- Patients should be advised that the medication is expected to improve bradykinesia and rigidity, while it has a variable effect on tremor and likely no effect on balance. Advise that the starting dose is low and the dose should only be increased as prescribed.
- After at least 2 weeks at target dose, assess for a clear and marked improvement in symptoms with patient self-report and by examining gait, rigidity, bradykinesia, and rest tremor.[17,34,45]
- Older patients should be titrated more slowly on dopaminergic treatment as they can develop side effects more easily.[47]

c) Refer to specialty care if the patient does not respond to trial of dopaminergic therapy [Expert Opinion].

Box 3: Initial Titration of Levodopa/Carbidopa [16,54]

Initial titration of levodopa/carbidopa is based on a tablet of **100 mg levodopa/25 mg carbidopa** taken orally 3 times daily, 30 minutes before meals:

	Breakfast	Lunch	Dinner
Week 1	Half a tablet	Half a tablet	Half a tablet
Week 2	1 tablet	Half a tablet	Half a tablet
Week 3	1 tablet	1 tablet	Half a tablet
Week 4	1 tablet	1 tablet	1 tablet

Note: Doses for ongoing treatment may be as high as 1,000 mg levodopa per day or higher. Bedtime doses with controlled release (CR) formulations may be considered, especially if there are troublesome symptoms overnight. **Do not use levodopa CR formulations during the day as absorption is delayed and variable.** Levodopa may need to be taken 30 minutes before or at least 60–90 minutes after a meal for optimal absorption. In later stages of Parkinson disease, patients could be counselled to consume protein-rich meals only at the end of day.

ONGOING MANAGEMENT

23. Motor symptoms can become more severe and difficult to manage as the disease progresses. Interventions are aimed at managing symptoms and improving quality of life, as there are currently no medication treatments that can delay the progression of the disease or mortality.[55]

Motor Symptoms

Pharmacotherapy for Motor Symptoms

24. There are 5 classes of pharmacologic treatments for managing motor symptoms [High Evidence]:
    - Levodopa-based, in combination with a dopa-decarboxylase inhibitor (carbidopa or benserazide)
    - Non-ergot dopamine agonists
    - Monoamine oxidase-B inhibitors (MAO-B)
    - Catechol-O-methyltransferase (COMT) inhibitor (used only in combination with levodopa for increased levodopa effect)
    - N-methyl-D-aspartate (NMDA) receptor antagonist (e.g. Amantadine)

    Appendix 2 lists the medications, starting and usual doses, and costs.

Levodopa-Based, in Combination With a Dopa-Decarboxylase Inhibitor (Carbidopa or Benserazide)

Note: Initiating carbidopa/levodopa is covered in Info point 22 and Box 3.

25. Avoid abrupt cessation of dopaminergic therapies (e.g., when NPO for surgery) as it may lead to neuroleptic malignant syndrome, which causes severe rigidity, parkinsonian symptoms, fever, autonomic instability, and cognitive dysfunction or psychosis, and has a significant risk of mortality.[56]