



DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 76-017

Food and Drug Administration
Rockville MD 20857

APR 28 2004

IVAX Pharmaceuticals, Inc.
Attention: Patricia Jaworski
140 Legrand Avenue
Northvale, NJ 07647

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated October 31, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act) for Gabapentin Tablets 100 mg, 300 mg, 400 mg, 600 mg, and 800 mg.

Reference is also made to your amendments dated March 1, 2001; May 21, November 19, and December 17, 2003; and February 13, and March 23, 2004. Reference is also made to the ANDA Suitability Petition submitted under Section 505(j)(2)(C) of the Act and approved on January 12, 2001. This petition allows you to include Gabapentin Tablets 100 mg, 300 mg, and 400 mg in this ANDA, even though these tablet strengths are not currently included in the approved labeling for the reference listed drug product, Neurontin Tablets of Pfizer Pharmaceuticals, Ltd.

We have completed the review of this abbreviated application, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of another ANDA applicant's current entitlement to 180-day generic drug exclusivity explained in greater detail below, we are unable to grant final approval to your Gabapentin Tablets, 600 mg and 800 mg at this time. Therefore, your Gabapentin Tablets 100 mg, 300 mg, and 400 mg are **approved**. Your Gabapentin Tablets 600 mg and 800 mg are regarded as **tentatively approved** and will not be eligible for final approval until the 180-day generic drug exclusivity period has expired.

The Division of Bioequivalence has determined that your Gabapentin Tablets 100 mg, 300 mg, and 400 mg can be expected to have the same therapeutic effect as that of the reference listed drug product upon which the Agency relied as the basis of safety and effectiveness. Your dissolution testing should be incorporated into your stability and quality control program using the same method proposed in your application.

The listed drug referenced in your application, Neurontin[®] Tablets, 600 mg and 800 mg of Pfizer Pharmaceuticals Ltd., is currently subject to periods of patent and market exclusivity. The following United States patents and their expiration dates appear in the Agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book":

<u>Patent Number</u>	<u>Expiration Date</u>
4,894,476 (the '476 patent)	November 2, 2008
6,054,482 (the '482 patent)	April 25, 2017

Your application contains paragraph IV certifications to each of these patents under Section 505(j)(2)(A)(vii)(IV) of the Act stating that these patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Gabapentin Tablets 100 mg, 300 mg, 400 mg, 600 mg, and 800 mg under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action is brought against IVAX Pharmaceuticals, Inc. (IVAX) for infringement of one or both of the patents which were the subjects of the paragraph IV certifications. This action must be brought against IVAX prior to the expiration of forty-five (45) days from the date the notice you provided under paragraph (2)(B)(i) was received by the patent and NDA holder(s). You have informed the Agency that IVAX complied with the requirements of Section 505(j)(2)(B) of the Act. As a result, Pfizer, Inc. initiated two separate patent infringement actions against IVAX for the '476 patent. The first action was filed with respect to Gabapentin Tablets 600 mg and 800 mg in the United States District Court for the District of New Jersey [Pfizer, Inc, Warner-Lambert Company, and Godecke

Aktiengesellschaft v. IVAX Pharmaceuticals, Inc., Civil Action No. CV-01-577 (JCL)]. The second action was filed with respect to Gabapentin Tablets 100 mg, 300 mg, and 400 mg, in the United States District Court for the District of New Jersey [Pfizer, Inc. and Warner-Lambert Company v. IVAX Pharmaceuticals, Inc., Civil Action No. CV-01-1538 (JCL)]. These suits were subsequently consolidated for pretrial proceedings in the U.S. District Court for the District of New Jersey (MDL Docket No. 1384. Litigation regarding IVAX's patent litigation remains ongoing.

You have informed the Agency that IVAX was not sued within the statutory 45 day period with regard to the '482 patent. With regard to the '476 patent, the Agency recognizes that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application, expired on September 30, 2003.

With this approval, IVAX is eligible for 180-day generic drug exclusivity for Gabapentin Tablets 100 mg, 300 mg, and 400 mg, as provided for under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments) in Section 505(j)(5)(B)(iv) of the Act. This is because the Agency has concluded that IVAX was the first ANDA applicant to submit a substantially complete ANDA for Gabapentin Tablets 100 mg, 300 mg, and 400 mg, containing paragraph IV certifications to each patent listed in the Orange Book. This exclusivity will begin to run from the earlier of (1) the date IVAX begins commercial marketing of Gabapentin Tablets 100 mg, 300 mg, and 400 mg under this ANDA, or (2) from the date of the applicable court decision finding the '476 patent to be invalid, unenforceable, or not infringed.

With respect to the "first commercial marketing" trigger for the commencement of exclusivity, please refer to 21 CFR 314.107(c)(4). The Agency expects that you will begin commercial marketing of this drug product in a prompt manner. Please submit correspondence to your application stating the date you began commercial marketing of your Gabapentin Tablets 100 mg, 300 mg, and 400 mg, or the date of a decision of the court holding the relevant patent invalid, unenforceable or not infringed.

If you have any questions concerning the effective date of approval of an abbreviated new drug application and the Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

Postmarketing reporting requirements for your Gabapentin Tablets 100 mg, 300 mg, and 400 mg under this abbreviated application 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.

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

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns for Gabapentin Tablets 100 mg, 300 mg, and 400 mg. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Please note that our decision to grant tentative approval to your Gabapentin Tablets 600 mg and 800 mg, is based upon information currently available to the Agency; (i.e., data in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This decision is subject to change on the basis of new information that may come to our attention.

As noted previously, we are unable to grant final approval to your Gabapentin Tablets 600 mg and 800 mg, at this time because an ANDA providing for the 600 mg and 800 mg strengths and containing paragraph IV certifications to the patents listed in the Orange Book was submitted to OGD by another applicant prior to the submission of your application. Accordingly, your Gabapentin Tablets 600 mg and 800 mg will be eligible for final approval beginning on the date that is one hundred and eighty days after the date the Agency received notice of the first commercial marketing of the 600 mg and 800 mg strengths under the previous application, or the date of a court decision described under Section 505(j)(5)(B)(iv), whichever event occurs earlier. For additional information, we refer you to the Agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1988).

In order to reactivate this application to provide for final approval of your Gabapentin Tablets 600 mg and 800 mg, you must submit a "Supplemental Application - Expedited Review Requested". This supplemental application should be submitted for prior approval approximately 90 days prior to the date you believe that your Gabapentin Tablets 600 mg and 800 mg will be eligible for final approval. The supplement should include a detailed explanation of why and when you believe final approval should be granted. It should also include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This supplemental application should be submitted even if no changes have been made to the application since the date of this tentative approval. Significant changes, as well as an update of the status of the manufacturing and testing facilities' compliance with cGMPs are subject to agency review before final approval of the supplemental application will be granted. We request that you categorize the changes as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt.

In addition to the supplemental application requested above, the Agency may request at any time prior to the date of final approval that you submit an additional document containing the requested information. Failure to submit either or, if requested, both documents may result in the rescission of the tentative approval status of your

application for Gabapentin Tablets 600 mg and 800 mg, or may result in a delay in the issuance of the final approval letter.

Please note that under Section 505 of the Act, your Gabapentin Tablets 600 mg and 800 mg may not be marketed without final Agency approval. The introduction or delivery for introduction into interstate commerce of your Gabapentin Tablets 600 mg and 800 mg before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, your Gabapentin Tablets 600 mg and 800 mg will not be deemed approved for marketing under 21 U.S.C. 355, and will not be listed in the "Orange Book".

For further information on the status of this application, or prior to submitting an amendment providing for the final approval of your Gabapentin Tablets 600 mg and 800 mg, Please contact Thomas Hinchliffe, Pharm.D., Project Manager, at (301) 827-5771.

Sincerely yours,

(b)(6)

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research