The Food and Drug Administration has approved pimavanserin for the indication of hallucinations and delusions associated with psychosis in Parkinson’s disease.

Pimavanserin became the first drug to receive approval from the FDA for this indication. It is also the only drug approved by the FDA that preferentially targets 5-HT2A receptors. These receptors are thought to play an important role in Parkinson’s disease psychosis.

The unique pharmacology of pimavanserin establishes a new class of drug — selective serotonin inverse agonists (SSIA) — by not only preferentially targeting 5-HT2A receptors, but also avoiding activity at dopamine and other receptors commonly targeted by antipsychotics.

Typical Parkinson’s disease therapy consists of drugs that stimulate dopamine to treat patients’ motor symptoms such as tremor, muscle rigidity, and difficulty with walking. Pimavanserin does not interfere with patients’ dopaminergic therapy, and therefore does not impair their motor function.

The approval of pimavanserin represents a new direction in the treatment of Parkinson’s disease psychosis, according to Michael S. Okun, MD, medical director of The National Parkinson Foundation. “Through its novel and selective mechanism of action, [pimavanserin] is a breakthrough treatment that works in a whole new way — treating hallucinations and delusions without blocking dopamine receptors and, therefore, not impairing motor function in Parkinson’s psychosis patients,” he said in a press statement.

The FDA approval of the drug, to be marketed under the brand name Nuplazid (Acadia Pharmaceuticals), was based largely on data from a phase 3 study, in which pimavanserin was shown in a 6-week clinical trial of 199 participants to significantly reduce the frequency and severity of psychotic symptoms compared with placebo on the Scale for Assessment of Positive Symptoms – Parkinson’s Disease (SAPS-PD). (The Lancet 2014; 383 (9916):533–540). This benefit was achieved without impairing motor function. The most common adverse reactions in this study were peripheral edema (7% pimavanserin vs. 3% placebo) and confusional state (6% pimavanserin vs. 3% placebo).

The FDA gave pimavanserin a Boxed Warning due to the increased risk of death associated with the use of atypical antipsychotic drugs to treat older people with dementia-related psychosis.

“Hallucinations and delusions can be profoundly disturbing and disabling,” said Mitchell Mathis, MD, director of the Division of Psychiatry Products in the FDA’s Center for Drug Evaluation and Research. “Nuplazid represents an important treatment for people with Parkinson’s disease who experience these symptoms.”

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