**NEW DRUGS CURB ‘OFF’ EPISODES IN ADVANCED PARKINSON’S**

**BY BRUCE JANCIN**

**DENVER BUREAU**

**San Francisco —** A single dose of subcutaneous apomorphine rapidly and effectively reverses for at least 90 minutes the hypomobility, or “off,” episodes that are common in patients with advanced Parkinson’s disease, William C. Koller, M.D., said at the annual meeting of the Mid-Atlantic Bureau of Neurology.

This injectable dopamine agonist, known as Apokyn, has received Food and Drug Administration approval as the first oral dopamine agonist to treat the acute or rescue therapy for off episodes in Parkinson’s disease patients.

Apokyn, which has been in Europe for over 10 years, will be commercially available in July, with distribution to be handled through a specialty pharmacy network, according to a spokesperson for Mylan Laboratories Inc.

Parkinson’s patients consider off episodes to be among the most frustrating aspects of the disease. Off episodes occur in about 50% of patients after 5 years of levodopa therapy.

The off episodes become increasingly frequent as the disease continues to progress.

These debilitating periods of loss of motor control are of two types: those that occur when a patient’s oral Parkinson’s disease medication wears off at the end of a dose, and those that occur unpredictably, according to Dr. Koller, who is with Mt. Sinai Medical Center, New York.

Off episodes occur because of a shortage of dopamine in movement centers in the brain. This episode respond to oral dopamine agonists, but only after a roughly 90-minute delay during which patients may encounter great difficulty in walking, eating, and talking.

An alternative to Apokyn in approaching the problem of off episodes is rasagiline, a potent once-daily second-generation MAO type-B inhibitor.

Rasagiline reduces the frequency of such episodes by blocking dopamine breakdown, although it’s not useful as rescue therapy during an episode, Dr. Koller said.

In addition, rasagiline has been shown in randomized trials to significantly improve motor function in general, and the disabling symptoms known as freezing of gait in particular, in patients who have advanced Parkinson’s disease, explained Nir Giladi, M.D., who is with Tel Aviv University.

Teva Neuroscience has filed a new drug application with the Food and Drug Administration seeking two indications for rasagiline: as monotherapy in early Parkinson’s disease and as an adjunct to levodopa in moderate to advanced disease.

Dr. Giladi reported on 454 levodopa-treated patients with advanced Parkinson’s disease and motor fluctuations who participated in a double-blind, randomized 18-week trial of 1 mg/day of rasagiline, 200 mg of entacapone taken three to eight times daily as an active comparator, or placebo.

The primary study end point was change in the Freezing of Gait Questionnaire from baseline to week 10. Patients who were in the rasagiline group showed a significant mean 1.17-point improvement from a baseline of 11.9 on the 24-point scale, while improvement in the entacapone group did not reach significance.

The study was part of a larger trial in which the addition of 1 mg/day of rasagiline in levodopa-treated patients reduced the total daily time that Parkinson’s symptoms weren’t controlled by 1.2 hours, or 21%.

Postural hypotension was the only adverse event more common with rasagiline than placebo, he added.

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