

# PALLIATIVE CARE PHARMACY PHAST PHACT



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## Palliative Care Pharmacy Team:

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to:  
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## TODAY'S TOPIC:

### What's New in Palliative Care Medications Drug #5: Istradefylline (Nourianz®)

#### Background:

Istradefylline (Nourianz®) is an adenosine A2A receptor antagonist approved for Parkinson's disease. In combination with levodopa/carbidopa

- Initial US approval: 2019
- Available as: 20mg and 40mg tablets

#### Importance:

Patients suffering from Parkinson's disease often complain of complications from motor fluctuations and dyskinesias. There are device-assisted and surgical treatments options for these patients but still patients experience wearing off. Palliative care providers often care for patients with Parkinson's disease; so knowledge about new pharmacological options is important.

#### Pharmacology:

<b>MoA:</b>	Istradefylline is an adenosine A2A receptor antagonist. The exact mechanism by which istradefylline exerts its therapeutic effect in Parkinson disease is unknown
<b>ADME:</b>	<ul style="list-style-type: none"><li>- A: Tmax: 4 hours</li><li>- M: Weak inducer and inhibitor of CYP3A4, substrate of CYP1A1 and CYP3A4</li><li>- E: T ½: 83 hours</li></ul>
<b>DIs:</b>	Concomitant use with strong CYP3A4 inducers may result in decreased istradefylline exposure Concomitant use with strong CYP3A4 inhibitors may result in increased istradefylline exposure

Key: MoA: Mechanism of Action; ADME: Absorption, Distribution, Metabolism, and Excretion; DI: Drug Interaction; Tmax: time until max concentration; T ½: terminal half-life; Cmax: max concentration; AUC: area under the curve

## Other Clinical Points:

<b>CIs:</b>	- Hypersensitivity
<b>Warnings and Precautions:</b>	- Neurologic: New or exacerbation of pre-existing dyskinesia has been reported when administered with levodopa - Psychiatric: Use not recommended in patients with major psychotic disorder due to risk of exacerbating psychosis
<b>Dosing:</b>	Administer 20mg orally once daily, initial titration is not needed; may increase to MAX 40mg once daily based on individual need and tolerability
<b>ADRs:</b>	- Gastrointestinal: Constipation (5-6%), Nausea (4-6%) - Neurologic: Dizziness (3-6%), Insomnia (1-6%)

Key: CI: contraindications; ADRs: adverse drug reactions

## The Literature:

- [Sci Rep. 2017 Dec 21;7\(1\):18018.](#)  
**The effect of istradefylline for Parkinson's disease: A meta-analysis.**
  - **Results:** Six studies satisfied our inclusion criteria. Istradefylline (40mg/day) decreased off time and improved motor symptoms of Parkinson's disease in homogeneous studies. Istradefylline at 20mg/day decreased off time and improved motor symptoms, but heterogeneity was found in the analysis of the former among studies. There was a significant effect of istradefylline on dyskinesia in homogeneous studies. Publication bias, however, was observed in the comparison of dyskinesia. Other adverse events showed no significant difference.
  - **Conclusion:** "The present meta-analysis suggests that istradefylline at 40mg/day could alleviate off time and motor symptoms derived from Parkinson's disease. Dyskinesia might be worsened, but publication bias prevents this from being clear."

## So... What does this all mean Jenn?

- Istradefylline has been available in Japan since 2013, and since have suggested impressive results. As above the meta-analysis suggests the only downside is dyskinesias may be worse
- Another great review article can be found [here](#)
- Currently istradefylline costs: \$60/tablet (or approximately \$1800/month)
- UPMC has not yet reviewed this agent
- Istradefylline should be considered for advanced patients with significant off time and motor symptoms – already receiving levodopa therapy – who do not significant struggle with dyskinesias
- It's mostly tolerable side effect profile may be more helpful with patients with complicated by depression or cognitive impairment – but use with caution with strong CYP 3A4 inducers or inhibitors

**CLINICAL PEARL: Istradefylline is an adenosine A2A receptor antagonist approved for Parkinson's disease in combination with levodopa/carbidopa.**