



I brake for moments, not for Parkinson's.TM

Add NOURIANZ[®], the only treatment for "off" time in Parkinson's disease (PD) that lifts the brake of adenosine,^{1,2} to help your patients brake for what matters to them.

Actor Portrayals.

NOURIANZ[®]
(istradefylline) tablets
20 mg | 40 mg 

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 Important Safety Information throughout.
Please see full [Prescribing Information](#) for NOURIANZ.

Around 1 million people in the United States are living with Parkinson's³

Within 5 years of initiating levodopa/carbidopa, 50% of patients with Parkinson's disease (PD) experience "off" time, including motor complications.⁴



Year 5

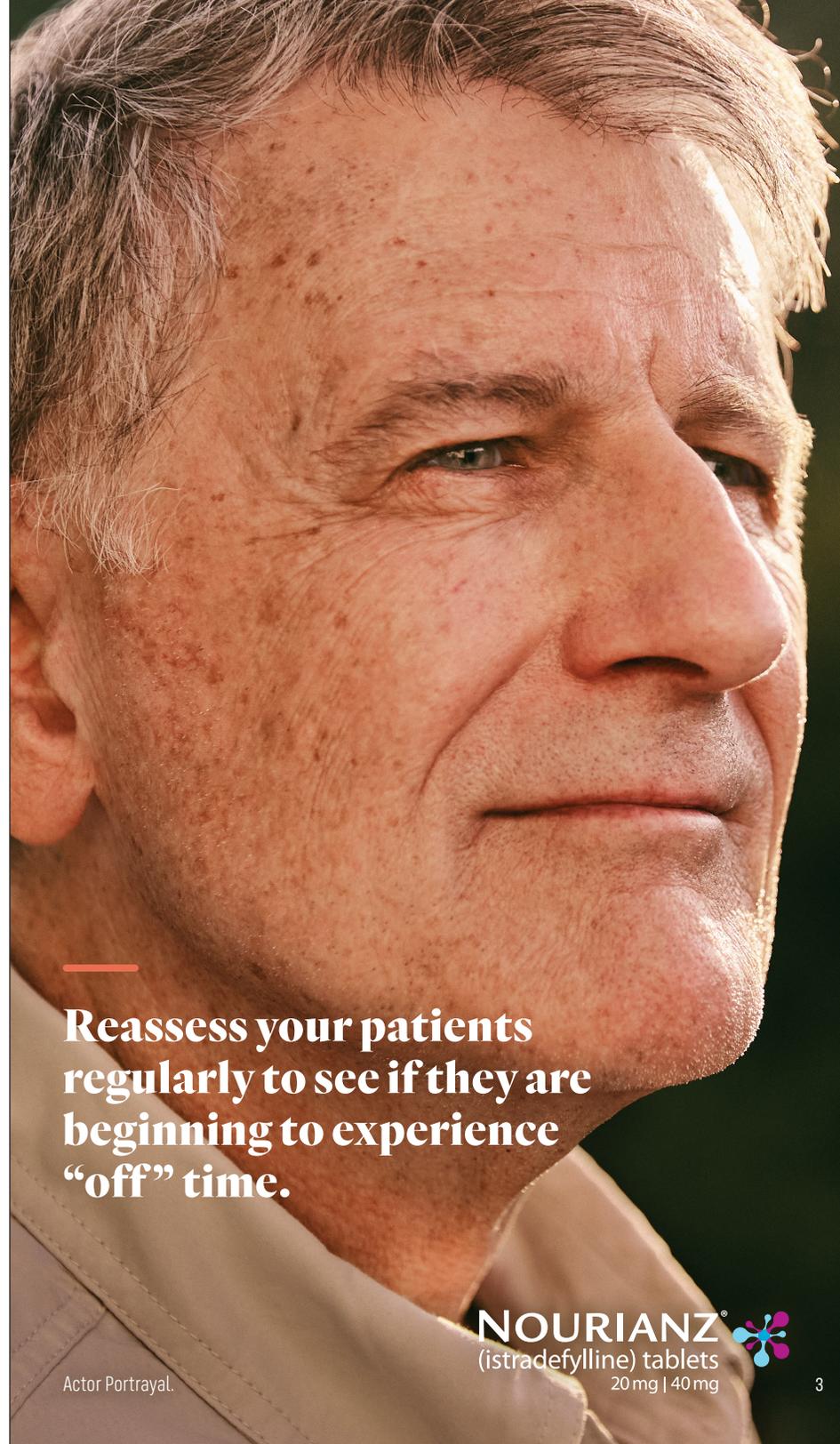
Patients taking levodopa/carbidopa to control symptoms of PD may still experience "off" time.⁵

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.

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Please see full [Prescribing Information](#) for NOURIANZ.



Reassess your patients regularly to see if they are beginning to experience "off" time.

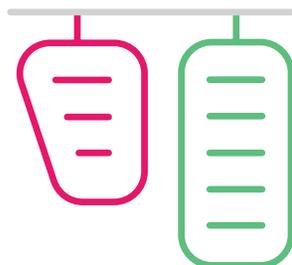
Actor Portrayal.

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There is more to the PD picture than just dopamine²

Both dopamine and adenosine regulate movement in PD.²

Stimulation of **adenosine** A_{2A} receptors is like applying the **brake** of a car, which suppresses movement.⁶⁻⁸



Stimulation of **dopamine** receptors is like pressing the **gas pedal**, which initiates movement.⁶⁻⁸

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.⁶⁻⁸

Important Safety Information (continued)

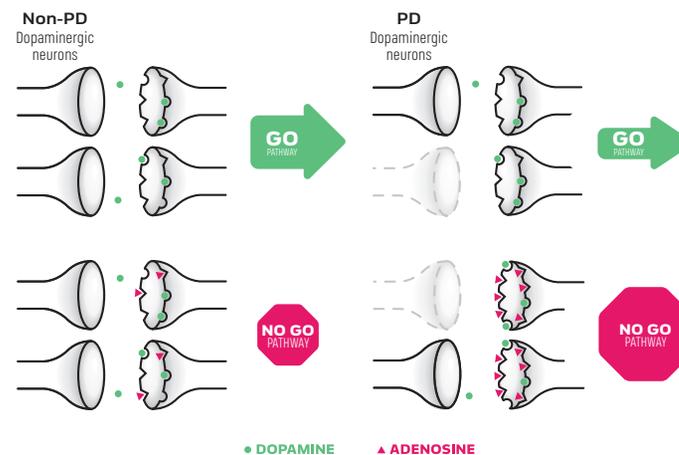
Warnings and Precautions (continued)

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.

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Understanding the go (direct) and no go (indirect) pathways in Parkinson's disease (PD)⁶

Imbalance among these pathways contributes to motor dysfunction.⁹



- Dopamine works in both go and no go pathways, while adenosine works in the no go pathway only⁶
- 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^{6,8}
- In patients with PD, dopamine levels are decreased, reducing the activity of the go pathway and increasing the activity of the no go pathway^{6,8}
- As PD progresses, adenosine A_{2A} receptor concentration increases and the effect of adenosine on the no go pathway becomes more prominent^{10,11}

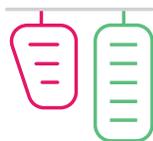
Important Safety Information (continued)

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.

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(istradefylline) tablets
20 mg | 40 mg

Only NOURIANZ® lifts the brake of adenosine in PD^{1,2}



NOURIANZ is a first-of-its-kind adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adults for reducing "off" time in PD.¹

The precise mechanism by which NOURIANZ exerts its therapeutic effect in PD is unknown.¹

In in vitro studies and in vivo animal studies, NOURIANZ was demonstrated to be an adenosine A_{2A} receptor antagonist.¹

Help your patients lift the brake of adenosine with NOURIANZ® (istradefylline).

Please see Important Safety Information throughout. Please see full [Prescribing Information](#) for NOURIANZ.

Actor Portrayals.

With a novel mechanism of action, NOURIANZ® works differently than other adjunct treatments for "off" time in Parkinson's disease (PD)^{1,12-15}

The precise mechanism of action by which NOURIANZ exerts its therapeutic effect in PD is unknown.¹

NOURIANZ blocks A_{2A} receptors.^{1,12-15}

| DRUG CLASS | DOPAMINERGIC ACTIVITY | A _{2A} RECEPTOR ACTIVITY |
|-------------------------------------|-----------------------|-----------------------------------|
| A _{2A} receptor antagonist | | • |
| Levodopa/carbidopa | • | |
| COMT inhibitor | • | |
| Dopamine agonist | • | |
| MAO-B inhibitor | • | |
| Other | • ^a | |

COMT, catechol-o-methyl transferase; MAO-B, monoamine oxidase B.

^aIncludes other classes of medication for PD, like anticholinergics and N-methyl-D-aspartate (NMDA) receptor antagonists, including amantadine, which may have effects on dopamine neurons.

- Dopaminergic treatments affect dopamine receptors in the striatum and in other areas of the brain and peripheral system^{16,17}
- NOURIANZ is highly selective for adenosine A_{2A} receptors¹¹
- In in vitro studies and in vivo animal studies, NOURIANZ was demonstrated to be an adenosine A_{2A} receptor antagonist¹

Important Safety Information (continued)

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.

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If levodopa/carbidopa is wearing off, add once-daily NOURIANZ.¹

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.

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Actor Portrayals.

NOURIANZ[®]: Clinical study description^{1,18}



Randomized, 12-week, multicenter, double-blind, placebo-controlled studies of NOURIANZ 20 mg and 40 mg as adjunctive treatment to levodopa treatment in patients with Parkinson's disease (PD) (mean age=65 years) experiencing "off" time (mean approximately 6 hours/day).

In Studies 1 & 2, patients were randomized to once-daily treatment with NOURIANZ 20 mg, 40 mg, or placebo with the primary endpoint of change from baseline in % of awake time spent in the "off" state:

- Study 1 (N=195) was conducted in the U.S. and Canada
- Study 2 (N=225) was conducted in the U.S.

In Studies 3 & 4, patients were randomized equally to treatment with NOURIANZ 20 mg, 40 mg, or placebo with the primary endpoint of change from baseline spent in "off" time/day:

- Study 3 (N=357) was conducted in Japan
- Study 4 (N=366) was conducted in Japan

Secondary endpoint in all 4 studies was change from baseline in "on" time without troublesome dyskinesia. Endpoints measured using 24-hour patient diaries.

All enrolled patients were on stable doses of baseline therapy for the duration of the studies. Baseline therapy was levodopa/carbidopa (Studies 1, 2, 3, and 4) or levodopa/benserazide (Studies 3 and 4) for all patients with or without other concomitant medications for PD, including dopamine agonists (85%), COMT inhibitors (38%), MAO-B inhibitors (40%), anticholinergics (13%), and/or amantadine (33%).

COMT, catechol-o-methyl transferase; MAO-B, monoamine oxidase B.

Important Safety Information (continued)

Adverse Reactions

The most common adverse reactions with an incidence $\geq 5\%$ 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.

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NOURIANZ is the first and only adjunct therapy that reduces "off" time by lifting the brake of adenosine^{1,2}

Studies 1 and 2: Change in "off" time from baseline to endpoint (12 weeks), daily awake "off" time (% of awake hours)^{1,18}

| | | BASELINE MEAN (% of awake time "off") | ENDPOINT, LS MEAN (% of awake time "off") |
|---------|----------------|---|---|
| STUDY 1 | NOURIANZ 40 mg | 38.44 n=129 | 27.17 n=126 |
| | Placebo | 37.19 n=66 | 32.67 n=65 |
| STUDY 2 | NOURIANZ 20 mg | 39.81 n=112 | 29.77 n=112 |
| | Placebo | 38.72 n=113 | 34.34 n=113 |
| | | CHANGE FROM BASELINE TO ENDPOINT (% of awake time "off") | DIFFERENCE FROM PLACEBO IN % OF AWAKE TIME "OFF" (P-value) |
| STUDY 1 | NOURIANZ 40 mg | -10.49 | -6.78 (P=0.007) |
| | Placebo | -3.71 | |
| STUDY 2 | NOURIANZ 20 mg | -9.49 | -4.57 (P=0.025) |
| | Placebo | -4.92 | |

▪ Pre-specified analysis for Study 1 was ANOVA, and for Study 2 was ANCOVA*

*Least squares mean change from baseline (ANOVA in Study 1, ANCOVA in Study 2). ANOVA, analysis of variance; ANCOVA, analysis of covariance.

Important Safety Information

Warnings and Precautions

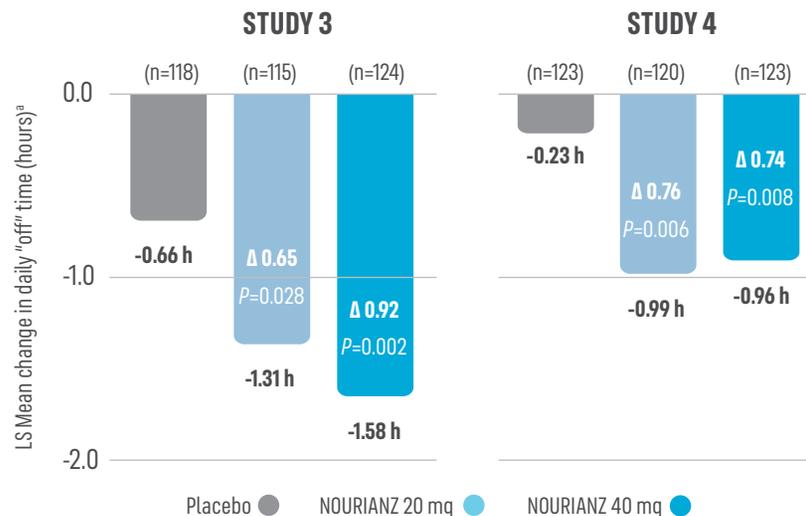
Dyskinesia: NOURIANZ in combination with levodopa may cause dyskinesia or exacerbate pre-existing dyskinesia. In clinical trials, 1% of patients treated with either NOURIANZ 20 mg or 40 mg discontinued treatment because of dyskinesia, compared to 0% for placebo.

Please see Important Safety Information throughout.

10 Please see full [Prescribing Information](#) for NOURIANZ.

Based on 24-hour patient diaries in Studies 3 & 4: NOURIANZ reduced "off" time^{1,18}

At Week 12, patients taking NOURIANZ in clinical trials saw a significant decrease in "off" time from baseline compared to placebo in all 4 studies (N=1,143 patients).¹



^aLeast squares (LS) mean change from baseline (ANCOVA). ANCOVA, analysis of covariance.

Important Safety Information (continued)

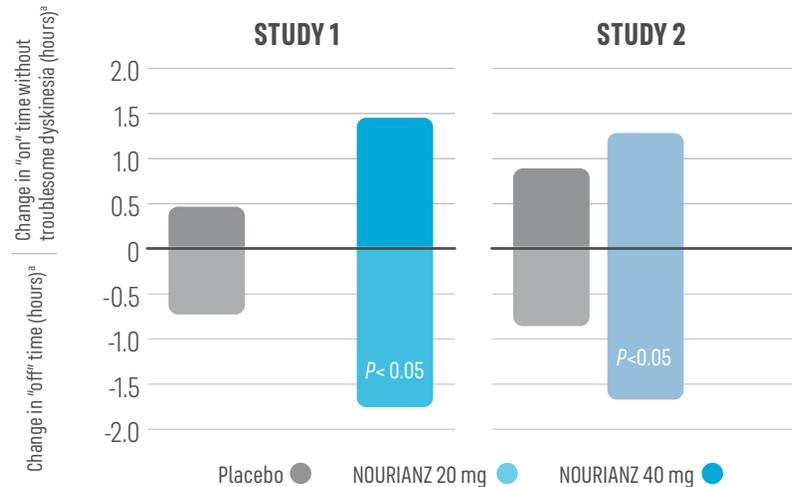
Warnings and Precautions (continued)

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.

"On" Time: Secondary Endpoint

Additional data suggests NOURIANZ® lifts the brake of adenosine to help increase good "on" time^{1,2}

Based on 24-hour patient diaries: NOURIANZ reduced "off" time and was shown to increase good "on" time without troublesome dyskinesia at Week 12^{1,18}



At Week 12, patients treated with NOURIANZ experienced an increase in good "on" time (a change from baseline in good "on" time without troublesome dyskinesia was a secondary efficacy endpoint).^{1,2}

- Increases from baseline with NOURIANZ 20 mg ranged from 0.90 to 1.35 hours. Nominal *P* values: *P*=0.135 in Study 2; *P*=0.085 in Study 3; *P*=0.008 in Study 4
- Increases from baseline with NOURIANZ 40 mg ranged from 0.85 to 1.45 hours. Nominal *P* values: *P*=0.026 in Study 1; *P*=0.048 in Study 3; *P*=0.008 in Study 4
- Increases from baseline with placebo ranged from 0.28 to 0.80 hours

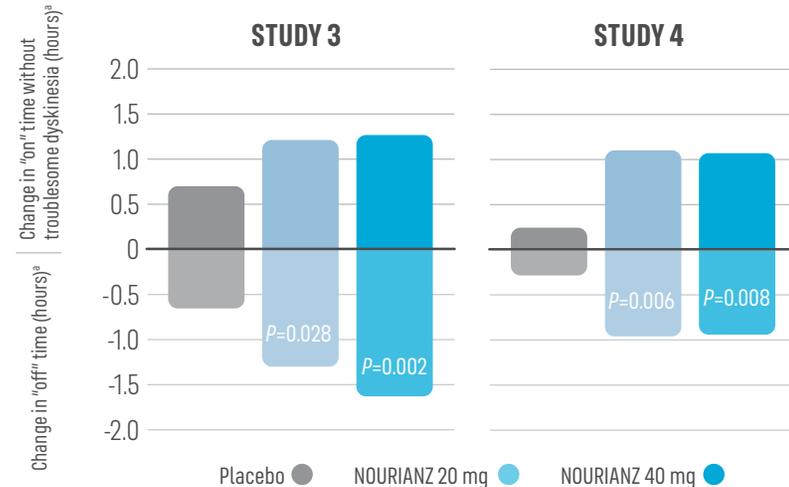
Important Safety Information (continued)

Warnings and Precautions (continued)

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.

12 Please see full [Prescribing Information](#) for NOURIANZ.



^aLeast squares mean change from baseline (ANOVA in Study 1, ANCOVA in Studies 2, 3, and 4). ANOVA, analysis of variance; ANCOVA, analysis of covariance.

Baseline therapy was levodopa/carbidopa and/or levodopa/benserazide for all patients with or without other concomitant medications for PD.

NOURIANZ in combination with levodopa may cause dyskinesia or exacerbate pre-existing dyskinesia.

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.

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NOURIANZ®: Safety data

Incidence of adverse reactions ≥2% in either dose of NOURIANZ and greater than placebo¹

The safety of NOURIANZ was evaluated in randomized, multicenter, double-blind, placebo-controlled trials with 734 patients.¹

| ADVERSE REACTIONS | PLACEBO (n=426) (%) | NOURIANZ 20 mg/day (n=356) (%) | NOURIANZ 40 mg/day (n=378) (%) |
|---|------------------------|--------------------------------------|--------------------------------------|
| Nervous system disorders | | | |
| Dyskinesia | 8 | 15 | 17 |
| Dizziness | 4 | 3 | 6 |
| Gastrointestinal disorders | | | |
| Constipation | 3 | 5 | 6 |
| Nausea | 5 | 4 | 6 |
| Diarrhea | 1 | 1 | 2 |
| Psychiatric disorders | | | |
| Hallucination ^a | 3 | 2 | 6 |
| Insomnia | 4 | 1 | 6 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | 1 | 1 | 3 |
| Investigations | | | |
| Blood alkaline phosphatase increased | 1 | 1 | 2 |
| Blood glucose increased | 0 | 1 | 2 |
| Blood urea increased | 0 | 1 | 2 |
| Respiratory, thoracic, and mediastinal disorders | | | |
| Upper respiratory tract inflammation | 0 | 1 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | 1 | 1 | 2 |

^aIncludes hallucinations (visual, olfactory, somatic, and auditory).

The trials included patients with PD taking a stable dose of levodopa/carbidopa (Studies 1, 2, 3, and 4) or levodopa/benserazide (Studies 3 and 4) with or without other medications for PD. Studies were 12-week studies of 734 patients (NOURIANZ 20 mg [n=356], NOURIANZ 40 mg [n=378]).^{1,2}

Please see Important Safety Information throughout.
Please see full [Prescribing Information](#) for NOURIANZ.

Treatment-emergent adverse reactions of special interest¹⁸

| ADVERSE REACTIONS | PLACEBO (n=426) (%) | NOURIANZ 20 mg/day (n=356) (%) | NOURIANZ 40 mg/day (n=378) (%) |
|--------------------------------|------------------------|--------------------------------------|--------------------------------------|
| Orthostatic hypotension | 5.4 | 6.7 | 6.9 |
| Falls ^a | 9.4 | 6.5 | 6.9 |
| Nausea and vomiting | 4.7 | 4.8 | 6.9 |
| Hallucination ^b | 2.8 | 2.2 | 5.8 |
| Sleep disturbance ^c | 0.7 | 0.8 | 1.6 |
| Increased liver enzymes | 2.6 | 0.8 | 1.9 |
| Impulse control disorder | - | - | 0.3 |
| Neutropenia ^d | - | 0.3 | 0.5 |

^aIncludes fractures and injuries.

^bIncludes hallucination, illusion, auditory, olfactory, somatic, visual, and mixed hallucination.

^cIncludes sleep disorder, irregular sleep phase, poor quality sleep, rapid eye movements, and abnormal sleep.

^dIncludes agranulocytosis, granulocytopenia, leukopenia, neutropenia, neutrophil count decreased, neutrophil percentage decreased, pancytopenia, and white blood cell count decreased.

NOURIANZ®: Discontinuation due to adverse reactions compared to placebo¹

Discontinuation rates due to adverse reactions¹

- 5% discontinuation rate with placebo
- 5% discontinuation rate with NOURIANZ 20 mg
- 6% discontinuation rate with NOURIANZ 40 mg

Discontinuations due to dyskinesia & hallucinations

- 1% of patients treated with either NOURIANZ 20 mg or 40 mg discontinued treatment because of dyskinesia, compared to 0% on placebo
- 1% of patients treated with NOURIANZ 40 mg discontinued due to hallucinations compared with 0% on placebo
- 0% of patients treated with NOURIANZ 20 mg discontinued due to hallucinations compared to 0% on placebo

NOURIANZ, in combination with levodopa, may cause dyskinesia or exacerbate pre-existing dyskinesia. The incidence of dyskinesia was 15% for NOURIANZ 20 mg, 17% for NOURIANZ 40 mg, and 8% for placebo.

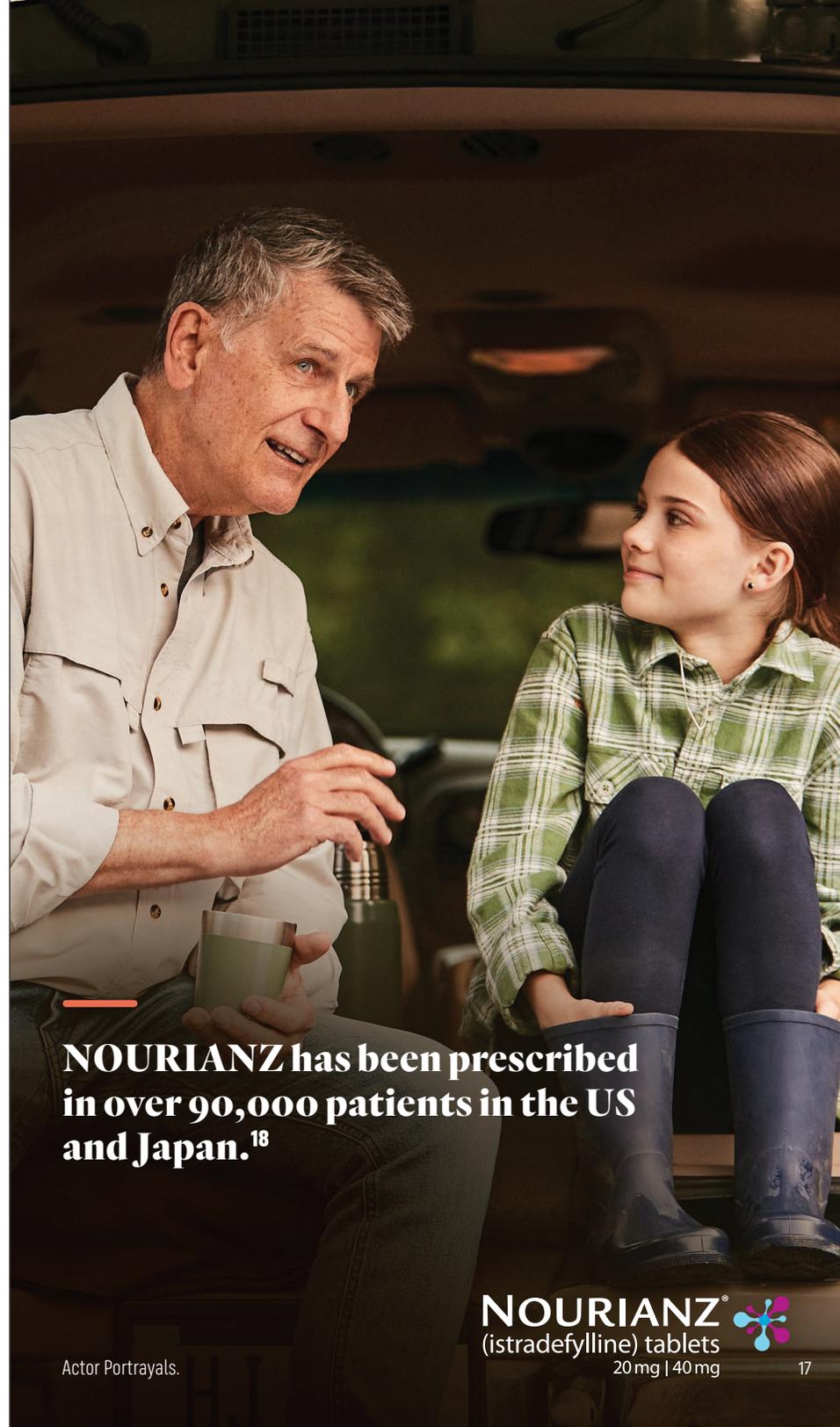
Important Safety Information (continued)

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.

Please see Important Safety Information throughout.
Please see full [Prescribing Information](#) for NOURIANZ.



NOURIANZ has been prescribed in over 90,000 patients in the US and Japan.¹⁸

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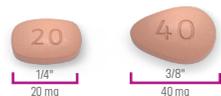
NOURIANZ®: A once-daily oral therapy that patients can take when it fits their schedule¹

Dosing for NOURIANZ can be flexible—it can be taken any time, with or without food.¹

NOURIANZ has¹:

- No food restrictions
- No time-of-day requirements
- No initial titration required

NOURIANZ comes in 2 dose strengths¹:



Not actual size.

Important Safety Information (continued)

Adverse Reactions

The most common adverse reactions with an incidence $\geq 5\%$ 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 throughout.
Please see full [Prescribing Information](#) for NOURIANZ.

Recommended dosage adjustments for NOURIANZ¹

- No dosage adjustments needed for mild, moderate, or severe renal impairment
- No dosage adjustment of levodopa/carbidopa is required when paired with NOURIANZ

| COADMINISTRATION OF NOURIANZ WITH: | DOSAGE RECOMMENDATIONS: |
|--|---|
| Strong CYP3A4 inhibitors | Maximum recommended dose of NOURIANZ is 20 mg/day |
| Strong CYP3A4 inducers | Avoid concomitant use |
| Tobacco smoking (≥ 20 cigarettes/day or equivalent of other tobacco product) | Recommended dose of NOURIANZ is 40 mg/day |

| ADMINISTRATION OF NOURIANZ IN PATIENTS WITH: | DOSING ADJUSTMENT/RECOMMENDATION: |
|--|---|
| Mild hepatic impairment | No dosage adjustment needed |
| Moderate hepatic impairment | Maximum recommended dose of NOURIANZ is 20 mg/day |
| Severe hepatic impairment | Avoid concomitant use |
| Mild, moderate, or severe renal impairment | No dosage adjustment needed |

Connect your patients to the support they need to help get started on NOURIANZ®



NOURIANZ CO-PAY ASSISTANCE

For eligible, commercially insured patients.
Terms and Conditions apply.

CO-PAY CARD PROGRAM

Eligible, commercially insured patients may pay as little as \$20 per month for each prescription of NOURIANZ.

Commercial Insurance

Kyowa Kirin offers co-pay assistance for eligible commercially insured patients. Review the co-pay assistance terms and conditions to determine if your patients with commercial insurance qualify.^{a,b}

No Insurance

Kyowa Kirin offers a patient assistance program for eligible uninsured patients. Download the application form to review the terms and conditions and determine if your patients without insurance qualify.^c

^aPatients must be US residents with an active primary commercial plan; patients with federal or state government insurance such as Medicare, Medicaid, and Tricare are not eligible for co-pay assistance. Other terms and conditions may apply.

^bCommercially insured patients do not need to participate in Kyowa Kirin Cares to be eligible for co-pay assistance.

^cPatients must be US residents with no active medical or pharmacy benefit insurance and an annual gross income ≤400% of the federal poverty level, confirmed by electronic income verification response or documented proof of income.



CONNECT WITH US TODAY

Find support for your patients at [KyowaKirinCares.com](https://www.kyowakirincares.com).

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 Important Safety Information throughout.
Please see full [Prescribing Information](#) for NOURIANZ.

References: 1. NOURIANZ [package insert]. Kyowa Kirin, Inc., Bedminster, NJ, USA. 2. Kalia LV, Brodchie 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. The voice of the patient: Parkinson's disease. Silver Spring, MD: US Food and Drug Administration; April 2016. <https://www.fda.gov/media/124392/download>. Accessed June 11, 2019. 4. Hickey P, Stacy M. Available and emerging treatments for Parkinson's disease: a review. *Drug Des Devel Ther*. 2011;5:241-254. 5. Stocchi F, Antonini A, Barone P, et al. Early detection of wearing off in Parkinson disease: the DEEP study. *Parkinsonism Relat Disord*. 2014;20(2):204-211. 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. 7. 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 8. Fuxe K, Marcellino D, Genedani S, Agnati L. Adenosine A_{2A} receptors, dopamine D2 receptors and their interactions in Parkinson's disease. *Mov Disord*. 2007;22(14):1990-2017. doi:10.1002/mds.21440 9. 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. 10. 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 11. 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. 12. Brichta L, Greengard P, Flajole M. Advances in the pharmacological treatment of Parkinson's disease: targeting neurotransmitter systems. *Trends Neurosci*. 2013;36(9):543-554. 13. Kaakkola S, Wurtman RJ. Effects of COMT inhibitors on striatal dopamine metabolism: a microdialysis study. *Brain Res*. 1992;587(2):241-249. 14. Kong P, Zhang B, Lei P, et al. Neuroprotection of MAO-B inhibitor and dopamine agonist in Parkinson disease. *Int J Clin Exp Med*. 2015;8(1):431-439. 15. Ossola B, Schendzielorz N, Chen SH, et al. Amantadine protects dopamine neurons by a dual action: reducing activation of microglia and inducing expression of GDNF in astroglia. *Neuropharmacology*. 2011;61(4):574-582. 16. Rubi B, Maechler P. Minireview: new roles for peripheral dopamine on metabolic control and tumor growth: let's seek the balance. *Endocrinology*. 2010;151(12):5570-5581. doi:10.1210/en.2010-0745 17. Gerlach M, Double K, Arzberger T, Leblhuber F, Tatschner T, Riederer P. Dopamine receptor agonists in current clinical use: comparative dopamine receptor binding profiles defined in the human striatum. *J Neural Transm (Vienna)*. 2003;110(10):1119-1127. 18. Data on file. Kyowa Kirin Pharmaceutical Development, Inc., Princeton, NJ.

If levodopa/carbidopa is wearing off, consider adding once-daily NOURIANZ® (istradefylline) for your adult patients experiencing “off” episodes.

NOURIANZ®
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20 mg | 40 mg

Add NOURIANZ[®] to help your patients have moments that matter to them¹

- The first and only adenosine A_{2A} receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes^{1,7,8}
- Efficacy and safety established in 4 pivotal clinical studies^{1,7,8}
- The most common adverse reactions include dyskinesia, dizziness, constipation, nausea, hallucination, and insomnia¹
- Once-daily dosing with the flexibility to be taken any time, with or without food¹

Actor Portrayal.

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.

Please see Important Safety Information throughout.
Please see full [Prescribing Information](#) for NOURIANZ.



Visit [NOURIANZHCP.com](https://www.nourianzhcp.com)
or scan this code to learn
more and to access helpful
patient materials.

Kyowa KIRIN

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"I Brake for Moments, Not for Parkinson's." is a trademark of Kyowa Kirin, Inc.

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NOURIANZ[®] 
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20mg | 40mg