Relimidex™

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For the use of Registered Medical Practitioner or a Hospital or a Laboratory only

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Anastrozole Tablets I.P
Composition
Each film-coated tablet contains:
Anastrozole 1 mg.
DESCRIPTION :
Anastrozole is a potent and selective non-steroidal aromatase inhibitor used in the treatment to breast cancer. Many breast cancer have estrogen receptors and growth of these tumors can be stimulated by estrogen. In postmenopausal women, the principal source of circulating estrogen (primarily estradiol) is conversion of adrenally generated and rostenedione to estrone by aromatase in peripheral tissues, such as adipose tissue with further conversion of estrone to estradiol. Many breast cancers also contain aromatase, the importance of tumor-generated estrogens is uncertain.
Treatment of breast cancer has included efforts to decrease estrogen levels. by ovariectomy premenopausally and by use of anti-estrogens and progestational and post agents both pre-and post-menopausally; and these interventions lead to decreased tumor, mass or delayed progression of tumor growth in some women. Anastrozole is a potent and selective non-steroidal aromatase inhibitor. It significantly lowers serum estradiol concentrations and has no detectable effect on formatin of adrenal corticosteroids or aldosterone.
Pharmacokinetics:
Absorption and Distribution
Inhibition of aromatase activity is primarily due to anastrozole, the parent drug. orally administered anastrozole is well absorbed into the systemic circulation Food does not affect the extent of absorption. Anastrozole has a mean terminal elimination half-life of approximately 50 hours in postmenopausal women. The major circulating metabolite of anastrozloe, triazole, lacks pharmacologic activity. The pharmacokinetic parameters are similar in patients and in healthy postmenopausal volunteers. The pharmacokinetics of anastrozole is linear over the dose range of 1 to 20 mg and do not change with repeated dosing. Consistent with the approximately 2-day terminal elimination half-life, plasma concentrations approach steady-state levels at about 7 days of once daily dosing and steady-state levels are approximately three-to four-fold higher; than levels observed after a single dose of anastrozole. Anastrozole is 40% bound to plasma proteins in the therapeutic range.
METABOLISM AND EXCRETION
Anastrozole is extensively metabolized with about 10% of the dose excreted in the urine as unchanged drug within 72 hours of dosing, and the remainder (about 60% of the dose) is excreted in the urine as metabolites. Metabolism of anastrozole occurs by N-dealkylation, hydroxylation and glucuronidation. Three metabolites of anastrozole have been identified in human plasma and urine. The known metabolites are triazole, a glucuronide conjugate of hydroxyanastrozole, and a glucuronide of anastrozole itself. Several minor (less than 5% of the radioactive dose) metabolites have not been identified.
Because renal elimination is not a significant pathway of elimination, total body clearance of anastrozole is unchanged even in severe (creatinine clearance less than 30 ml/min/1.73 m^2) renal impairment, dosing adjustment in patients with renal dysfunctions is not necessary. Dosage adjustment is also unnecessary in patients with stable hepatic cirrhosis.
INDICATIONS:
- Adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer.
-First-line treatment of postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer.
- Treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy.
Patients with ER-negative disease and patients who did not respond to previous tamoxifen therapy rarely respond to anastrozole.
DOSAGE AND ADMINISTRATION
The dose of anastrozole is one 1 mg tablet taken once a day. For patients with advanced breast cancer, anastrozole should be continued until tumor progression. For adjuvant treatment of early breast cancer in postmenopausal women, the optimal duration of therapy is unknown.
Patients with Hepatic Impairment
Hepatic metabolism accounts for approximately 85% of anastrozole Elimination. Although clearance of anastrozole was decreased in patients with cirrhosis due to alcohol abuse, plasma anastrozole concentration stayed in the usual range seen in patients without liver disease. Therefore, no changes in dose are recommended for patients with mid-to-moderate hepatic impairment. although patients should be monitored for side effects. Anastrozole has not been studied in patients with severe hepatic impairment.
Patients with Renal Impairment
No changes indose are necessary for patients with renal impairment.
Use In The Elderly
No dosage adjustment is necessary.
Contraindications
Hypersensitivity reaction to the drug or to any of the excipients.
Warnings and Precautions
Keep out of reach of children. Pregnancy must be excluded. Anastrozole should be administered under the supervision of a qualified physician experienced in the use of anticancer agents.
LABORATORY TESTS
During the ATAC trial, more patients receiving anastrozole were reported to have an elevated serum cholesterol compared to patients receiving tamoxifen (7% versus 3% respectively)
Drug Interactions
Anastrozole inhibited in vitro metabolic reactions catalyzed by cytochromes P4501 A2, 2C8/9, and 3A4 but only at relatively high concentrations. Anastrozole did not inhibit P450 o2A6 or the polymorphic P450 2D6 in human liver microsomes. Antipyrine. Anastrozole did not alter the pharmacokinetic of antipyrine. Although there have been no formal Interaction studies other than with antipyrine, based on these in vivo and in vitro studies, it is unlikely that co-administration of a 1 mg dose of anastrozole with other durgs will results in clinically significant drug inhibition of cytochrome P450- mediated metabolism of the other durgs.
Warfarin : An Interaction study with warfarin showed no clinically significant effect of anastrozole on warfarin pharmacokinetics or anticoagulant activity.
Tamoxifen: Clinical and pharmacokinetic results from the ATAC trial suggest that tamoxifen should not be administered with anastrozole. Co-administration of anastrozole and tamoxifen resulted in a reduction of anastrozole plasma levels by 27% compared with those achieved with anastrozole alone.
Estrogen-containing therapies. These should not be used with anastrozole as they may diminish its pharmacologic action.
Other Endocrine Effects :
No increase in thyroid stimulating hormone (TSH) was reported during the administration of anastrozole. Anastrozole does not possess direct progestogenic, androgenic, or estrogenic activity in animals, but does perturb the circulating levels of progesterone, androgens and estrogens.

DRUG/LABORATORY TEST INTERACTIONS
No Clinically significant changes in the results of clinical laboratory tests have been observed.
PREGNANCY :
Pregnancy Category D
Anastrozole can cause fetal harm when administrated to a pregnant women using anastrozole. If anastrozole is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patients should be apprised of the potential hazard to the fetus or potential risk for loss of the pregnancy.
NURSING MOTHERS
It is not known if anastrozole is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when anastrozole is administered to a nursing woman.
Pediatric use
The safety and efficacy of anastrozole in pediatric patients have not been established.
Geriatric use
Response rates and time to progression were similar for the over 65 and yonger patients.
Adverse Reactions
Anastrozole is generally well tolerated. The principal adverse events are asthenia, pharyngitis, nausea, dizziness, headache, rash, hot flashes, dry mouth, pain. peripheral edema, back pain, pelvic pain, dyspnea, depression, vomiting.
Chest pain cough, paresthesia, diarrhoea, vaginal hemorrhage, constipation, weight gain, abdominal pain, sweating, anorexia increased appetite and bone pain.
Other less frequent adverse experiences reported in patients receiving anastrozole 1 mg are listed below.
Body as a whole, flusyndorme; fever, neck pain; malaise; accidental injury.
INFECTION
Cardiovascular ; Hypertension; thrombophlibitis
Hepatic Gamma GT increase ; SGOT increased; SGPT increased Hematologic; Anemia; leukopenia
Metabolic and Nutritional ; Alkaline phosphatase increased; weight loss mean serum total cholesterol levels increased by 0.5 mm/L among patients receiving anastrozole Increases in LDL cholesterol have been shown to contribute to these changes.
MUSCULOSKELETAL; MYALGIA; arthralgia; pathological fracture, joint pain/stiffness cytoiliom Nervous; Somnolence; confusion; insomnia; anxiety; nervousness Respiratory. Sinusitis; bronchitis; rhinitis.
Skin and Appendages: Hair thinning; pruritus, rash including very rare cases of mucocutaneous disorders such as erythema multiforme and stevens johnson syndrome.,
Urogenital : Urinary tract Infection; breast pain.
OVERDOSE:
Clinical trails have been conducted with 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 result in life-threatening symptoms has not been established. In rats, lethality was observed after single oral doses that were greater than 100 mg/kg (about 800 times the recommended human dose on a mg/m2 basis) and was associated with severe irritation to the stomach (necrosis, gastritis, ulceration, and hemorrhage). In an oral acute toxicity study in the dog the median lethal dose was greater than 45 mg / kg / day. There is no specific antidote to overdosage and treatment must be symptomatic in the management of an overdose, consider 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 patients, is indicated.
STORAGE:
Store in a cool dry place.
PRESENTATION
Blister of 10 Tablets