ANAST-1

(Anastrozole Tablets 1 mg)

CAUTION: CYTOTOXIC AGENT

Name and strength of active ingredient
Anastrozole 1 mg

Dosage form
Film Coated Tablet

Product Description
White to off white, round, biconvex, film coated tablets with "AHI" debossing on one side and plain on other side.

Pharmacodynamic properties
Pharmacotherapeutic group: enzyme inhibitors
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.

Daily doses of Anastrozole up to 10 mg do not have any effect on cortisol or aldosterone secretion, measured before or after standard ACTH challenge testing. Corticoid supplements are therefore not needed.

As with all treatment decisions, women with breast cancer and their physician should assess the relative benefits and risks of the treatment.

When Anastrozole and tamoxifen were co-administered, the efficacy and safety were similar to tamoxifen when given alone, irrespective of hormone receptor status. The exact mechanism of this is not yet clear. It is not believed to be due to a reduction in the degree of estradiol suppression produced by Anastrozole.

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 is independent of age in postmenopausal women.

Pharmacokinetics has not been studied in children.

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.

Indication/Usage
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.

Recommended Dose
Adults including the elderly: One 1 mg tablet to be taken orally once a day.

Children and adolescents: Not recommended for use in children.
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.

Route of Administration
Oral

Contraindication
Anastrozole is contraindicated in:

- Patients with known hypersensitivity to anastrozole or to any of the excipients.
- 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.

Oestrogen-containing therapies should not be co-administered with Anastrozole as they would negate its pharmacological action.
Concurrent tamoxifen therapy.

Warnings & Precaution
Anastrozole is not recommended for use in children, as safety and efficacy have not been established in this group of patients.

The menopause should be defined biochemically in any patient where there is doubt about hormonal status.

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 e.g. DEXA scanning 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.
Adequate data to show the effect of bisphosphonates on bone mineral density loss caused by anastrozole, or their utility when used prophylactically, are not currently available.

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.

Interaction with other medicaments
Antipyrine and cimetidine clinical interaction studies indicate that the co-administration of Anastrozole with other medicinal products 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 medicinal products.

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.

Front Side

Pregnancy and Lactation
Anastrozole is contraindicated in pregnant or lactating women.

Side effects/Adverse Reactions
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The frequencies of undesirable effects are following: 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 data).

Very common (≥1/10)	Vascular	Hot flushes, mainly mild or moderate in nature
	Psychiatric disorder	Depression
Common (≥1/100 to <1/10)	General	Asthenia, mainly mild or moderate in nature
	Musculoskeletal, connective tissue and bone	Joint pain/stiffness, mainly mild or moderate in nature
	Reproductive system and breast	Vaginal dryness, mainly mild or moderate in nature
	Skin and subcutaneous tissue	Hair thinning, mainly mild or moderate in nature
		Rash, mainly mild or moderate in nature
	Gastrointestinal	Nausea, mainly mild or moderate in nature
		Diarrhoea, mainly mild or moderate in nature
	Nervous system	Headache, mainly mild or moderate in nature
		Carpal tunnel syndrome
	Hepatobiliary disorders	Increases in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase
Uncommon (≥1/1,000 to <1/100)	Reproductive system and breast	Vaginal bleeding, mainly mild or moderate in nature*
	Metabolism and nutrition	Anorexia, mainly mild in nature
		Hypercholesterolaemia, mainly mild or moderate in nature
	Gastrointestinal	Vomiting, mainly mild or moderate in nature
	Nervous system	Somnolence, mainly mild or moderate in nature
	Hepatobiliary	Increases in gamma-GT and bilirrubin, hepatitis
Very rare (<1/10,000)	Skin and subcutaneous	Erythema multiforme Stevens-Johnson syndrome Allergic tissue reactions including angioedema, urticaria and anaphylaxis

*Vaginal bleeding has been reported uncommonly, mainly in patients with advanced breast cancer during the first few weeks after changing from existing hormonal therapy to treatment with Anastrozole. If bleeding persists, further evaluation should be considered.

As Anastrozole lowers circulating oestrogen levels, it may cause a reduction in bone mineral density placing some patients at a higher risk of fracture.

Signs & Symptoms of overdose and Treatment
There is limited clinical experience of accidental overdose. 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 overdose 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.

Shelf life
36 months

Pack size
PVC/PVDC -Alu Blister of 10 tablets. Each Carton contains 3 such blister. (3 x 10T)

Manufactured by:
INTAS
INTAS PHARMACEUTICALS LTD.
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Marketing Authorization Holder:
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INP103

Back Side

File Name : RANS01I521-ANAST-1(MALAYSIA)PIL
Size : 175 x 275 (mm)
Colour : Pantone Black
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