Supplementary Online Content


eTable. Subject Inclusion and Exclusion Criteria

This supplementary material has been provided by the authors to give readers additional information about their work.
eTable. Subject Inclusion and Exclusion Criteria

**Inclusion criteria:**

- Age 30 to 80 years at screening.
- Diagnosis of idiopathic PD, based on medical history and neurological examination, with >3-year duration and at Hoehn and Yahr stage I to IV during an “Off” phase.
- Levodopa-responsive, and on a stable L-dopa regimen (3-10 doses per day of any oral L-dopa preparation, immediate- or controlled-release, plus benserazide or carbidopa and with or without a catechol-O-methyltransferase inhibitor). May also be receiving a dopamine agonist, an anticholinergic, and/or amantadine, at stable dosage for at least the 4 weeks prior to screening.
- Be experiencing motor fluctuations, with >1.5 hr/d of “Off” time (excluding morning akinesia).
- If female, be either post-menopausal for ≥2 years, surgically sterilized (or have undergone hysterectomy), or willing to use an adequate method of contraception.
- Be able to maintain an accurate and complete diary (18-hour), with the help of a caregiver, recording “On” time, “On” time with non-troublesome dyskinesia, “On” time with troublesome dyskinesia, “Off” time, and time asleep.
- Be willing and able to participate in the trial, and to provide written, informed consent.

**Exclusion criteria:**

- Any indication of forms of parkinsonism other than idiopathic PD.
- Late-stage PD, as manifested by severe, disabling peak-dose or biphasic dyskinesia and/or wide or unpredictable symptom fluctuations.
- Stereotactic surgery for PD.
- Current diagnosis of a clinically significant medical condition other than PD.
- Clinically significant abnormalities by physical examination, electrocardiography, or laboratory tests.
- Severe dizziness or fainting on standing, due to postural hypotension.
- Current diagnosis or history of retinal disease or severely diminished visual acuity.
- Current or recent drug or alcohol abuse, within the 3 months prior to screening.
- History of, or current psychosis, or a score ≥3 on UPDRS Part I, Item 2 (thought disorder) at screening.
- Evidence of dementia or cognitive dysfunction, as indicated by a score <22 on the MMSE or a score ≥3 on UPDRS Part I, Item 1 (mentation) at screening.
- Depression, as indicated by a score >17 on the GRID-HAMD 17-item scale at screening.
• History of hypersensitivity or contraindications to L-dopa, other anti-Parkinsonian agents, anticonvulsants, or drugs similar to safinamide.

• Use of monoamine oxidase inhibitors, opioids, serotonin-norepinephrine reuptake inhibitors, or tricyclic or tetracyclic antidepressants within the 8 weeks prior to screening.

• Use of oral neuroleptics within the 4 weeks prior to screening, or depot neuroleptics within one injection cycle.

• Use of drugs known to be capable of influencing safinamide absorption, metabolism, or elimination, within the 4 weeks prior to screening.

• History of safinamide treatment.

• Participation in a clinical trial within the 30 days prior to screening, or treatment with any investigational compound within 30 days or 5 half-lives, whichever is longer.

• If female, being pregnant or lactating.

GRID-HAMD = Hamilton Rating Scale of Depression, 17-item grid version. MMSE = Mini Mental State Examination. PD = Parkinson’s disease. UPDRS = Unified Parkinson’s Disease Rating Scale.