MEDISON
Delivering Innovative Healthcare

**רופא/ה, רוקח/ת נכבד/ה,**

**הריני להודיעכם כי העלון לרופא של התכשיר עודכן:**

| | |
|---|---|
| **Xadago 50mg** | **קסדגו 50מ"ג** |
| **Xadago 100mg** | **קסדגו 100מ"ג** |

**Film-coated tablets**

**Per os**

**מרכיב פעיל: Safinamide (as methansulfonate)**

**התוויה מאושרת:**

Xadago is indicated for the treatment of adult patients with idiopathic Parkinson's disease (PD) as add-on therapy to a stable dose of Levodopa (L-dopa) alone or in combination with other PD medicinal products in mid-to late-stage fluctuating patients.

בעלון לרופא נעשו עדכונים הבאים:

**4. CLINICAL PARTICULARS**

**4.2 Special warnings and precautions for use**

Potential for retinal degeneration in patients with ~~presence/~~prior history of retinal disease
Xadago should not be administered to patients with ophthalmological history that would put them at increased risk for potential retinal effects (e.g., ~~albino patients,~~ family history of hereditary retinal disease, ~~retinitis pigmentosa, any active retinopathy,~~ or history of uveitis) see sections 4.3 and 5.3.

**4.3 Interaction with other medicinal products and other forms of interaction**

*In vivo* and *in vitro* pharmacodynamic drug interactions
~~*Tyramine/safinamide interaction*~~

~~Results of one intravenous and two short term oral tyramine challenge studies, as well as results of home monitoring of blood pressure after meals during chronic dosing in two therapeutic trials in PD patients, did not detect any clinically important increase in blood pressure. Three therapeutic studies performed in PD patients without any tyramine restriction, also did not detect any evidence of~~

~~tyramine potentiation. Xadago can, therefore, be used safely without any dietary tyramine restrictions.~~

*In vivo* and *in vitro* pharmacokinetic drug interactions

~~There was no effect on the clearance of safinamide in patients with PD receiving safinamide as adjunct to chronic L-dopa and/or DA-agonists and safinamide treatment did not change the pharmacokinetic profile of co-administered L-dopa.~~

~~In an *in vivo* drug-drug interaction study performed with ketoconazole, there was no clinically relevant effect on the levels of safinamide. Human studies evaluating the interaction of safinamide with CYP1A2 and CYP3A4 substrates (caffeine and midazolam), did not demonstrate any clinically significant effects on the pharmacokinetic profile of safinamide. This is in line with the results of the *in vitro* tests in which no meaningful CYP induction or inhibition by safinamide was observed and it was shown that CYP enzymes play a minor role in the biotransformation of safinamide (see section 5.2)~~

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Safinamide is almost exclusively eliminated via metabolism, largely by high capacity amidases that have not yet been characterized. Safinamide is eliminated mainly in the urine. In human liver microsomes (HLM), the N-dealkylation step appears to be catalysed by CYP3A4, as safinamide clearance in HLM was inhibited by ketoconazole by 90%. ~~There are currently no marketed medicinal products known to cause clinically significant drug-drug interactions through inhibition or induction of amidase enzymes.~~

**4.6 Fertility, pregnancy and lactation**

Pregnancy

~~No clinical data for safinamide on exposed pregnancies is available~~There are no or limited amount of data from the use of safinamide in pregnant women. ~~Animal s~~Studies in animals have shown ~~adverse reactions when exposed to safinamide during pregnancy or lactation~~reproductive toxicity (see section 5.3). ~~Women of childbearing potential should be advised not to become pregnant during safinamide therapy. Xadago should not be given during pregnancy.~~Xadago is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

~~Safinamide is expected to be excreted in milk as adverse reactions have been observed in rat pups exposed via milk~~Available pharmacodynamic/toxicological data in animals have shown excretion of safinamide in milk (for details see ~~section~~ 5.3). A risk for the breast-fed child cannot be excluded. Xadago should not be ~~given to breast-feeding women~~used during breast-feeding.

**4.7 Effects on ability to drive and use machines**

~~Xadago has no or negligible influence on the ability to drive and use machines, however,~~Somnolence and dizziness may occur during Xadago treatment, therefore patients should be cautioned about using hazardous machines, including motor vehicles, until they are reasonably certain that Xadago does not affect them adversely.

**4.8 Undesirable effects**

Summary of the safety profile

~~The overall safety profile of Xadago is based on the clinical development program performed in over 3000 subjects, of whom over 500 were treated for more than 2 years~~Dyskinesia was the most common adverse reaction reported in safinamide patients when used in combination with L-dopa alone or in combination with other PD treatments.

Serious adverse reactions are known to occur with the concomitant use of SSRIs, SNRIs, tricyclic/tetracyclic antidepressants and MAO inhibitors, such as hypertensive crisis (high blood pressure, collapse), neuroleptic malignant syndrome (confusion, sweating, muscle rigidity, hyperthermia, CPK increase), serotonin syndrome (confusion, hypertension, muscle stiffness, hallucinations), and hypotension. With MAO-inhibitors there have been reports of drug interactions with concomitant use of sympathomimetic medicinal products.

Description of selected ~~A~~adverse ~~Drug R~~reactions ~~(ADRs)~~

~~Dyskinesia was the most common adverse reaction reported in safinamide patients when used in combination with L-dopa alone or in combination with other PD treatments.~~ Dyskinesia occurred early in treatment, was rated “severe”, led to discontinuation in very few patients (approx. 1.5%), and did not require reduction of dose in any patient.

העלון לרופא והעלון לצרכן נמצאים בקישור וכן מפורסמים במאגר התרופות באתר משרד הבריאות וניתן לקבלם מודפס על ידי פניה לבעל הרישום.

בברכה,
שרון עמיר
רוקחת ממונה
מדיסון פארמה בע"מ