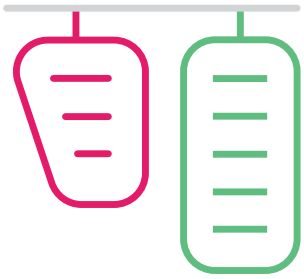
There is more to the Parkinson's disease (PD) picture than just dopamine[1]

Both dopamine and adenosine regulate movement in PD.[1]

Actor Portrayals.

Stimulation of **adenosine** A_{2A} receptors is like applying the **brake pedal of a car**, which suppresses movement.[2-4]



Stimulation of **dopamine** receptors is like pressing the **gas pedal**, which initiates movement.[2-4]

In PD, motor dysfunction occurs when there is a deficiency of dopamine and an overactivation of adenosine A_{2A} receptors. Levodopa/carbidopa acts on the gas, but not the brake.[2-4]

Lift the brake of adenosine to help reduce "off" time in PD.[1,5]

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.

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.

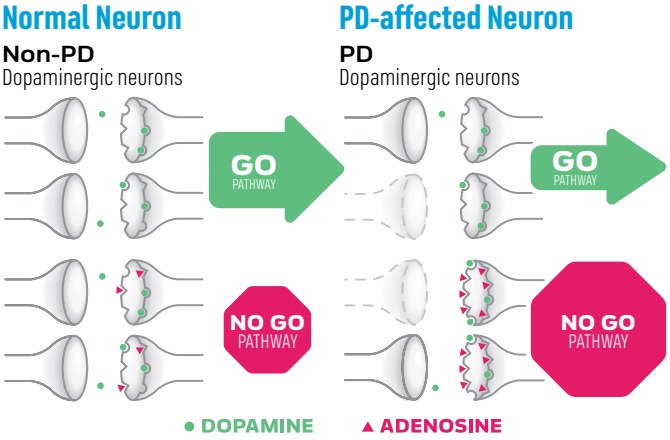
Impulse Control / Compulsive Behaviors: Patients treated with NOURIANZ and one or more medication(s) for the treatment of Parkinson's disease (including levodopa) may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense 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.

Please see Important Safety Information throughout.
Please see full Prescribing Information for NOURIANZ.

NOURIANZ®
(istradefylline) tablets
20 mg | 40 mg

Understanding the go (direct) and no go (indirect) pathways in Parkinson's disease (PD)[2]

Imbalance among these pathways contributes to motor dysfunction.[6]



- Dopamine works in both go and no go pathways, while adenosine works in the no go pathway only[2]
- Adenosine is a product of cellular metabolism that is present in both non-PD and PD brains
- In normal movement, balance between the pathways facilitates movement signals from the basal ganglia, enabling motor activity[2,4]
- In patients with PD, dopamine levels are decreased, reducing the activity of the go pathway and increasing the activity of the no go pathway[2,4]
- As PD progresses, adenosine A_{2A} receptor concentration increases and the effect of adenosine on the no go pathway becomes more prominent[7,8]

Choose NOURIANZ®, the first and only adjunct therapy that reduces "off" time by lifting the brake of adenosine.[1,5]

The precise mechanism by which NOURIANZ exerts its therapeutic effect in PD is unknown.[5]
In in vitro studies and in vivo animal studies, NOURIANZ was demonstrated to be an adenosine A_{2A} receptor antagonist.[5]

Important Safety Information (continued)

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.

Scan this code or visit **NOURIANZHCP.com** to watch the MOA video and learn more.

Please see Important Safety Information throughout. Please see full Prescribing Information for NOURIANZ.

References: 1. 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. **2.** 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. **3.** Varani K, Vincenzi F, Tosi A, et al. A_{2A} adenosine receptor overexpression and functionality, as well as TNF-α levels, correlate with motor symptoms in Parkinson's disease. *FASEB J*. 2010;24(2):587-598. doi:10.1096/fj.09-141044. **4.** Fuxe K, Marcellino D, Genedani S, Agnati L. Adenosine A_{2A} receptors, dopamine D_2 receptors and their interactions in Parkinson's disease. *Mov Disord*. 2007;22(14):1990-2017. doi: 10.1002/mds.21440. **5.** NOURIANZ [package insert]. Kyowa Kirin, Inc., Bedminster, NJ, USA. **6.** 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. **7.** Morelli M, Blandini F, Simola N, Hauser RA. A_{2A} receptor antagonism and dyskinesia in Parkinson's disease. *Parkinsons Dis*. 2012;2012:489853. doi: 10.1155/2012/489853. **8.** Jenner P. Istradefylline, a novel adenosine A_{2A} receptor antagonist, for the treatment of Parkinson's disease. *Expert Opin Investig Drugs*. 2005;14(6):729-738.

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PM-US-NOU-0400 January 2022

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