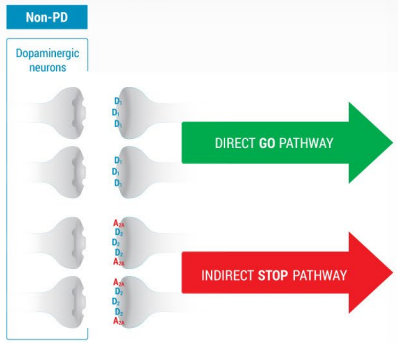
IN PARKINSON'S DISEASE (PD)

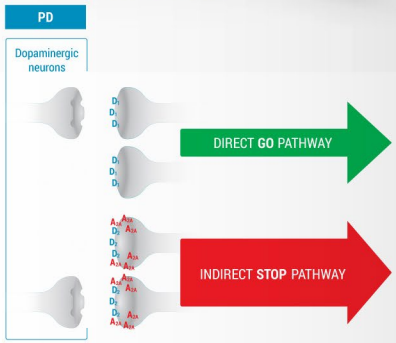
THERE IS MORE TO CONSIDER THAN DOPAMINE... [1,2]

The first and only adenosine A_{2A} receptor antagonist for "off" time in PD [1]

Normal Neuron



PD-affected Neuron



...there is also adenosine

- In addition to the degeneration of dopaminergic neurons, there is also an increased density of A_{2A} receptors[3,4]
- The resulting overactivity of the indirect "STOP" pathway may further impact motor functionality[3]
- There is only one available treatment for PD that specifically targets adenosine A_{2A} receptors[1,4]

Choose **NOURIANZ™ (istradefylline)** for your patients with PD who are experiencing **"off" episodes** while being treated with levodopa/carbidopa [1]

Indication

NOURIANZ™ (istradefylline) is an adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes.

Important Safety Information

Warnings and Precautions

Dyskinesia: NOURIANZ in combination with levodopa may cause dyskinesia or exacerbate pre-existing dyskinesia. In clinical trials, 1% of patients treated with either NOURIANZ 20 mg or 40 mg discontinued treatment because of dyskinesia, compared to 0% for placebo.

Please see additional Important Safety Information on next page, and click here full Prescribing Information .

NOURIANZ™
(istradefylline) tablets
20 mg | 40 mg

Mechanism of disease: A visual representation of the roles of dopamine and adenosine

The role of dopamine...
The stimulation of D_1 and D_2 dopamine receptors is like pushing down on the gas pedal of a car, which initiates movement[5,6]

The role of adenosine...
The stimulation of adenosine A_{2A} receptors is like applying the brake, which suppresses movement[5,6]

▶ Learn more at NourianzHCP.com

Use the QR code to watch a video on how NOURIANZ works

Important Safety Information (continued)

Warnings and Precautions (continued)

Hallucinations / Psychotic Behavior: Because of the potential risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with NOURIANZ. Consider dosage reduction or discontinuation if a patient develops hallucinations or psychotic behaviors while taking NOURIANZ.

Impulse Control / Compulsive Behaviors: Patients treated with NOURIANZ and one or more medication(s) for the treatment of Parkinson's disease (including levodopa) may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges. In clinical trials, 1 patient treated with NOURIANZ 40 mg was reported to have impulse control disorder, compared to no patient on NOURIANZ 20 mg or placebo.

Drug Interactions

The maximum recommended dosage in patients taking strong CYP3A4 inhibitors is 20 mg once daily. Avoid use of NOURIANZ with strong CYP3A4 inducers.

Specific Populations

Pregnancy: Based on animal data, may cause fetal harm.
Hepatic impairment: The maximum recommended dosage of NOURIANZ in patients with moderate hepatic impairment is 20 mg once daily. Avoid use in patients with severe hepatic impairment.

Adverse Reactions

The most common adverse reactions with an incidence ≥5% and occurring more frequently than with placebo were dyskinesia (15%, 17%, and 8%), dizziness (3%, 6%, and 4%), constipation (5%, 6%, and 3%), nausea (4%, 6%, and 5%), hallucination (2%, 6%, and 3%), and insomnia (1%, 6%, and 4%) for NOURIANZ 20 mg, 40 mg, and placebo, respectively.

You are encouraged to report suspected adverse reactions to Kyowa Kirin, Inc. at 1-844-768-3544 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Important Safety Information on previous page, and click here full Prescribing Information .

References: 1. NOURIANZ [package insert]. Kyowa Kirin, Inc., Bedminster, NJ, USA. **2.** Kalia LV, Brotchie JM, Fox SH. Novel nondopaminergic targets for motor features of Parkinson's disease: review of recent trials. *Mov Disord*. 2013;28(2):131-144. **3.** Morelli M, Di Paolo T, Wardas J, Calon F, Xiao D, Schwarzschild MA. Role of adenosine A_{2A} receptors in parkinsonian motor impairment and L-DOPA-induced motor complications. *Prog Neurobiol*. 2007;83(5):293-309. **4.** Mishina M, Ishiwata K, Naganawa M, et al. Adenosine A_{2A} receptors measured with [^{11}C]TMSX PET in the striata of Parkinson's disease patients. *PLoS One*. 2011;6(2):e17338. doi:10.1371/journal.pone.0017338. **5.** Kulisevsky J, Poyurovsky M. Adenosine A_{2A}-receptor antagonism and pathophysiology of Parkinson's disease and drug-induced movement disorders. *Eur Neurol*. 2012;67(1):4-11. **6.** Mori A. Mode of action of adenosine A_{2A} receptor antagonists as symptomatic treatment for Parkinson's disease. *Int Rev Neurobiol*. 2014;119:87-116.

KYOWA KIRIN

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