Zortex®

Anastrozole

FORMS AND PRESENTATION
Zortex®: Film coated tablets: Box of 30.
COMPOSITION
Zortex®: Each film coated tablet contains Anastrozole 1mg.
Excipients: lactose, sodium starch glycolate, povidone, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol.
PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Therapeutic class: Endocrine therapy.
ATC code: L02BG03.
Anastrozole is a potent and highly selective non-steroidal aromatase inhibitor. In postmenopausal women, estradiol is produced primarily from the conversion of androstenedione to estrone through the aromatase enzyme complex in peripheral tissues. Estrone is subsequently converted to estradiol. Reducing circulating estradiol levels has been shown to produce a beneficial effect in women with breast cancer. In postmenopausal women, Anastrozole at a daily dose of 1 mg produced estradiol suppression of greater than 80% using a highly sensitive assay.
Anastrozole does not possess any progestogenic, androgenic or oestrogenic activity.
Pharmacokinetic Properties
Absorption of Anastrozole is rapid and maximum plasma concentrations typically occur within two hours of dosing (under fasted conditions). Anastrozole is eliminated slowly with a plasma elimination half-life of 40 to 50 hours. Food slightly decreases the rate but not the extent of absorption. The small change in the rate of absorption is not expected to result in a clinically significant effect on steady-state plasma concentrations during once daily dosing of Anastrozole tablets. Approximately 90 to 95% of plasma Anastrozole steady-state concentrations are attained after 7 daily doses. There is no evidence of time or dose-dependency of Anastrozole pharmacokinetic parameters.
Anastrozole pharmacokinetics are independent of age in postmenopausal women.
In boys with pubertal gynaecomastia, Anastrozole was rapidly absorbed, was widely distributed, and was eliminated slowly with a half-life of approximately 2 days. Clearance of Anastrozole was lower in girls than in boys and exposure higher. Anastrozole in girls was widely distributed and slowly eliminated, with an estimated half-life of approximately 0.8 days.
Anastrozole is only 40% bound to plasma proteins.
Anastrozole is extensively metabolised by postmenopausal women with less than 10% of the dose excreted in the urine unchanged within 72 hours of dosing. Metabolism of Anastrozole occurs by N-dealkylation, hydroxylation and glucuronidation. The metabolites are excreted primarily via the urine. Triazole, the major metabolite in plasma, does not inhibit aromatase.
The apparent oral clearance of Anastrozole in volunteers with stable hepatic cirrhosis or renal impairment was in the range observed in healthy volunteers.
INDICATIONS
Treatment of advanced breast cancer in postmenopausal women. Efficacy has not been demonstrated in oestrogen receptor negative patients unless they had a previous positive clinical response to tamoxifen.
Adjuvant treatment of postmenopausal women with hormone receptor positive early invasive breast cancer.
Adjuvant treatment of early breast cancer in hormone receptor positive postmenopausal women who have received 2 to 3 years of adjuvant tamoxifen.
CONTRAINDICATIONS
Anastrozole is contraindicated in:
- premenopausal women.
- pregnant or lactating women.
- patients with severe renal impairment (creatinine clearance less than 20 ml/min).
- patients with moderate or severe hepatic disease.
- patients with known hypersensitivity to Anastrozole or to any of the excipients.

Oestrogen-containing therapies should not be co-administered with Anastrozole as they would negate its pharmacological action.
Concurrent tamoxifen therapy: tamoxifen should not be co-administered with Anastrozole, as this may diminish its pharmacological action.
PRECAUTIONS
Anastrozole is not recommended for use in children as safety and efficacy have not been established in this group of patients.
Anastrozole should not be used in boys with growth hormone deficiency in addition to growth hormone treatment. Anastrozole must not be used in girls with growth hormone deficiency in addition to growth hormone treatment. Long-term safety data in children and adolescents are not available.
There are no data to support the safe use of Anastrozole in patients with moderate or severe hepatic impairment, or patients with severe impairment of renal function (creatinine clearance less than 20 ml/min).
Women with osteoporosis or at risk of osteoporosis, should have their bone mineral density formally assessed by bone densitometry at the commencement of treatment and at regular intervals thereafter. Treatment or prophylaxis for osteoporosis should be initiated as appropriate and carefully monitored.
There are no data available for the use of Anastrozole with LHRH analogues. This combination should not be used outside clinical trials.
As Anastrozole lowers circulating oestrogen levels it may cause a reduction in bone mineral density with a possible consequent increased risk of fracture. The use of bisphosphonates may stop further bone mineral loss caused by Anastrozole in postmenopausal women and could be considered.
This product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Ability to drive and use machines
Anastrozole is unlikely to impair the ability of patients to drive and operate machinery. However, asthenia and somnolence have been reported with the use of Anastrozole and caution should be observed when driving or operating machinery while such symptoms persist.
PREGNANCY AND LACTATION
Anastrozole is contraindicated in pregnant or lactating women.
DRUG INTERACTIONS
Antipyrine and cimetidine clinical interaction studies indicate that the co-administration of Anastrozole with other drugs is unlikely to result in clinically significant drug interactions mediated by cytochrome P450.
A review of the clinical trial safety database did not reveal evidence of clinically significant interaction in patients treated with Anastrozole who also received other commonly prescribed drugs. There were no clinically significant interactions with bisphosphonates.
Oestrogen-containing therapies should not be co-administered with Anastrozole as they would negate its pharmacological action.
Tamoxifen should not be co-administered with Anastrozole, as this may diminish its pharmacological action.
ADVERSE EFFECTS
Very Common (≥ 10%) :
Hot flushes, Asthenia, Joint pain/stiffness, Headache, Nausea, Rash
Common (≥ 1% and <10%):
Hair thinning (Alopecia), Allergic reactions, Diarrhea, Vomiting, Somnolence, Carpal Tunnel Syndrome,Increases in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase.Vaginal dryness, Vaginal bleeding , Anorexia, Hypercholesterolaemia
Uncommon (≥ 0.1% and <1%):
Increases in gamma-GT and bilirubin, Hepatitis, urticaria, Trigger finger
Rare (≥0.01% and < 0.1%)
Erythema multiforme, Anaphylactoid reaction.
DOSAGE AND ADMINISTRATION
Adults including the elderly: 1 tablet to be taken orally once a day.
Children: Zortex® is not recommended for use in children due to insufficient data on safety and efficacy.
Renal impairment: No dose change is recommended in patients with mild or moderate renal impairment.
Hepatic impairment: No dose change is recommended in patients with mild hepatic disease.
For early disease, the recommended duration of treatment should be 5 years.
OVERDOSAGE
There is limited clinical experience of accidental overdosage. In animal studies, Anastrozole demonstrated low acute toxicity. Clinical trials have been conducted with various dosages of Anastrozole, up to 60 mg in a single dose given to healthy male volunteers and up to 10 mg daily given to postmenopausal women with advanced breast cancer; these dosages were well tolerated. A single dose of Anastrozole that results in life-threatening symptoms has not been established. There is no specific antidote to overdosage and treatment must be symptomatic.
In the management of an overdose, consideration should be given to the possibility that multiple agents may have been taken. Vomiting may be induced if the patient is alert. Dialysis may be helpful because Anastrozole is not highly protein bound. General supportive care, including frequent monitoring of vital signs and close observation of the patient, is indicated.
STORAGE CONDITIONS
Store below 30°C.
Keep in original pack in intact conditions.

Date of revision: November 2014.

This is a medicament
- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

Council of Arab Health Ministers
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