First Transdermal Drug OK'd for Parkinson's

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For the first time, a transdermal drug delivery system is available for treating Parkinson's disease patients, a treatment option that provides both practical and theoretical benefits for this population, according to experts not involved in clinical trials of the product.

The Food and Drug Administration has approved a transdermal patch that contains rotigotine, a nonergotamine dopamine agonist that previously was not available in any form in the United States, for treating the signs and symptoms of early-stage idiopathic Parkinson's disease. Approval, which came in May, was based on three randomized, double-blind placebo-controlled studies in the United States and abroad of 1,154 patients with early Parkinson's, who were not taking other medications for Parkinson's. The patch will be marketed under the trade name Neupro by Schwarz Pharma LLC and was expected to be available in U.S. pharmacies by June 22-30, according to a spokesperson for the German company. At press time, the price was not available.

The option of a transdermal delivery system for patients who are tired of taking many pills is a clear advantage, said Dr. David Standaert, professor of neurology and director of the division of movement disorders at the University of Alabama at Birmingham. The pharmacology of rotigotine is a little different from that of the most widely used dopamine agonists, pramipexole and ropinirole, but the main difference is the transdermal system, he said in an interview.

Another advantage is that the continuous delivery of medication over 24 hours provides a stable blood level, which theoretically, could be an improvement over current treatments, he said. Recent research suggests that the peaks and troughs with conventional dopaminergic drugs may be responsible for some of the problems associated with oral therapy—end of the dose "wearing off" and dyskinesia—and possibly hallucinations and neuropsychiatric effects as well.

However, there is no evidence yet that the steady level provided by the patch will translate into long-term clinical benefits, he emphasized. "Many of us think it will, but I don't think we have the proof of that yet." Dr. Standaert, who also is the director of the university's Center for Neurodegeneration and Experimental Therapeutics, was not involved in rotigotine studies, some of which were conducted there before he arrived. He has no financial ties to the manufacturer but has consulted on the pharmacologic properties of rotigotine to UCB, the U.S. pharmaceutical company that is in the process of acquiring Schwarz Pharma.

"This is an exciting step in that there are a lot of both theoretical and practical advantages to finally having patch therapy for Parkinson's," agreed Dr. Michael Pourfar, a neurologist in the division of movement disorders, at North Shore University Hospital, Manhasset, N.Y. Because there are effective dopamine agonists available for Parkinson's, he said he would not want patients to feel like they need to change their medications. "But I do think this is something that will improve quality of life for many people," he added in an interview, noting that for some patients, the patch could replace as many as six pills per day. He has not been involved in trials of rotigotine and has no financial ties to the manufacturer.

Rotigotine is delivered continuously though the silicone-based patch that is applied to clean, dry, intact skin and is replaced every 24 hours. It is available in three strengths: 2 mg, 4 mg, and 6 mg/24 hr. The recommended dosing is to start at 2 mg. When additional therapeutic effects are needed, the dose may be increased weekly by 2 mg/24 hours if tolerated, according to the package insert. In studies, the lowest effective dose was 4 mg/24 hours, and in dose-ranging studies, doses above 6 mg/24 hours were not more effective than the lower doses and were associated with a higher rate of adverse reactions. The patch should be applied to sites on the front of the abdomen, thigh, hip, flank, shoulder, or upper arm at about the same time every day, avoiding reapplication to the same site more than once every 14 days.

The change from baseline for the combined scores for the activities of daily living and motor components of the Unified Parkinson's Disease Rating Scale (UPDRS) was the primary outcome in the three studies, which enrolled early-stage Parkinson's disease patients who were not on dopamine agonist treatment, and whose mean age was 60-63 years. In one of the trials, a 28-week multicenter North American study, 277 patients received up to a 6 g/24 hours dose of rotigotine or placebo. The mean reduction in the combined UPDRS score from baseline was 4.0, compared with a mean 1.39 increase from baseline among those on placebo, a difference of 5.3 that was statistically significant.

The most common side effects in the three trials included dizziness, nausea, vomiting, drowsiness, and insomnia, "most of which are typical for this class of drugs," according to the FDA statement announcing the approval. Nearly 40% of those on the patch had application site reactions–mostly mild or moderate–compared with 14% among those who received a placebo patch. The drug's label includes a warning about sulfite sensitivity, because the delivery system contains a sulfite that may cause allergic reactions.

The rotigotine patch is not approved for advanced disease, but it is being studied in this population. In a recently published placebo-controlled 24-week study of the rotigotine patch in 351 patients with advanced Parkinson's, those treated with two doses of the patch had significant reductions in the amount of daily "off" time than those on placebo (Neurology 2007;68:1262-7). ■