Parkinson's Today: Emerging Treatments and the Critical Role of the Multidisciplinary Healthcare Team

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Movement Disorders Specialist

IPMDC Medical Director

Inova™

Inova
Parkinson's and
Movement Disorders Center
10 YEARS

Disclosures

D. Falconer has received consultancy or speaker fees from Abbott Laboratories, Abbvie, Amneal, Acorda, GE HealthCare, Kyowa Kirin, Neurocrine, Merz, Medtronic, and Supernus.

Dr. Falconer also receives compensation as an FTC and Justice Department subject matter expert.

What's on Tap?

Learning objectives:

- Describe the core features and progression of Parkinson's disease, including key motor and non-motor symptoms.
- Identify current pharmacologic treatments for Parkinson's disease with emphasis on newer and emerging treatment options.
- Differentiate targeted therapies (e.g. deep brain stimulation, focused ultrasound, botulinum toxin injections, and subcutaneous pump/device therapies) and their appropriate use cases.
- Explain the structure and role of a comprehensive movement disorders center in optimizing patient outcomes.
- Recognize the role of multidisciplinary healthcare providers in supporting individuals with Parkinson's disease and facilitating appropriate referrals.

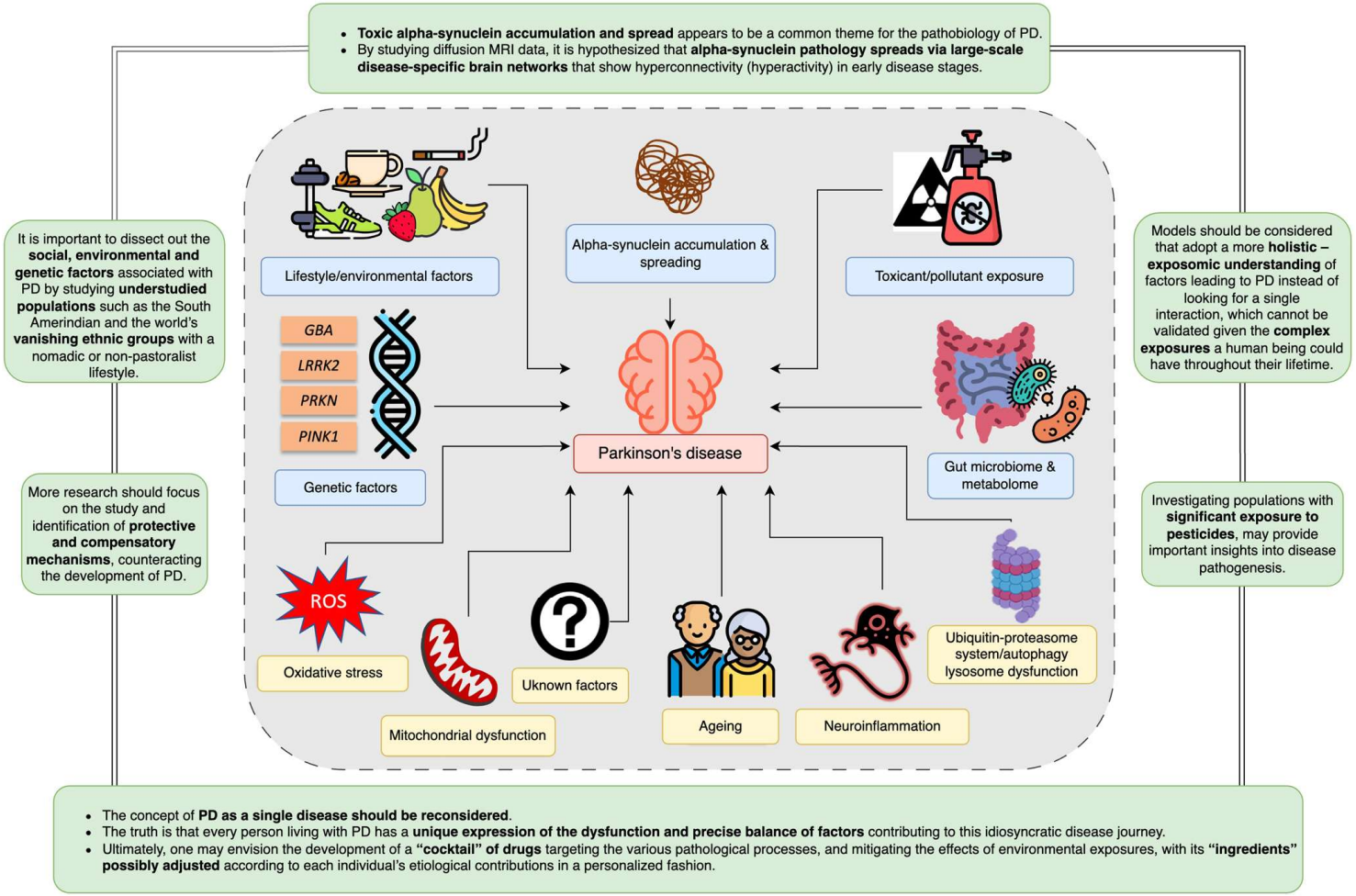
What is Parkinson's?

Simply a chemical deficiency!

Causes?

Classically
NOT inherited
~ 10%

Life expectancy is the same as someone without Parkinson's - if adequately treated.



Müller-Nedebock, A.C., Dekker, M.C.J., Farrer, M.J. *et al.* Different pieces of the same puzzle: a multifaceted perspective on the complex biological basis of Parkinson's disease. *npj Parkinsons Dis.* **9**, 110 (2023). https://doi.org/10.1038/s41531-023-00535-8

How do we diagnose Parkinson's?

Movement disorder specialist

- Additional fellowship training in movement disorders
- Focus is primarily on movement disorders = more up to date on latest treatments and understand the variation in movement patients
- Knows the questions to ask patients
- General neurologist sees a wider range of neurological conditions, like headache, stroke, epilepsy, MS, etc.

An expert general neurologist
≠ a Movement Disorders Specialist

- Symptoms/History/Exam
  + Response to Medications
- DaTscan
  (GE Healthcare is a sponsor)
  Syn-One Skin Biopsy
  (details to follow)
- "Parkinsonism"
  is not a diagnosis

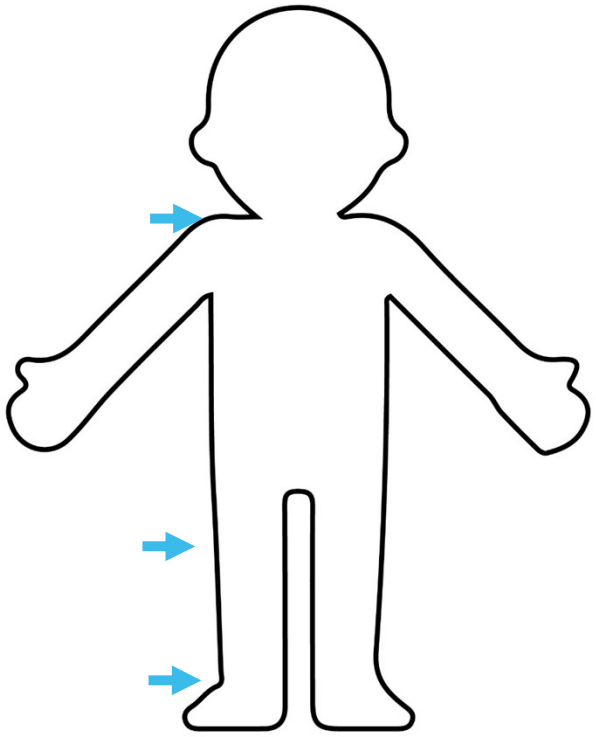
Syn-One skin biopsy

Checks for the deposit of phosphorylated alpha-synuclein in the skin

FDA approved to assist with a diagnosis of Parkinsonism.

95% accuracy

Life expectancy is the same as someone without Parkinson's if adequately treated.



What happens if you have reduced dopamine?

Motor and Non-motor Symptoms

Systems which function inappropriately due to reduction in Dopamine or one of its byproducts

Motor Symptoms

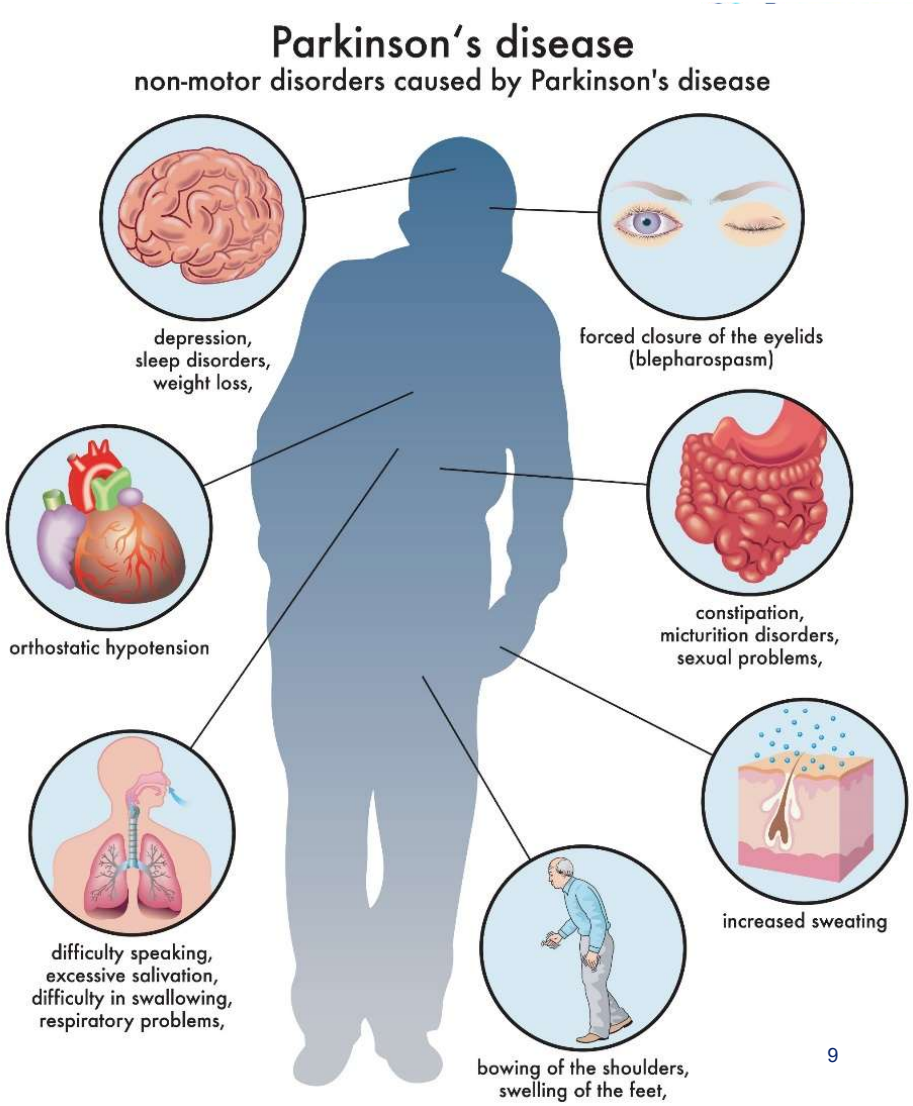
- Resting tremor
- Tremor with position
- Bradykinesia (slowness)
- Rigidity (stiffness)
- Dystonia
- Slow walking, shuffle, reduced arm swing
- Balance issues
- Reduced facial expression
- Speech changes (hypophonia)

Examples of Non-motor symptoms

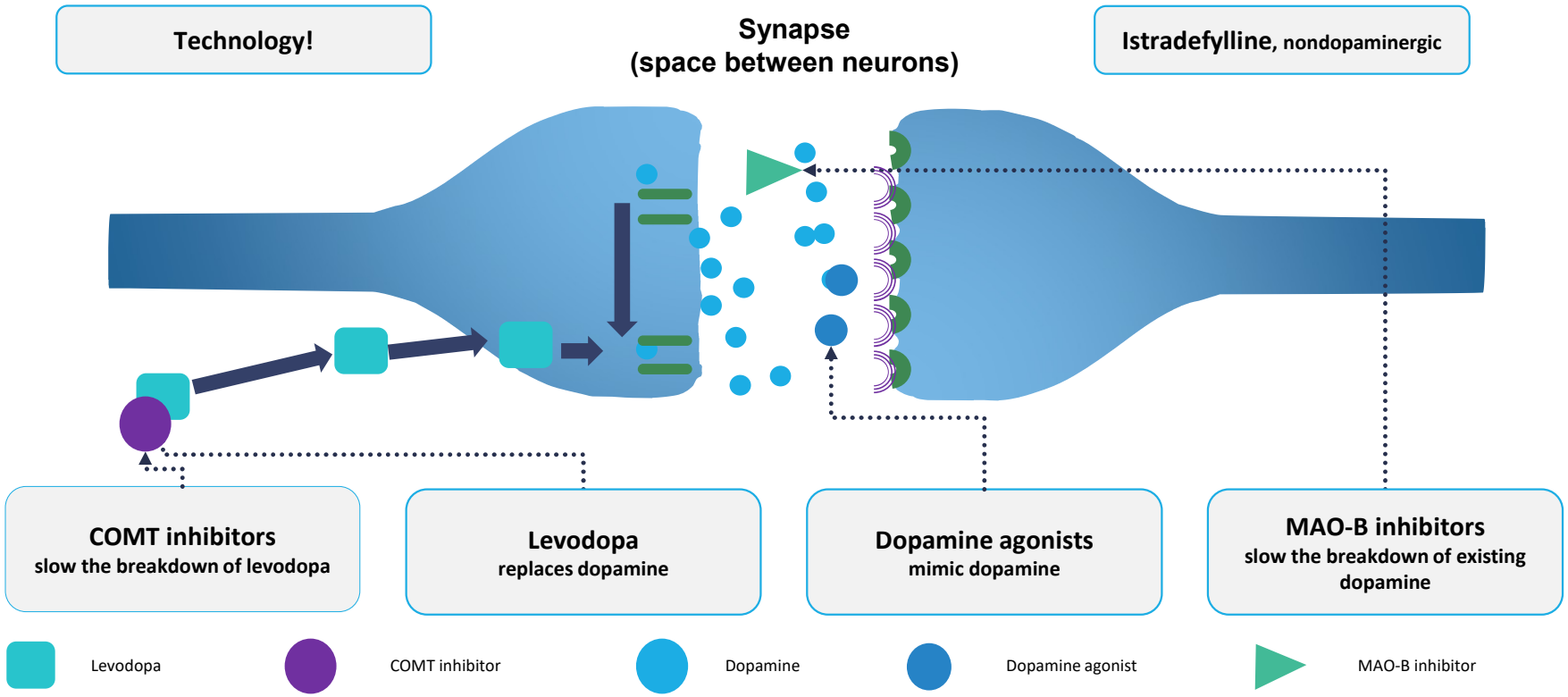
Can present years before diagnosis*

- Loss of sense of smell*
- Constipation*
- Talking in sleep or acting out dreams*
- Anxiety / depression*

- Bladder issues
- Excessive saliva/drooling
- Fatigue
- Vision changes
- Cognitive changes / hallucinations
- Lightheadedness / dizziness on standing
- Skin problems
- Problems sweating



Different avenues of treatment



COMT = catechol-*O*-methyltransferase.
MAO-B = monoamine oxidase-B.

Kalia LV et al. *Lancet.* 2015;386:896–912

Inova™

RYTARY®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES

CREXONT®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
35mg/140mg · 52.5mg/210mg
70mg/280mg · 87.5mg/350mg

New toolbox and growing

VYALEV™
240 mg/mL+12 mg/mL solution for infusion
foslevodopa/foscarbidopa

ONAPGO™
(apomorphine HCl)
injection, for subcutaneous use • 4.9 mg/mL

NUPLAZID™
(pimavanserin) tablets

Parkinson's and
Movement Disorders Center

NUEDEXTA®
(dextromethorphan HBr and quinidine sulfate) capsules
20 mg
10 mg

Dopamine Agonist

Carbidopa/Levodopa formulation

MAOB inhibitor

NOURIANZ™
(istradefylline) tablets
20 mg | 40 mg

COMT inhibitor

Neupro®
(Rotigotine Transdermal System)

A2a agonists

Amantadine derivatives

Rescue Therapies

APOKYN® Be on. Live life.
apomorphine hydrochloride injection

Inbrija™
(levodopa inhalation powder)
42 mg capsules

Symptom specific therapies

XADAGO®
(safinamide) tablets

Ongentys®
(opicapone) capsules

GOCOVRI®
(amantadine) extended release capsules

Carbidopa/Levodopa

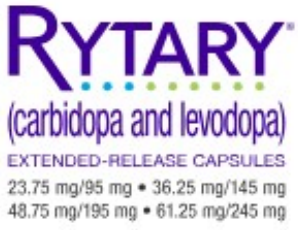
Tablets

Sinemet

Dhivy

Parcopa

Capsules



Now generic
Carbidopa/ Levodopa ER

Brand name is still available
Ask for "authorized generic".

Technology

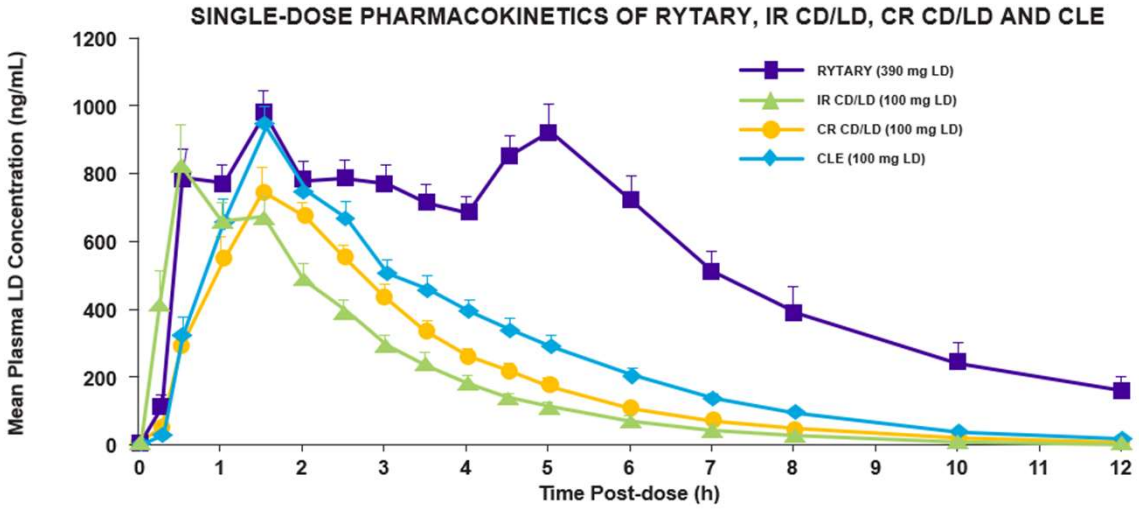
Longer lasting carbidopa/levodopa 2015

Rytary™ (carbidopa/levodopa)
Amneal

RYTARY®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
23.75 mg/95 mg • 36.25 mg/145 mg
48.75 mg/195 mg • 61.25 mg/245 mg

History of evolution
of levodopa delivery -------->

- Equivalent dose of Rytary on average 1.2 more hours of "on time" compared to IR.

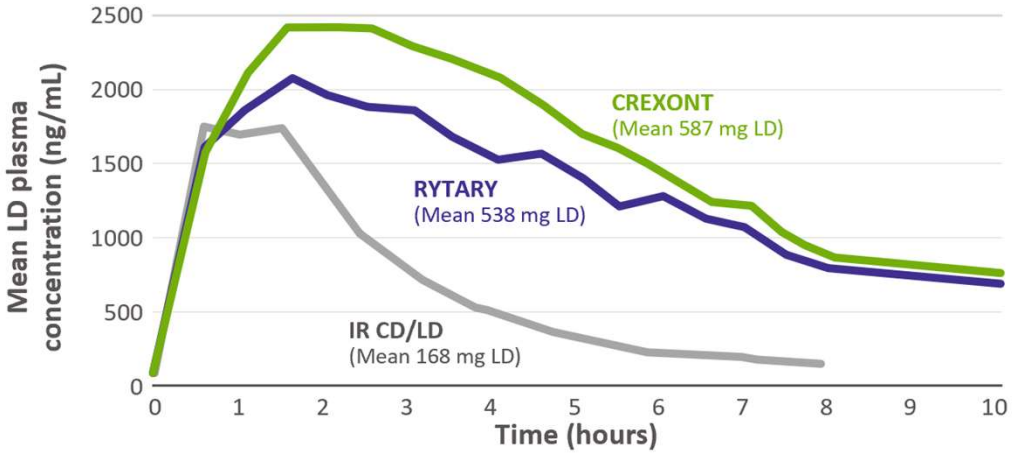


Longer lasting carbidopa/levodopa 2025

Crexont ™ (carbidopa/levodopa)
Amneal

CREXONT®
(carbidopa and levodopa)
EXTENDED-RELEASE CAPSULES
35mg/140mg · 52.5mg/210mg
70mg/280mg · 87.5mg/350mg

- Capsule/bead formula.
- Adhesive polymer.
- 4.8 hrs above 50% Cmax, 3x daily (avg)
- 1.6 hr longer on time per dose (avg)



1. Hauser RA et al. *JAMA Neurol.* 2023;80(10):1062-1069.

Rescue options

Apokyn™ (apomorphine injection)
Supernus

Rapid onset dopamine agonist via injection

For different types of OFF episodes:

- Rapid off, wearing off
- Dose failure / unexpected off
- Delayed on
- First AM symptoms or exercise intolerance

Achieve ON within 10-20 minutes

Inbrija™ (levodopa inhalation powder)
Merz

Rapid onset levodopa through inhaler

For different types of OFF episodes:

- Rapid off, wearing off
- Dose failure / unexpected off
- Delayed on
- First AM symptoms or exercise intolerance

Achieve ON within 10 minutes, can take up to 5x daily

Maximizing levodopa

Ongentys™ (opicapone)
Amneal

- 1x daily peripheral COMT inhibitor
- Significant boost in levodopa availability.
- 1.95 improvement in off time, Δ1.01hr

Amantadine, off time + dyskinesia control

Gocovri™ (amantadine ER)

Supernus

- 1x daily delayed release, extended release.
- Dyskinesia AND Off Time
- 41% reduction in dyskinesia,
  21% reduction in off time (avg)
  45% more good ON time daily

Non-dopaminergic approach

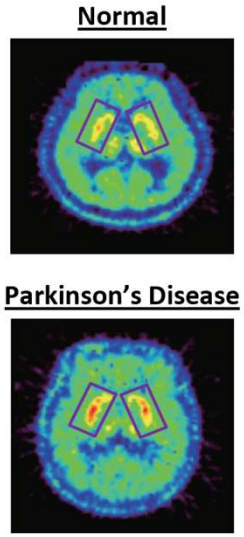
Nourianz™ (istradefylline)

NOURIANZ™ (istradefylline) tablets 20 mg | 40 mg

Indicated as adjunctive treatment to levodopa in adult patients with Parkinson's disease (PD) experiencing wearing off phenomena. Can help with freezing gait.

- Indirect pathway – adenosine A2a receptor antagonist
- Addition reduced levodopa dose escalation over 37 weeks[1] and 72 months[2]
- Effective in tremor dominant and postural instability and gait difficulty subtypes (*post hoc*)[3].

A_{2a} Receptor PET imaging[1]



Increase in A_{2a} Receptors with PD progression[1]

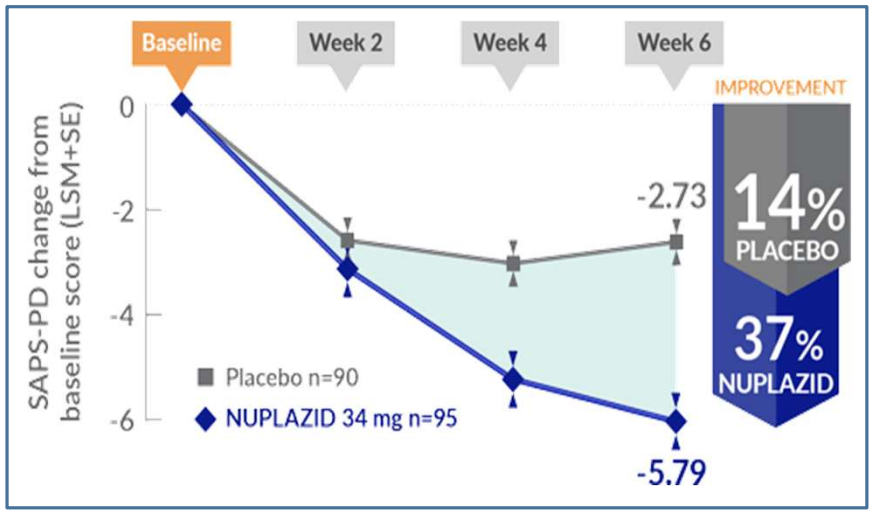
1.Hatano T et al. Impact of Istradefylline on Levodopa Dose Escalation in Parkinson's Disease: ISTRA ADJUST PD Study, a Multicenter, Open-Label, Randomized, Parallel-Group Controlled Study. Neurol Ther. 2024 Apr;13(2):323-338.
2.Hattori N et al. Real-world evidence on levodopa dose escalation in patients with Parkinson's disease treated with istradefylline. PLoS One. 2023 Dec 22;18(12):e0269969
3.Torres-Yaghi et al. Istradefylline effects on tremor dominance (TD) and postural instability and gait difficulty (PIGD). Clin Park Relat Disord. 2023 Oct 14;9:100224.

Hallucinations and Psychosis

Nuplazid™ (Pimavanserin)
Acadia-

NUPLAZID™
(pimavanserin) tablets

- First antipsychotic medication specifically designed for hallucinations and 'psychosis' associated with Parkinson's Dementia and Lewy Body Dementia.
- Serotonin Agonist with no impact on dopamine receptors
- + SAPS-PD improvement with no change in UPDRS
- More effective when prescribed sooner, when hallucinations are beginning.



Hacksell, Uli et al. "On the Discovery and Development of Pimavanserin: A Novel Drug Candidate for Parkinson's Psychosis." *Neurochemical Research*39.10 (2014): 2008–2017. *PMC*. Web. 4 June 2015.

Timing of Medications

- Very little flexibility in scheduling
- 4 hours means 4 hours apart
- Timing of protein and meals with some oral medications

Why do medicines not work for some people?

- Progression of the disease
- Parkinsonism (PSP, MSA, CBD)
- Other conditions
- Expectations:
  Some symptoms don't respond that well
  e.g. fatigue, mood, cognition
- Not taking meds as prescribed
- Not on optimal combination of meds
- Meds are underdosed
- Not enough time has lapsed to allow meds to work

How the gut impedes absorption

- Diet
- Dehydration
- Constipation

What about when the medicines 'stop working'

Longer acting medicines

Complimentary medicines

Targeted Technologies

Targeted Technology

- Botulinum toxin injections
- Vyalev / Onapago Subcutaneous Pump/Device
- Focused Ultrasound (FUCS)
- Deep Brain Stimulation

Technology – Foslevodopa Pump

Vyalev™ (foscarbidopa/foslevodopa)
Abbvie

- 24-hour subq foslevodopa pump
- 2.72 hr increased ON time
- 83% waking in the ON state, reduced sleep disturbance (36%)
- Replaces oral levodopa

Pahwa R, Soileau MJ, Standaert DG, et al. Rapid onset of good ON-time and improvement in motor-state stability in aPD patients after treatment with continuous subcutaneous foslevodopa/foscarbidopa. Poster presented at: The International Congress of Parkinson's Disease and Movement Disorders (MDS); September 15-18, 2022; Madrid, Spain.
Hauser RA, Bergmans B, Malaty I, et al. Effects of continuous subcutaneous infusion of foslevodopa/foscarbidopa on sleep dysfunction in people with Parkinson's. Poster presented at: The American Academy of Neurology 76th Annual Meeting (AAN); April 13-18, 2024; Denver, CO

Technology – Apomorphine Pump

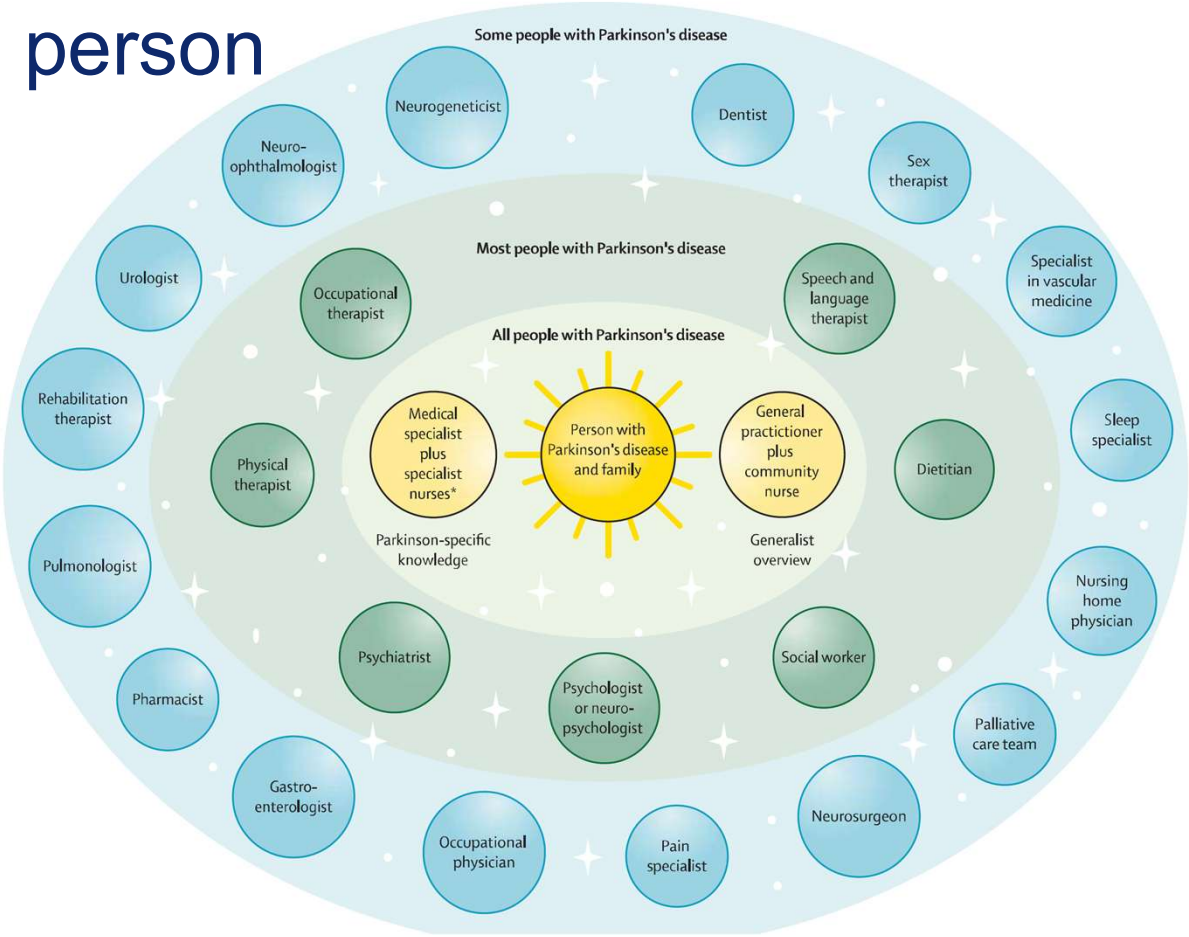
Onapgo™ (apomorphine infusion)
Supernus

- Add on subq pump during waking hours
- 2.8+ hr increased ON time
- Added in addition to foundational oral therapies

Caring for the whole person

It takes a village . . .

Caring for people with Parkinson's requires an interdisciplinary healthcare team!



Therapies Are Important

Therapies are key to helping people with Parkinson's keep doing things and have a better life.

Physical Therapy (PT):
Helps with balance, walking, strength, and stopping falls. (lower body)

Speech-Language Pathology (SLP):
Helps with clear talking, voice loudness, trouble swallowing, and cognition.

Check out
ipmdc.org/therapy
For our list of teams with experts.

Occupational Therapy (OT):
Helps with daily tasks and activities, finding tools to make things easier, and staying independent. Driver rehabilitation. (upper body)

Living well with Parkinson's

***Movement is medicine*!**

The right medications +

Challenging Exercise

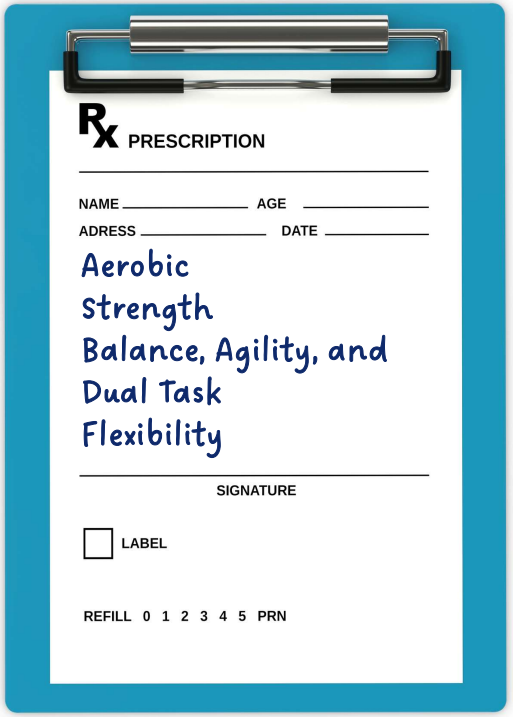
Social interaction

Eating well

Reducing stress

Getting enough sleep

Staying mentally active



Parkinson's and Movement Disorders Center

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Parkinson's and Movement Disorders Center

CARING FOR PATIENTS WITH PARKINSON'S

Medications - On time, every time:

- Parkinson medications must be given **on time every time** as prescribed by their neurologist.
- There is no "window" with prescribed times
- A Parkinson's patient's medications should NOT be changed without consulting the patient's neurologist.
- Changing the patients medications to formulary meds can exacerbate their Parkinson's disease, create harm and extend their hospitalization.

For patients with Parkinson's disease, it is important that in addition to being treated for the condition that led to their hospitalization, their treatment for Parkinson's disease continues as prescribed by their neurologist.

Contraindicated medications to avoid:

Haloperidol (Haldol) and most neuroleptics

- Phenothiazines & antiemetics: prochlorperazine (Compazine), metoclopramide (Reglan), promethazine (Phenergan) and droperidol (Inapsine)
- Commonly prescribed opiod medications are contraindicated with selective MAO-B inhibitors such as rasagiline (Azilect), selegiline (l-deprenyl, Eldepryl), and selegiline HCL oral disintegrating (Zelapar)

Medications considered safe

- Pimavanserin (Nuplazid), quetiapine (Seroquel) and clozapine (Clozaril)
- Trimethobenzamide (Tigan) and ondansetron (Zofran)

More information at ipmdc.org/hospital

We recommend:

- The patient and/or caregiver be allowed to self-administer the patient's Parkinson medications.
- Patients be permitted to use medications from their home supply, in their original containers.
- The caregiver be present where possible, to advocate for the patient.
- Should a nasogastric tube be required, carbidopa/levodopa 25/100 immediate release tablets can be crushed and administered via the tube.

Sonia Gow
Program and Community Care Manager
Inova Parkinson's and Movement Disorders Center (IPMDC)
sonia.gow@inova.org | 703.375.9987 | ipmdc.org | inova.org/move

Contact Inova Neurosciences 24/7
571.472.4200

Inova™

Caring for Patients With Parkinson's

AVOID:

haloperidol (Haldol™) and most neuroleptics
(blocks dopamine – can impact swallowing)

Forms available at: **ipmdc.org/hospital**

- For emergency responders
- Emergency contact into
- Medications list
- Medical history
- Hospital Go Bag check list
- Communication card

How can you help?

- Learn as much as you can about movement and memory disorders.
  - Thank you for joining us today!
  - Sign up for *IPMDC News for Health Care Professionals* for updates on IPMDC and Inova Neurosciences programs

- We appreciate your feedback for what you want to know, and how we can help you help our patients.
  Contact sonia.gow@inova.org.