DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

FEB - 2 2001

Mr. Robert Miranda
Associate Director
Drug Regulatory Affairs
Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, NJ 07936

RE: NDA: 20-726
Femara® (letrozole) Tablets
MACMIS ID # 9583

Dear Mr. Miranda:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of a Press Release (January 10, 2001) and an advertisement in the journal *Oncology* (2000;14(11):1522) for Femara (letrozole) Tablets. DDMAC finds this promotional material to be false, misleading, or otherwise in violation of the Federal Food, Drug, and Cosmetic Act and the regulations promulgated there under. Specifically, the Novartis Pharmaceuticals Corporation (Novartis) promotional material broadens the drug's approved indication, lacks fair balance, inadequately communicates the approved indication, and fails to provide information in brief summary as required for prescription drug advertisements.

Press Release (January 10, 2001)

An advertisement for a prescription drug is false, lacking in fair balance, or otherwise misleading if it contains a representation or suggestion, not approved for use in the labeling, that a drug is better, more effective, useful in a broader range of conditions or patients than has been demonstrated by substantial evidence. In the press release dated January 10, 2001, Novartis states "Supporting the filing was a Phase III randomized controlled trial of 324 postmenopausal women with large localized or locally advanced breast cancer tumors who were given Femara or tamoxifen as pre-operative treatment to reduce tumor size before breast-conserving surgery. Clinical responses after four months of preoperative therapy were significantly better for Femara than for tamoxifen (55% versus 36%)." Femara is not approved for "pre-operative treatment to reduce tumor size before breast-conserving surgery" and, therefore, this statement broadens the indication for Femara and promotes an unapproved new use.

Journal Advertisement (*Oncology* 2000;14(11):1522)

Your journal advertisement lacks fair balance, inadequately communicates the approved indication, and fails to provide information in brief summary as required for prescription drug advertisements. Specifically, the advertisement makes the claim "Soon there will be a significant change in the way you look at hormonal therapy" but fails to provide information regarding the risks associated with the use of Femara. For example, the approved product labeling (APL) warns that Femara may cause fetal harm when administered to pregnant women.

Furthermore, this journal advertisement fails to provide the approved indication for use of Femara (i.e., the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy). This required information was not communicated in any part of your journal advertisement.

Lastly, regulations require that advertisements for prescription drugs present a true statement of information in brief summary relating to side effects, contraindications and effectiveness. Your journal advertisement does not contain any of this required information.

Novartis should immediately cease distribution of these and other similar promotional materials for Femara that contain the same or similar claims or presentations. Novartis should submit a written response to DDMAC on or before February 16, 2001, describing its intent and plans to comply with the above. In its letter to DDMAC, Novartis should include the date on which this and other similarly violative materials were discontinued.

Novartis should direct its response to me by facsimile at (301) 594-6771 or by written communication at the Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. In all future correspondence regarding this matter, please refer to MACMIS ID 9583 in addition to the NDA number. DDMAC reminds Novartis that only written communications are considered official.

Sincerely,

/S/

Joseph A. Grillo, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing, Advertising and Communications

Press Releases

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FDA Approves Femara (letrozole tablets) As First-Line Hormonal Treatment for Advanced Breast Cancer in Postmenopausal Women -- Largest Study of its Kind Shows Novartis Drug Is More Effective Than Current Gold Standard

Prescribing Information

East Hanover, NJ, January 10, 2001 – Novartis Oncology announced today that the U.S. Food and Drug Administration has approved Femara® (letrozole tablets) for the first-line treatment of postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer. Most postmenopausal women with advanced breast cancer fall into these tumor receptor categories.

Approval of the new indication followed a priority review by the FDA and a unanimous recommendation from the FDA's Oncologic Drugs Advisory Committee. The recommendation was based on data from the largest single study ever to evaluate a hormonal therapy in this setting. The study found that Femara was significantly more effective than tamoxifen in multiple efficacy endpoints. Tamoxifen has traditionally been the standard of therapy for this indication.

"Femara shows great promise for becoming the new first-line therapy of choice for postmenopausal women with advanced breast cancer," said Robert Smith, MD, South Carolina Oncology Associates and a lead investigator in the first-line study. "It is the first therapy to challenge tamoxifen in multiple endpoints, including time to progression, response rates and overall clinical benefit."

Study Details

The Phase III trial on which the FDA based its decision was a head-to-head, randomized, double-blind multi-center trial comparing the use of Femara versus tamoxifen in more than 900 postmenopausal women who had locally advanced (stage IIIB) disease, metastatic breast cancer, or recurrences not amenable to treatment with surgery or radiotherapy.

The study demonstrated that Femara delays progression of advanced breast cancer for 9.4 months, as compared to 6.0 months for

tamoxifen. Results also indicated significant differences between Femara and tamoxifen with respect to overall tumor response rates (30% vs. 20%), clinical benefit (49% vs. 38%) and time to treatment failure (9.1 months vs. 5.7 months / 40 weeks vs. 25 weeks). Femara and tamoxifen were equally well tolerated.

Supporting the filing was a Phase III randomized controlled trial of 324 postmenopausal women with large localized or locally advanced breast cancer tumors who were given Femara or tamoxifen as pre-operative treatment to reduce tumor size before breast-conserving surgery. Clinical responses after four months of preoperative therapy were significantly better for Femara than for tamoxifen (55% versus 36%).

"Novartis is pleased that the FDA has recognized Femara's strong efficacy and safety profile and has deemed it worthy of the first-line indication," said David Epstein, President, Novartis Oncology. "We look forward to soon being able to offer Femara as first-line hormonal therapy all over the world to postmenopausal women with advanced breast cancer."

About Femara

Femara, an aromatase inhibitor, is a once-a-day oral treatment that was first approved for marketing in 1997 for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy. In July 2000, Novartis submitted a supplemental New Drug Application (sNDA) for first-line therapy in advanced breast cancer and, in August 2000, the sNDA received a priority review designation from the FDA.

In postmenopausal women, the primary source of estrogen is from fat, liver, muscle, and breast tissue through a process that turns adrenal androgens into estrogen, which stimulates the growth of certain hormone-dependent cancer cells. A breast tumor itself also may generate estrogen. Femara works by binding to the enzyme aromatase and blocking it from converting adrenal androgens to estrogen in these tissues.

"FDA approval of this new indication means that thousands of postmenopausal women with advanced breast cancer will finally have a more effective hormonal treatment option," said David Parkinson, MD, Vice President, Clinical Research at Novartis Oncology. "Novartis Oncology is proud to be at the forefront of the development of this and other products that can make a significant difference in patients' lives."

Femara is currently available in more than 75 countries worldwide as a treatment for advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy. Regulatory submissions for the first-line indication have also been filed globally; the drug is also being studied in the adjuvant setting.

Advanced Breast Cancer

More than 120,000 women in the United States have advanced breast cancer, the second leading cause of cancer death among American women. Approximately half of the 182,000 newly diagnosed cases of breast cancer each year are already in an advanced stage when they are detected.

Contraindications and Adverse Effects

Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients. Femara is generally well-tolerated. The adverse reactions in the first-line study were generally mild to moderate and were consistent with those seen in the second-line studies. The most commonly reported adverse events for Femara vs. tamoxifen were bone pain (20% vs. 18%), hot flushes (18% vs. 15%), back pain (17% vs. 17%), nausea (15% vs. 16%), dyspnea or labored breathing (14%vs. 15%), arthralgia (14% vs. 13%), fatigue (11% vs.

11%) and coughing (11% vs. 10%).

This release contains certain "forward-looking statements" relating to the Company's business, which can be identified by the use of forward-looking terminology such as "believes," "will," "breakthrough," or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of new products expected to be introduced by the Company and anticipated customer demand for such products. Such statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the Company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Some of these are uncertainties relating to unexpected regulatory delays, government regulation or competition in general, as well as factors discussed in the Company's Form 20F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

About Novartis

Novartis Oncology is a business unit under Novartis AG. It has operations within Novartis Pharma AG in Switzerland as well as Novartis Pharmaceuticals Corporation in the United States. Novartis (NYSE: NVS) is a world leader in healthcare with core businesses in pharmaceuticals, consumer health, generics, eye-care, and animal health. In 1999, the Group achieved sales of CHF 25.4 billion (USD 16.9 billion) and invested approximately CHF 3.6 billion (USD 2.4 billion) in R&D. Headquartered in Basel, Switzerland, Novartis employs about 66,000 people and operates in over 140 countries around the world. For further information please consult www.novartis.com.

Press Contact: Gloria Stone, 973-781-5587

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November 2000

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