Finasteride

Finar

5 mg Film-Coated Tablet

Urological (Testosterone-5-alpha reductase Inhibitor)

FORMULATION:
Each film-coated tablet contains:
Finasteride.....5 mg

PRODUCT DESCRIPTION:
Brick red coloured, round shaped, biconvex film-coated tablet with break line on one side and plain on other side.

CLINICAL PHARMACOLOGY:
The development and enlargement of the prostate gland is dependent on the potent androgen, 5α- dihydrotestosterone (DHT). Type II 5α-reductase metabolizes testosterone to DHT in the prostate gland, liver and skin. DHT induces androgenic effects by binding to androgen receptors in the cell nuclei of these organs.

Finasteride is a competitive and specific inhibitor of Type II 5α-reductase with which it slowly forms a stable enzyme complex. Turnover from this complex is extremely slow (t½ ~ 30 days). This has been demonstrated both *in vivo* and *in vitro.* Finasteride has no affinity for the androgen receptor. In man, the 5α-reduced steroid metabolites in blood and urine are decreased after administration of Finasteride.

Pharmacodynamics
In man, a single 5-mg oral dose of Finasteride produces a rapid reduction in serum DHT concentration, with the maximum effect observed 8 hours after the first dose. The suppression of DHT is maintained throughout the 24-hour dosing interval and with continued treatment. Daily dosing of Finasteride at 5 mg/day for up to 4 years has been shown to reduce the serum DHT concentration by approximately 70%. The median circulating level of testosterone increased by approximately 10-20% but remained within the physiologic range. In a separate study in healthy men treated with Finasteride 1 mg per day (n=82) or placebo (n=69), mean circulating levels of testosterone and estradiol were increased by approximately 15% as compared to baseline, but these remained within the physiologic range.

In patients receiving Finasteride 5 mg/day, increases of about 10% were observed in luteinizing hormone (LH) and follicle-stimulating hormone (FSH), but levels remained within the normal range. 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 patients with benign prostatic hyperplasia (BPH), Finasteride has no effect on circulating levels of cortisol, prolactin, thyroid-stimulating hormone, or thyroxine. No clinically meaningful effect was observed on the plasma lipid profile (i.e., total cholesterol, low density lipoproteins, high density lipoproteins and triglycerides) or bone mineral density.

Adult males with genetically inherited Type II 5α-reductase deficiency also have decreased levels of DHT. Except for the associated urogenital defects present at birth, no other clinical abnormalities related to Type II 5α-reductase deficiency have been observed in these individuals. These individuals have a small prostate gland throughout life and do not develop BPH.

In patients with BPH treated with Finasteride (1-100 mg/day) for 7-10 days prior to prostatectomy, an approximate 80% lower DHT content was measured in prostatic tissue removed at surgery, compared to placebo; testosterone tissue concentration was increased up to 10 times over pretreatment levels, relative to placebo. Intraprostatic content of PSA was also decreased.

In healthy male volunteers treated with Finasteride for 14 days, discontinuation of therapy resulted in a return of DHT levels to pretreatment levels in approximately 2 weeks. In patients treated for three months, prostate volume, which declined by approximately 20%, returned to close to baseline value after approximately three months of discontinuation of therapy.

Pharmacokinetics
Finasteride is absorbed after oral doses, and peak plasma concentrations are achieved in 1 to 2 hours. The mean bioavailability has variously been reported as 63% and 80%. It is about 90% bound to plasma protein. Finasteride crosses the blood-brain barrier, and is distributed into semen. It is metabolised in the liver, primarily by the cytochrome P450 isoenzyme CYP3A4, and excreted in urine and faeces as metabolites. The mean terminal half-life is about 6 hours in patients under 60 years of age but may be prolonged to about 8 hours in those 70 years of age or older.

INDICATIONS:
Used in the management of benign prostatic hyperplasia.

DOSAGE AND ADMINISTRATION:
Finasteride is an azasteroid that inhibits the type-2 isoform of 5α-reductase, the enzyme responsible for conversion of testosterone to the more active dihydrotestosterone, and therefore has anti-androgenic properties. It is given by mouth in a dose of 5 mg daily in the management of benign prostatic hyperplasia to cause regression of the enlarged prostate and to improve symptoms; it may reduce the incidence of acute urinary retention and the need for surgery. Response may be delayed and treatment for 6 months or more may be required to assess whether benefit has been achieved.
In the treatment of male-pattern baldness (alopecia androgenetica) in men, Finasteride is given by mouth in a dose of 1 mg daily. In general, use for 3 months or more is required before benefit is seen, and effects are reversed within 12 months of ceasing therapy.

CONTRAINDICATIONS:
Contraindicated in women who are or may become pregnant. In addition, it is recommended that women in this category should not handle crushed or broken Finasteride tablets.
Finasteride has been detected in semen, therefore use of a condom is recommended if the patient's partner is, or may become, pregnant.

PRECAUTIONS:
Finasteride should be used with caution in hepatic impairment. When used for benign prostatic hyperplasia, Finasteride should be used with caution in men at risk of obstructive uropathy. Patients should be evaluated for prostatic carcinoma before and during therapy. Use of Finasteride decreases concentrations of serum markers of prostate cancer such as prostate specific antigen (PSA) by up to 50% even when cancer is present, and reference values should be adjusted accordingly; the ratio of free to total PSA (percent free PSA) remains constant.

PREGNANCY AND LACTATION:
Finasteride is contraindicated for use in women when they are or may potentially be pregnant.
Because of the ability of Type II 5α-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including Finasteride, may cause abnormalities of the external genitalia of a male fetus when administered to a pregnant woman.
Exposure to Finasteride: Risk to Male Fetus: Women should not handle crushed or broken tablets of Finasteride when they are 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.
Finasteride is not indicated for use in women.
It is not known whether Finasteride is excreted in human milk.

ADVERSE DRUG REACTIONS:
The most commonly reported adverse effects of Finasteride are decreased libido, erectile dysfunction, ejaculation disorders, and reduced volume of ejaculate.
Breast tenderness and enlargement (gynaecomastia) may occur, and there have been reports of hypersensitivity reactions such as swelling of the lips and face, pruritus, urticaria, and rashes. Testicular pain has also been reported.

DRUG INTERACTIONS:
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 have included antipyrine, digoxin, propranolol, theophylline, and warfarin and no clinically meaningful interactions were found.
Other Concomitant Therapy: Although specific interaction studies were not performed, Finasteride was concomitantly used in clinical studies with acetaminophen, acetylsalicylic acid, α-blockers, angiotensin-converting enzyme (ACE) inhibitors, analgesics, anti-convulsants, beta-adrenergic blocking agents, diuretics, calcium channel blockers, cardiac nitrates, HMG-CoA reductase inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), benzodiazepines, H2 antagonists and quinolone anti-infectives without evidence of clinically significant adverse interactions.

OVERDOSE AND TREATMENT:
Patients have received single doses of Finasteride up to 400 mg and multiple doses of Finasteride up to 80 mg/day for three months without adverse effects. 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 1500 mg/m^2 (500 mg/kg) and in female and male rats at single oral doses of 2360 mg/m^2 (400 mg/kg) and 5900 mg/m^2 (1000 mg/kg), respectively.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

AVAILABILITY:
Alu/PVC Blister Pack of 10's (Box of 30's)

DRP-4725-01
Date of First Authorization: June 20, 2022
Date of Revision of Package Insert: October 4, 2024

Manfactured by:
Unicure Remedies Pvt. Ltd.
F/25, BIDC Estate, Gorwa,
Baroda-390 016, India

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Ambica International Corporation
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Merville Park Subd., Parañaque, Metro Manila