Rytary™ (carbidopa/levodopa) — New Drug Approval

- On January 8, 2015, Impax Pharmaceuticals announced the FDA approval of Rytary (carbidopa/levodopa) extended-release oral capsules, for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.
- Rytary is a combination product containing an aromatic amino acid decarboxylase inhibitor (carbidopa) and a dopamine precursor (levodopa). Formulated as immediate-release and extended-release beads, Rytary provides both initial and extended levodopa plasma concentrations.
- The safety and efficacy of Rytary were based on clinical trials in both early and advanced Parkinson's disease patients.
  - In patients with early Parkinson's disease, Rytary demonstrated significant improvement from baseline over placebo, as determined by the Unified Parkinson's Disease Rating Scale.
  - In patients with advanced Parkinson's disease, the percentage of "off" time during waking hours was less with Rytary compared to immediate-release carbidopa/levodopa (23.8% vs. 29.8%, $p < 0.05$).
- Rytary is contraindicated in patients who are currently taking a nonselective monoamine oxidase inhibitor (eg, phenelzine and tranylcypromine) or have recently (within 2 weeks) taken a nonselective MAO inhibitor.
- Warnings and precautions of Rytary include: falling asleep during activities of daily living and somnolence, withdrawal-emergent hyperpyrexia and confusion, cardiovascular ischemic events, hallucinations/psychosis, impulse control/compulsive behaviors, dyskinesia, peptic ulcer disease, glaucoma, and melanoma.
- The common adverse events in early Parkinson's disease (≥ 5 % and greater than placebo) with Rytary use were nausea, dizziness, headache, insomnia, abnormal dreams, dry mouth, dyskinesia, anxiety, constipation, vomiting, and orthostatic hypotension.
- The common adverse events in advanced Parkinson's disease (≥ 5 % and greater than oral immediate-release carbidopa/levodopa) with Rytary use were nausea and headache.
- In levodopa-naïve patients, the recommended starting dose is 23.75 mg/95 mg taken orally three-times daily (TID) for the first 3 days. On the fourth day, the dose may be increased to 36.25 mg/145 mg TID.
  - The maximum daily dose of Rytary is 612.5 mg/2,450 mg.
  - For patients who have difficulty swallowing intact capsules, the capsule may be opened and sprinkled on a small amount of applesauce for immediate consumption.

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— The dosages of other carbidopa and levodopa products are not interchangeable with the dosages of Rytary. To convert patients from immediate-release carbidopa/levodopa to Rytary, determine the recommended starting dosage of Rytary using the table below.

Conversion from Immediate-Release Carbidopa/Levodopa to Rytary

	Recommended Starting Dosage of Rytary	
Total Daily Dose of Levodopa in immediate-release Carbidopa/Levodopa	**Total Daily Dose of Levodopa in Rytary**	**Rytary Dosing Regimen**
400 mg – 549 mg	855 mg	Three capsules of Rytary 23.75 mg/95 mg TID*
550 mg – 749 mg	1,140 mg	Four capsules of Rytary 23.75 mg/95 mg TID
750 mg – 949 mg	1,305 mg	Three capsules of Rytary 36.25 mg/145 mg TID
950 mg – 1,249 mg	1,755 mg	Three capsules of Rytary 48.75 mg/195 mg TID
≥ 1,250 mg	2,340 mg or 2,205 mg	Four capsules of Rytary 48.75 mg/195 mg TID, or three capsules of Rytary 61.25 mg/245 mg TID

* TID = three time daily

- Impax plans to launch Rytary in February of 2015. Rytary capsules will be available in multiple strengths containing carbidopa and levodopa as follows: 23.75 mg/95 mg, 36.25 mg/145 mg, 48.75 mg/195 mg, 61.25 mg/245 mg.