Health Canada Endorsed Important Safety Information on Femara* (letrozole)

NOVARTIS

November 17, 2005

Dear Health Care Professional:

Subject: Contraindication of Femara* (letrozole) in premenopausal women

Following discussions with Health Canada, Novartis is advising you of concerns about the use of the aromatase inhibitor Femara* (letrozole) for the purpose of ovulation induction in the treatment of infertility. Novartis is aware that Femara* has been or is being used to treat infertility even though statements in the Canadian Product Monographs warn physicians about potential embryo- and fetotoxicity with or without teratogenicity. There have been post-market reports of congenital anomalies in infants of mothers exposed to Femara* for the treatment of infertility.

Femara* (letrozole) is contraindicated in women with premenopausal endocrine status, in pregnancy, and/or lactation due to the potential for maternal and fetal toxicity and fetal malformations.

Novartis is committed to the safe use of its medications. As a manufacturer and distributor of Femara* (letrozole), it is our regulatory and compliance responsibility to duly remind all concerned physicians that the use of letrozole for the purpose of ovulation induction is not within the scope of the approved indications. For your information, the approved indications for Femara* and important information on contraindications and reproductive toxicology are described below:

Extracted from the respective Femara* (letrozole) Product Monographs dated March 22, 2004 and Sept. 22, 2005:

- ***Indications and Clinical Use***
  Femara (letrozole) is indicated for the treatment of first-line therapy in postmenopausal women with advanced breast cancer. It is also indicated for the hormonal treatment of advanced/metastatic breast cancer in women with natural or artificially-induced postmenopausal status, who have disease progression following antiestrogen therapy.*

  Femara (letrozole) is also indicated for use in the extended adjuvant treatment of hormone receptor-positive early breast cancer in postmenopausal women who have received approximately 5 years of prior standard adjuvant tamoxifen therapy.*

- ***Contraindications***
  Femara (letrozole) is contraindicated in premenopausal endocrine status, pregnancy, and lactation.*

- ***Warnings***
  Reproductive Toxicology
  Letrozole was evaluated for maternal toxicity as well as embryotoxic, fetotoxic and teratogenic potential in female rats following oral administration of daily doses of 0.003, 0.01 or 0.03 mg/kg on gestation days 6 through 17. Oral administration of letrozole to pregnant rats resulted in teratogenicity and maternal toxicity at 0.03 mg/kg. Embryotoxicity and fetotoxicity were seen at doses ≥ 0.003 mg/kg and there was an increase in the incidence of fetal malformation among the animals treated. However it is not known whether this was an indirect consequence of the pharmacological activity of Femara (inhibition of estrogen biosynthesis) or a direct drug effect.*

Novartis recommends the use of Femara* within the labeled indications. Your professional commitment in this regard has an important role in protecting the well being of your patients.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse drug reaction reporting programmes. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments.

Health Canada depends on health care professionals to report any fetal or maternal toxicity or any other serious and/or unexpected adverse reactions in patients receiving Femara* to Novartis or Health Canada at the following addresses:

Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, (QC) H9S 1A9
Phone:1-800-363-8883 (Medical information)

Any suspected adverse reaction can also be reported to:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

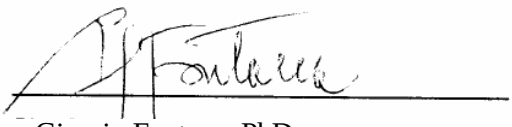
The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries, please refer to contact information:
Marketed Health Products Directorate
mhpd_dpsc@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

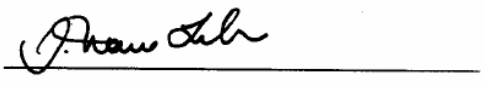
For the full prescribing information consult the Novartis website at: http://www.novartis.ca

Should you have any questions or require additional information regarding the use of Femara* (letrozole) please contact Novartis Pharmaceuticals Canada Inc., at 1-800-363-8883 from 8:30 AM to 4:30 PM Monday to Friday Eastern Standard Time.

Novartis Pharmaceuticals Canada Inc.



Pier-Giorgio Fontana, PhD
Vice-President
Regulatory Affairs



Jean-Marie Leclerc, M.D. FRCP (c)
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[Pr] Femara* is a registered trademark