

ZELAPAR® (selegiline HCl) Fact Sheet

About Zelapar Orally Disintegrating Tablets

Zelapar is a selective and irreversible monoamine oxidase type-B (MAO-B) inhibitor approved by the U.S. Food and Drug Administration (FDA) on June 14, 2006 as a once-daily adjunct therapy for Parkinson's disease (PD) patients being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy.

Mechanism of Action

The mechanisms accounting for selegiline's beneficial adjunctive action in the treatment of Parkinson's disease are not fully understood. However, MAO-B inhibitors, such as Zelapar, are thought to block the metabolism of dopamine by MAO and enhance endogenous dopamine as well as dopamine produced by exogenously administered levodopa. Zelapar is the first Parkinson's disease treatment to use a novel delivery system called Zydis® Technology, which allows the oral tablets to dissolve within seconds in the mouth and deliver more active drug at a lower dose. Because of this unique technology, Zelapar significantly bypasses the gut and first-pass hepatic metabolism and is primarily absorbed into the systemic circulation through the oral mucosa.

“Off” and “On” Time

As Parkinson's disease progresses, it becomes increasingly difficult to adequately control symptoms with medications. Parkinson's disease patients may experience many hours during the day in which their symptoms return as a result of medication wearing off. This wearing off is known as “off” time, or the hours in which a patient's medication is wearing off causing partial or total return of symptoms of Parkinson's disease, such as motor complications and dyskinesia. “On” time refers to the period of time when medication generally controls symptoms of Parkinson's disease.

Treatment with Zelapar has been shown to reduce the amount of “off” time, on average, by 2.2 hours per day. Because each Parkinson's disease patient reacts differently to treatment, doctors and patients must work closely to find a treatment plan right for them.

Parkinson's disease (PD)

Parkinson's disease is a chronic, progressive disorder of the central nervous system that belongs to a group of conditions called motor system disorders. It occurs when nerve cells (neurons) in an area of the brain, known as the substantia nigra, die or become impaired. Normally, these cells produce a vital chemical known as dopamine. Dopamine allows smooth, coordinated function of the body's muscles and movement. The symptoms of Parkinson's disease appear when approximately 80 percent of the dopamine-producing cells are damaged.

Parkinson's disease affects both men and women equally. It shows no social, ethnic, economic or geographic boundaries. In the United States, 1.5 million Americans currently have Parkinson's disease and it is estimated that 60,000 new patients are diagnosed each year. While the condition usually develops after the age of 65, 40 percent of people diagnosed are under age 60.

According to testimony before the U.S. Senate Committee on Aging, Parkinson's disease costs the United States an estimated \$25 billion (1999 dollars) per year.

The process of making a Parkinson's disease diagnosis can be difficult. There is no X-ray or blood test that can confirm Parkinson's disease. A physician arrives at the diagnosis only after a thorough examination. Blood tests and brain scans known as magnetic resonance imaging (MRI) may be performed to rule out other conditions that have similar symptoms. People suspected of having Parkinson's disease should consider seeking the care of a neurologist who specializes in Parkinson's disease.

Administration and Dosage

Zelapar is indicated as a once-daily oral adjunct therapy for Parkinson's disease patients being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy. Treatment should be initiated with 1.25 mg (one tablet) given once-daily for at least six weeks. After six weeks, the dose may be escalated to 2.5 mg (two tablets) given once-daily if a desired benefit has not been achieved and the patient is tolerating Zelapar. The citrus flavored tablets are placed on the tongue and dissolve in the mouth within seconds. Zelapar should be taken at the same time in the morning before breakfast and without liquid. Patients should avoid ingesting food or liquid for five minutes before and after taking Zelapar.

Clinical Studies

Treatment with Zelapar has been shown to significantly reduce "off" time after one week of treatment. Patients who increased their once daily dose from 1.25 mg (one tablet) to 2.5 mg (two tablets), experienced additional reductions in "off" time within the following two weeks.

The effectiveness of Zelapar as an adjunct to levodopa/carbidopa in the treatment of Parkinson's disease was established in a multi-center, double-blind, randomized, placebo-controlled, parallel-group study. Patients received either 1.25 mg of the drug or placebo each day for the first six weeks and then 2.5 mg of the drug or placebo once-daily for the following six weeks.

At the end of 12 weeks, Zelapar-treated patients had, on average, a reduction of 2.2 hours per day less "off" time compared to baseline, and placebo-treated patients had 0.6 hours per day less "off" time. The observed reduction in "off" time between the two treatment groups compared to baseline was statistically significant ($p < 0.001$).

The most common adverse events reported by patients treated with Zelapar were comparable to placebo and included nausea (11%), dizziness (11%), pain (8%), headache (7%), insomnia (7%), rhinitis (7%), dyskinesia (6%), skin disorders (6%), stomatitis (5%), back pain (5%) and dyspepsia (5%).

Important Safety Information

Zelapar is contraindicated in patients with a known hypersensitivity to any formulation of selegiline or any of the inactive ingredients of Zelapar. Serious, sometimes fatal reactions have been precipitated with the concomitant use of meperidine (e.g. Demerol® and other tradenames) and MAO inhibitors including selective MAO-B inhibitors. These reactions have been characterized by coma, severe hypertension or hypotension, severe respiratory depression, convulsions, malignant hyperpyrexia, excitation, peripheral vascular collapse and death. In addition, the combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. Severe toxicity has also been reported in patients receiving the combination of tricyclic antidepressants and conventional selegiline and selective serotonin reuptake inhibitors and conventional selegiline. Zelapar should not be administered along with other selegiline products.

Zelapar may potentiate the dopaminergic side effects of levodopa and may cause or worsen preexisting dyskinesia. Decreasing the dose of levodopa may improve this side effect.

5.2 percent of patients discontinued Zelapar therapy due to adverse events (vs. one percent with placebo). Zelapar should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

For full prescribing information, please visit www.zelapar.com, or for product-related questions, call Valeant Pharmaceuticals International at 1-877-361-2719.

Valeant

Valeant Pharmaceuticals International (NYSE:VRX) is a global, publicly traded, science-based specialty pharmaceutical company that develops, manufactures and markets products primarily in the areas of neurology, infectious disease and dermatology. For more information about Valeant please visit www.valeant.com.

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