Xadago (safinamide)

XADAGO®
(safinamide) tablets

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Xadago
- **Generic name:** Safinamide
- **Pharmacological class:** MAO-B inhibitor
- **Strength and Formulation:** 50mg, 100mg; tabs
- **Manufacturer:** US WorldMeds
- **How supplied:** Bottle—30, 90
- **Legal Classification:** Rx

Indications

- As adjunct to levodopa/carbidopa in patients with **Parkinson's disease** experiencing "off" episodes

Limitations of Use

- **Not effective** as monotherapy for treating Parkinson's disease

Dosage & Administration

- Initially 50mg once daily (at same time of day); may increase to 100mg once daily after 2 weeks as tolerated
- **Moderate hepatic impairment** (Child-Pugh B): max 50mg once daily
- Taper gradually upon discontinuation

Considerations for Special Populations

- **Pregnancy:** Category C
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Elderly:** No overall differences in safety or efficacy
- **Hepatic impairment:** See Contraindications

Contraindications

- Severe hepatic impairment (Child-Pugh C)
- Concomitant other MAOIs including linezolid, opioids (eg, meperidine, methadone, propoxyphene, tramadol), SNRIs, tricyclic, tetracyclic, or triazolopyridine antidepressants, cyclobenzaprine, methylphenidate, amphetamine and their derivatives, St. John's wort, dextromethorphan

Warnings/Precautions

- Monitor for new onset or uncontrolled **hypertension**
- Avoid **tyramine-rich** (>150mg) foods (see full labeling)
- **Dyskinesia**: reduce daily dose of levodopa or dopaminergic agent
- Consider reducing dose or discontinuing therapy if hallucinations, psychotic disorders, urges/compulsive behaviors develop

Warnings/Precautions

- Consider discontinuing if excessive daytime **sleepiness** or if sudden onset of sleep occurs
- History of retinal/macular degeneration, uveitis, inherited retinal conditions, family history of hereditary retinal disease, albinism, retinitis pigmentosa, active retinopathy; monitor periodically for visual changes
- **Discontinue** if severe hepatic impairment develops

Interactions

- See **Contraindications**
- Allow at least 14 days after discontinuing safinamide before starting MAOIs, opioids, serotonergics
- Possible hypertensive crisis with excess dietary tyramine (see full labeling)
- Monitor for hypertension and reaction to dietary tyramine if concomitant with isoniazid
- Concomitant **SSRIs**: use lowest effective dose and monitor for serotonin syndrome

Interactions

- Monitor for hypertension if concomitant with **sympathomimetics** (eg, nasal, oral, ophthalmic, decongestants or cold remedies)
- Concomitant with **BCRP substrates** (eg, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, rosuvastatin, sulfasalazine, topotecan); monitor
- May be **antagonized** by dopamine antagonists (eg, antipsychotics, metoclopramide)

Adverse Reactions

- Dyskinesia
- Fall
- Nausea
- Insomnia
- Serotonin syndrome
- Withdrawal-emergent hyperpyrexia and confusion
- Retinal pathology

Mechanism of Action

- Inhibition of MAO-B activity, by blocking the catabolism of dopamine, is thought to result in an increase in dopamine levels and a subsequent increase in dopaminergic activity in the brain

Clinical Studies

- **Study 1** and **Study 2** were double-blind, placebo-controlled, multi-national, 24-week studies in Parkinson's disease (PD) patients with "Off" time during treatment with carbidopa/levodopa and other PD medications (eg, dopamine agonists, COMT inhibitors, anticholinergics, and/or amantadine)

Clinical Studies

- **Primary efficacy endpoint:** change from baseline in total daily “On” time without troublesome dyskinesia based on 18-hour patient diaries done at least 3 days before scheduled visits
- **Secondary endpoints:** “Off” time during the diary period, reduction in UPDRS Part III scores

Clinical Studies

- In **Study 1** (n=645), patients were randomized to Xadago 50mg daily, Xadago 100mg daily, or placebo
- Both Xadago doses significantly increased **“On” time** vs. placebo
  - **Xadago 50mg:** 0.50 (95% CI: 0.03, 0.96; *P*=0.0356)
  - **Xadago 100mg:** 0.53 (95% CI: 0.07, 1.00; *P*=0.0238)

Clinical Studies

- Both Xadago doses significantly reduced “Off” time
  - **Xadago 50mg:** -0.55 (95% CI: -0.93, -0.17; *P*=0.0049)
  - **Xadago 100mg:** -0.57 (95% CI: -0.95, -0.19; *P*=0.0037)
- Both Xadago doses significantly reduced UPDRS Part III scores
  - **Xadago 50mg:** -1.75 (95% CI: -3.24, -0.36; *P*=0.0212)
  - **Xadago 100mg:** -2.48 (95% CI: -3.97, -1.00; *P*=0.0011)

Clinical Studies

- In **Study 2** (n=549), patients were randomized to Xadago 100mg daily or placebo for up to 24 weeks
- Xadago significantly increased **“On” time** vs. placebo (least squares difference 0.99, 95% CI: 0.58, 1.39; *P*<0.001)

Clinical Studies

- Xadago significantly reduced **“Off” time** vs. placebo (-1.06, 95% CI: -1.43, -0.69; *P*<0.001)
- Xadago significantly reduced **UPDRS Part III scores** vs. placebo (-1.70, 95% CI: -2.89, -0.50; *P*=0.005)
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/xadago/drug/34690/