Letrozole (Femara®)

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Drug name: Letrozole is marketed by the trade name Femara® (Novartis Pharmaceuticals Corporation, East Hanover, NJ).

Classification: Hormone oncological. Letrozole is a third-generation aromatase inhibitor. Aminoglutethimide is an example of a first-generation aromatase inhibitor.

Action: Letrozole is a competitive inhibitor of aromatase that blocks the conversion of androgens into estrogens, thus lowering the amount of estrogen in the bloodstream. This then restricts the supply of estrogen to cancers, such as some breast cancers. In postmenopausal women, estrogens are derived mainly from the action of the aromatase enzyme.

Indication: Letrozole is indicated for treating advanced breast cancer in postmenopausal women. The drug is considered a first-line treatment of hormone receptor positive or unknown, locally advanced, or metastatic breast cancer.

In an open label, multicenter, randomized, phase IIIb/IV trial published in *European Journal of Cancer,* letrozole demonstrated higher activity than anastrozole (Arimidex®, AstraZeneca Pharmaceuticals LP, Wilmington, DE) as a second-line therapy for advanced breast cancer after failure of tamoxifen (Rose et al., 2003).

New England Journal of Medicine recently published results of a randomized trial, led by the National Cancer Institute of Canada on behalf of several cooperative groups and the pharmaceutical company, concluding that taking letrozole therapy for at least 2.4 years, after the completion of standard tamoxifen (5 years), significantly improves disease-free survival (Goss et al., 2003). The optimal duration of treatment and long-term toxicities has not been established. Because of the preliminary findings, this trial was terminated early, thus leaving a follow-up period that was exceptionally short (2.4 years) (Bryant & Wolmark, 2003; Burstein, 2003).

Metabolism: Letrozole is metabolized through the liver by cytochrome P-450 isoenzymes 3A4 and 2A6, reducing plasma estrogen levels.

Excretion: Letrozole is excreted in the urine.

Half-life: The drug has a half-life of two days and steady state plasma concentration after two to six weeks of daily dosing of 2.5 mg.

Effect on blood counts: No toxicities have been reported.

Adverse reactions and effects: The most serious side effect reported with letrozole is thromboembolism, but this was limited to less than 1%. The most common side effects include arthritis, arthralgia, myalgia, hot flashes, headaches, fatigue, nausea, vomiting, constipation, diarrhea, rash, edema, cough, hypertension, and anorexia. Letrozole has been shown to increase bone resorption but is not necessarily associated with an increase of osteoporosis.

Route: Letrozole is administered as an oral medication.

Dosage and administration: The recommended daily dosage of letrozole is 2.5 mg.

Interactions: Specific drug interactions have not been reported. Taking contraceptives combined with estrogen may interfere with aromatase inhibitor efficacy. No added benefit occurs when letrozole is given with tamoxifen.

Contraindications: Letrozole is contraindicated in patients with known hypersensitivity to the drug/class or components. Caution should be used when administering letrozole to patients with impaired liver or renal function. The drug may cause fetal harm when administered to pregnant women.

Availability: Letrozole is available in 2.5 mg tablets. The average cost for 30 tablets is $197.

Nursing implications: Nurses evaluating the use of letrozole should do the following.

- Assess menopausal status of patients with breast cancer. Therapy with aromatase inhibitors alone does not suppress estrogen production adequately in women who are still ovulating.
- Assess patients for history of thromboembolism and liver or renal insufficiency.
- Review patients' current medications (prescription and nonprescription, including vitamins and herbs).
- Monitor patients' vital signs, with ongoing assessment of blood pressure.
- Inform patients that an assistance program and reimbursement information are available by calling 800-282-7630. (A trial script voucher program also is available).
- Assess for side effects. The most severe is thromboembolism.

Patient education: Patients receiving letrozole should be taught the following.

- Take letrozole as directed, with or without food.
- For gastrointestinal upset, eat small meals.
- Report chest pain, palpitations, shortness

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