

LTC Pharmacy

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Managing Parkinson's Disease

A conundrum upon diagnosing Parkinson's disease is whether to start a patient on levodopa or a "levodopa-sparing" regimen of a dopamine agonist or a monoamine oxidase inhibitor (MAOBI).

New results of a trial comparing the long-term effectiveness of the three drug classes should help PA/LTC clinicians decide how to preserve patients' quality of life as long as possible. An international team of researchers based in London published the results from the open-label, randomized PD MED trial online in *The Lancet* in June.

The findings favored starting carbidopa/levodopa over MAOBIs (e.g., selegiline, rasagiline) and dopamine agonists (e.g., ropinirole, pramipexole). The researchers noted that, at 7 years, 72% of dopamine agonist users, 50% of MAOBI users, and 7% of levodopa users had stopped taking their medications. Levodopa did not lose its effectiveness, and both patients and clinicians gave slightly, but statistically significant, better mobility and quality-of-life scores to patients initiating levodopa therapy.

Furthermore, MAOBIs appeared at least as effective as dopamine agonists as levodopa-sparing therapy. Keep an eye out for the next PD MED results, which will look at the management of patients with advanced PD.

Rotigotine Patch (Neupro Patch)

Last year, the Neupro patch reemerged as a treatment option, after being off the market since 2008 because of problems with the patch's drug delivery. The patch is indicated for all stages of Parkinson's disease and for restless legs syndrome. Rotigotine is a dopamine agonist that appears to work as well, and it has similar side effects to other dopamine antagonists, such as pramipexole (Mirapex) and ropinirole (Requip). Putting such a drug in a patch was supposed to offer less "off" time for Parkinson's patients than the oral agents do, but this has not been proven.

Labeling advises starting Neupro at 2 mg/day for early stage Parkinson's or 4 mg/day for advanced stage. If needed, the dose may be increased 2 mg/day at weekly intervals, up to 6 mg/day for early stage disease and up to 8 mg/day for advanced-stage disease. For restless legs syndrome, labeling advises starting Neupro at 1 mg/day and increasing, as needed, by 1 mg/day weekly, up to 3 mg/day.

To reduce skin irritation, it is critical to change the site of the patch daily and not use the same site more than once every 14 days. Patients should be monitored for peripheral edema, which

is commonly seen with dopamine agonists. If this occurs, consider lowering the dose or switching to another medication class, noting that diuretics do not help.

When choosing an agent, it is important to look not only at efficacy and safety, but also at cost and a patient's preference. Neupro costs about the same as extended-release pramipexole dihydrochloride (Mirapex ER) and ropinirole extended-release tablets (Requip XL), but much more than generic pramipexole or ropinirole.

Pimavanserin for Psychosis

When a dopaminergic therapy appears to be causing psychosis, we are faced with the choice of reducing the dose of the drug or adding an antipsychotic. Regulatory scrutiny of PA/LTC for the off-label use of antipsychotics, as well as the potential effects of antipsychotics on worsening motor control, makes this a daunting choice.

Hope is on the horizon. Pimavanserin is a new chemical entity that recently advanced to phase 3 development as potentially the first drug approved in the United States for the treatment of Parkinson's disease psychosis. ACADIA Pharmaceuticals also has the drug in phase 2 development for Alzheimer's disease psychosis and has successfully completed a phase 2 trial of pimavanserin as adjunct therapy for schizophrenia.

The medication is formulated as a tablet and can be taken orally once a day. It selectively blocks the 5-HT_{2A} receptor, which plays an important role in psychosis. Pimavanserin appears not to compromise Parkinson's therapy, but more research needs to explore whether this agent is an effective therapy for Parkinson's psychosis and a safer alternative to antipsychotics.

Pharmacy Tip

Parkinson's medications are not interchangeable, but confusion exists when carbidopa/levodopa is ordered. Is it the combination product with entacapone, or is it the controlled release vs. the immediate release, which is approximately 30% less bioavailable? These potential errors in managing Parkinson's, though generally minor, are something that all of us need to be aware of.

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