)

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.

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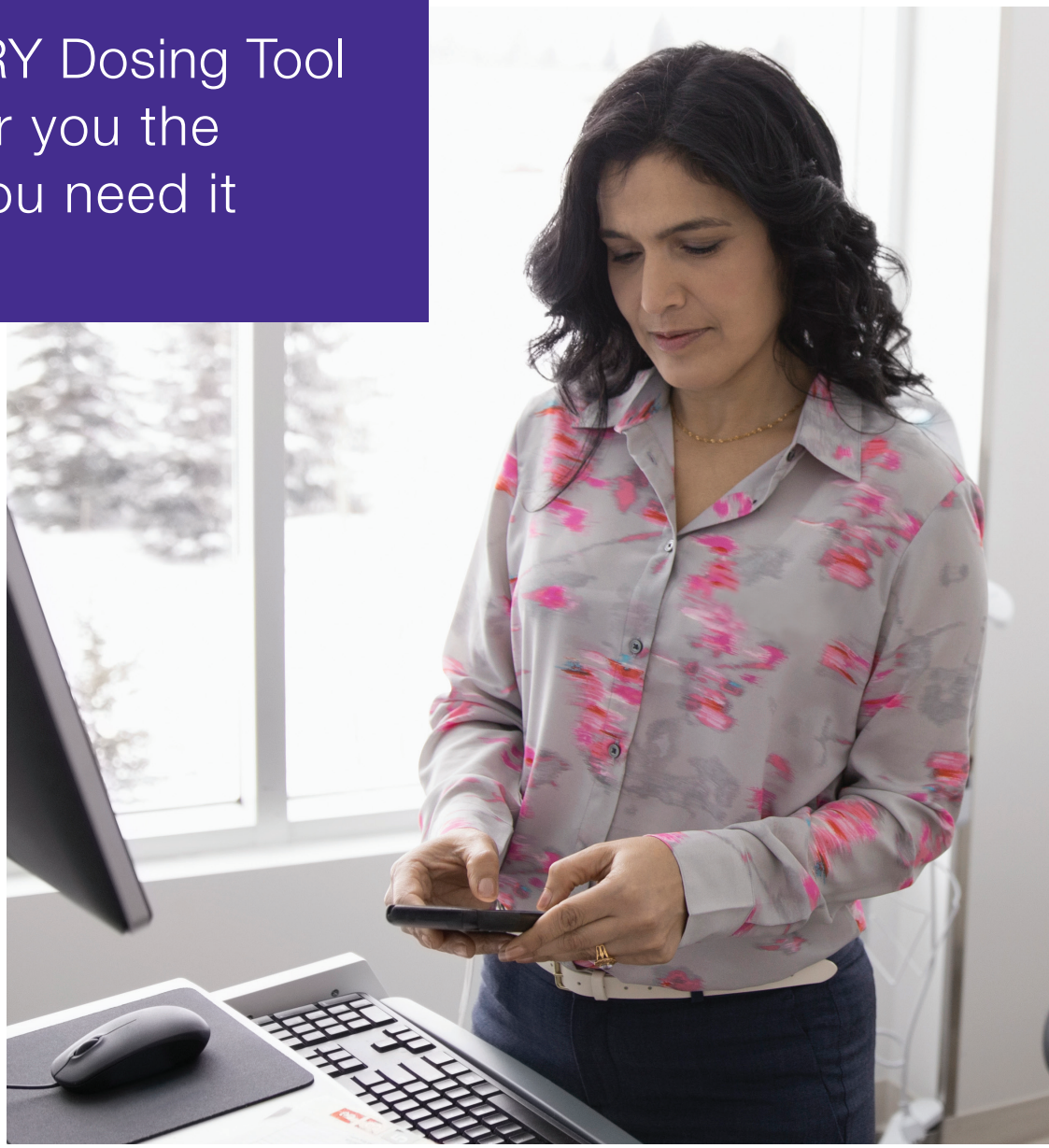
The RYTARY Dosing Tool is ready for you the moment you need it



There's no app to download and no log-in to remember

Add it to your bookmarks or save it to your smartphone's home screen for easy access

The RYTARY Dosing Tool currently performs best on these browsers

Visit dosingRYTARY.com or point your smartphone camera here to help with your dosing decisions.

References: 1. RYTARY [package insert]. Bridgewater, NJ: Amneal Specialty, a division of Amneal Pharmaceuticals LLC; 2019. **2.** 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. **3.** 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.

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