The Expert Institute for Parkinson's Disease

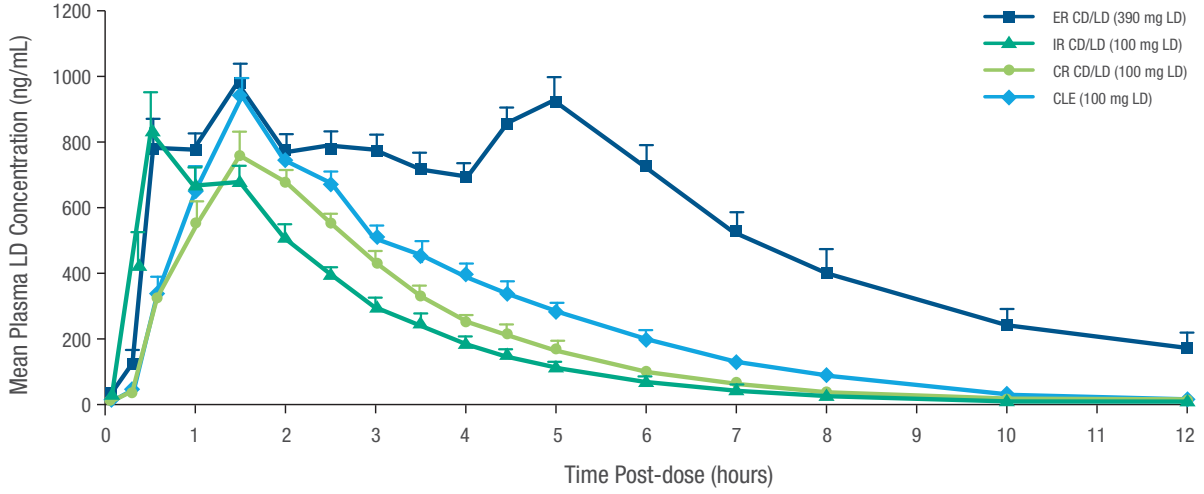
Choosing the Optimal Levodopa Treatment for Patients With PD and Motor Fluctuations

Why Choose ER CD/LD Instead of CR CD/LD?

	ER CD/LD	CR CD/LD
Description	Capsule contains both IR and ER beads to provide an initial rapid increase in LD concentrations and a subsequent delayed and extended LD release[1,2]	Polymeric-based drug delivery that slowly erodes and releases CD/LD[3]
Advantages	Sustained levodopa plasma levels for about 4-5 hours[1,2]	Sometimes administered for nighttime use to supplement IR[4]
Limitations	• Not interchangeable with IR CD/LD on a 1:1 basis[1,5] • Conversion from IR to ER is based on a patient's total daily LD dose[1,5]	• Delayed absorption of about an hour[3] • CR does not significantly reduce "Off" time in patients with moderate to severe motor fluctuations vs IR[3] • Less systemically bioavailable and less predictable symptom relief than IR[6]

ER CD/LD Sustains Levodopa Levels Longer Than Other CD/LD Treatments

Single-Dose Pharmacokinetics of ER CD/LD, IR CD/LD, CR CD/LD and CLE in Healthy Volunteers[2]*



With ER, the initial LD concentration increase was similar to IR, but LD concentrations were sustained for 4 to 5 hours following the peak.[5]

*LD plasma concentration profiles collected after single-dose administration in healthy volunteers (N=22).[2]

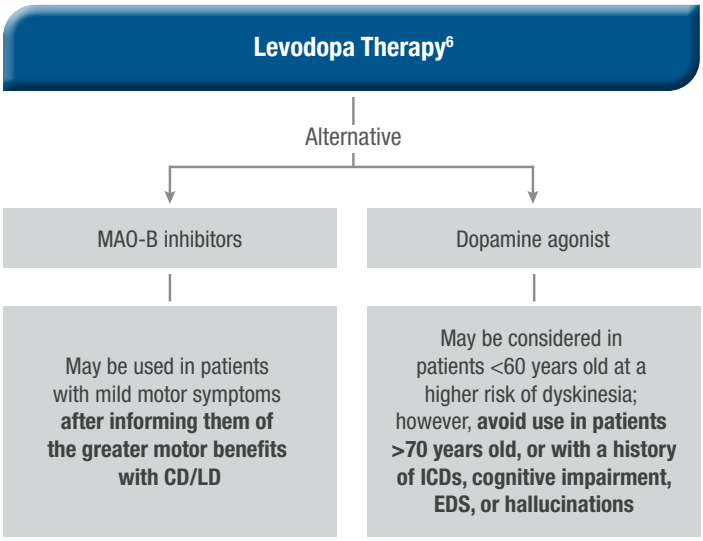
CD=carbidopa; CLE=carbidopa/levodopa/entacapone; CR=controlled-release; ER=extended-release; IR=immediate-release; LD=levodopa; PD=Parkinson's disease.

Clinical Practice Guidelines for PD Treatment

AAN Guidelines Recommend First-Line Levodopa Therapy for Patients With Early PD and Motor Symptoms[6]

Selecting a **levodopa therapy** for patients with early PD*:

- Clinicians should initially prescribe IR CD/LD rather than CR CD/LD or CLE in patients with early PD[3]
  - **CR CD/LD has lower bioavailability and less predictable symptom relief compared to IR CD/LD**, which may necessitate treatment discontinuation in later stages of the disease due to dose failures
  - CLE may be helpful for patients who experience end-of-dose wearing-off, which is not commonly associated with early PD



MDS Guidelines Do Not Recommend CR CD/LD for PD Treatment in Patients With Motor Fluctuations[7]

- Both IR and ER CD/LD are clinically effective for the treatment of motor fluctuations
- CR CD/LD is not considered clinically useful for patients with motor fluctuations on optimized levodopa therapy

Most Common Adverse Events With ER CD/LD[8]

In ADVANCE-PD, the most common adverse events (≥2%) reported with ER CD/LD (n=201) vs IR CD/LD (n=192), respectively, were insomnia (3% vs 1%), nausea (3% vs 2%), fall (3% vs 2%), dizziness (2% vs 1%), dyskinesia (2% vs 1%), diarrhea (2% vs 1%), peripheral edema (2% vs 2%), upper respiratory tract infection (2% vs 2%), urinary tract infection (2% vs 2%), sleep disorder (2% vs 2%), weight decreased (2% vs 0%), back pain (1% vs 2%), arthralgia (1% vs 2%), vomiting (<1% vs 2%), and depression (<1% vs 3%).

*Early PD is defined as Hoehn & Yahr stages 1 or 2, or within 2 years of disease onset.[6]

AAN=American Academy of Neurology; EDS=excessive daytime sleepiness; ICD=impulse control disorder; MAO-B=monoamine oxidase B; MDS=International Parkinson and Movement Disorder Society.

References: 1. RYTARY [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; 2019. **2.** Hsu A et al. *J Clin Pharmacol*. 2015;55(9):995-1003. **3.** SINEMET CR [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2018. **4.** Dhall R, Kreitzman DL. *Neurology*. 2016;86(14 suppl 1):S13-S24. **5.** Mittur A et al. *Clin Pharmacokinet*. 2017;56(9):999-1014. **6.** Pringsheim T et al. *Neurology*. 2021;97(20):942-957. **7.** Fox SH et al. *Mov Disord*. 2018;33(8):1248-1266. **8.** Hauser RA et al. *Lancet Neurol*. 2013;12(4):346-356.