DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21641/S-016, S-017

SUPPLEMENT APPROVAL

Teva Pharmaceuticals USA
Attention: Dennis Ahern
Senior Director, Regulatory Affairs
41 Moores Road
PO Box 4011
Frazer, PA 19355

Dear Mr. Ahern:

Please refer to your following Supplemental New Drug Applications (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Azilect® (rasagiline mesylate) Tablet, 0.5 mg and 1 mg:

Supplement 016

Dated: May 18, 2012
Received: May 18, 2012
Amendments: October 3, 2013, and March 25, 2014

This "Prior Approval" supplemental new drug application proposes the following changes to the Full Prescribing Information:

- Use in Specific Populations (8.1): inclusion of Phase IV study results relative to embryo fetal development in rabbit
- Clinical Pharmacology (12.3): inclusion of Phase IV study results relative to the effect of levodopa/carbidopa on rasagiline pharmacokinetics

Supplement 017

Dated: July 31, 2013
Received: August 1, 2013
Amendments: August 29, 2013, September 17, 2013, October 30, 2013, and February 4, 2014

This "Prior Approval" supplemental new drug application proposes the inclusion of efficacy and safety results pertaining to the study entitled "A Double-blind, Placebo-controlled, Randomized, Multicenter Study to Assess the Safety and Clinical Benefit of Rasagiline as an Add-on Therapy to Stable Doses of Dopamine Agonists in the Treatment of Early Parkinson's Disease" (ANDANTE) into the prescribing information.

In addition, we note drugs that have an effect on central dopaminergic activity may lead to certain adverse reactions that warrant a detailed description in the Prescribing Information. Therefore, to be consistent and thorough, the following class language was added to the "Warnings and Precautions" section of the Azilect Prescribing Information:

- Patients Falling Asleep During Activities of Daily Living
- Impulse Control/Compulsive Behaviors

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable because Parkinson's disease is currently considered an adult-related condition that does not occur in pediatrics.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

0023-6 To conduct a large, simple, randomized, placebo controlled trial of rasagiline added to standard therapy in approximately 5000 Parkinson's disease patients for a duration of 36 months to assess the relative risk of melanoma.

The timetable listed in your approval letter dated May 16, 2006, states that you will conduct this study according to the following schedule:

Protocol Submission Date:	January 20, 2006
Study Start Date:	February 28, 2007
Final Report Submission Date:	May 31, 2012 (ongoing review of the data by Data Safety Monitoring Board (DSMB) during the study)

In a submission dated February 1, 2013, you requested the following revised milestones because negotiations regarding the Final Protocol are not complete:

Protocol Submission Date:	January 20, 2006
Study Start Date:	October 15, 2014
Final Report Submission Date:	September 15, 2016 (ongoing review of the data by Data Safety Monitoring Board (DSMB) during the study)

Submit clinical protocols to your IND 045958 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. As noted in our correspondence dated February 14, 2013, the original schedule serves as the basis for defining the status of a postmarketing commitment, even if a revised schedule has been proposed. Your annual progress reports, required under 21 CFR 314.81(b)(2)(vii), must include both the original and revised schedules, and the reason for the revision. Because these submission dates differ from those specified in the milestones listed in the May 16, 2006, approval letter, we consider this postmarketing commitment delayed. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Tracy Peters, Senior Regulatory Project Manager, at (301) 796-2953.

Sincerely,

{See appended electronic signature page}

Eric Bastings, M.D.
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS
05/29/2014