DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 078388

Barr Laboratories, Inc.
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated June 26, 2006, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Donepezil Hydrochloride Orally-Disintegrating Tablets, 5 mg and 10 mg.

Reference is also made to the tentative approval letter issued by this office on April 9, 2010, and to your amendments dated November 15, 2006; February 5, and May 3, 2007; and June 28, September 24, and November 24, 2010.

This letter corrects the **approval** letter issued by this office on November 26, 2010, in which we stated that Barr Laboratories, Inc. was eligible for 180 days of generic drug exclusivity. This letter serves as the official document, retaining the approval date of November 26, 2010.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Donepezil Hydrochloride Orally-Disintegrating Tablets, 5 mg and 10 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Aricept ODT, 5 mg and 10 mg, respectively, of Eisai, Inc. (Eisai). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

The reference listed drug (RLD) upon which you have based your ANDA, Eisai's Aricept ODT, 5 mg and 10 mg, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos. 7,727,548 (the '548 patent) and 7,727,552 (the '552 patent) are scheduled to expire on June 23, 2022, and March 26, 2018, respectively.

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each of these patents is invalid, unenforceable, or will not be infringed by your

manufacture, use, or sale of Donepezil Hydrochloride Orally-Disintegrating Tablets, 5 mg and 10 mg, under this ANDA. You have notified the agency that Barr Laboratories, Inc. (Barr) complied with the requirements of section 505(j)(2)(B) of the Act, and that no action for infringement was brought against Barr with respect to either of these patents within the statutory 45-day period. It is also noted that these patents were listed after submission of your ANDA.

With respect to 180-day generic drug exclusivity, we note that Barr was the first ANDA applicant for Donepezil Hydrochloride Orally-Disintegrating Tablets, 5 mg and 10 mg, to submit a substantially complete ANDA with paragraph IV certifications to the '548 and '552 patents. The Agency has determined, however, that Barr forfeited its eligibility for 180-day exclusivity period when it failed to obtain tentative approval of this ANDA within 30 months after the date on which the ANDA was filed.[1] See section 505(j)(5)(D)(I)(IV) of the Act.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

The agency approved a revision to the labeling of the RLD within 60 days of the expiration of the '841 patent, which expired on November 25, 2010. This revision to the labeling of the RLD does not include a change to the WARNINGS section, and the agency has not determined that the continued presence of the labeling in effect before the revision will adversely impact the safe use of the drug. The agency has also determined that your ANDA meets the applicable standards for approval under section 505(j), and was otherwise eligible for approval but for expiration of the '841 patent. Therefore, under section 505(j)(10) of the Act, your ANDA is eligible for approval with labeling that differs from that of the RLD. You are hereby notified that you are required to change the labeling of your product to contain the revision that was approved on November 24, 2010, for Aricept Tablets, 5 mg and 10 mg. We note your commitment dated November 24, 2010, to submit a "Supplement – Changes Being Effected" containing such revised labeling no later than 60 days from the date of the notification.

We note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Post-marketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory

[1] Barr's ANDA 078388 was received (filed) on June 30, 2006, for the 10 mg strength, and an amendment for the 5 mg strength was received on December 12, 2006. The 30 month periods from these dates expired on December 30, 2008, and June 12, 2009, respectively. ANDA 078388 was not tentatively approved until April 9, 2010. The agency finds that this failure to obtain tentative approval by either December 30, 2008, or June 12, 2009, was not caused by a change in or a review of the requirements for approval, nor was a related citizen petition submitted that was subject to section 505(q) of the Act.

requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly 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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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 via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

11/26/2010

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.