Finasteride

Atepros®

5 mg Film-Coated Tablet
5α - Reductase Inhibitor

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

PRODUCT DESCRIPTION
Finasteride 5 mg is a biconvex film-coated, blue tablet, 5/16" in diameter, plain on both sides.

CLINICAL PHARMACOLOGY

Pharmacodynamics
Finasteride is a member of the 4-azasteroid family of compounds. It is a competitive and specific inhibitor of Type II 5α-reductase. Type II 5α-reductase is an intracellular enzyme which converts testosterone into the more potent androgen 5-dihydrotestosterone (DHT), the principal androgen responsible for stimulation of prostatic growth.

Benign prostatic hyperplasia (BPH), the abnormal enlargement of the prostate gland dependent upon the conversion of testosterone to DHT within the prostate, produces manifestations such as weak urinary stream, difficulty in initiating urination, urinary frequency and urgency. Inhibition of the conversion of testosterone to DHT by finasteride leads to reduced prostatic size and improvement of urinary flow and associated manifestations of urinary obstruction.

Finasteride has no androgenic, antiandrogenic, or other steroid hormone-related properties.

Pharmacokinetics
Finasteride is rapidly and almost completely absorbed after oral administration. Peak plasma concentrations (Cmax) are attained two hours after an oral dose of 5 mg finasteride and absorption is complete after 6 to 8 hours. There is slow accumulation of the drug during chronic administration. Steady state concentrations of finasteride 5 mg daily are 8 to 10 µg/L.

Oral bioavailability is 80%. Food does not affect absorption or bioavailability of finasteride. Finasteride is extensively bound to plasma proteins (~93%); its volume of distribution is 76 liters.

Small amounts of finasteride are excreted in seminal fluid in subjects receiving finasteride 5 mg daily but the amount of finasteride in ejaculate is only 1 to 2% of the minimum daily oral dose needed to produce a measurable reduction in circulating DHT levels. Finasteride crosses the blood-brain barrier. The extent to which finasteride is excreted in breast milk is unknown.
Finasteride is eliminated relatively rapidly from plasma and its terminal elimination half-life is 6 hours.

Finasteride is metabolized extensively in the liver primarily through the cytochrome P450 3A4 enzyme subfamily. Its metabolites, t-butyl side chain monohydroxylated and monocarboxylic acid metabolites, possess < 20% the 5α-reductase inhibitory activity of finasteride. These metabolites are excreted in both the urine (39%) and feces (57%) with only trace amounts of finasteride excreted unchanged in urine (0.04%) or feces. Finasteride's total body clearance is 165 mL/min.

No dosage adjustment in the elderly (≥ 70 years old) is required although finasteride's elimination rate in these patients increases to 8 hours compared with 6 hours in younger subjects (45-60 years old).

INDICATIONS
- Treatment and control of benign prostatic hyperplasia (BPH) in men with enlarged prostate to:
  - Cause regression of the enlarged prostate, improve urinary flow and alleviate symptoms associated with BPH
  - Reduce the risk of acute urinary retention
  - Reduce the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy

Note: Finasteride is not indicated in the following:
- **Patients who are candidates for immediate surgery**
- **To reduce the risk of developing prostate cancer in healthy men.**

DOSAGE AND ADMINISTRATION
Usual recommended dose: Orally, 5 mg once a day
Or, as prescribed by a physician.

- May be administered with or without food.
- Although early symptomatic improvement may be observed, treatment for least 6 months may be necessary to determine clinical benefit of finasteride therapy. Monitor clinical response through periodic follow-up evaluations.
- No dosage adjustment necessary for the elderly and for patients with renal impairment (creatinine clearance as low as 9 mL/min).

CONTRAINDICATIONS
- Hypersensitivity to finasteride or to any ingredient in the product
- Women, who are, or may potentially be pregnant
- Children

WARNINGS AND PRECAUTIONS
The long term (> 10 years) beneficial and adverse effects of finasteride have not been established.

The use of finasteride for the control of prostatic hyperplasia in asymptomatic patients has not been studied.

General
Finasteride has been detected in the semen and has been shown to cause abnormalities of the external genitalia in male offspring. Therefore, the exposure of the female sexual partner to the finasteride-treated patient's semen should be avoided or finasteride-treated patients discontinue therapy when the partner is or may become pregnant. (see **Statement on Usage for High-Risk Groups**)

Effects on Prostate-Specific Antigen (PSA) and the Use of PSA in Prostate Cancer Detection
Finasteride may interfere with the interpretation of PSA determinations. PSA may be elevated in patients with BPH, prostate cancer or other prostatic disease. Although finasteride causes a decrease in PSA even in patients with prostate cancer, this should not be interpreted as efficacy of finasteride on prostate cancer.

In most patients, a rapid decrease in PSA is observed within the first months of therapy, after which time PSA levels stabilize to a new baseline. The post-treatment baseline is approximately half of the pre-treatment value. Therefore, PSA values should be doubled for comparison in patients treated with finasteride for six months or more compared to normal ranges in untreated men.

Carefully evaluate (consider patient compliance to therapy) when sustained increases in serum PSA concentrations is observed during finasteride therapy.

Increased Risk of High-Grade Prostate Cancer
5α-reductase inhibitors such as finasteride may increase the risk of development of high-grade prostate cancer. An increased risk of prostate cancer (Gleason score 8-10) was observed in men (≥ 55 years old) with normal digital rectal examination and baseline PSA levels of <3 ng/mL who took finasteride 5 mg/day (finasteride 1.8% vs placebo 1.1%) in the 7-year Prostate Cancer Prevention Trial (PCPT). This was similar to the results from the REduction by DUtasteride of prostate Cancer Events (REDUCE) trial (4-year placebo-controlled) using another 5α-reductase inhibitor, dutasteride (1% dutasteride vs 0.5% placebo). Whether the effect of 5α-reductase inhibitors to reduce prostate volume, or study-related factors had an influence in the results of these studies is not known.

Evaluation for Other Urological Conditions
Before starting finasteride therapy, perform appropriate patient evaluation to identify conditions which might mimic BPH such as infection, prostate cancer, stricture disease, hypotonic bladder, or other neurogenic disorders. Other screening tests for prostate cancer, including digital rectal examination should also be performed before starting finasteride therapy and periodically thereafter.

Carefully monitor patients with large residual urinary volume and/or diminished urinary flow for obstructive uropathy. Finasteride may not be the appropriate therapy for these patients. The possibility of surgery should be an option.

Effect on Semen Characteristics
Patients should be informed on the possibility of having a reduced volume of ejaculate during finasteride treatment. Although this does not appear to interfere with normal sexual function, impotence and decreased libido have been observed in patients treated with finasteride.

Breast Cancer in Men
During clinical trials and postmarketing studies, breast cancer was reported in men taking finasteride 5 mg. Patients should promptly inform their attending physician of any changes in their breasts (e.g., lumps, pain, nipple discharge) since breast changes including breast enlargement (gynecomastia), tenderness and neoplasms have been reported.

Sexual Function
Increased duration of treatment with finasteride did not result in increased sexual adverse experiences. New reports of drug-related sexual adverse experiences decreased with duration of treatment.

Laboratory Test Findings
Finasteride has been shown to have no effect on circulating levels of cortisol, estradiol, prolactin, thyroid stimulating hormone, or thyroxine in patients with BPH. There was no clinically significant effect observed on the plasma lipid profile (i.e., total cholesterol, low density lipoproteins, high density lipoproteins, and triglycerides) or bone mineral density. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) was shown to increase by about 10% in finasteride-treated patients but levels remained within the normal range. Treatment with finasteride, however, did not alter the response of LH and FSH to gonadotropin-releasing hormone which indicates that the hypothalamic-pituitary-testicular axis was not affected.

PSA levels are decreased in patients treated with finasteride and therefore, consideration should be given when PSA laboratory determinations are evaluated.

There is no difference observed in standard laboratory parameters in patients treated with placebo or finasteride. Percent free PSA (free total PSA ratio) is not significantly decreased by finasteride. The ratio of free to total PSA remains constant even under the influence of finasteride and therefore no adjustment to its value is necessary when free PSA is used as an aid to the detection of prostate cancer.

Ability to Use and/or Drive Machinery
There is no data that finasteride affects the ability to drive and/or use machinery.

INTERACTIONS WITH OTHER MEDICAMENTS
No clinically important drug interactions have been identified and finasteride does not appear to significantly affect the cytochrome P450-linked drug-metabolizing enzyme system. Concomitant drugs that have been studied include propranolol, digoxin, glibenclamide, warfarin, theophylline, and antipyrine.

Finasteride has also been used concomitantly with analgesics including paracetamol, α-blockers, angiotensin-converting enzyme (ACE) inhibitors, anticonvulsants, benzodiazepines, beta-blockers, calcium-channel blockers, cardiac nitrates, diuretics, H_1-antagonists, HMG-CoA reductase inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), and quinolone anti-infectives without evidence of clinically significant adverse interactions.

STATEMENT ON USAGE FOR HIGH-RISK GROUPS
Pregnancy (Risk to Male Fetus) Pregnancy Category X

Finasteride is contraindicated in women when they are or may potentially be pregnant.

Women are advised not to handle crushed or broken finasteride tablets when they are pregnant or may potentially become pregnant because of the possibility of finasteride absorption and subsequent potential risk to a male fetus. Because of the ability of type II 5-reductase inhibitors to inhibit conversion of testosterone to DHT, exposure of pregnant women to these drugs (including finasteride) may cause abnormalities of the external genitalia of 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.

Exposure of the female sexual partner to the patient's semen should also be avoided when the partner is or may become pregnant since finasteride has been detected in the semen. Discontinuation of finasteride therapy should also be considered.

Lactation
Finasteride is not indicated for use in women and its distribution into human milk is not known.

Infants and Children
Finasteride is not indicated for use in pediatric patients. The safety and efficacy of finasteride has not been established in this age group.

Geriatric
Dosage adjustment is not necessary in elderly patients.

Hepatic Insufficiency
Since finasteride is extensively metabolized in the liver, exercise caution in administering finasteride in patients with liver function abnormalities.

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

UNDESIRABLE EFFECTS
Finasteride is generally well tolerated and its adverse effects are usually mild and transient.

Cardiovascular: Palpitation, hypotension, postural hypotension,
Metabolic and Nutritional: Peripheral edema
Hypersensitivity: Hypersensitivity reactions including rash, pruritus, urticaria, and swelling of the lips and face.
Hepatobiliary: Increased hepatic enzymes
Reproductive System and Breast Disorders: Ejaculation disorders (including decreased volume of ejaculate), breast enlargement/gynecomastia, sexual function disorder, breast pain/tenderness, impotence, testicular pain, erectile dysfunction, male breast cancer, prostate cancer
CNS: Decreased libido, dizziness, somnolence, depression
Body as a whole: Asthenia, headache
Respiratory: Rhinitis, dyspnea
Gastrointestinal: Abdominal pain, diarrhea, flatulence, and nausea.
Ocular and Otic: Lens changes or opacities

OVERDOSAGE AND MANAGEMENT
No adverse effects were reported when finasteride single doses of up to 400 mg and multiple doses up to 80 mg daily were taken for up to three months.

No specific treatment for finasteride overdosage is recommended.

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

AVAILABILITY: Finasteride (ATEPROS®) 5mg Film-Coated Tablet in Strip Foil x 10's (Box of 30's)

STORAGE: Store at temperatures not exceeding 30ºC.

Manufactured by Amherst Laboratories, Inc.
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