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

PRESCRIBING INFORMATION

FINASTERIDE TABLETS IP 1 mg

FINALO

COMPOSITION

Each film coated tablet contains:
Finasteride IP 1 mg
Excipients: Q.S.
Colour: Titanium Dioxide IP

DESCRIPTION

Finasteride, a synthetic 4-azasteroid compound, is a specific inhibitor of steroid Type II 5(alpha)-reductase, an intracellular enzyme that converts the androgen testosterone into 5(alpha)- dihydrotestosterone (DHT).
Finasteride is 4-azaandrost-1-ene-17-carboxamide, *N* -(1,1- dimethylethyl)-3-oxo-,(5(alpha),17(beta))-. The empirical formula of finasteride is $C_{23}H_{36}N_2O_2$ and its molecular weight is 372.55.

CLINICAL PHARMACOLOGY

Finasteride is a competitive and specific inhibitor of Type II 5(alpha)-reductase, an intracellular enzyme that converts the androgen testosterone into DHT. Two distinct isozymes are found in mice, rats, monkeys, and humans: Type I and II. Each of these isozymes is differentially expressed in tissues and developmental stages. In humans, Type I 5(alpha)-reductase is predominant in the sebaceous glands of most regions of skin, including scalp, and liver. Type I 5(alpha)-reductase is responsible for approximately one-third of circulating DHT. The Type II 5(alpha)-reductase isozyme is primarily found in prostate, seminal vesicles, epididymides, and hair follicles as well as liver, and is responsible for two-thirds of circulating DHT.

In humans, the mechanism of action of finasteride is based on its preferential inhibition of the Type II isozyme. For both isozymes, the inhibition by finasteride is accompanied by reduction of the inhibitor to dihydrofinasteride and adducts formation with NADP+. The turnover for the enzyme complex is slow. Finasteride has no affinity for the androgen receptor and has no androgenic, antiandrogenic, estrogenic, antiestrogenic, or progestational effects. Inhibition of Type II 5(alpha)-reductase blocks the peripheral conversion of testosterone to DHT, resulting in significant decreases in serum and tissue DHT concentrations. Finasteride produces a rapid reduction in serum DHT concentration, reaching 65% suppression within 24 hours of oral dosing with a 1-mg tablet. Mean circulating levels of testosterone and estradiol were increased by approximately 15% as compared to baseline, but these remained within the physiologic range.

In men with male pattern hair loss (androgenetic alopecia), the balding scalp contains miniaturized hair follicles and increased amounts of DHT compared with hairy scalp. Administration of finasteride decreases scalp and serum DHT concentrations in these men. The relative contributions of these reductions to the treatment effect of finasteride have not been defined. By this mechanism, finasteride appears to interrupt a key factor in the development of androgenetic alopecia in those patients genetically predisposed.

Pharmacokinetics

Absorption
Finasteride is well absorbed following oral administration. In a study in 15 healthy young male subjects, the mean bioavailability of finasteride 1-mg tablets has been 65% (range 26-170%), based on the ratio of area under the curve (AUC) relative to an intravenous (IV) reference dose. At steady state following dosing with 1 mg/day (n=12), maximum finasteride plasma concentration averaged 9.2 ng/mL (range, 4.9-13.7 ng/mL) and was reached 1 to 2 hours postdose; AUC (0-24 hr) was 53 ng•hr/mL (range, 20-154 ng•hr/mL). Bioavailability of finasteride is not affected by food.

Distribution
Mean steady-state volume of distribution is around 76 liters.
Approximately 90% of circulating finasteride is bound to plasma proteins. There is a slow accumulation phase for finasteride after multiple dosing. Finasteride has been found to cross the blood-brain barrier.
Semen levels have been measured in 35 men taking finasteride 1 mg/day for 6 weeks. In 60% (21 of 35) of the samples, finasteride levels were undetectable (<0.2 ng/mL). The mean finasteride level was 0.26 ng/mL and the highest level measured was 1.52 ng/mL. Using the highest semen level measured and assuming 100% absorption from a 5-mL ejaculate per day, human exposure through vaginal absorption would be up to 7.6 ng per day, which is 750 times lower than the exposure from the no-effect dose for developmental abnormalities in Rhesus monkeys and 650-fold less than the dose of finasteride (5 µg) that had no effect on circulating DHT levels in men.

Metabolism
Finasteride is extensively metabolized in the liver, primarily via the cytochrome P450 3A4 enzyme subfamily. Two metabolites, the t-butyl side chain monohydroxylated and monocarboxylic acid metabolites, have been identified that possess no more than 20% of the 5(alpha)-reductase inhibitory activity of finasteride.

Excretion
Part of oral dose (39%) is excreted in urine as metabolites; 57% is excreated in feces. No unchanged drug is found in urine. Mean terminal half-life is approximately 5-6 hours in men 18-60 years of age and 8 hours in men more than 70 years of age.

Special Populations

Pediatric: Finasteride pharmacokinetics have not been investigated in patients <18 years of age.

Gender: Finasteride is not indicated for use in women.

Geriatric: No dosage adjustment is necessary in the elderly. Although the elimination rate of finasteride is decreased in the elderly, these findings are of no clinical significance.

Race: The effect of race on finasteride pharmacokinetics has not been studied.

Renal Insufficiency: No dosage adjustment is necessary in patients with renal insufficiency.

Hepatic Insufficiency: The effect of hepatic insufficiency on finasteride pharmacokinetics has not been studied. Caution should be used in the administration of finasteride in patients with liver function abnormalities, as finasteride is metabolized extensively in the liver

Drug Interaction
No drug interactions of clinical importance have been identified. Finasteride does not appear to affect the cytochrome P450-linked drug-metabolizing enzyme system. Compounds that have been tested in man include antipyrine, digoxin, propranolol, theophylline, and warfarin and no clinically meaningful interactions were found.

Other concomitant therapy: Although specific interaction studies were not performed, finasteride doses of 1 mg or more were concomitantly used in clinical studies with acetaminophen, acetylsalicylic acid (alpha)-blockers, analgesics, angiotensin- converting enzyme (ACE) inhibitors, anticonvulsants, benzodiazepines, beta blockers, calcium-channel blockers, cardiac nitrates, diuretics, H 2 antagonists, HMG-CoA reductase inhibitors, prostaglandin synthetase inhibitors (NSAIDs), and quinolone anti-infectives without evidence of clinically significant adverse interactions.

Laboratory Test Interactions
Finasteride has no effect on circulating levels of cortisol, thyroid-stimulating hormone, or thyroxine, nor does it affect the plasma lipid profile (e.g., total cholesterol, low-density lipoproteins, high-density lipoproteins and triglycerides) or bone mineral density. In studies with finasteride, no clinically meaningful changes in luteinizing hormone (LH), follicle-stimulating hormone (FSH) or prolactin were detected. In healthy volunteers, treatment with finasteride did not alter the response of LH and FSH to gonadotropin-releasing hormone indicating that the hypothalamic-pituitary-testicular axis was not affected.

In clinical studies, finasteride showed reduction in blood PSA level. These findings should be taken into account for proper interpretation of serum PSA when evaluating men treated with finasteride.

INDICATIONS AND USAGE

Finasteride is indicated for the treatment of male pattern hair loss (androgenetic alopecia) in men only. Safety and efficacy have been demonstrated in men between 18 to 41 years of age with mild to moderate hair loss of the vertex and anterior mid-scalp area. Efficacy in bitemporal recession has not been established. Finasteride is not indicated in women and children.

DOSAGE AND ADMINISTRATION

The recommended dosage is 1 mg orally once a day. Finasteride may be administered with or without meals. In general, daily use for three months or more is necessary before benefit is observed. Continued use is recommended to sustain benefit, which should be re-evaluated periodically. Withdrawal of treatment leads to reversal of effect within 12 months.

CONTRAINDICATIONS
Finasteride is contraindicated in the following:

Pregnancy. Finasteride use is contraindicated in women when they are or may potentially be pregnant. Because of the ability of Type II 5(alpha)-reductase inhibitors to inhibit the conversion of testosterone to DHT, finasteride may cause abnormalities of the external genitalia of a male fetus of a pregnant woman who receives finasteride. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the pregnant woman should be apprised of the potential hazard to the male fetus.
Hypersensitivity to any component of this medication.

WARNINGS
Finasteride is not indicated for use in pediatric patients or women.

EXPOSURE OF WOMEN - RISK TO MALE FETUS
Women should not handle crushed or broken Finasteride tablets when they are pregnant or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male fetus. Finasteride tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

PRECAUTIONS

General
Caution should be used in the administration of Finasteride in patients with liver function abnormalities, as finasteride is metabolized extensively in the liver.

Information for Patients
Women should not handle crushed or broken. Finasteride tablets when they are pregnant or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male fetus.Finasteride tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

Physicians should instruct their patients to promptly report any changes in their breasts such as lumps, pain or nipple discharge. Breast changes including breast enlargement, tenderness and neoplasm have been reported.

Pregnancy
Teratogenic Effects: Pregnancy Category X
Finasteride use is contraindicated in women when they are or may potentially be pregnant. Because of the ability of Type II 5(alpha)-reductase inhibitors to inhibit the conversion of testosterone to DHT, finasteride may cause abnormalities of the external genitalia of a male fetus of a pregnant woman who receives finasteride. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the pregnant woman should be apprised of the potential hazard to the male fetus.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No evidence of a tumorogenic effect was observed in a 24-month study in Sprague-Dawley rats receiving doses of finasteride up to 160 mg/kg/day in males and 320 mg/kg/day in females.

In a 19-month carcinogenicity study in CD-1 mice, a statistically significant (p</=0.05) increase in the incidence of testicular Leydig cell adenomas was observed at a dose of 250 mg/kg/day (1,824 times the human exposure). In mice at a dose of 25 mg/kg/day (184 times the human exposure, estimated) and in rats at a dose of >/=40 mg/kg/day (312 times the human exposure) an increase in the incidence of Leydig cell hyperplasia was observed. A positive correlation between the proliferative changes in the Leydig cells and an increase in serum LH levels (2-3 fold above control) has been demonstrated in both rodent species treated with high doses of finasteride.
No evidence of mutagenicity was observed in an *in vitro* bacterial mutagenesis assay, a mammalian cell mutagenesis assay, or in an *in vitro* alkaline elution assay.

In sexually mature male rabbits treated with finasteride at 80 mg/kg/day (4,344 times the estimated human exposure) for up to 12 weeks, no effect on fertility, sperm count, or ejaculate volume was seen.

Nursing Mothers
Finasteride is not indicated for use in women.
It is not known whether finasteride is excreted in human milk.

Pediatric Use
Finasteride is not indicated for use in pediatric patients.
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical efficacy studies with finasteride did not include subjects aged 65 and over. Based on the pharmacokinetics of finasteride 5 mg, no dosage adjustment is necessary in the elderly for finasteride. However the efficacy of finasteride in the elderly has not been established.

Adverse reactions
Finasteride is generally well tolerated and adverse reaction are usually mild.

Genito-Urinary: impotence, decrease volume of ejaculate, decrease libido, Nonbeneficial decreased prostate-specific antigen serum levels (PSA). The incidence of these adverse reaction decreases with duration of therapy. Resolution occurs after discontinuation of therapy.

General: allergic reactions including rash, itching, hives and swelling of the lips and face; problems with ejaculation; breast tenderness and enlargement; and testicular pain.

OVERDOSAGE
In clinical studies, single doses of finasteride up to 400 mg and multiple doses of finasteride up to 80 mg/day for three months did not result in adverse reactions. Until further experience is obtained, no specific treatment for an overdose with finasteride can be recommended.

Significant lethality was observed in male and female mice at single oral doses of 1,500 mg/m^2 (500 mg/kg) and in female and male rats at single oral doses of 2,360 mg/m^2 (400 mg/kg) and 5,900 mg/m^2 (1,000 mg/kg), respectively.

STORAGE AND HANDLING
Store in a cool dry place, protect from light.
Keep out of reach of children.
FOR USE BY MEN ONLY

Women should not handle crushed or broken. Finasteride tablets when they are pregnant or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male fetus. Finasteride tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets are not broken or crushed.

PRESENTATION
FINALO is available in strip of 10 tablets.

Manufactured by:
INTAS
INTAS PHARMACEUTICALS LTD.
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