Carbidopa-Levodopa: Revving Up Relief – Choose Your Formula!

Braylee Wardwell, PharmD & Constance Chan, PharmD
PGY-2 Ambulatory Care Pharmacy Residents
Department of Pharmacy | UConn Health
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Disclosures

- Drs. Chan and Wardwell have no actual or potential conflict of interest associated with this presentation.

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Abbreviations

- PD: Parkinson's Disease
- COMT: catechol-O-methyltransferase
- MAO-B: monoamine oxidase B
- MAOI: monoamine oxidase inhibitors
- BBB: blood brain barrier
- CNS: Central nervous system
- CD-LD: carbidopa-levodopa
- LD: levodopa
- Tx: Treatment
- BID: twice daily
- TID: three times daily
- ER: extended release
- CR: controlled release
- IR: immediate release
- PK: pharmacokinetics
- PD: pharmacodynamic
- MD: maintenance dose
- FDA: Food and Drug Administration
- PEG-J: percutaneous endoscopic gastrostomy
- ADE: Adverse drug events

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Pharmacists Objectives

Describe the role of carbidopa-levodopa in Parkinson’s disease and the use of different carbidopa-levodopa formulations

Recognize the differences between each carbidopa-levodopa formulation

Discuss the appropriate patient who may benefit from transitioning to a different formulation of carbidopa-levodopa

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Pharmacy Technicians Objectives

- Describe the functions of the carbidopa-levodopa and how it aids in treatment for patients with Parkinson's disease
- List different forms of carbidopa-levodopa
- Identify when to refer patients with questions about Parkinson's disease to a pharmacist

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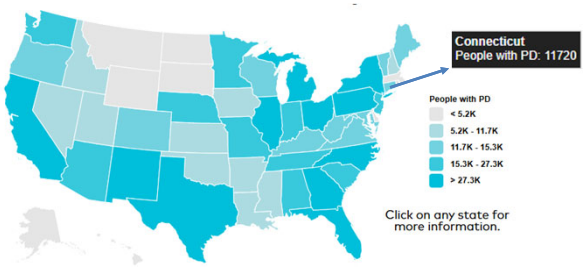
Parkinson's Disease Background

- Neurodegenerative disorder that causes both motor and nonmotor symptoms
- Destruction of substantia nigra neurons → lose dopamine producing cells
- Norepinephrine is destroyed as well
- Cause still unknown – many theories
  - Environmental model
  - Genetic component



Pringsheim T, et al. *Neurology*. 2021;97(20):942-957; Parkinson's disease: Causes, symptoms, and treatments. https://www.nia.nih.gov/health/parkinsons-disease#:~:text=Parkinson's%20disease%20is%20a%20brain,gradually%20and%20worsen%20over%20time.; DeMaagd G, et al. P T. 2015;40(8):504-532; Statistics. https://www.parkinson.org/understanding-parkinsons/statistics

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Epidemiology

- Nearly 1 million people in the US are living with Parkinson's Disease
- Second-most common neurodegenerative disease
- Nearly 90,000 people in the US are diagnosed with PD each year
- Incidences of Parkinson's disease increases with age, but an estimated 4% of people with PD are diagnosed before age 50
- Men are 1.5x more likely to have Parkinson's Disease than women

Statistics. https://www.parkinson.org/understanding-parkinsons/statistics

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Signs and Symptoms

Motor symptoms		**Mental status changes**	
• Bradykinesia • Dizziness or fainting • Drooling • Dyskinesia • Dystonia • Facial masking	• Micrographia • Postural instability (trouble with balance & falls) • Rigidity • Stooped posture • Tremor • Trouble moving or walking	• Confusion (towards end stages of disease) • Dementia/Lewy Body disorder • Psychosis (paranoia, hallucination) • Sleep disturbances	
Autonomic symptoms		**Other symptoms**	
• Urinary incontinence • Constipation • Diaphoresis	• Orthostatic blood pressure changes • Paroxysmal flushing • Sexual disturbances	• Difficulty swallowing, chewing, and speaking • Fatigue • Oily skin/ seborrheic dermatitis	• Pedal edema • Weight loss • Impulse control disorders • REM sleep behavior disorder • Punding

Movement symptoms. https://www.parkinson.org/understanding-parkinsons/movement-symptoms; Non-movement symptoms. https://www.parkinson.org/understanding-parkinsons/non-movement-symptoms

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Pharmacological Treatments for PD

Initial practice recommendations:

- No current disease-modifying pharmacologic treatments
- Symptomatic treatment only
- "Wait and see" approach

Goals of anti-parkinson drugs

- Restore dopamine receptor function
- Inhibition of muscarinic cholinergic receptors

Dopamine precursors	Levodopa Carbidopa
Dopamine agonists	Pramipexole Ropinirole Rotigotine Apomorphine Bromocriptine
COMT inhibitors	Entacapone Opicapone Tolcapone
MAO-B inhibitors	Rasagiline Selegiline Safinamide
Anticholinergics	Benztropine Trihexyphenidyl
Miscellaneous	Amantadine

Pringsheim T, et al. *Neurology*. 2021;97(20):942-957; Patel T, et al. *Can Pharm J (Ott)*. 2014;147(3):161-170

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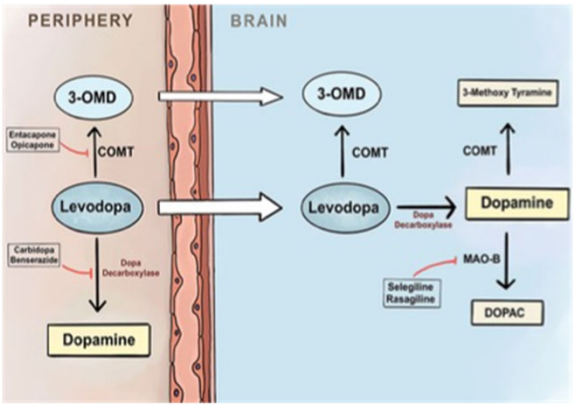
Levodopa

- Prodrug - immediate precursor of dopamine
- Very little of drug enters brain due to extracerebral metabolism
- Over time becomes less effective due to:
  - Progressive loss of dopaminergic neurons
  - Some patients require reduced doses to prevent side effects



Ramesh S, Arachchige ASPM. AIMS Neurosci. 2023;10(3):200-231; Di Stefano A, et al. Curr Pharm Des. 2011;17(32):3482-3493; Lenka A, et al. *Expert Rev Neurother*. 2022;22(6):489-498.

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Levodopa Pharmacokinetics

Absorption:

- Absorbed in small intestine
- Affected by pH and gastric emptying (except enteral suspension & subcutaneous infusion pump)
- Take oral formulations 1 hour before or 2 hours after protein
- High-fat, high-calorie meals delay oral absorption (↑2 hrs)

Distribution

- Plasma level time to peak in 0.5 to 4.5 hrs

Metabolism

- Mainly through dopa decarboxylation and O-methylation

Excretion

- Unchanged in urine

Carbidopa and Levodopa. Lexi-Drugs. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at http://online.lexi.com

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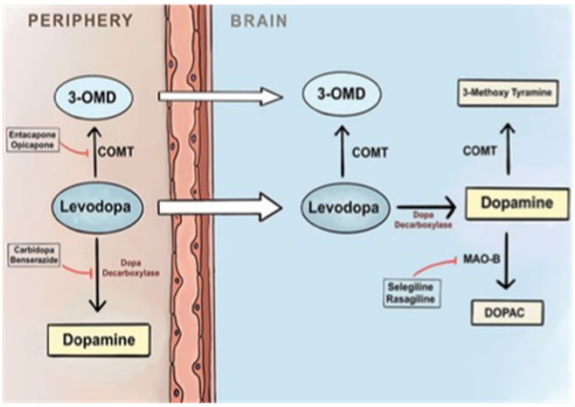
Carbidopa

- Decarboxylase Inhibitor
- Does not cross BBB
- Allows for higher CNS concentration of dopamine with lower doses of levodopa
- Reduces nausea



Zhu H, et al. PLoS One. 2017;12(9):e0183484; Lenka A, et al. *Expert Rev Neurother*. 2022;22(6):489-498

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Carbidopa - Levodopa

- Contraindications
  - Concurrent use with nonselective MAOIs or use within the last 14 days
- Side effects
  - Dyskinesia
  - Nausea and vomiting
  - Orthostatic hypotension
  - Psychiatric behavior abnormalities (e.g. hallucinations)

Carbidopa and Levodopa. Lexi-Drugs. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at http://online.lexi.com

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Knowledge Question

What is the primary role of carbidopa-levodopa in the management of Parkinson's disease?

a) Carbidopa and levodopa directly increase dopamine production in the brain
b) Levodopa converts to dopamine in the brain, and carbidopa prevents its breakdown
c) Carbidopa and levodopa work by inhibiting the breakdown of dopamine in the brain

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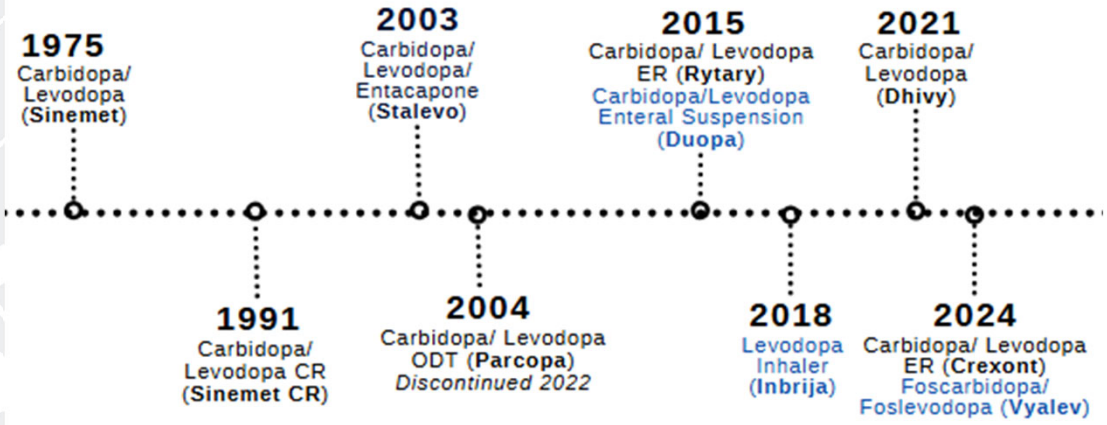
Timeline of CD-LD Formulations



Blue: Non-oral formulation
Black: oral formulation

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Carbidopa-Levodopa Formulations

Generic	Brand	Role in Therapy
CD-LD IR	Sinemet	• First-line therapy for CD-LD
	Dhivy	• Quartered pills for incremental dosing
CD-LD CR	Sinemet CR	• To prolong effects of CD-LD • May consider bedtime dose for nighttime symptoms
Levodopa inhaler	Inbrija	• Rescue therapy for "off" periods in advanced PD
CD-LD Enteral Suspension	Duopa	• Gel infusion via PEG-J tube for advanced PD with delayed gastric emptying
CD-LD/ Entacapone	Stalevo	• Reduces pill burden
CD-LD ER	Rytary	• Provides symptomatic relief for longer • For patients with difficulty swallowing (beads can be sprinkled on food) • Better absorption with tartaric acid, but more nausea reported
	Crexont	• Longer, more consistent release than Rytary
Foscarbidopa/ Foslevodopa	Vyalev	• Subcutaneous form providing steady levodopa levels within 24 hours

Understand the Differences in Carbidopa/Levodopa Formulations for Parkinson Disease. https://www.pharmacytimes.com/view/understand-the-differences-in-carbidopa-levodopa-formulations-for-parkinson-disease; Carbidopa/Levodopa Formulations & Parkinson's Disease. https://www.apdaparkinson.org/carbidopa-levodopa-formulations-and-parkinsons-disease/; An Overview of Levodopa Formulations. https://davidphinneyfoundation.org/levodopa-formulations/

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Carbidopa-Levodopa Formulations

Generic	Brand	Dose	Bioavailability of Levodopa (Compared to IR)	Time to Peak (Levodopa)	Half-Life (Levodopa in Presence of Carbidopa
CD-LD IR	Sinemet Dhivy	Initial: 25/100mg 2-3x/day Usual max levodopa dose: 2g/day	-	0.5-1hr	1.5-2hrs
CD-LD CR	Sinemet CR	Initial: 50/200mg BID Max levodopa dose: 2.4g/day	75%	1.5-2hrs	1.6hrs
Levodopa inhaler	Inbrija	84 mg/dose, up to 5x/day as needed Max: 420 mg/day	70%	0.17-2hr	2.3hrs
CD-LD Enteral Suspension	Duopa	Split between morning bolus, continuous, & extra bolus Max levodopa dose: 2g/day	81-98%	2.5hrs	1.5hrs
CD-LD/ Entacapone	Stalevo	Max daily dose: - Tablets with <200mg Levodopa: 8 tablets/day - Tablets with 200mg Levodopa: 6 tablets/day	-	1-2hrs	1.7hrs
CD-LD ER	Rytary	Initial: 23.75/95mg TID Max levodopa dose: 2.45g/day	70%	1- 4.5hr	1.9hrs
	Crexont	Initial: 35/140 mg BID Max levodopa dose: 2.1g/day	88-99%	1hr	2hr
Foscarbidopa/ Foslevodopa	Vyalev	Continuous infusion rate is based on total levodopa dosage (TLD) Max levodopa daily dose: 3525mg	-	2hr*	1.5hr

**Steady-state levodopa was achieved within 2 hours when administered as a loading dose followed by continuous infusion in healthy volunteers*

Carbidopa and Levodopa. Lexi-Drugs. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at http://online.lexi.com; Levodopa. Lexi-Drugs. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at http://online.lexi.com; Crexont. Package insert. Amneal Pharmaceuticals LLC; 2024.; Vyalev. Package insert. AbbVie Inc; 2024

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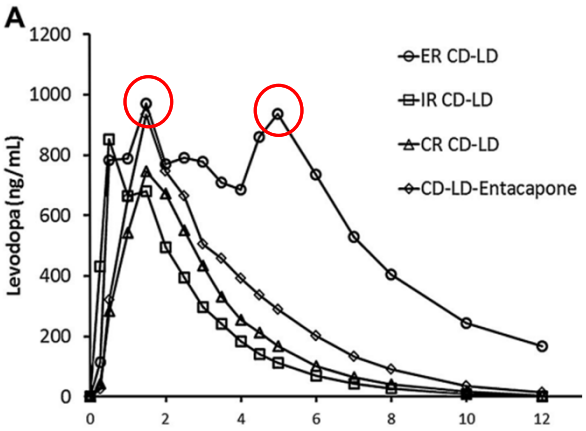
Comparison of the Pharmacokinetics of Different Carbidopa-Levodopa Formulations

- **Design:**
  - Randomized, single-dose, open-label, 4-sequence, 4-treatment crossover study
- **Objective:**
  - To assess PK of CD-LD ER vs IR vs CR vs with entacapone formulations
- **Treatment groups: (washout period at least 6 days)**
  - ER (Rytary 48.75-195mg): 2 capsules
  - IR (Sinemet 25–100mg): 1 tablet
  - CR (Sinemet CR 25–100mg): 1 tablet
  - CD-LD-Entacapone (Stalevo 25-100-200mg): 1 tablet
- **Population**
  - N = 24 patients



Hsu A, et al. *J Clin Pharmacol.* 2015;55(9):995-1003

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Knowledge Question

How does the formulation of carbidopa-levodopa in Sinemet CR differ from the immediate-release version?

a) It increases peak dopamine levels in the brain

b) It reduces the amount of carbidopa needed to enhance levodopa absorption

c) It provides a slower, more continuous release of levodopa

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New Carbidopa-Levodopa Formulations

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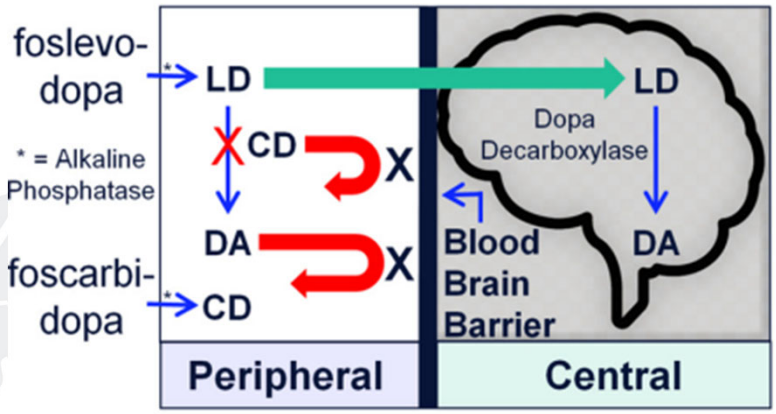
Foscarbidopa-Foslevodopa (Vyalev)

Subcutaneous administration with FDA approval October 17th, 2024



Rosebraugh M, et al. *Ann Neurol*. 2021;90(1):52-61.

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Foslevodopa-Foscarbidopa (Vyalev) Trial

Design:

- 12-week randomized, double-blind, double-dummy, active-controlled study

Population:

- 30 years or older with PD, on ≥ 400mg/day of LD, and ≥2.5 h/day of "off" time
- n=74 foslevodopa-foscarbidopa + oral placebo capsules
- n=67 oral CD-LD IR + placebo continuous infusion

Dose:

- Home CD-LD doses converted to IR doses, rounded to 100mg LD
- Patients received CD-LD IR for 2-3 weeks before randomization
- On day of randomization patients received loading dose of oral CD-LD IR, and foslevodopa-foscarbidopa

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Séileau MJ, et al. *Lancet Neurol*. 2022;21(12):1099-1109; Vyalev. Package insert. AbbVie INC; 2024.

24

Foslevodopa-Foscarbidopa (Vyalev) Trial

Outcomes Baseline → 12 weeks

- Daily "on" time: Tx group 1.75 hours MORE on time, 95% CI (0.46 to 3.05); p=0.0083
- Daily "off" time: Tx group 1.79 hours LESS off time, 95% CI (−3.03 to −0.54); p=0.0054
- ADEs foscarbidopa-foslevodopa group: erythema 27%, pain 26%, cellulitis 19%, oedema 12%.

Where foscarbidopa-foslevodopa may be beneficial

- Daily "off" time of >2.5hr
- High pill burden or dosing frequency
- Hard time swallowing pills

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Soileau MJ, et al. *Lancet Neurol.* 2022;21(12):1099-1109; Vyalev. Package insert. AbbVie INC; 2024.

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Foscarbidopa-Foslevodopa (Vyalev) Pump

Pump Placement

- Into abdomen ≥ 2 inches from navel
- Replace infusion set every 3 days ≥ 1 inch away from sites used in past 12 days

Pump Settings

- Neurologist programs pump based on daily IR levodopa dose and adjust settings based on symptoms
- Pump can be disconnected <1hr/day for showers

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AbbVie Inc. How the VYALEV™ (foscarbidopa/foslevodopa) Pump Works. VYALEV™ (foscarbidopa/foslevodopa). Published 2025. . https://www.vyalev.com/vyalev-pump; Soileau MJ, et al. Lancet Neurol. 2022;21(12):1099-1109. . Vyalev. Package insert. AbbVie INC; 2024.

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Foscarbidopa-Foslevodopa (Vyalev) Dose Calculation

Loading Dose = $\frac{\text{First morning dose of IR levodopa x 1.3}}{240}$

Used if starting foscarbidopa-foslevodopa infusion, or went without infusion >3 hrs.

Maintenance Dose = $\frac{\text{[Total IR equivalent of levodopa daily x 1.3]/240}}{\text{number of hours patient is typically awake}}$

Patient transfers pre-mixed drug from vial to syringe and connects to pump for continuous delivery. Syringe is replaced minimum of every 24 hours, or when it is empty.

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Vyalev. Package insert. AbbVie INC; 2024.

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Knowledge Question

What is a key difference between Carbidopa-Levodopa IR and Foscarbidopa-Foslevodopa?

a. Carbidopa-Levodopa IR causes peaks and troughs of levodopa, Foscarbidopa-Foslevodopa is formulated to give more consistent levodopa
b. Carbidopa-Levodopa IR is dosed once daily, while Foscarbidopa-Foslevodopa is dosed multiple times daily
c. Carbidopa-Levodopa IR is dosed using levodopa concentration levels, Foscarbidopa-Foslevodopa is dosed using carbidopa concentration levels

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c. Carbidopa-Levodopa IR is dosed using levodopa concentration levels, Foscarbidopa-Foslevodopa is dosed using carbidopa concentration levels

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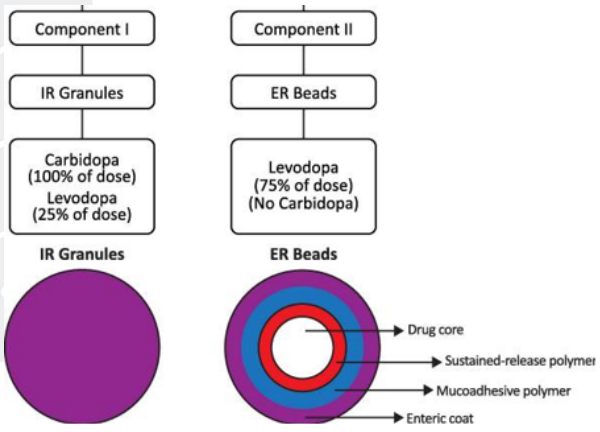
Carbidopa - Levodopa ER (Crexont)

Combined IR and ER formulation with FDA approval August 8th, 2024



Starting CREXONT. https://crexont.com/starting-crexont/. LeWitt P, et al. *Clin Park Relat Disord*. 2023;8:100197.

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Carbidopa-levodopa ER (Crexont) vs Carbidopa-Levodopa IR

Design:

- 20-week, randomized, double-blind, double-dummy, active-controlled, phase 3 clinical trial

Population:

- PD on ≥400mg/day of levodopa, and ≥2.5 h/day of "off" time
- n=256 CD-LD ER
- n=250 CD-LD IR

Dose:

- Patients converted to CD-LD IR and doses optimized over 3 weeks
- CD-LD ER dose based upon optimized CD-LD IR dose

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

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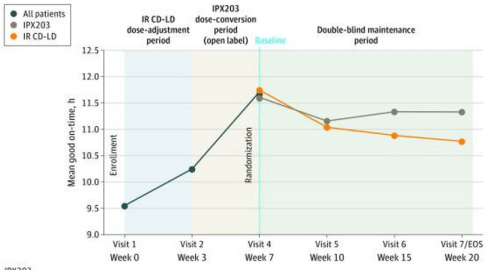
Carbidopa-levodopa ER (Crexont) vs Carbidopa-Levodopa IR

Outcome Baseline → 20 weeks

- Daily "on" time: CD-LD ER group had 1.55 hours MORE on time; 95% CI, 1.37-1.73; P < .001
- Daily "off" time: CD-LD ER group had 0.48 LESS off time; 95% CI, −0.90 to −0.06; P = 0.03
- ADEs CD-LD ER group: dyskinesia 6.8%, nausea 4.9%, dry mouth 4.2%.



Where CD-LD ER (Crexont) may be beneficial

- Daily "off" time of >2.5hr
- High pill burden or dosing frequency

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

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Carbidopa-Levodopa ER (Crexont) vs Carbidopa-Levodopa ER (Rytary) vs Carbidopa-Levodopa IR

Design:

- Randomized, open-label, 3-treatment, single-dose crossover study

Population:

- 40 years or older, advanced PD, on LD ≥ 400mg/day for minimum of 4 weeks
- N=25

Dose:

- All 3 treatment doses based on home CD-LD doses
- 100mg dose of CD-LD IR = 360 mg of CD-LD ER (Crexont) or 340 mg of CD-LD ER (Rytary)

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Modi NB, et al. *ClinNeuropharmacol*. 2019;42(1):4-8.

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Carbidopa-Levodopa ER (Crexont) vs Carbidopa-Levodopa ER (Rytary) vs Carbidopa-Levodopa IR

- **Outcome**
  - Daily "on" time: CD-LD ER (Crexont)
    - 2.6 hours MORE "on" time than CD-LD IR ($P < 0.0001$) and
    - 0.9 hours MORE "on" time than CD-LD ER (Rytary) ($P = 0.0259$)
  - Daily "off" time: CD-LD ER (Crexont)
    - 2.7 hours LESS of "off" time than CD-LD IR ($P < 0.0001$) and
    - 0.9 hours LESS of "off" time than CD-LD ER (Rytary) ($P = 0.023$)
- **Conclusion**
  - Levodopa concentrations were sustained longer with CD-LD ER (Crexont) than with CD-LD IR or CD-LD ER (Rytary)

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Modi NB, et al. *ClinNeuropharmacol*. 2019;42(1):4-8.

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Crexont Maintenance Dose Calculation

Total Daily IR Levodopa Dose	IR Levodopa Single Dose	Recommended Crexont Starting Dose of Levodopa
Less than 500mg daily	100mg	280mg BID
	150mg	420mg BID
	200mg	560mg BID
Equal to or greater than 500mg daily	100mg	280mg TID
	150mg	420mg TID
	200mg	560mg TID
	Greater than 200mg	700mg TID

Starting CREXONT - Crexont Site. Crexont Site. Published October 7, 2024.

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When to consider using new dosage forms of carbidopa-levodopa?

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Motor Complications of Dopaminergic Medications

"Wearing off" phenomenon

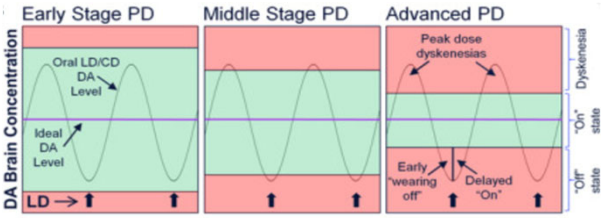
- Levodopa's effect fades causing symptoms to return
- Higher dose and frequency helps but may cause dyskinesias
- On/off fluctuations: can occur in late-stage PD - "off" (no effect) vs. "on" (with dyskinesias)

Freezing of gait

- "Feet are stuck to the floor"
- Increases risk for falls and subsequent fractures

Levodopa-induced dyskinesia

- Involuntary movements like chorea (most common), dystonia, or ballism
- Peak-dose (at levodopa peak), diphasic (before and after ON period), and OFF-period dystonia



Freitas ME, et al. *Semin Neurol.* 2017;37(2):147-157.; Rosebraugh M, et al. *Ann Neurol.* 2021;90(1):52-61.

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Transitioning CD-LD IR to Alternative Formulation

	Foscarbidopa-foslevodopa (Vyalev)	CD-LD ER (Crexont)	CD-LD ER (Rytary)	CD-LD CR (Sinemet CR)	CD-LD/Entacapone (Stalevo)	CD-LD enteral suspension (Duopa)	Levodopa inhaler (Inbrija)
"Off" time ≥2.5 h/day	x	x					
Pill burden	x	x	x	x	x	x	x
Increased dosing frequency	x	x	x	x	x	x	
Increased motor complications	x	x	x		x		
Delayed gastric emptying	x					x	

Vyalev. Package insert. AbbVie INC; 2024; Crexont. Package insert. AmnealPharmaceuticals LLC; 2024; Sinemet CR. Package insert. Merck & Co; 2014.; Duopa. Package insert. AbbVie INC; 2015; Stalevo. Package insert. Novartis Pharmaceuticals Corporation; 2010; Rytary. Package insert. Impax Pharmaceuticals; 2015; Inbrija. Package insert. Acorda Therapeutics, Inc; 2020.

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Case Question

AL is a 55-year-old with Parkinson's disease. He takes carbidopa-levodopa IR 25mg/100mg two tablets four times daily. He has a hard time with his current number of pills and breakthrough symptoms between doses. Which of the following alternative dose of carbidopa-levodopa would be appropriate for AL?

a. Carbidopa-levodopa ER (Crexont) 420mg three times daily

b. Carbidopa-levodopa ER (Rytary) 195mg twice daily

c. Foscarbidopa-foslevodopa (Vyalev) 0.27mg/hr

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Carbidopa-levodopa IR Conversion

Carbidopa-levodopa ER (Crexont)

Daily IR Levodopa Dose	IR Levodopa Single Dose	Crexont Dose of Levodopa
<500mg daily	100mg	280mg BID
	150mg	420mg BID
	200mg	560mg BID
≥500mg daily	100mg	280mg TID
	150mg	420mg TID
	200mg	**560mg TID**
	> 200mg	700mg TID

560mg TID = 1680mg levodopa

Carbidopa-levodopa CR (Sinemet CR)

~10-30% more than Levodopa IR dose

800mg x 1.1 = 880mg to
800mg x 1.3 = 1040mg

1 tablet 50mg/200mg + 1 tablet 25mg/100mg every 8 hours = 900mg levodopa

Crexont. Package insert. AmnealPharmaceuticals LLC; 2024; Sinemet CR. Package insert. Merck & Co; 2014.

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Carbidopa-levodopa IR Conversion

CD-LD/Entacapone (Stalevo)	CD-LD enteral suspension (Duopa)
>600 mg/day levodopa IR, may need dose reduction with addition of entacapone Titrate with individual products first (carbidopa/levodopa IR) + entacapone 200 mg, then switch to Stalevo 1 tablet 37.5/150/200 mg QID= 600mg levodopa	**Morning dose** $\frac{[\text{IR levodopa 1st dose x } 0.8]}{20} + 3\text{ml}$ $\frac{[200\text{mg IR x } 0.8]}{20} + 3\text{ml} = 11\text{ml}$ **Daily dose** $\frac{[\text{Total IR levodopa dose} - \text{IR levodopa 1st dose}]/20}{16}$ $\frac{[800\text{mg} - 200\text{mg}]/20}{16} = 1.8\text{ml/hr}$

Duopa. Package insert. AbbVie INC; 2015; Stalevo. Package insert. Novartis Pharmaceuticals Corporation; 2010.

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Carbidopa-levodopa IR Conversion

Carbidopa-levodopa ER (Rytary)

Daily IR Levodopa Dose	Total Daily Dose Levodopa in Rytary	Rytary Regimen
400mg to 549mg	855mg	3 capsules 23.75mg/95mg TID
550mg to 749mg	1140mg	4 capsules 23.75mg/95mg TID
750mg to 949 mg	**1305mg**	**3 capsules 36.25mg/145mg TID**
950mg to 1249mg	1755mg	3 capsules 48.75mg/195mg TID
≥1250mg	2340mg or	4 capsules 48.75mg/195mg TID or
	2205mg	3 capsules 61.25mg/245mg TID

(3 x 145mg) x 3 = 1305mg levodopa

Foscarbidopa-foslevodopa (Vyalev)

$$\frac{[Total\ IR\ equivalent\ of\ levodopa\ daily\ x\ 1.3]/240}{number\ of\ hours\ patient\ is\ typically\ awake}$$

$$\frac{[800mg\ IR\ x\ 1.3]/240}{16} = 0.27\text{ml/hr}$$

Rytary. Package inset. Impax Pharmaceuticals; 2015; Vyalev. Package insert. AbbVie INC; 2024.

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Case Question

AL is a 55-year-old with Parkinson's disease. He takes carbidopa-levodopa IR 25mg/100mg two tablets four times daily. He has a hard time with his current number of pills and breakthrough symptoms between doses. Which of the following alternative dose of carbidopa-levodopa would be appropriate for AL?

a. Carbidopa-levodopa ER (Crexont) 420mg three times daily

b. Carbidopa-levodopa ER (Rytary) 195mg twice daily

c. Foscarbidopa-foslevodopa (Vyalev) 0.27mg/hr

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Future Directions for CD-LD Formulations

- ND0612
  - 24h/day SC Infusion of CD-LD
  - Successfully showed efficacy and safety data in phase 3 trial
- Accordion Pill
  - CR oral tablet with extended absorption time window
  - Phase 3 trial failed to decrease "off" time
    - Showed increased tolerability of higher levels of levodopa
  - New phase 3 trial is being planned

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Conclusion

- Levodopa converts to dopamine in the brain, and carbidopa prevents its breakdown
- New formulations of CD-LD decrease “off” time and increase “on” time for PD patients compared to CD-LD IR formulations
- Optimization of CD-LD regimens depends on patient specific factors

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1 Kaitlyn advised to have both truncated and reference slide
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Carbidopa-Levodopa: Revving Up Relief – Choose Your Formula!

Braylee Wardwell, PharmD & Constance Chan, PharmD
PGY-2 Ambulatory Care Pharmacy Residents
Department of Pharmacy | UConn Health

June 2025

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1 Kaitlyn advised to have both truncated and reference slide
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