Coastal Neurological Medical Group, Inc.

Dee E. Silver, M.D.

We're here to help!

Movement Disorders
Neurodegenerative Diseases
Neuro-Ophthalmology
Botulinum Toxin Injection
Migraine Headaches

9850 Genesee Avenue Suite 860
La Jolla, California 92037
Phone 858-453-3842 Fax 858-535-9390
www.coastalneurological.com
www.pdasd.org

Neurological Rehabilitation
DBS Programming
Electromyography
Electroencephalography
Electronystagmography

Rytary - released January 8, 2015

Rytary is an extended release oral L-DOPA formulation that is comprised of small beads. The beads contain L-DOPA and are absorbed in the small intestine. The beads release L-DOPA slowly as it goes through the small intestine. The transit time from the beginning of the small intestine to the cecum (end of the small intestine) is about four hours. The beads with L-DOPA dissolve in relationship to the change in pH of the small intestine and dissolve also because of the characteristics of the polymer which makes up the small bead. Rytary has been studied in three separate clinical trails. Each trail showed that the plasma level when taking Rytary has a sustained high level for five to six hours. This is much different than the half life of L-DOPA, which is 90 minutes. To obtain an equivalent plasma level for 100 mg of L-DOPA immediate release, it takes about two to three times greater dosing with Rytary. The advantage of this new formulation of L-DOPA is that there will be significant reduction in the need for frequent dosing. Most patients can get a very good response with improved off-time by taking the pill three to four times a day.

In the trial, improvement in the "off" time was 1.17 hours on average. There was more on-time with less troublesome dyskinesias. In these trials, which were double-blind and some crossover, the effectiveness of Rytary compared to placebo was measured by a number of different scales including the PDQ 39 and the UPDRS scale and the Clinical Global Improvement and the Patient Global Improvement Scale. One trial called the Advanced Trial had the patients take three weeks of immediate release carbidopa and levodopa, then switch to six weeks of Rytary, and then the patients were randomized between immediate release L-DOPA and Rytary. It was shown that when compared to the immediate release L-DOPA, patients from Rytary had improvement in "off" time by 1.17 hours. Importantly, the range of those who improved was from 0.5 hour to 3.0 hours, giving a significant range of improvement. Other measurements also showed improvement. There were some cases that had more 'on' time, but dyskinesias were made worse.

The ASCEND trial compared Rytary versus entacapone. This trail compared carbidopa, levodopa and the entacapone 3-in-1 pill to Rytary. There was significantly less "off"-time and more "on" time without troublesome dyskinesias with Rytary as compared to the 3-in-1 pill. Other measurements also showed improvement. The great advantage of Rytary may be the possibility of reducing "off" time, the number of pills and doses per day, and especially when using it with entacapone, it may be less costly.

The doses will be 2:1 Rytary to immediate release L-DOPA. Rytary will come in at 95-mg, 145-mg and 195-mg pills. An example of the exchange, which probably will be able to be done overnight, would be that a 25/100 carbidopa-levodopa pill can be substituted with a 195-mg Rytary pill. It can be given without a meal, but also may be given at times with a meal.

The study showed that if a fatty meal was given at bedtime and a Rytary pill was given, it may prolong the plasma level for up to seven to eight hours. This would be of benefit since it may reduce off-time during the sleeping hours and maybe in the morning. The drug has 80% bioavailability. The adverse side effects of Rytary are similar to L-DOPA.

Rytary will be a very helpful medication in treating patients who have off-time and who may be taking too many pills a day and too frequently. Usage in the general Parkinson population will give us a much better idea how beneficial this drug will be and in whom it will benefit the most. I would expect for now it would be important to try this drug in different settings, but in the clinical trial there were many patients that had significant benefit when the immediate release L-DOPA was switched to Rytary. It may well delay the need for DBS in some cases and it would be my feeling that it would be used before the L-DOPA intestinal gel procedure, which is an invasive procedure and has a great deal of commitment needed by the patient, caregiver and the doctor. Its release is still pending.

The released drug should be available in mid to late January or early February. Please review Dr. Dee Silver's YouTube programs (at- www.tinyurl.com/doctorsilver), especially the program "Management of PD", "Management of Advanced PD" and "Understanding PD in Depth View".

Duodopa, an intestinal gel of L-Dopa, was also released on 01/12/2015. This treatment uses an invasive procedure, placing a tube through the abdominal wall into the GI tract and needs intermittent gel placed through the tube. There are significant adverse complications with this procedure; please also review the above mentioned YouTube videos.