Tamodex
Tablet

DRUG INTERNATIONAL LTD.

Composition : **Tamodex-10 :** Each film coated tablet contains Tamoxifen 10 mg as Tamoxifen Citrate USP.
Tamodex-20 : Each film coated tablet contains Tamoxifen 20 mg as Tamoxifen Citrate USP.

Pharmacology : Tamodex is a nonsteroidal agent that has demonstrated potent antiestrogenic properties in animal test systems. The antiestrogenic effects may be related to its ability to compete with estrogen for binding sites in target tissues such as breast. Absorption and Distribution: Following a single oral dose of 20 mg Tamoxifen, an average peak plasma concentration of 40 ng/mL (range 35 to 45 mg/mL) occurred approximately 5 hours after dosing. The decline in plasma concentrations of Tamoxifen is biphasic with a terminal elimination half-life of about 5 to 7 days. The average peak plasma concentration of N-desmethyl Tamoxifen is 15 mg/mL (range 10 to 20 mg/mL). Chronic administration of 10 mg Tamoxifen given twice daily for 3 months to patients results in average steady-state plasma concentrations of 120 ng/mL (range 67-183 mg/mL) for Tamoxifen and 336 mg/mL (range 148-654 mg/mL) for N-desmethyl Tamoxifen. Metabolism: Tamoxifen is extensively metabolized after oral administration. N-desmethyl Tamoxifen is the major metabolite found in patients' plasma. Excretion: Tamoxifen have shown that approximately 65% of the administered dose was excreted from the body over a period of 2 weeks with fecal excretion as the primary route of elimination. Half-life: About 5 to 7 days over a period of 2 weeks with fecal excretion as the primary route of elimination. Half-life: About 5 to 7 days.

Indications : Metastatic Breast Cancer: Tamodex is effective in the treatment of metastatic breast cancer in women and men. In premenopausal women with metastatic breast cancer, Tamodex is an alternative to oophorectomy or ovarian irradiation. Available evidence indicates that patients whose tumors are estrogen receptor positive are more likely to benefit from Tamodex therapy. Adjuvant Treatment of Breast Cancer: Tamodex is indicated for the treatment of node-positive breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation. In some Tamodex adjuvant studies, most of the benefit to date has been in the subgroup with four or more positive axillary nodes. Ductal Carcinoma in Situ (DCIS): In women with DCIS, following breast surgery and radiation, Tamodex is indicated to reduce the risk of invasive breast cancer. Current data from clinical trials support five years of adjuvant Tamodex therapy for patients with breast cancer. Reduction in Breast Cancer Incidence in High Risk Women: Tamodex is indicated to reduce the incidence of breast cancer in women at high risk for breast cancer. Tamodex is indicated only for high-risk women. "High risk" is defined as women at least 35 years of age with a 5-year predicted risk of breast cancer 1.67%, as calculated by the Gail Model.

Dosage and administration : For patients with breast cancer, the recommended daily dose is 20-40 mg. Dosages greater than 20 mg per day should be given in divided doses (morning and evening). In three single agent adjuvant studies in women, one 10 mg Tamoxifen Citrate tablet was administered two or three times a day for two years. Ductal Carcinoma in Situ (DCIS): The recommended dose is Tamodex 20 mg daily for 5 years. Reduction in Breast Cancer Incidence in High Risk Women: The recommended dose is Tamodex 20 mg daily for 5 years. There are no data to support the use of Tamodex other than for 5 years. Or, as directed by the registered physicians.

Contraindication : It is contraindicated in patients with known hypersensitivity to the drug or any of its ingredients. Tamodex is contraindicated in women who require concomitant coumarin-type anticoagulant therapy or in women with a history of deep vein thrombosis or pulmonary embolus. Warning: Effects in Metastatic Breast Cancer Patients: As with other additive hormonal therapy (estrogens and androgens), hypercalcemia has been reported in some breast cancer patients with bone metastases within a few weeks of starting treatment with Tamodex. Effects on the Uterus-Endometrial Cancer and Uterine Sarcoma: An increased incidence of uterine malignancies has been reported in association with Tamodex treatment. The underlying mechanism is unknown, but may be related to the estrogen-like effect of Tamodex. Most uterine malignancies seen in association with Tamodex are classified as adenocarcinoma of the endometrium. Non-Malignant Effects on the Uterus: An increased incidence of endometrial changes including hyperplasia and polyps have been reported in association with Tamodex treatment. There have been a few reports of endometriosis and uterine fibroids in women receiving Tamodex. Ovarian cysts have also been observed in a small number of premenopausal patients with advanced breast cancer who have been treated with Tamodex. It has been reported to cause menstrual irregularity or amenorrhea. Thromboembolic Effects of Tamodex: There is evidence of an increased incidence of thromboembolic events, including deep vein thrombosis and pulmonary embolism, during Tamodex therapy. When it is coadminstered with chemotherapy, there may be a further increase in the incidence of thromboembolic effects.

Precautions : Decreases in platelet counts, usually to infrequently lower, have been occasionally reported in patients taking Tamodex for breast cancer. In patients with significant thrombocytopenia, rare hemorrhagic episodes have occurred, but it is uncertain if these episodes are due to Tamodex therapy. Leukopenia has been observed, sometimes in association with anemia and/or thrombocytopenia. There have been rare reports of neutropenia and pancytopenia in patients receiving Tamodex; this can sometimes be severe. In the NSABP P-1 trial, 6 women on Tamodex and 2 on placebo experienced grade 3-4 drops in platelet counts 50,000/mm3).

Side Effects : Adverse reactions to Tamodex are relatively mild and rarely severe enough to require discontinuation of treatment in breast cancer patients. Continued clinical studies have resulted in further information which better indicates the incidence of adverse reactions with Tamodex as compared to placebo.

Use in Pregnancy and Lactation : Pregnancy Category D. It can cause fetal harm when administered to a pregnant woman. Tamoxifen has been reported to inhibit lactation. It is not known if Tamodex is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Tamodex, women taking Tamodex should not breast feed.

Use in Child : The long-term effects of Tamodex therapy for girls aged two to 10 years have not been established. In adults treated with Tamodex, an increase in incidence of uterine malignancies, stroke and pulmonary embolism has been noted.

Drug Interactions : # When Tamodex is used in combination with coumarin-type anticoagulants, a significant increase in anticoagulant effect may occur. Where such coadministration exists, careful monitoring of the patient's prothrombin time is recommended. # There is an increased risk of thromboembolic events occurring when cytotoxic agents are used in combination with Tamodex. # Tamoxifen reduced Letrozole plasma concentrations by 37%. The effect of tamoxifen on metabolism and excretion of other antineoplastic drugs, such as cyclophosphamide and other drugs that require mixed function oxidases for activation, is not known. # One patient receiving Tamodex with concomitant phenobarbital exhibited a steady state serum level of tamoxifen lower than that observed for other patients (ie, 26 ng/mL vs. mean value of 122 ng/mL). However, the clinical significance of this finding is not Known. Rifampin induced the metabolism of Tamoxifen and significantly reduced the plasma concentrations of Tamoxifen in 10 patients. Aminoglutethimide reduces Tamoxifen and N-desmethyl Tamoxifen plasma concentrations. Medroxyprogesterone reduces plasma concentrations of N-desmethyl, but not Tamoxifen. # Based on clinical and pharmacokinetic results from the Anastrozole adjuvant trial, Tamodex should not be administered with Anastrozole.

Overdose : Acute overdosage in humans has not been reported. In a study of advanced metastatic cancer patients which specifically determined the maximum tolerated dose of Tamodex in evaluating the use of very high doses to reverse multidrug resistance, acute neurotoxicity manifested by tremor, hyperreflexia, unsteady gait and dizziness were noted. These symptoms occurred within 3-5 days of beginning Tamodex and cleared within 2-5 days after stopping therapy. No permanent neurologic toxicity was noted. One patient experienced a seizur several days after Tamodex was discontinued and neurotoxic symptoms had resolved. The causal relationship of the seizure to Tamodex therapy is unknown. Doses given in these patients were all greater than 400 mg/m2 loading dose, followed by maintenance doses of 150 mg/m2 of Tamodex given twice a day. No specific treatment for overdosage is known; treatment must be symptomatic.

Storage : Store below 30°C in a cool & dry place, away from sunlight & keep out of reach of children.

Packaging : **Tamodex-10:** Each box contains 30 tablets in a blister pack.
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