Dear Healthcare Professional,

Please be informed that the AZILECT® Product Monograph has been updated.

- The monograph format is in line with the new Product Monograph template
- Updated Contraindications section:

**IMPORTANT**

Wording from the updated Contraindications section is included below in its entirety. Please review carefully.

*Meperidine and Other Analgesics:* AZILECT is contraindicated for use with meperidine. Serious, sometimes fatal reactions have been precipitated with 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. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with meperidine.

For similar reasons, AZILECT should not be administered with the analgesic agents tramadol, methadone, tapentadol, and propoxyphene.

*Other Drugs:* AZILECT should not be used with the antitussive agent dextromethorphan. The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. AZILECT is also contraindicated for use with St. John’s wort, and cyclobenzaprine (a tricyclic muscle relaxant).

*MAO inhibitors:* AZILECT should not be administered along with other MAO inhibitors because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with MAO inhibitors.
Updated Warnings and Precautions section - Use of antidepressants

Antidepressants: Severe CNS toxicity associated with hyperpyrexia and death has been reported with the combined treatment of an antidepressant (e.g. selective serotonin reuptake inhibitors-SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, tetracyclic antidepressants, triazolopyridine antidepressants) and non-selective MAOIs (NARDIL, PARNATE) including the reversible MAOI, moclobemide or selective MAO-B inhibitors, selegiline and rasagiline (AZILECT). These adverse reactions are often described as “serotonin toxicity” or “serotonin syndrome” a potentially serious condition which can result in death. The symptoms of serotonin syndrome have included behavioral and cognitive/mental status changes (e.g., confusion, hypomania, hallucinations, agitation, delirium, headache, and coma), autonomic effects (e.g., syncope, shivering, sweating, high fever/hyperthermia, hypertension, hypotension, tachycardia, nausea, diarrhea), and somatic effects (e.g., muscular rigidity, myoclonus, muscle twitching, hyperreflexia manifested by clonus, and tremor). In the post-marketing period, non-fatal cases of serotonin syndrome have been reported in patients treated with antidepressants concomitantly with AZILECT.

Since the mechanisms of these reactions are not fully understood, it seems prudent, in general, to avoid the combination of AZILECT and tricyclic, tetracyclic or triazolopyridine antidepressants, as well as AZILECT and selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with a tricyclic, tetracyclic, triazolopyridine, SSRI, or SNRI antidepressant. Similarly, at least 14 days should elapse after discontinuing treatment with a tricyclic, tetracyclic, triazolopyridine, SSRI, or SNRI antidepressant before starting AZILECT. Because of the long half-lives of fluoxetine and its active metabolite, at least five weeks (perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses) should elapse between discontinuation of fluoxetine and initiation of AZILECT.
Updated Warnings and Precautions section - Tyramine/rasagiline interaction

Tyramine/rasagiline interaction: Dietary tyramine restriction is not ordinarily required with ingestion of most foods and beverages that may contain tyramine, during treatment with recommended doses of AZILECT. However, certain foods (e.g., aged cheeses, such as Stilton cheese) may contain very high amounts (i.e., > 150 mg) of tyramine and could potentially cause a hypertensive “cheese” reaction in patients taking AZILECT even at the recommended doses due to increased sensitivity to tyramine. Patients should be advised to avoid foods (e.g., aged cheese) containing a very large amount of tyramine while taking recommended doses of AZILECT because of the potential for large increases in blood pressure. Selectivity for inhibiting MAO-B diminishes in a dose-related manner as the dose is progressively increased above the recommended daily doses.

Updated Information for Patients section

Information for Patients

Patients receiving AZILECT should be given the following instructions by the physician:

- Patients should be told that taking more than 1 mg may cause serious side effects which could include a severe headache, seizures, and a sudden rise in blood pressure. Patients should be told to seek immediate emergency medical assistance if they experience these side effects. Patients should contact their doctor or pharmacist immediately if they experience any other unusual symptoms they have not had before or are not mentioned here.

- Patients who are taking ciprofloxacin and other CYP1A2 inhibitors and patients with mild hepatic impairment should use 0.5mg daily of AZILECT.

- The possibility exists that very tyramine-rich foods (e.g., aged cheese such as Stilton) could possibly cause an increase in blood pressure. Patients should be advised to avoid certain foods containing a very large amount of tyramine (e.g., aged cheese) while taking recommended doses of AZILECT because of the potential for large increases in blood pressure. If patients eat food very rich in tyramine and do not feel well after eating, they should contact their healthcare provider.

- Patients should be cautioned of the possibility of developing hallucinations and instructed to report them to their health care provider promptly should they develop.

- Patients should be advised to inform their physician if they are taking, or planning to take, any prescription or over-the-counter drugs especially with antidepressants and over-the-counter cold medications since there is a potential for interaction with AZILECT. Patients should not use meperidine with AZILECT.
Patients taking AZILECT as adjunct to levodopa should be advised there is the possibility of increased dyskinesia and postural hypotension.

Patients are advised to monitor for melanomas frequently and on a regular basis because patients with Parkinson’s disease have a higher risk of developing melanoma than the general population. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g. dermatologists).

Patients should be instructed to take AZILECT as prescribed. If a dose is missed the next dose should be taken at the usual time on the following day. The patient should not doubleup the dose of AZILECT.

Patients should be told to contact their healthcare provider if they wish to discontinue AZILECT.

**Updated Drug Interactions section:**

Concomitant use of sympathomimetic medications

*Sympathomimetic medications:* The concomitant use of AZILECT and sympathomimetic medications was not allowed in clinical studies. Severe hypertensive reactions have followed the administration of sympathomimetics and non-selective MAO inhibitors. One case of hypertensive crisis has been reported in a patient taking the recommended doses of a selective MAO-B inhibitor and a sympathomimetic medication (ephedrine). Elevated blood pressure was reported in another patient taking the recommended dose of AZILECT and ophthalmic drops with a sympathomimetic medication (tetrahydrozoline). Because AZILECT is a selective MAOI, hypertensive reactions are not ordinarily expected with the concomitant use of sympathomimetic medications. Nevertheless, caution should be exercised when concomitantly using recommended doses of AZILECT with any sympathomimetic medications including nasal, oral, and ophthalmic decongestants and cold remedies.
Teva Canada Innovation thanks you for your interest in AZILECT®.

We invite you to consult the updated Product Monograph at www.tevacanadainnovation.com/English/products/. For more information, contact your Teva Canada Innovation representative. For your convenience, a copy of the updated AZILECT® Prescribing Information is included with this communication.

AZILECT® (rasagiline mesylate) is indicated for the treatment of the signs and symptoms of idiopathic Parkinson’s disease as initial monotherapy and as adjunct therapy to levodopa.

AZILECT® may cause hallucinations and as adjunct to levodopa there is the possibility of increased dyskinesia and postural hypotension. AZILECT® should not be used at daily doses exceeding the maximum recommended (1 mg/day) because of the risks associated with nonselective inhibition of MAO-B. Patients should be advised to avoid foods (e.g., aged cheese) containing a very large amount of tyramine while taking recommended doses of AZILECT® because of the potential for large increases in blood pressure. It is recommended, in general, to avoid the combination of AZILECT® and tricyclic, tetracyclic or triazolopyridine antidepressants, as well as AZILECT® and selective serotonin re-uptake inhibitors or serotonin-norepinephrine reuptake inhibitors. Patients taking concomitant ciprofloxacin and other CYP1A2 inhibitors should use 0.5 mg daily of AZILECT®.

No significant differences in safety profile were observed based on age or gender.

Overall, in phase II/III clinical trials, the long-term safety profile was similar to that observed with shorter duration exposure.

The most commonly observed adverse events that occurred in ≥5% of patients and were at least 1.5 times the incidence in the placebo group were dyskinesia (18%, 10%), accidental injury (12%, 5%), weight loss (9%, 3%), postural hypotension (9%, 3%), vomiting (7%, 1%), anorexia (5%, 1%), arthralgia (8%, 4%), abdominal pain (5%, 1%), nausea (12%, 8%), constipation (9%, 5%), dry mouth (6%, 3%), rash (6%, 3%), ecchymosis (5%, 3%), somnolence (6%, 4%) and paresthesia (5%, 3%) for AZILECT® 1 mg as adjunct therapy.

The most commonly observed adverse events that occurred in ≥5% of patients and were at least 1.5 times the incidence in the placebo group were flu syndrome (5%, 1%), arthralgia (7%, 4%), depression (5%, 2%), dyspepsia (7%, 4%) and falls (5%, 3%) in patients receiving AZILECT® 1 mg as monotherapy.

* This is not a complete list of updates to the AZILECT® Product Monograph. Please consult the new Product Monograph for complete information.

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