SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Letroz 2.5mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:
Letrozole …… 2.5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablet.

4. CLINICAL PARTICULARS

4.1 *Therapeutic indications*

- Adjuvant treatment of postmenopausal women with hormone receptor positive invasive early breast cancer.
- 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-oestrogens.
- Neo-adjuvant treatment of postmenopausal women with hormone receptor positive, HER-2 negative breast cancer where chemotherapy is not suitable and immediate surgery not indicated.

Efficacy has not been demonstrated in patients with hormone receptor negative breast cancer.

4.2 *Posology and method of administration*

Posology

Adult and elderly patients

The recommended dose of **Letroz** is 2.5 mg once daily. No dose adjustment is required for elderly patients.

In patients with advanced or metastatic breast cancer, treatment with **Letroz** should continue until tumour progression is evident.

In the adjuvant and extended adjuvant setting, treatment with **Letroz** should continue for 5 years or until tumour 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 (see sections 4.4).

In the neoadjuvant setting, treatment with **Letroz** could be continued for 4 to 8 months in order to establish optimal tumour reduction. If the response is not adequate, treatment with **Letroz** should be discontinued and surgery scheduled and/or further treatment options discussed with the patient.

Paediatric population
Letroz 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 have been reported 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 ≥10 ml/min. Insufficient data have been reported in cases of renal insufficiency with creatinine clearance lower than 10 ml/min (see sections 4.4 and 5.2).

Hepatic impairment
No dose adjustment of letrozole is required for patients with mild to moderate hepatic insufficiency (ChildPugh A or B). Insufficient data have been reported for patients with severe hepatic impairment. Patients with severe hepatic impairment (ChildPugh C) require close supervision (see sections 4.4 and 5.2).

Method of administration

Letroz should be taken orally and can be taken with or without food.

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 2.5 mg recommended dose, over proportionality in systemic exposure was observed (see section 5.2).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Premenopausal endocrine status
- Pregnancy (see section 4.6)
- Breast-feeding (see section 4.6)

4.4 *Special warnings and precautions for use*

Menopausal status
In patients whose menopausal status is unclear, luteinising hormone (LH), folliclestimulating hormone (FSH) and/or oestradiol 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 a creatinine clearance lower than 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 C), systemic exposure and terminal half-life were approximately doubled compared to healthy volunteers. Such patients should therefore be kept under close supervision (see section 5.2).

Bone effects

Letrozole is a potent oestrogen-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. In the adjuvant setting a sequential treatment schedule (letrozole 2 years followed by tamoxifen 3 years) could also be considered depending on the patient's safety profile (see sections 4.2 and 4.8).

Tendonitis and tendon rupture
Tendonitis and tendon ruptures (rare) may reported. Close monitoring of the patients and appropriate measures (e.g. immobilisation) must be initiated for the affected tendon (see section 4.8).

Other warnings
Co-administration of letrozole with tamoxifen, other anti-oestrogens or oestrogencontaining therapies should be avoided as these substances may diminish the pharmacological action of letrozole (see section 4.5).

Excipients
Letroz contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not receive this medicine.

4.5 *Interaction with other medicinal products and other forms of interaction*

Metabolism of letrozole is partly mediated via CYP2A6 and CYP3A4. Cimetidine, a weak, unspecific inhibitor of CYP450 enzymes, did not affect the plasma concentrations of letrozole. The effect of potent CYP450 inhibitors is unknown.

There is no clinical experience reported till date on the use of letrozole in combination with oestrogens or other anticancer agents, other than tamoxifen. Tamoxifen, other antioestrogens or oestrogen-containing therapies may diminish the pharmacological action of letrozole. In addition, co-administration of tamoxifen with letrozole has been reported to substantially decrease plasma concentrations of letrozole. Co-administration of letrozole with tamoxifen, other anti-oestrogens or oestrogens should be avoided.

In vitro, letrozole inhibits the cytochrome P450 isoenzymes 2A6 and, moderately, 2C19, but the clinical relevance is unknown. Caution is therefore indicated when giving letrozole concomitantly with medicinal products whose elimination is mainly dependent on these isoenzymes and whose therapeutic index is narrow (e.g. phenytoin, clopidrogel).

4.6 *Fertility, Pregnancy and lactation*

Women of perimenopausal status or childbearing potential

Letrozole should only be used in women with a clearly established postmenopausal status (see section 4.4). 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

Based on reported human experience in which there have been isolated cases of birth defects (labial fusion, ambiguous genitalia), letrozole may cause congenital malformations when administered during pregnancy. Reported studies in animals have shown reproductive toxicity (see section 5.3).

Letrozole is contraindicated during pregnancy (see sections 4.3 and 5.3).

Lactation

It is unknown whether letrozole and its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.

Letrozole is reported to be contraindicated during breastfeeding (see section 4.3).

Fertility

The pharmacological action of letrozole is to reduce oestrogen production by aromatase inhibition. In premenopausal women, the inhibition of oestrogen synthesis leads to feedback increases in gonadotropin (LH, FSH) levels. Increased FSH levels in turn stimulate follicular growth, and can induce ovulation.

4.7 *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 reported with the use of letrozole and

somnolence has been reported uncommonly, caution is advised when driving or using machines.

4.8 *Undesirable effects*

Summary of the safety profile

The frequencies of adverse reactions for letrozole are mainly based on reported data collected from clinical trials.

Up to approximately one third of the patients treated with letrozole in the metastatic setting and approximately 80% of the patients in the adjuvant setting as well as in the extended adjuvant setting experienced adverse reactions. The majority of the adverse reactions reported during the first few weeks of treatment.

The most frequently reported adverse reactions in reported clinical studies were hot flushes, hypercholesterolaemia, arthralgia, fatigue, increased sweating and nausea.

Important additional adverse reactions that may reported with letrozole are: skeletal events such as osteoporosis and/or bone fractures and cardiovascular events (including cerebrovascular and thromboembolic events). The frequency category for these adverse reactions is described in Table 1.

Tabulated list of adverse reactions

The frequencies of adverse reactions for letrozole are mainly based on reported data collected from clinical trials.

The following adverse drug reactions, listed in Table 1, were reported from clinical studies and from post-marketing experience with letrozole:

Table 1:

Adverse reactions are ranked under headings of frequency, the most frequent first, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available reported data).

Infections and infestations	
Uncommon:	Urinary tract infection
Neoplasms benign, malignant and unspecified (including cysts and polyps)	

Uncommon:	Tumour pain[1]
Blood and lymphatic system disorders	
Uncommon:	Leukopenia
Immune system disorders	
Not known:	Anaphylactic reaction
Metabolism and nutrition disorders	
Very common:	Hypercholesterolaemia
Common:	Decreased appetite, increased appetite
Psychiatric disorders	
Common:	Depression
Uncommon:	Anxiety (including nervousness), irritability
Nervous system disorders	
Common:	Headache, dizziness
Uncommon:	Somnolence, insomnia, memory impairment, dysaesthesia (including paraesthesia, hypoaesthesia), dysgeusia, cerebrovascular accident, carpal tunnel syndrome
Eye disorders	
Uncommon	Cataract, eye irritation, blurred vision
Cardiac disorders	
Common:	Palpitations[1]
Uncommon:	Tachycardia, ischaemic cardiac events (including new or worsening angina, angina requiring surgery, myocardial infarction and myocardial ischaemia)
Vascular disorders	
Very common:	Hot flushes
Common:	Hypertension
Uncommon:	Thrombophlebitis (including superficial and deep vein thrombophlebitis)
Rare:	Pulmonary embolism, arterial thrombosis, cerebral infarction
Respiratory, thoracic and mediastinal disorders	
Uncommon:	Dyspnoea, cough
Gastrointestinal disorders	
Common:	Nausea, dyspepsia[1], constipation, abdominal pain, diarrhoea, vomiting
Uncommon:	Dry mouth, stomatitis[1]
Hepatobiliary disorders	
Uncommon:	Increased hepatic enzymes, hyperbilirubinemia, jaundice
Not known:	Hepatitis
Skin and subcutaneous tissue disorders	

Very common:	Hyperhidrosis
Common:	Alopecia, rash (including erythematous, maculopapular, psoriaform, and vesicular rash), dry skin
Uncommon:	Pruritus, urticaria
Not known:	Angioedema, toxic epidermal necrolysis, erythema multiforme
Musculoskeletal and connective tissue disorders	
Very common:	Arthralgia
Common:	Myalgia, bone pain[1], osteoporosis, bone fractures, arthritis
Uncommon:	Tendonitis
Rare:	Tendon rupture
Not known:	Trigger finger
Renal and urinary disorders	
Uncommon:	Pollakiuria
Reproductive system and breast disorders	
Common:	Vaginal haemorrhage
Uncommon:	Vaginal discharge, vulvovaginal dryness, breast pain
General disorders and administration site conditions	
Very common:	Fatigue (including asthenia, malaise)
Common:	Peripheral oedema, chest pain
Uncommon:	General oedema, mucosal dryness, thirst, pyrexia
Investigations	
Common:	Weight increased
Uncommon:	Weight decreased

[1] Adverse drug reactions reported only in the metastatic setting

Some adverse reactions have been reported with notably different frequencies in the adjuvant treatment setting. The following tables provide information on significant differences in letrozole versus tamoxifen monotherapy and in the letrozole -tamoxifen sequential treatment therapy:

Table 2: Adjuvant letrozole monotherapy versus tamoxifen monotherapy – adverse events with significant differences

	Letrozole, incidence rate		**Tamoxifen, incidence rate**	
	During treatment	**Any time after randomization**	**During treatment**	**Any time after randomization**

	(Median 5 years)	**(Median 8 years)**	**(Median 5 years)**	**(Median 8 years)**
Bone fracture	10.2%	14.7%	7.2%	11.4%
Osteoporosis	5.1%	5.1%	2.7%	2.7%
Thromboembolic events	2.1%	3.2%	3.6%	4.6%
Myocardial infarction	1.0%	1.7%	0.5%	1.1%
Endometrial hyperplasia / endometrial cancer	0.4%	2.3%	2.9%	

Note: "During treatment" includes 30 days after last dose. "Any time" includes follow-up period after completion or discontinuation of reported study treatment. Differences were based on risk ratios and 95% confidence intervals.

Table 3: Sequential treatment versus letrozole monotherapy – adverse events with significant differences

	Letrozole monotherapy	**Letrozole->tamoxifen**	**Tamoxifen->letrozole**
	5 years	**2 years-> 3 years**	**2 years-> 3 years**
Bone fractures	10.0%	7.7%*	9.7%
Endometrial proliferative disorders	0.7%	3.4%**	1.7%**
Hypercholesterolaemia	52.5%	44.2%*	40.8%*
Hot flushes	37.6%	41.7%**	43.9%**
Vaginal bleeding	6.3%	9.6%**	12.7%**

* Significantly less than with letrozole monotherapy
** Significantly more than with letrozole monotherapy
Note : Reporting period is during treatment or within 30 days of stopping treatment

Description of selected adverse reactions

Cardiac adverse reactions

In the adjuvant setting, in addition to the reported data presented in Table 2, the following adverse events were reported for letrozole and tamoxifen, respectively (at median treatment duration of 60 months plus 30 days): angina requiring surgery (1.0% vs. 1.0%); cardiac failure (1.1% vs. 0.6%); hypertension (5.6% vs. 5.7%); cerebrovascular accident/transient ischaemic attack (2.1% vs. 1.9%).

In the extended adjuvant setting for letrozole (median duration of treatment 5 years) and placebo (median duration of treatment 3 years), respectively: angina requiring surgery
(0.8% vs. 0.6%); new or worsening angina (1.4% vs. 1.0%); myocardial infarction (1.0%
vs. 0.7%); thromboembolic event* (0.9% vs. 0.3%); stroke/transient ischaemic attack* (1.5% vs. 0.8%) were reported.

Events marked * were statistically significantly different in the two treatment arms.

Skeletal adverse reactions
For skeletal safety reported data from the adjuvant setting, please refer to Table 2.

In the extended adjuvant setting, significantly more patients treated with letrozole experienced bone fractures or osteoporosis (bone fractures, 10.4% and osteoporosis, 12.2%) than patients in the placebo arm (5.8% and 6.4%, respectively). Median duration of treatment was 5 years for letrozole, compared with 3 years for placebo.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorisation holder or, where applicable, via the national reporting system.
https://pv.pharmacyboardkenya.org/

4.9 *Overdose*

Isolated cases of overdose with letrozole have been reported.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 *Pharmacodynamic properties*
Pharmacotherapeutic group: Endocrine therapy. Hormone antagonist and related agents: aromatase inhibitor, ATC code: L02BG04.

Pharmacodynamic effects
The elimination of oestrogen-mediated growth stimulation is a prerequisite for tumour response in cases where the growth of tumour tissue depends on the presence of oestrogens and endocrine therapy is used. In postmenopausal women, oestrogens are mainly derived from the action of the aromatase enzyme, which converts adrenal androgens primarily androstenedione and testosterone to oestrone and oestradiol. The suppression of oestrogen

biosynthesis in peripheral tissues and the cancer tissue itself can therefore be achieved by specifically inhibiting the aromatase enzyme.

Letrozole is a nonsteroidal aromatase inhibitor. It inhibits the aromatase enzyme by competitively binding to the haem of the aromatase cytochrome P450, resulting in a reduction of oestrogen biosynthesis in all tissues where present.

In healthy postmenopausal women, single doses of 0.1 mg, 0.5 mg, and 2.5 mg letrozole suppress serum oestrone and oestradiol by 75%, 78% and 78% from baseline respectively. Maximum suppression is achieved in 48-78 hours.

In postmenopausal patients with advanced breast cancer, daily doses of 0.1 mg to 5 mg suppressed plasma concentration of oestradiol, oestrone, and oestrone sulphate by 7595% from baseline in all patients treated. With doses of 0.5 mg and higher, many values of oestrone and oestrone sulphate were below the limit of detection in the assays, indicating that higher oestrogen suppression is achieved with these doses. Oestrogen suppression was maintained throughout treatment in all these patients.

Letrozole is highly specific in inhibiting aromatase activity. Impairment of adrenal steroidogenesis has not been observed. No clinically relevant changes were found in the plasma concentrations of cortisol, aldosterone, 11-deoxycortisol, 17hydroxyprogesterone, and ACTH or in plasma renin activity among postmenopausal patients treated with a daily dose of letrozole 0.1 to 5 mg. The ACTH stimulation test performed after 6 and 12 weeks of treatment with daily doses of 0.1 mg, 0.25 mg, 0.5 mg, 1 mg, 2.5 mg, and 5 mg did not indicate any attenuation of aldosterone or cortisol production. Thus, glucocorticoid and mineralocorticoid supplementation is not necessary.

No changes were noted in plasma concentrations of androgens (androstenedione and testosterone) among healthy postmenopausal women after 0.1 mg, 0.5 mg, and 2.5 mg single doses of letrozole or in plasma concentrations of androstenedione among postmenopausal patients treated with daily doses of 0.1 mg to 5 mg, indicating that the blockade of oestrogen biosynthesis does not lead to accumulation of androgenic precursors. Plasma levels of LH and FSH are not affected by letrozole in patients, nor is thyroid function as evaluated by TSH, T4, and T3 uptake test.

5.2 *Pharmacokinetics properties*

Absorption

Letrozole is reported to be rapidly and completely absorbed from the gastrointestinal tract (mean absolute bioavailability: 99.9%). Food slightly reported to decreases the rate of absorption (median t_{max} 1 hour fasted versus 2 hours fed; and mean C_{max} 129 ± 20.3 nmol/litre fasted versus 98.7 ± 18.6 nmol/litre fed) 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 reported to be approximately 60%, mainly to albumin (55%). The concentration of letrozole in erythrocytes is about 80% of that in plasma. After administration of 2.5 mg ^{14}C-labelled letrozole, approximately 82% of the radioactivity in plasma was reported to be unchanged compound. Systemic exposure to metabolites is therefore low. Letrozole is reported to be rapidly and extensively distributed to tissues. Its apparent volume of distribution at steady state is reported to be about 1.87 ± 0.47 l/kg.

Biotransformation

Metabolic clearance to a pharmacologically inactive carbinol metabolite is the major elimination pathway of letrozole (CL_m = 2.1 l/h) but is relatively slow when compared to hepatic blood flow (about 90 l/h). The cytochrome P450 isoenzymes 3A4 and 2A6 were found to be capable of converting letrozole to this metabolite. Formation of minor unidentified metabolites and direct renal and faecal excretion play only a minor role in the overall elimination of letrozole. Within 2 weeks after administration of 2.5 mg ^{14}Clabelled letrozole to healthy postmenopausal volunteers, 88.2 ± 7.6% of the radioactivity was recovered in urine and 3.8 ± 0.9% in faeces. At least 75% of the radioactivity recovered in urine up to 216 hours (84.7 ± 7.8% of the dose) was attributed to the glucuronide of the carbinol metabolite, about 9% to two unidentified metabolites, and 6% to unchanged letrozole.

Elimination

The apparent terminal elimination half-life in plasma is reported to about 2 to 4 days. After daily administration of 2.5 mg steady state levels are reported to reached within 2 to 6 weeks. Plasma concentrations at steady state are approximately 7 times higher than concentrations measured after a single dose of 2.5 mg, 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 nonlinearity in the pharmacokinetics of letrozole upon daily administration of 2.5 mg. Since steady state levels are maintained over time, it can be concluded that no continuous accumulation of letrozole reported.

Linearity/nonlinearity

The pharmacokinetics of letrozole were reported to be dose proportional after single oral doses up to 10 mg (dose range: 0.01 to 30 mg) and after daily doses up to 1.0 mg (dose range: 0.1 to 5mg). After a 30 mg single oral dose there was a slightly dose over proportional increase in AUC value. The dose over proportionality is likely to be the result of a saturation of metabolic elimination processes. Steady levels were reached after 1 to 2 months at all dosage regimens tested (0.1 - 5.0 mg daily).

Special populations

Elderly

Age had no effect on the pharmacokinetics of letrozole.

Renal impairment

In a reported study involving volunteers with varying degrees of renal function (24-hour creatinine clearance 9-116 ml/min) no effect on the pharmacokinetics of letrozole was found after a single dose of 2.5 mg. In addition to the above reported study assessing the influence of renal impairment on letrozole, a covariate analysis was performed on the reported data of two pivotal studies. Calculated creatinine clearance (CL_{cr}) reported no statistically significant association between letrozole plasma trough levels at steady state (C_{min}). Futhermore, data of reported studies in second line metastatic breast cancer reported no evidence of an adverse effect of letrozole on CL_{cr} or an impairment of renal function.

Therefore, no dose adjustment is reported to be required for patients with renal impairment (CL_{cr} ≥10 mL/min). Little information is reported in patients with severe impairment of renal function (CL_{cr} <10 mL/min).

Hepatic impairment

In a similar reported study involving subjects with varying degrees of hepatic function, the mean AUC values of the volunteers with moderate hepatic impairment (Child-Pugh B) was 37% higher than in normal subjects, but still within the range seen in subjects without impaired function. In a reported study comparing the pharmacokinetics of letrozole after a single oral dose in eight male subjects with liver cirrhosis and severe hepatic impairment (Child-Pugh C) to those in healthy volunteers, AUC and t½ increased by 95 and 187%, respectively. Thus, letrozole should be administered with caution to patients with severe hepatic impairment and after consideration of the risk/benefit in the individual patient.

5.3 Preclinical safety data

In a variety of reported preclinical safety studies conducted in standard animal species, there was no evidence of systemic or target organ toxicity.

Letrozole reported a low degree of acute toxicity in rodents exposed up to 2000 mg/kg. In dogs letrozole caused signs of moderate toxicity at 100 mg/kg.

In a reported repeated dose toxicity studies in rats and dogs up to 12 months, the main findings observed can be attributed to the pharmacological action of the compound. The no adverse effect level was 0.3 mg/kg in both species.

Oral administration of letrozole to female rats resulted in decreases in mating and pregnancy ratios and increases in pre-implantation loss.

Both *in vitro* and *in vivo* investigations of letrozole's mutagenic potential reported no indications of any genotoxicity.

In a reported 104 week rat carcinogenicity study, no treatment related tumours were noted in male rats. In female rats, a reduced incidence of benign and malignant mammary tumours at all the doses of letrozole was found.

In a reported 104 week mouse carcinogenicity study, no treatment-related tumors were noted in male mice. In female mice, a generally dose-related increase in the incidence of benign ovarian granulosa theca cell tumors was observed at all doses of letrozole tested. These tumors were considered to be related to the pharmacological inhibition of estrogen synthesis and may be due to increased LH resulting from the decrease in circulating estrogen.

Letrozole was reported to be embryotoxic and foetotoxic in pregnant rats and rabbits following oral administration at clinically relevant doses. In rats that had live foetuses, there was an increase in the incidence of foetal malformations including domed head and cervical/centrum vertebral fusion. An increased incidence of foetal malformations was not seen in the rabbit. It is not known whether this was an indirect consequence of the pharmacological properties (inhibition of oestrogen biosynthesis) or a direct drug effect (see sections 4.3 and 4.6).

Reported preclinical observations were confined to those associated with the recognised pharmacological action, which is the only safety concern for human use derived from animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
microcrystalline sodium
corn starch
povidone
sodium starch glycolate
colloidal anhydrous silica
magnesium stearate
opadry yellow.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30 ° C. Protect from light.

6.5 Nature and contents of container

Letroz is available as a strip of 5 tablets.

6.6 Special precautions for disposal and other handling

Not Applicable

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

Marketing Authorisation holder:

Sun Pharmaceutical Industries Limited,
Sun House, 201 B/1, Western Express Highway,
Goregaon (East), Mumbai, 400063
India.

Manufacturing site address:
Sun Pharmaceutical Industries Limited
Halol- Baroda Highway, Dist.- Panchmahal,
Halol-389350, Gujarat,
India

8. MARKETING AUTHORISATION NUMBER(S)

H2008/18878/675

9. DATE OF RENEWAL OF THE REGISTRATION

10/08/2026

10. DATE OF REVISION OF THE TEXT

10/08/2026