Estrolet Tablets

ایسٹرو لیٹ گولیاں

(Letrozole Tablets USP)

(لیٹروزول)

COMPOSITION: Each film coated tablet contains:
Letrozole USP ... 2.5mg. [USP Specs.]

INDICATIONS: Adjuvant treatment of postmenopausal women with hormone receptor positive invasive early breastcancer. Extended adjuvant treatment of hormone-dependent invasive breast cancer in postmenopausal women who have received prior standard adjuvant tamoxifen therapy for 5 years.First-line treatment in postmenopausal women with hormone-dependent advanced breast cancer. Advanced breast cancer after relapse or disease progression, in women with natural or artificially induced postmenopausal endocrine status, who have previously been treated with anti-estrogens.
Neo-adjuvant treatment of postmenopausal women with hormone receptor positive, HER-2 negativebreast cancer where chemotherapy is not suitable and immediate surgery not indicated.

CONTRA-INDICATIONS: Hypersensitivity to the active substance or to any of the excipients, premenopausal endocrine status, pregnancy and breast-feeding.

PHARMACOLOGY: Mechanism of action: Letrozole is a nonsteroidal competitive inhibitor of the aromatase enzyme system; it inhibits the conversion of androgens to estrogens. In adult non tumor and tumor bearing female animals, letrozole is as effective as ovariectomy in reducing uterine weight, elevating serum LH, and causing the regression of estrogen-dependent tumors. In contrast to ovariectomy, treatment with letrozole does not lead to an increase in serum FSH. Letrozole selectively inhibits gonadal steroidogenesis but has no significant effect on adrenal mineralocorticoid or glucocorticoid synthesis.

PHARMACOKINETIC: Absorption: Letrozole is rapidly and completely absorbed from the gastrointestinal tract (mean absolute bioavailability: 99.9%). Food slightly decreases the rate of absorption but the extent of absorption (AUC) is not changed. The minor effect on the absorption rate is not considered to be of clinical relevance and therefore Letrozole may be taken without regard to mealtimes.
Distribution: Plasma protein binding of Letrozole is approximately 60%, mainly to albumin (55%). The concentration of Letrozole in erythrocytes is about 80% of that in plasma. Letrozole is rapidly and extensively distributed to tissues. Its apparent volume of distribution at steady state is about 1.87 ± 0.47 L/kg.
Biotransformation: Metabolism to a pharmacologically-inactive carbinol metabolite (4, 4'-methanolbisbenzonitrile) and renal excretion of the glucuronide conjugate of this metabolite is the major pathway of Letrozole clearance. Of the radiolabel recovered in urine, at least 75% was the glucuronide of the carbinol metabolite, about 9% was two unidentified metabolites, and 6% was unchanged Letrozole.
Elimination: The apparent terminal elimination half-life in plasma is about 2 to 4 days. After daily administration of 2.5mg steady-state levels are reached within 2 to 6 weeks. Plasma concentrations at steady state are approximately 7 times higher than concentrations measured after a single dose of 2.5mg, while they are 1.5 to 2 times higher than the steady-state values predicted from the concentrations measured after a single dose, indicating a slight non-linearity in the pharmacokinetics of Letrozole upon daily administration of 2.5mg. Since steady-state levels are maintained over time, it can be concluded that no continuous accumulation of Letrozole occurs.

DOSAGE AND ADMINISTRATION:
Adults and elderly patients: The recommended dose of Letrozole is 2.5mg once daily. No dose adjustment is required for elderly patients.
In patients with advanced or metastatic breast cancer, treatment with Letrozole should continue until tumor progression is evident. In the adjuvant and extended adjuvant setting, treatment with Letrozole should continue for 5 years or until tumor relapse occurs, whichever is first. In the adjuvant setting a sequential treatment schedule (Letrozole 2 years followed by tamoxifen 3 years) could also be considered.
In the neoadjuvant setting, treatment with Letrozole could be continued for 4 to 8 months in order to establish optimal tumor reduction. If the response is not adequate, treatment with Letrozole should be discontinued and surgery scheduled and/or further treatment options discussed with the patient.
Pediatric population: Letrozole is not recommended for use in children and adolescents. The safety and efficacy of Letrozole in children and adolescents aged up to 17 years have not been established. Limited data are available and no recommendation on a posology can be made.
Renal impairment: No dosage adjustment of Letrozole is required for patients with renal insufficiency with creatinine clearance =10ml/min. Insufficient data are available in cases of renal insufficiency with creatinine clearance lower than 10ml/min.
Hepatic impairment: No dose adjustment of Letrozole is required for patients with mild to moderate hepatic insufficiency (Child-Pugh A or B). Insufficient data are available for patients with severe hepatic impairment. Patients with severe hepatic impairment (Child-Pugh C) require close supervision.
Method of administration: Letrozole should be taken orally and can be taken with or without food.
Missed dose: A missed dose should be taken as soon as the patient remembers. However, if it is almost time for the next dose (within 2 or 3 hours), the missed dose should be skipped, and the patient should go back to her regular dosage schedule. Doses should not be doubled because with daily doses over the 2.5mg recommended dose, over-proportionality in systemic exposure was observed.

SPECIAL POPULATIONS:
Elderly People: Age had no effect on the pharmacokinetics of Letrozole.
Renal impairment: Renal impairment (24-hour creatinine clearance: 9 to 116mL/min), had no effect on the pharmacokinetics of single doses of 2.5mg of Letrozole, and had no effect on steady-state plasma Letrozole concentrations.

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Therefore, no dose adjustment is required for patients with renal impairment (CLcr =10ml/min). Little information is available in patients with severe impairment of renal function (CLcr <10ml/min).
Hepatic impairment: Letrozole should be administered with caution to patients with severe hepatic impairment and after consideration of the risk/benefit in the individual patient.

OVERDOSAGE: No specific treatment for overdose is known; treatment should be symptomatic and supportive.

WARNINGS & PRECAUTIONS: Menopausal status: In patients whose menopausal status is unclear, luteinizing hormone (LH), follicle-stimulating hormone (FSH) and/or estradiol levels should be measured before initiating treatment with Letrozole. Only women of postmenopausal endocrine status should receive Letrozole.
Renal impairment: Letrozole has not been investigated in a sufficient number of patients with creatinine clearance lower than 10ml/min. The potential risk/benefit to such patients should be carefully considered before administration of Letrozole.
Hepatic impairment: In patients with severe hepatic impairment (Child-Pugh C), systemic exposure and terminal half-life were approximately doubled compared to healthy volunteers. Such patients should therefore be kept under close supervision.
Bone effects: Letrozole is a potent estrogen-lowering agent. Women with a history of osteoporosis and/or fractures, or who are at increased risk of osteoporosis, should have their bone mineral density formally assessed prior to the commencement of adjuvant and extended adjuvant treatment and monitored during and following treatment with Letrozole. Treatment or prophylaxis for osteoporosis should be initiated as appropriate and carefully monitored.
Other Warnings: Co-administration of Letrozole with tamoxifen, other anti-estrogens or estrogen-containing therapies should be avoided as these substances may diminish the pharmacological action of Letrozole. As the tablets contain lactose, Letrozole is not recommended for patients with rare hereditary problems of galactose intolerance, of severe lactase deficiency or of glucose-galactose malabsorption.

DRUG INTERACTIONS: Tamoxifen: Clinical experience in the second-line breast cancer trials (AR/BC2 and AR/BC3) indicates that the therapeutic effect of Letrozole therapy is not impaired if Letrozole is administered immediately after tamoxifen.
Cimetidine: A pharmacokinetic interaction study with cimetidine showed no clinically significant effect on Letrozole pharmacokinetics.
Warfarin: An interaction study with warfarin showed no clinically significant effect of Letrozole on warfarin pharmacokinetics.
Other anticancer agents: There is no clinical experience to Letrozole dose on the use of Letrozole in combination with other anticancer agents.

FERTILITY, PREGNANCY AND LACTATION:
Women of perimenopausal status or child-bearing potential: Letrozole should only be used in women with a clearly established postmenopausal status. As there are reports of women regaining ovarian function during treatment with Letrozole despite a clear postmenopausal status at start of therapy, the physician needs to discuss adequate contraception when necessary.
Pregnancy: Letrozole is contraindicated during pregnancy. Letrozole may cause congenital malformations when administered during pregnancy.
Breast-feeding: It is unknown whether Letrozole and its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.Letrozole is contraindicated during breast-feeding.
Fertility: The pharmacological action of Letrozole is to reduce estrogen production by aromatase inhibition. In premenopausal women, the inhibition of estrogen synthesis leads to feedback increases in gonadotropin (LH, FSH) levels. Increased FSH levels in turn stimulate follicular growth, and can induce ovulation.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Letrozole has minor influence on the ability to drive and use machines. Since fatigue and dizziness have been observed with the use of Letrozole and somnolence has been reported uncommonly, caution is advised when driving or using machines.

ADVERSE REACTIONS: Very common: Hypercholesterolaemia, hot flushes, increased sweating, arthralgia and fatigues.
Common: Anorexia, appetite increase,depression, headache, dizziness, palpitations, hypertension, nausea, dyspepsia, constipation, abdominal pain, diarrhoea, vomiting, alopecia, rash, dry skin, myalgia, bone pain, osteoporosis, bone fractures, arthritis, vaginal bleeding, peripheral oedema, chest pain and weight increase.
Uncommon: Urinary tract infection, tumour pain, leucopenia, general oedema, anxiety, irritability, somnolence, insomnia, memory impairment, dysaesthesia, taste disturbance, cerebrovascular accident, carpal tunnel syndrome, cataract, eye irritation, blurred vision, tachycardia, ischaemic cardiac events (including new or worsening angina, angina requiring surgery, myocardial infarction and myocardial ischaemia), Thrombophlebitis, ischemic cardiac events,dyspnoea, cough, dry mouth, stomatitis, increased hepatic enzymes, hyperbilirubinemia, jaundice., pruritus, urticaria, tendonitis, increased urinary frequency, vaginal discharge, vaginal dryness, breast pain, pyrexia, mucosal dryness, thirst, and weight loss.
Rare: Pulmonary embolism, arterial thrombosis, cerebrovascular infarction, tendon rupture.
Very rare: Angioedema.
Not Known: Anaphylactic reactions, hepatitis, toxic epidermal necrolysis, erythema multiforme and trigger finger.

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Estrolet Tablets (Letrozole 2.5mg Tablets) is available in pack size of 10's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: ۳۰ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
NABIQASIM INDUSTRIES (PVT) LTD.
PHARMA 17/24, Korangi Industrial Area, Karachi-Pakistan.

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