

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-083

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-083

NDA APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Michelle Campbell
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Campbell:

Please refer to your new drug application (NDA) dated September 8, 2006, received September 8, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Exelon® Patch (rivastigmine transdermal system).

We acknowledge receipt of your submissions dated:

January 8, 2007
January 22, 2007
February 21, 2007

March 2, 2007
May 24, 2007
June 20, 2007

June 28, 2007
July 2, 2007
July 5, 2007

This new drug application provides for the use of Exelon® Patch (rivastigmine transdermal system) for the treatment of mild to moderate dementia of the Alzheimer's type and the treatment of mild to moderate dementia associated with Parkinson's Disease.

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

The following dissolution method and specifications are acceptable for quality control. When major changes are made in the future, in vivo studies will be required.

Dissolution Method:

Apparatus: USP Apparatus 6 (cylinder)
Medium: 0.9% Sodium Chloride solution
Temperature: 32°C ± 0.5 °C
Speed: 50 rpm

Dissolution Specifications: The following are the regulatory specifications for the Exelon patches:

Table: Release and stability acceptance criteria for Exelon Patch 4.6 mg/24 hours and 9.5 mg/24 hours

Time Points	Percent Released
2 hours	b(4)
4 hours	
7 hours	

In regard to your proposed comparability protocol for any post approval drug manufacturing site change, you have not provided data to show that the in vitro human skin permeation for the product correlates to in vivo performance when changes are made to the product. In the absence of this information, your proposal to do in vitro testing cannot be accepted and a bioequivalence study will be required.

Submit final printed carton and container labels that are identical to the July 5, 2007 submitted carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission **“Final Printed Carton and Container Labels for approved NDA 22-083.”** Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, “SPL for approved NDA 22-083”.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

Please submit one market package of the drug product when it is available.

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 Melina Griffis, R.Ph., Sr. Regulatory Project Manager, at (301) 796-1078.

Sincerely,

{See appended electronic signature page}

Russell Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and
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/s/

Russell Katz

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