CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-541/S-006

CHEMISTRY REVIEW

DIVISION OF ONCOLOGY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-541

REVIEW DATE: August 29, 2000

SUBMISSION TYPE	DOC. DATE	CDER DATE	ASSIGNED DATE
SE-006	November 1, 1999	November 1, 1999	November 3, 1999

NAME & ADDRESS OF APPLICANT:

Zeneca Pharmaceuticals (US Agent)
1800 Concord Pike- P.O.Box 15437
Wilmington, DE 19850-5437

DRUG PRODUCT NAME:

Proprietary:	Arimidex tablet
Nonproprietary/USAN:	Anastrozole
Code Name/Number:	ZD1033

PHARMACOL. CATEGORY/INDICATION: Aromatase inhibitor for treatment of breast cancer in post menopausal women

DOSAGE FORM:	Tablet
STRENGTHS:	1 mg
ROUTE OF ADMINISTRATION:	Oral, QD
DISPENSED:	_x_ Rx ____ OTC

REMARKS/COMMENTS:
No new CMC information is available since the approval of NDA 20-541. A categorical exclusion for an environmental assessment is requested for this efficacy supplement (page 44, v6.2).

CONCLUSIONS & RECOMMENDATIONS:
A categorical exclusion for an environmental assessment for the efficacy supplement-006 is requested under 21CFR 25.31 with the following statements:

- Additional approval of this supplement will not result in the total amount of ARIMIDEX introduced into the environment, exceeding a concentration of 1ppb of the material in the aquatic environment.
- The applicant has no knowledge that any exceptional circumstances exist that would require any additional controls in order to protect the environment.

The provided justifications fall under the limits of 1ppb provision in 21CFR 25.31(b) and the extraordinary circumstance provision. The exclusion request is adequate.

/S/

Sung K. Kim, Ph.D.,
Review Chemist, HFD-150

cc:
Orig. NDA 20-541
HFD-150/Division File
HFD-150/S.Kim
HFD-150-/ABaird
HFD-150/R.Wood
R/D Init. by: /S/ 8-30-00

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville MD 20857

CLINICAL INSPECTION SUMMARY

DATE: August 14, 2000

TO: Amy Baird, Regulatory Project Manager
Oluwo Odujinrin, M.D., Clinical Reviewer
Division of Oncology Drug Products, HFD-150

THROUGH: Antoine El-Hage, Ph.D., Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

FROM: Gerald R. Hajarian

SUBJECT: Evaluation of Clinical Inspections

NDA: NDA 20-541/S-006

APPLICANT: AstraZeneca UK

DRUG: Arimidex® (anastrozole) Tablets

CHEMICAL CLASSIFICATION:

THERAPEUTIC CLASSIFICATION: Standard Review

INDICATION: Treatment of advanced breast cancer in postmenopausal woman

CONSULTATION REQUEST DATE: March 30, 2000

ACTION GOAL DATE: September 1, 2000

I. BACKGROUND:

Inspection assignments were issued on May 2, 2000 for one foreign clinical investigator (Jean-Marc Nabholz, M.D.) and one domestic clinical investigator (Aman U. Buzdar, M.D.) for the purpose of validating data in support of pending NDA 20-541/S-006. The Canadian site was inspected because it was considered pivotal in support of this supplemental application. The establishment inspection report (EIR) for Dr. Nabholz has not yet been received. This evaluation is based on a review of the Form FDA 483 and a teleconference with the investigator.

II. RESULTS (by site):

NAME	CITY	STATE or COUNTRY	ASSIGNED DATE	EIR RECEIVED	CLASSIFICATION
Buzdar	Houston	TX	5/2/00	7/00	NAI
Nabholz	Edmonton	Canada	5/2/00	Pending	VAI

A. Aman U. Buzdar, M.D.

Twenty subjects were enrolled and 7 subjects' records were audited. No major objectionable conditions were noted and no Form FDA 483 was issued. The data appear to be acceptable.

B. Jean-Marc Nabholz, M.D.

Forty-two subjects were enrolled. Although minor deficiencies were noted, for example, (1) failure to retain original informed consent forms for 13 subjects (consent was documented via microfiche); (2) failure to use the current version of the informed consent for 4 subjects; and (3) failure to include three sub-investigators on the Form FDA 1572, the data appear to be acceptable.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS:

Although there were minor deficiencies noted in the conduct of Dr. Nabholz's study which are described above, the data from the two sites appear acceptable for use in support of pending NDA 20-541/S-006. As noted above, this summary is based partially on the Form FDA 483 and a teleconference with the FDA investigator regarding Dr. Nabholz's study. Should the EIR for Dr. Nabholz contain significant additional findings, you will be notified.

Key to Classifications
NAI = No deviation from regulations. Data acceptable
VAI = Minor deviations(s) from regulations. Data acceptable
VAIr= Deviation(s) form regulations, response requested. Data acceptable
OAI = Significant deviations for regulations. Data unreliable
Pending = Inspection not completed

/S/

Gerald R. Hajarian
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

CONCURRENCE:

/S/

Antoine El-Hage, Ph.D., Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

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