1.5 Product Information

1.5.3 Patient information leaflet

(For All Products not subject to Medical Prescription)

LETERO (Letrozole Tablets USP 2.5 mg).

PACKAGE LEAFLET: INFORMATION FOR THE USER

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours
- If you get any side effects, talk to your doctor or pharmacist.

In this leaflet:

1. WHAT LETROZOLE TABLETS USP 2.5 MG IS AND WHAT IT IS USED FOR

Adjuvant Treatment of Early Breast Cancer

Letrozole Tablets 2.5 mg (letrozole) is indicated for the adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer.

Extended Adjuvant Treatment of Early Breast Cancer

Letrozole Tablets 2.5 mg is indicated for the extended adjuvant treatment of early breast cancer in postmenopausal women, who have received 5 years of adjuvant tamoxifen therapy. The effectiveness of Letrozole Tablets 2.5 mg in extended adjuvant treatment of early breast cancer is

based on an analysis of disease-free survival in patients treated with Letrozole Tablets 2.5 mg for a median of 60 months

First and Second-Line Treatment of Advanced Breast Cancer

Letrozole Tablets 2.5 mg is indicated for first-line treatment of postmenopausal women with hormone receptor positive or unknown, locally advanced or metastatic breast cancer. Letrozole Tablets 2.5 mg is also indicated for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE LETROZOLE TABLETS USP 2.5 MG

- Pregnancy: Letrozole can cause fetal harm.
- Known hypersensitivity to the active substance, or to any of the excipients.

3. HOW TO TAKE LETROZOLE TABLETS USP 2.5 MG

Recommended Dose

The recommended dose of Letrozole Tablets 2.5 mg is one 2.5 mg tablet administered once a day, without regard to meals.

Use in Adjuvant Treatment of Early Breast Cancer

In the adjuvant setting, the optimal duration of treatment with letrozole is unknown. In both the adjuvant study and the post approval adjuvant study, median treatment duration was 5 years. Treatment should be discontinued at relapse

Use in Extended Adjuvant Treatment of Early Breast Cancer

In the extended adjuvant setting, the optimal treatment duration with Letrozole Tablets 2.5 mg is not known. The planned duration of treatment in the study was 5 years. In the final updated analysis, conducted at a median follow-up of 62 months, the median treatment duration for Letrozole Tablets 2.5 mg was 60 months. Seventy-one (71%) percent of patients were treated for at least 3 years and 58% of patients completed at least 4.5 years of extended adjuvant treatment. The treatment should be discontinued at tumor relapse

Use in First and Second-Line Treatment of Advanced Breast Cancer

In patients with advanced disease, treatment with Letrozole Tablets 2.5 mg should continue until tumor progression is evident

Use in Hepatic Impairment

No dosage adjustment is recommended for patients with mild to moderate hepatic impairment, although Letrozole Tablets 2.5 mg blood concentrations were modestly increased in subjects with moderate hepatic impairment due to cirrhosis. The dose of Letrozole Tablets 2.5 mg in patients with cirrhosis and severe hepatic dysfunction should be reduced by 50%. The recommended dose of Letrozole Tablets 2.5 mg for such patients is 2.5 mg administered every other day. The effect of hepatic impairment on Letrozole Tablets 2.5 mg exposure in noncirrhotic cancer patients with elevated bilirubin levels has not been determined.

Use in Renal Impairment

No dosage adjustment is required for patients with renal impairment if creatinine clearance is greater than or equal to 10 mL/min

4. POSSIBLE SIDE EFFECTS

Bone Effects

Use of Letrozole Tablets 2.5 mg may cause decreases in bone mineral density (BMD). Consideration should be given to monitoring BMD. Results of a safety study to evaluate safety in the adjuvant setting comparing the effect on lumbar spine (L2-L4) BMD of adjuvant treatment with letrozole to that with tamoxifen showed at 24 months a median decrease in lumbar spine BMD of 4.1% in the letrozole arm compared to a median increase of 0.3% in the tamoxifen arm (difference = 4.4%) ($P < 0.0001$). Updated results from the BMD substudy (MA-17B) in the extended adjuvant setting demonstrated that at 2 years patients receiving letrozole had a median decrease from baseline of 3.8% in hip BMD compared to a median decrease of 2.0% in the placebo group. The changes from baseline in lumbar spine BMD in letrozole and placebo treated groups were not significantly different .

In the adjuvant trial (BIG 1-98) the incidence of bone fractures at any time after randomization was 14.7% for letrozole and 11.4% for tamoxifen at a median follow-up of 96 months. The incidence of osteoporosis was 5.1% for letrozole and 2.7% for tamoxifen. In the extended adjuvant trial (MA-17), the incidence of bone fractures at any time after randomization was 13.3% for letrozole and

7.8% for placebo at a median follow-up of 62 months. The incidence of new osteoporosis was 14.5% for letrozole and 7.8% for placebo.

Cholesterol

Consideration should be given to monitoring serum cholesterol. In the adjuvant trial (BIG 1-98), hypercholesterolemia was reported in 52.3% of letrozole patients and 28.6% of tamoxifen patients. Grade 3-4 hypercholesterolemia was reported in 0.4% of letrozole patients and 0.1% of tamoxifen patients. Also in the adjuvant setting, an increase of greater than or equal to 1.5 x upper limit of normal (ULN) in total cholesterol (generally nonfasting) was observed in patients on monotherapy who had baseline total serum cholesterol within the normal range (i.e., less than =1.5 x ULN) in 155/1843 (8.4%) patients on letrozole vs 71/1840 (3.9%) patients on tamoxifen Lipid lowering medications were required for 29% of patients on letrozole and 20% on tamoxifen .

Hepatic Impairment

Subjects with cirrhosis and severe hepatic impairment who were dosed with 2.5 mg of Letrozole Tablets 2.5 mg experienced approximately twice the exposure to Letrozole Tablets 2.5 mg as healthy volunteers with normal liver function . Therefore, a dose reduction is recommended for this patient population. The effect of hepatic impairment on Letrozole Tablets 2.5 mg exposure in cancer patients with elevated bilirubin levels has not been determined .

Fatigue and Dizziness

Because fatigue, dizziness, and somnolence have been reported with the use of Letrozole Tablets 2.5 mg, caution is advised when driving or using machinery until it is known how the patient reacts to Letrozole Tablets 2.5 mg use.

Laboratory Test Abnormalities

No dose-related effect of Letrozole Tablets 2.5 mg on any hematologic or clinical chemistry parameter was evident. Moderate decreases in lymphocyte counts, of uncertain clinical significance, were observed in some patients receiving Letrozole Tablets 2.5 mg 2.5 mg. This depression was transient in about half of those affected. Two patients on Letrozole Tablets 2.5 mg developed thrombocytopenia; relationship to the study drug was unclear. Patient withdrawal due to laboratory abnormalities, whether related to study treatment or not was infrequent.

Embryo-Fetal Toxicity

Based on post-marketing reports, findings from animal studies and the mechanism of action, Letrozole Tablets 2.5 mg can cause fetal harm and is contraindicated for use in pregnant women. In post-marketing reports, use of letrozole during pregnancy resulted in cases of spontaneous abortions and congenital birth defects. Letrozole caused embryo-fetal toxicities in rats and rabbits at maternal exposures that were below the maximum recommended human dose (MHRD) on a mg/m^2 basis. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during therapy with Letrozole Tablets 2.5 mg and for at least 3 weeks after the last dose.

5. HOW TO STORE LETROZOLE TABLETS USP 2.5 MG

Store below 30°C and protect from moisture.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Letrozole Tablets USP 2.5 mg contains

The active substance is Letrozole USP. Each film coated tablet contains: 2.5 mg of Letrozole USP.

The other ingredients are

Lactose monohydrate (Pharmatose 200 M)

Povidone (Plasdone K-29/32)

Croscarmellose Sodium (Ac-Di-Sol)

Magnesium stearate

Opadry Yellow 03B82401

What Letrozole Tablets USP 2.5 mg looks like and contents of the pack

Dark yellow coloured, round shaped, slightly biconvex bevel edged film coated tablets debossed with '5' on one side and 'H' on the other side.

Container pack: 30's HDPE Container

Marketing Authorization Holder and Manufacturer

Marketing Authorisation Holder:

Name: Hetero Labs Limited

Business Address: 7-2-A2, Hetero Corporate,
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Country: INDIA

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