Arofrez®

Letrozole USP 2.5 mg

Composition

Arofrez® tablet 2.5 mg: Each film coated tablet contains Letrozole USP 2.5 mg.

Pharmacology

Letrozole is a non-steroidal aromatase inhibitor and is highly specific in inhibiting aromatase activity. It inhibits the aromatase enzyme by competitively binding to the haem group of aromatase, a cytochrome P450 enzyme which catalyzes conversion of androgens to estrogens (specifically, androstenedione to estrone and testosterone to estradiol) resulting in a significant reduction of oestrogen biosynthesis in peripheral tissues and cancer tissue. Aromatase inhibition by letrozole appears to be specific, with sparing of other cytochrome P450 enzymes of the same class involved in glucocorticoid and mineralocorticoid synthesis.

Indications

- Adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer.
- Adjuvant treatment of postmenopausal women with early breast cancer (positive or unknown oestrogen or progesterone receptor status) who have received 5 years of adjuvant tamoxifen therapy (extended adjuvant therapy).
- First-line treatment in postmenopausal women with hormone-dependent advanced breast cancer.
- Treatment of advanced breast cancer in women with natural or artificially induced postmenopausal status, who have previously been treated with antioestrogens.
- Pre-operative therapy in postmenopausal women with localized hormone receptor positive breast cancer, to allow subsequent breast-conserving surgery in women not originally considered candidates for this type of surgery. Subsequent treatment after surgery should be in accordance with standard of care.

Dosage and Administration

Adult and elderly patients

The recommended dose of Letrozole is 2.5 mg once daily. In the adjuvant and extended adjuvant setting, treatment with Letrozole should continue for 5 years or until tumor relapse occurs, whichever comes first. In patients with metastatic disease, treatment with Letrozole should continue until tumor progression is evident. No dose adjustment is required for elderly patients.

Children

Not applicable.

Patients with hepatic and/or renal impairment

No dosage adjustment is required for patients with hepatic impairment or renal impairment (creatinine clearance =10 mL/min.). However, patients with severe hepatic impairment (Child-Pugh score C) should be kept under close supervision

Contraindications

- Known hypersensitivity to the active substance or to any of the excipients.
- Premenopausal endocrine status; pregnancy, lactation.

Warnings and Precautions

Renal impairment

Letrozole has not been investigated in patients with creatinine clearance <10 mL/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 score C), systemic exposure and terminal half-life were approximately doubled compared to healthy volunteers. Such patients should therefore be kept under close supervision.

Side Effects

Common:

Hot flushes, Increased level of cholesterol (hypercholesterolemia), Fatigue, Increased sweating, Pain in bones and joints (arthralgia), Skin rash, Headache, Dizziness, Malaise (generally feeling unwell), gastrointestinal disorders such as nausea, vomiting, indigestion, constipation, diarrhea. Increase in or loss of appetite ,Pain in muscles ,Thinning or wasting of your bones (osteoporosis), leading to bone fractures in some cases ,Swelling of arms, hands, feet, ankles (edema) ,Depression ,Weight increase ,Hair loss ,Raised blood pressure (hypertension), Abdominal pain, Dry skin, Vaginal bleeding, Palpitations, rapid heart rate, Joint stiffness (arthritis), Chest pain.

Rare:

Nervous disorders such as anxiety, nervousness, irritability, drowsiness, memory problems,
Somnolence, insomnia, Pain or burning sensation in the hands or wrist (carpal tunnel syndrome)
Impairment of sensation, especially that of touch ,Eye disorders such as blurred vision, eye irritation ,Skin disorders such as itching (urticarial) ,Vaginal discharge or dryness
Dryness of mucous membranes, Weight decrease, Urinary tract infection, increased frequency of urination, Cough, Increased level of enzymes, yellowing of the skin and eyes, High blood levels of bilirubin (a breakdown product of red blood cells)

Use in Pregnancy & Lactation

Pregnancy

Letrozole is contraindicated during pregnancy.

Lactation

Letrozole is contraindicated during lactation.

Use in Children & Adolescents

Children and adolescents should not use this medicine.

Drug Interactions

There is no clinically significant drug interactions from coadministration of letrozole with cimetidine and warfarin & other anticancer agents. Letrozole inhibits in vitro the cytochrome P450-isozymes 2A6, and moderately 2C19. CYP2A6 does not play a major role in drug metabolism. Thus, clinically relevant interactions with CYP2C19 are unlikely to occur.

Overdose

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

Storage

Store at temperature not exceeding 30°C in a dry place. Protect from light and moisture.

Packing

Arofrez® tablet 2.5mg: Each box contains 1x10's and 3x10's tablets in Alu-Alu blister.

Medicine: Keep out of reach of children

Healthcare

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