DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 078003

APPROVAL

IVAX Pharmaceuticals, Inc.
(An indirect and wholly owned subsidiary of Teva Pharmaceuticals USA)
425 Privet Road
Horsham, PA 19044

Attention: Rich Leone
Senior Director, Regulatory Affairs, U.S. Generics

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 25, 2005, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Esomeprazole Magnesium Delayed-release Capsules USP, 20 mg and 40 mg.

Reference is also made to the complete response letter issued by this office on July 11, 2014, and to your amendments dated August 22, October 29, and December 12, 2014; and January 5, 2015.

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.[1] The Division of Bioequivalence has determined your Esomeprazole Magnesium Delayed-release Capsules USP, 20 mg and 40 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Nexium Delayed-release Capsules, 20 mg and 40 mg, of AstraZeneca Pharmaceuticals LP (AstraZeneca).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows:

Dissolution Testing should be conducted using the following FDA-recommended method:

Medium	Acid stage: 0.1N HCl Buffer stage: Sodium Phosphate Buffer, pH 6.8
Volume	Acid stage: 300 mL Buffer stage: 1000 mL
Temperature	37 °C
Apparatus	II (Paddle)
Rotational Speed	100 rpm

[1] The agency has determined that the applicant who was first to file a substantially complete ANDA with a paragraph IV certification to one or more of the patents listed for the reference listed drug (RLD) has forfeited its eligibility for 180-day generic drug exclusivity under section 505(j)(5)(B)(iv) of the Act.

Specifications	Acid stage: NMT 10% in 120 minutes Buffer stage: NLT 75% in 30 minutes

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Special Supplement – Changes Being Effected when there are no revisions to the "interim" specifications or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, AstraZeneca's Nexium Delayed-release Capsules, 20 mg and 40 mg, is subject to periods of patent protection. The following unexpired patents and expiration dates (with pediatric exclusivity added) are currently listed[2] in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"):

U.S. Patent No.	Expiration Date
5,714,504 (the '504 patent)	August 3, 2015
5,900,424 (the '424 patent)	November 4, 2016
6,147,103 (the '103 patent)	April 9, 2019
6,166,213 (the '213 patent)	April 9, 2019
6,191,148 (the '148 patent)	April 9, 2019
6,369,085 (the '085 patent)	November 25, 2018
6,428,810 (the '810 patent)	May 3, 2020
7,411,070 (the '070 patent)	November 25, 2018
8,466,175 (the '175 patent)	November 25, 2018

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 Esomeprazole Magnesium Delayed-release Capsules USP, 20 mg and 40 mg, under this ANDA. You have notified the agency that IVAX Pharmaceuticals, Inc., an indirect and wholly owned subsidiary of Teva Pharmaceuticals USA (Teva), complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation was initiated against Teva for infringement of the '504, '810, and '085 patents within the statutory 45-day period in the United States District Court for the District of New Jersey [AstraZeneca AB, Aktiebolaget Hässle, AstraZeneca LP, KBI Inc., and KBI-E Inc. v. Ivax Corporation, Ivax Pharmaceuticals, Inc., Zenith Laboratories, Inc., Teva Pharmaceutical Industries Ltd., and Teva Pharmaceuticals USA., Civil Action No. 06 CV 1057] and that in the same court, litigation was initiated against Teva for infringement of the '070 patent within the statutory 45-day period [AstraZeneca AB, Aktiebolaget Hässle, AstraZeneca LP, KBI Inc., and KBI-E Inc. v. Ivax Corporation, Ivax Pharmaceuticals, Inc., Ivax Pharmaceuticals NV, Inc., Teva Pharmaceutical Industries Ltd., Teva Pharmaceuticals USA, Inc., and Cipla, Ltd., Civil Action No. 08 CV 4993]. You also notified the agency of the dismissal of these cases.

[2] Also listed is U.S. Patent No. 5,690,960 (the '960 patent) which expired on November 25, 2014. A pediatric exclusivity period associated with the '960 patent expires on May 25, 2015.

With respect to the pediatric exclusivity period scheduled to expire on May 25, 2015 that is associated with the '960 patent, you have provided a copy of a letter from AstraZeneca that waives this exclusivity period, effective from December 15, 2014. This ANDA is therefore eligible for approval.

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.

Please 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.

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

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
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 Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

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,

William P. Rickman -S

Digitally signed by William P. Rickman -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300043242, cn=William P. Rickman -S
Date: 2015.01.26 12:19:11 -05'00'

For Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research