

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-726

ADMINISTRATIVE DOCUMENTS

MC LABELING
COMMENTS

LABELING REVIEW: FEMARA (LETROZOLE)

4 23 17 TERRY
LABELING, MTC,

NDA: 20726
DRUG: Letrozole (Femara™)
APPLICANT: Ciba-Geigy
M.O.: G. Schechter, M.D.
DATE: April 22, 1997
Revised April 23, 1997

I. DESCRIPTION:

See Chemistry Review

II. CLINICAL PHARMACOLOGY:

A. Mechanism of Action:

Lines 26 - 28:

should be changed to :

to more accurately reflect the various treatments used when the cancer is hormonally responsive regardless of menopausal state.

Lines 34 - 35:

should be changed to:

B. Animal Pharmacology:

See Pharm/Tox Review

C. Pharmacokinetics:

See Biopharm Review and

Special Populations - Hepatic Insufficiency:

Lines 92 - 95:

should be changed to:

Pharmacodynamics:

See Biopharm Review

Clinical Studies:

Lines 135 - 136:

should be changed to:

Lines 136 - 137:

should be changed to:

Lines 139 - 144:

should be changed to:

Lines 148 -150:

must be changed to:

Line 152-156:

should be changed to :

Line 156: ‘

would read better as:

Line 169 - 172: Delete

Comment: Unadjusted analyses will be used in the label.

Line 176 - 177: Delete

Line 179: Change “

to:

Line 179 - 184: Delete:
following:

and insert the

Line 185 - 191: Delete

and insert:

Line 192 - 193: Delete.

Lines 194 - 226: See attached sheet for correction to the table.

1 Page (Table)

Deleted

Lines _____ Delete

III. INDICATIONS AND USAGE

Lines 235 - 237:

must be changed to read:

IV. CONTRAINDICATIONS

Lines 240 - 241:

would read better as:

See Pharmacology Review

IV. PRECAUTIONS

General

Line 252 - 253:

would read better as”

Laboratory Test:

Lines 262 - 263: Delete

and insert:

Lines 264:
changed to:

must be

Line 266:

must be changed to:

Comment: Grade 3/4 abnormalities in one or more of the following liver function studies (bilirubin, SGOT, SGPT, or gamma GT) in study participants who did not have documented liver metastases were reported for thirteen study participants on AR/BC2 and for eleven patients on AR/BC3 treated with Femara or in 24/737 (3.3%) of patients.

Drug Interactions

See Biopharm Review

Carcinogenesis, Mutagenesis, Impairment of Fertility

Pregnancy

Pediatric Use

See Pharmacology Review

Geriatric Use

Acceptable as written

ADVERSE EVENTS

Line 316 - 317: Delete

and insert:

Line 317 - 324: Delete
and insert:

Lines 326 - 328: Delete

and insert:

Lines 330 -332:

must be changed to:

Table of Adverse Events Occurring in > 5% of Patients Regardless of Causality:

See the attached table with the corrected numbers (%) based on the information contained in Vol. 1.96 and Vol 12.1 of NDA 20-726.

Lines 335 -336: Delete

OVERDOSAGE

1 page (table)

Deleted

Lines 341: Change

to:

Line 343 - 345:

should be changed

to:

Line 345 - 346: Delete

DOSAGE & ADMINISTRATION

Adults and elderly patients:

Line 253: Delete the word ^{do not alter} so that the sentences reads:

Hepatic and/or Renal Impairment

Acceptable as written

HOW SUPPLIED

See Chemistry Review

*Renowned Schuchter MD
6/27/97
JR Johnson, MD
6-27-97*

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA/PLA # 20-726 Supplement # — Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-150 Trade (generic) name/dosage form: Femara (letrozole tablets) Action: AP AE NA

Applicant Novartis Pharmaceutical Therapeutic Class ANTI-NEOPLASTIC HORMONES

Indication(s) previously approved _____ Pediatric labeling of approved indication(s) is adequate inadequate

Indication in this application ADVANCED BREAST CANCER IN POSTMENOPAUSAL WOMEN FOLLOWING ANTI-ESTROGEN THERAPY (For supplements, answer the following questions in relation to the proposed indication.)

1. **PEDIATRIC LABELING IS ADEQUATE.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric subgroups. Further information is not required.
2. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.
- a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
- b. The applicant has committed to doing such studies as will be required.
- (1) Studies are ongoing.
- (2) Protocols were submitted and approved.
- (3) Protocols were submitted and are under review.
- (4) If no protocol has been submitted, explain the status of discussions on the back of this form.
- c. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.
3. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in children. Explain, on the back of this form, why pediatric studies are not needed. (OVER) →
4. **EXPLAIN.** If none of the above apply, explain, as necessary, on the back of this form.

EXPLAIN, AS NECESSARY, ANY OF THE FOREGOING ITEMS ON THE BACK OF THIS FORM.

Jane Spillman
Signature of Preparer and Title (PM, CSO, MO, other)

June 20, 1997
Date

cc: Orig NDA/PLA # 20-726
HFD-150 /Div File
NDA/PLA Action Package
HFD-510/GTroendle (plus, for CDER APs and AEs, copy of action letter and labeling)
J. Spillman

EXPLANATION

3. CHILDREN DO NOT GET BREAST CANCER.

(BREAST CANCER IS EXTREMELY RARE IN THE PEDIATRIC AGE GROUP)

R. S. S. S.
7/20/97

Ciba Pharmaceuticals Division
Ciba-Geigy Corporation

NDA 20-726

Femara™
(Ietrozole / CGS 20267)

DEBARMENT CERTIFICATION STATEMENT (21 U.S.C. 335a)

Ciba-Geigy Corporation hereby certifies that, to the best of its knowledge, it did not and will not use in any capacity the services of any person debarred under section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act, in connection with this application.

Signed Robert A. Spicandy Date 7/22/96
for Adrian L. Birch
Executive Director
Drug Regulatory Affairs

Consult #591 (HFD-150)

DEC 4 1996

FEMARA

letrozole tablets

The LNC noted two potential look alike/sound alike conflicts with the proposed proprietary name: FEMSTAT and FEMCARE. but the LNC feels these trademarks have only a slight potential for confusion since they are different dosage forms.

The LNC has no reason to find the proposed proprietary name unacceptable.

W. R. King 11/8/96, Chair
CDER Labeling and Nomenclature Committee

cc: NDA 20-726
HFD-150 / Div Files
/ L. Zhou
/ P. Dietze
/ E. Tagyesi
/ D. Spillman