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

FINAST

1. Generic Name

FINASTERIDE TABLETS I.P. 5 MG

2. Qualitative and quantitative composition

Each film coated tablet contains
Finasteride I.P…….5 Mg
Colour: Titanium dioxide I.P.

The excipients are Lactose Monohydrate, MCC, Starch -1500 LM Grade Sodium Starch Glycolate, Docusate Sodium, Magnesium Stearate HydroxyPropyl Methylcellulose, Propylene Glycol, Titanium Dioxide, Talc Methylene Chloride, Isopropyl Alcohol.

3. Dosage form and strength

Dosage form: Tablet

Strength: Finasteride 5 mg film-coated tablets

4. Clinical particulars

4.1 Therapeutic indication

It is use in treatment of benign prostatic hypertrophy only.

4.2 Posology and method of administration

Posology

The recommended dose of Finast as directed by physician.

The recommended dose of FINAST is one tablet 5 mg taken once a day with or without food.

Combination with Alpha-Blocker

The recommended dose of FINAST is one tablet 5 mg taken once a day in combination with the alpha-blocker doxazosin.

Method of administration

Oral use

It can be administered with or without a meal.

4.3 Contraindications

Hypersensitivity to any component of this medication.

Pregnancy. Finasteride use is contraindicated in females when they are or may potentially be pregnant. Because of the ability of Type II 5α-reductase inhibitors to inhibit the conversion of testosterone to 5α-dihydrotestosterone (DHT), finasteride may cause abnormalities of the external genitalia of a male fetus of a pregnant female who receives finasteride. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the pregnant female should be apprised of the potential hazard to the male fetus. In female rats, low doses of finasteride administered during pregnancy have produced abnormalities of the external genitalia in male offspring.

4.4 Special warnings and precautions for use

General

Effects on Prostate Specific Antigen (PSA) and the Use of PSA in Prostate Cancer Detection

In reported studies, FINAST reduced serum PSA concentration by approximately 50% within six months of treatment. This decrease is predictable over the entire range of PSA values in patients with symptomatic BPH, although it may vary in individuals.

For interpretation of serial PSAs in men taking FINAST, a new PSA baseline should be established at least six months after starting treatment and PSA monitored periodically thereafter. Any confirmed 3 increase from the lowest PSA value while on FINAST may signal the presence of prostate cancer and should be evaluated, even if PSA levels are still within the normal range for men not taking a 5α- reductase inhibitor. Non-compliance with FINAST therapy may also affect PSA test results. To interpret an isolated PSA value in patients treated with FINAST for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. These adjustments preserve the utility of PSA to detect prostate cancer in men treated with FINAST.

FINAST may also cause decreases in serum PSA in the presence of prostate cancer. The ratio of free to total PSA (percent free PSA) remains constant even under the influence of FINAST. If clinicians elect to use percent free PSA as an aid in the detection of prostate cancer in men undergoing finasteride therapy, no adjustment to its value appears necessary.

Increased Risk of High-Grade Prostate Cancer

Men aged 55 and over with a normal digital rectal examination and PSA ≤3.0 ng/mL at baseline taking finasteride 5 mg/day in the 7-year Prostate Cancer Prevention Trial (PCPT) had an increased risk of Gleason score 8-10 prostate cancer (finasteride 1.8% vs placebo 1.1%). Similar results were observed in a 4-year placebo-controlled clinical trial with another 5α-reductase inhibitor (dutasteride, AVODART) (1% dutasteride vs 0.5% placebo). 5α- reductase inhibitors may increase the risk of development of high-grade prostate cancer. Whether the effect of 5α-reductase inhibitors to reduce prostate volume, or study-related factors, impacted the results of these studies has not been established.

Exposure of Females — Risk to Male Fetus

FINAST is contraindicated in pregnant females and in females who may potentially be pregnant and not indicated for use in females. Based on animal studies and the mechanism of action, FINAST may cause abnormal development of external genitalia in a male fetus if administered to a pregnant female. Females who are pregnant or may potentially be pregnant should not handle crushed or broken FINAST tablets. FINAST tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed. If a pregnant female comes in contact with crushed or broken FINAST tablets, the contact area should be washed immediately with soap and water.

Pediatric Patients and Females

FINAST is not indicated for use in pediatric patients or females.

Effect on Semen Characteristics

Treatment with FINAST for 24 weeks to evaluate semen parameters in healthy male volunteers revealed no clinically meaningful effects on sperm concentration, mobility,

morphology, or pH. A 0.6 mL (22.1%) median decrease in ejaculate volume with a concomitant reduction in total sperm per ejaculate was observed. These parameters remained within the normal range and were reversible upon discontinuation of therapy with an average time to return to baseline of 84 weeks.

Consideration of Other Urological Conditions

Prior to initiating treatment with FINAST, consideration should be given to other urological conditions that may cause similar symptoms. In addition, prostate cancer and BPH may coexist. Patients with large residual urinary volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy. These patients may not be candidates for finasteride therapy.

4.5 Drugs interactions

Cytochrome P450-Linked Drug Metabolizing Enzyme System

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, FINAST 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.

4.6 Use in special populations

Pregnancy

Risk Summary

FINAST is contraindicated in pregnant females and not indicated for use in females. Based on animal studies and the mechanism of action, FINAST may cause abnormal development of external genitalia in a male fetus if administered to a pregnant female.

In a reported embryo-fetal development study in rats, there was a dose-dependent increase in hypospadias that occurred in 3.6 to 100% of male offspring of pregnant rats administered oral finasteride during the period of major organogenesis at doses approximately 0.1 to 86 times the maximum recommended human dose (MRHD) of 5 mg/day (based on AUC at animal doses of 0.1 to 100 mg/kg/day). Decreased 7 prostatic and seminal vesicular weights, delayed preputial separation and transient nipple development were also observed in male offspring at oral maternal doses approximately 0.03 times the MRHD (based on AUC at animal dose of 0.03 mg/kg/day), along with decreased anogenital distance in male offspring at oral maternal doses approximately 0.003 times the MRHD (based on AUC at animal dose of 0.003 mg/kg/day).

FINAST is a Type II 5α-reductase inhibitor that prevents conversion of testosterone to 5α - dihydrotestosterone (DHT), a hormone necessary for normal development of male genitalia. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the male fetus.

Abnormal male genital development is an expected consequence when conversion of testosterone to 5α-dihydrotestosterone (DHT) is inhibited by 5α-reductase inhibitors. These outcomes are similar to those reported in male infants with genetic 5α-reductase deficiency. Females could be exposed to finasteride through contact with crushed or broken FINAST tablets or semen from a male partner taking FINAST. With regard to finasteride exposure through the skin, FINAST tablets are coated and will prevent skin contact with finasteride during normal handling if the tablets have not been crushed or broken. Females who are pregnant or may potentially be pregnant should not handle crushed or broken FINAST tablets because of possible exposure of a male fetus. With regard to potential finasteride exposure through semen, three studies have been conducted that measured finasteride concentrations in semen in men receiving FINAST 5 mg/day. In these studies the highest amount of finasteride in semen was estimated to be 50- to 100-fold less than the dose of finasteride (5 ·g) that had no effect on circulating DHT levels in men.

Data

Human Data

In 2 reported studies, healthy subjects (n=69) receiving FINAST 5 mg/day for 6-24 weeks, finasteride concentrations in semen ranged from undetectable (<0.1 ng/mL) to 10.54 ng/mL. In an earlier study using a less sensitive assay, finasteride concentrations in semen of 16 subjects receiving FINAST 5 mg/day ranged from undetectable (<1.0 ng/mL) to 21 ng/mL. Using the highest semen level measured and assuming 100% absorption would be up to 105 ng per day, which is 50- to 100-fold less than the dose of finasteride (5 □g) that had no effect on circulating DHT levels in men.

Animal Data

In a reported embryo-fetal development study, pregnant rats received finasteride during the period of major organogenesis (gestation days 6 to 17). At maternal doses of oral finasteride approximately 0.1 to 86 times the maximum recommended human dose (MRHD) of 5 mg/day (based on AUC at animal doses of 0.1 to 100 mg/kg/day) there was a dose-dependent increase in hypospadias that occurred in 3.6 to 100% of male offspring. Exposure multiples were estimated using data from nonpregnant rats. Days 16 to 17 of gestation is a critical period in male fetal rats for differentiation of the external genitalia. At oral maternal doses approximately 0.03 times the MRHD (based on AUC at animal dose of 0.03 mg/kg/day), male offspring had decreased prostatic and seminal vesicular weights, delayed preputial separation and transient nipple development. Decreased anogenital distance occurred in male offspring of pregnant rats that received approximately 0.003 times the MRHD (based on AUC at animal dose of 0.003 mg/kg/day). No abnormalities were observed in female offspring at any maternal dose of finasteride.

No developmental abnormalities were observed in the offspring of untreated females mated with finasteride treated male rats that received approximately 61 times the MRHD (based on AUC at animal dose of 80 mg/kg/day). Slightly decreased fertility was observed in male offspring after administration of about 3 times the MRHD (based on AUC at animal dose of 3 mg/kg/day) to female rats during late gestation and lactation. No effects on fertility were seen in female offspring under these conditions.

No evidence of male external genital malformations or other abnormalities were observed in rabbit fetuses exposed to finasteride during the period of major organogenesis (gestation days 6-18) at maternal oral doses up to 100 mg/kg/day, (finasteride exposure levels were not measured in rabbits). However, this study may not have included the critical period for finasteride effects on development of male external genitalia in the rabbit.

The fetal effects of maternal finasteride exposure during the period of embryonic and fetal development were evaluated in the rhesus monkey (gestation days 20-100), in a species and development period more predictive of specific effects in humans than the studies in rats and rabbits. Intravenous administration of finasteride to pregnant monkeys at doses as high as 800 ng/day (estimated 8 maximal blood concentration of 1.86 ng/mL or about 143 times the highest estimated exposure of pregnant females to finasteride from semen of men taking 5 mg/day) resulted in no abnormalities in male fetuses. In confirmation of the relevance of the rhesus model for human fetal development, oral administration of a dose of finasteride (2 mg/kg/day or approximately 18,000 times the highest estimated blood levels of finasteride from semen of men taking 5 mg/day) to pregnant monkeys resulted in external genital abnormalities in male fetuses. No other abnormalities were observed in male fetuses and no finasteride-related abnormalities were observed in female fetuses at any dose.

Lactation

Risk Summary

FINAST is not indicated for use in females.

Females and Males of Reproductive Potential

Infertility

Females
FINAST is not indicated for use in females.

Males
Treatment with FINAST for 24 weeks to evaluate semen parameters in healthy male volunteers revealed no clinically meaningful effects on sperm concentration, mobility, morphology, or pH. A 0.6 mL (22.1%) median decrease in ejaculate volume with a concomitant reduction in total sperm per ejaculate was observed. These parameters remained within the normal range and were reversible upon discontinuation of therapy with an average time to return to baseline of 84 weeks.
There have been postmarketing reports of male infertility and/or poor seminal quality; normalization or improvement of seminal quality has been reported after discontinuation of finasteride.

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

Geriatric Use
Of the total number of subjects included in PLESS, 1480 and 105 subjects were 65 and over and 75 and over, respectively. No overall differences in safety or effectiveness were

observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. No dosage adjustment is necessary in the elderly.

Hepatic Impairment
Caution should be exercised in the administration of FINAST in those patients with liver function abnormalities, as finasteride is metabolized extensively in the liver.

Renal Impairment
No dosage adjustment is necessary in patients with renal impairment.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Clinical Trials Experience

Because reported studies are conducted under widely varying conditions, adverse reactions rates observed in the Reported studies of a drug cannot be directly compared to rates in the Reported studies of another drug and may not reflect the rates observed in practice.

4-Year Placebo-Controlled Study (PLESS)

In PLESS, 1524 patients treated with FINAST and 1516 patients treated with placebo were evaluated for safety over a period of 4 years. The most frequently reported adverse reactions were related to sexual function. 3.7% (57 patients) treated with FINAST and 2.1% (32 patients) treated with 4 placebo discontinued therapy as a result of adverse reactions related to sexual function, which are the most frequently reported adverse reactions.

Table 1 presents the only clinical adverse reactions considered possibly, probably or definitely drug related by the investigator, for which the incidence on FINAST was ≥1% and greater than placebo over the 4 years of the study. In years 2-4 of the study, there was no significant difference between treatment groups in the incidences of impotence, decreased libido and ejaculation disorder.

Table : 1 Drug-Related Adverse Experiences

	Year 1 (%)		Year 2,3 and 4* (%)	
	Finasteride	**Placebo**	**Finasteride**	**Placebo**
Impotence	8.1	3.7	5.1	5.1
Decreased Libido	6.4	3.4	2.6	2.6
Decreased Volume of Ejaculate	3.7	0.8	1.5	0.5
Ejaculation Disorder	0.8	0.1	0.2	0.1
Breast Enlargement	0.5	0.1	1.8	1.1

Breast Tenderness	0.4	0.1	0.7	0.3
Rash	0.5	0.2	0.5	0.1

*Combined Years 2-4

N = 1524 and 1516, finasteride vs placebo, respectively

Phase III Studies and 5-Year Open Extensions

The adverse experience profile in the 1-year, placebo-controlled, Phase III studies, the 5-year open extensions, and PLESS were similar.

Medical Therapy of Prostatic Symptoms (MTOPS) Study

In the MTOPS reported study, 3047 men with symptomatic BPH were randomized to receive FINAST 5 mg/day (n=768), doxazosin 4 or 8 mg/day (n=756), the combination of FINAST 5 mg/day and doxazosin 4 or 8 mg/day (n=786), or placebo (n=737) for 4 to 6 years.

The incidence rates of drug-related adverse experiences reported by 2% of patients in any treatment group in the MTOPS Study are listed in Table 2.

The individual adverse effects which occurred more frequently in the combination group compared to either drug alone were: asthenia, postural hypotension, peripheral edema, dizziness, decreased libido, rhinitis, abnormal ejaculation, impotence and abnormal sexual function (see Table 2). Of these, the incidence of abnormal ejaculation in patients receiving combination therapy was comparable to the sum of the incidences of this adverse experience reported for the two monotherapies.

Combination therapy with finasteride and doxazosin was associated with no new clinical adverse experience.

Four patients in MTOPS reported the adverse experience breast cancer. Three of these patients were on finasteride only and one was on combination therapy.

The MTOPS Study was not specifically designed to make statistical comparisons between groups for reported adverse experiences. In addition, direct comparisons of safety data between the MTOPS study and previous studies of the single agents may not be appropriate based upon differences in patient population, dosage or dose regimen, and other procedural and study design elements.

Table 2: Incidence ≥2% in One or More Treatment Groups
Drug-Related Clinical Adverse Experiences in MTOPS

Adverse Experience	Placebo (N=737) (%)	Doxazosin 4 mg or 8 mg* (N=756) (%)	Finasteride (N=768) (%)	Combination (N=768) (%)
Body as a whole				
Asthenia	7.1	15.7	5.3	16.8
Headache	2.3	4.1	2.0	2.3

Cardiovascular				
Hypotension	0.7	3.4	1.2	1.5
Postural Hypotension	8.0	16.7	9.1	17.8
Metabolic and Nutritional				
Peripheral Edema	0.9	2.6	1.3	3.3
Nervous				
Dizziness	8.1	17.7	7.4	23.2
Libido Decreased	5.7	7.0	10.0	11.6
Somnolence	1.5	3.7	1.7	3.1
Respiratory				
Dyspnea	0.7	2.1	0.7	1.9
Rhinitis	0.5	1.3	1.0	2.4
Urogenital				
Abnormal Ejaculation	2.3	4.5	7.2	14.1
Gynecomastia	0.7	1.1	2.2	1.5
Impotence	12.2	14.4	18.5	22.6
Sexual Function Abnormal	0.9	2.0	2.5	3.1

*Doxazosin dose was achieved by weekly titration (1 to 2 to 4 to 8 mg). The final tolerated dose (4 mg or 8 mg) was administered at end-Week 4. Only those patients tolerating at least 4 mg were kept on doxazosin. The majority of patients received the 8-mg dose over the duration of the study.

Long-Term Data

High-Grade Prostate Cancer

The reported PCPT trial was a 7-year randomized, double-blind, placebo-controlled trial that enrolled 18,882 men ≥55 years of age with a normal digital rectal examination and a PSA ≤3.0 ng/mL. Men received either FINAST (finasteride 5 mg) or placebo daily. Patients were evaluated annually with PSA and digital rectal exams. Biopsies were performed for elevated PSA, an abnormal digital rectal exam, or the end of study. The incidence of Gleason score 8-10 prostate cancer was higher in men treated with finasteride (1.8%) than in those treated with placebo (1.1%). In a 4-year placebo-controlled clinical trial with another 5α-reductase inhibitor (dutasteride, AVODART), similar results for Gleason score 8-10 prostate cancer were observed (1% dutasteride vs 0.5% placebo).

No clinical benefit has been demonstrated in patients with prostate cancer treated with FINAST.

Breast Cancer

During the reported 4- to 6-year placebo- and comparator-controlled MTOPS study that enrolled 3047 men, there were 4 cases of breast cancer in men treated with finasteride but no cases in men not treated with finasteride. During the 4-year, placebo-controlled PLESS study that enrolled 3040 men, there were 2 cases of breast cancer in placebo-

treated men but no cases in men treated with finasteride. During the 7- year placebo-controlled Prostate Cancer Prevention Trial (PCPT) that enrolled 18,882 men, there was 1 case of breast cancer in men treated with finasteride, and 1 case of breast cancer in men treated with placebo. The relationship between long-term use of finasteride and male breast neoplasia is currently unknown.

Sexual Function

There is no evidence of increased sexual adverse experiences with increased duration of treatment with FINAST. New reports of drug-related sexual adverse experiences decreased with duration of therapy.

Postmarketing Experience

The following additional adverse events have been reported in postmarketing experience with FINAST. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure:

- Hypersensitivity reactions, such as pruritus, urticaria, and angioedema (including swelling of the lips, tongue, throat, and face)

- Testicular pain

- Hematospermia

- Sexual dysfunction that continued after discontinuation of treatment, including erectile dysfunction, decreased libido and ejaculation disorders (e.g. reduced ejaculate volume). These events were reported rarely in men taking FINAST for the treatment of BPH. Most men were older and were taking concomitant medications and/or had co-morbid conditions. The independent role of FINAST in these events is unknown.

- Male infertility and/or poor seminal quality were reported rarely in men taking FINAST for the treatment of BPH. Normalization or improvement of poor seminal quality has been reported after discontinuation of finasteride. The independent role of FINAST in these events is unknown.

- Depression

- Male breast cancer.

The following additional adverse event related to sexual dysfunction that continued after

Discontinuation of treatment has been reported in postmarketing experience with finasteride at lower doses used to treat male pattern baldness. Because the event is reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate its frequency or establish a causal relationship to drug exposure:

- Orgasm disorders

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

4.9 Overdose

Patients have received single doses of FINAST up to 400 mg and multiple doses of FINAST up to 80 mg/day for three months without adverse effects. Until further

experience is obtained, no specific treatment for an overdose with FINAST can be recommended.

Significant lethality was observed in male and female mice at single oral doses of 1500 mg/m2 (500 mg/kg) and in female and male rats at single oral doses of 2360 mg/m2 (400 mg/kg) and 5900 mg/m2 (1000 mg/kg), respectively.

5. Pharmacological properties

5.1 Mechanism of action

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.

5.2 Pharmacodynamics properties

In man, a single 5-mg oral dose of FINAST 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 FINAST 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 FINAST 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 FINAST 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 BPH, FINAST 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 pre-treatment levels, relative to placebo. Intraprostatic content of PSA was also decreased.

In healthy male volunteers treated with FINAST for 14 days, discontinuation of therapy resulted in a return of DHT levels to pre-treatment 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.

5.3 Pharmacokinetic properties

Absorption.

In a reported study of 15 healthy young subjects, the mean bioavailability of finasteride 5-mg tablets was 63% (range 34-108%), based on the ratio of area under the curve (AUC) relative to an intravenous (IV) reference dose. Maximum finasteride plasma concentration averaged 37 ng/mL (range, 27-49 ng/mL) and was reached 1-2 hours post dose. Bioavailability of finasteride was not affected by food**.**

Distribution

Mean steady-state volume of distribution was 76 liters (range, 44-96 liters). Approximately 90% of circulating finasteride is bound to plasma proteins. There is a slow accumulation phase for finasteride after multiple dosing. After dosing with 5 mg/day of finasteride for 17 days, plasma concentrations of finasteride were 47 and 54% higher than after the first dose in men 45-60 years old (n=12) and □70 years old (n=12), respectively. Mean trough concentrations after 17 days of dosing were 6.2 ng/mL (range, 2.4- 9.8 ng/mL) and 8.1 ng/mL (range, 1.8-19.7 ng/mL), respectively, in the two age groups. Although steady state was not reached in this study, mean trough plasma concentration in another study in patients with BPH (mean age, 65 years) receiving 5 mg/day was 9.4 ng/mL (range, 7.1-13.3 ng/mL; n=22) after over a year of dosing.

Finasteride has been shown to cross the blood brain barrier but does not appear to distribute preferentially to the CSF.

In reported 2 studies of healthy subjects (n=69) receiving FINAST 5 mg/day for 6-24 weeks, finasteride concentrations in semen ranged from undetectable (<0.1 ng/mL) to 10.54 ng/mL. In an earlier study using a less sensitive assay, finasteride concentrations in the semen of 16 subjects receiving FINAST 5 mg/day ranged from undetectable (<1.0 ng/mL) to 21 ng/mL. Thus, based on a 5-mL ejaculate volume, the amount of finasteride in semen was estimated to be 50- to 100-fold less than the dose of finasteride (5 □g) 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 5α-reductase inhibitory activity of finasteride.

Excretion

In healthy young subjects (n=15), mean plasma clearance of finasteride was 165 mL/min (range, 70- 279 mL/min) and mean elimination half-life in plasma was 6 hours (range, 3-16 hours). Following an oral dose of 14C-finasteride in man (n=6), a mean of 39% (range, 32-46%) of the dose was excreted in the urine in the form of metabolites; 57% (range, 51-64%) was excreted in the feces.

The mean terminal half-life of finasteride in subjects □70 years of age was approximately 8 hours (range, 6-15 hours; n=12), compared with 6 hours (range, 4-12 hours; n=12) in subjects 45-60 years of age. As a result, mean AUC (0-24 hr) after 17 days of dosing was 15% higher in subjects □70 years of age than in subjects 45-60 years of age (p=0.02).

Table 3: Mean (SD) Pharmacokinetic Parameters in Healthy Young Subjects (n=15)	
	Mean (□ SD)
Bioavailability	63% (34-108%)*
Clearance (mL/min)	165 (55)
Volume of Distribution (L)	76 (14)
Half-Life (hours)	6.2 (2.1)

*Range

Pediatric

Finasteride pharmacokinetics have not been investigated in patients <18 years of age. Finasteride is not indicated for use in pediatric patients.

Gender

Finasteride is not indicated for use in females.

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.

Table 4: Mean (SD) Noncompartmental Pharmacokinetic Parameters after Multiple Doses of 5 mg/day in Older Men		
	Mean (□ SD)	
	45-60 years old (n=12)	**270 years old (n=12)**
AUC (ng•hr/mL)	389 (98)	463 (186)
Peak Concentration (ng/mL)	46.2 (8.7)	48.4 (14.7)
Time to Peak (hours)	1.8 (0.7)	1.8 (0.6)
Half-Life (hours)*	6.0 (1.5) 8.2 (2.5)	8.2 (2.5)

*First-dose values; all other parameters are last-dose values

Race

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

Hepatic Impairment

The effect of hepatic impairment on finasteride pharmacokinetics has not been studied. Caution should be exercised in the administration of FINAST in those patients with liver function abnormalities, as finasteride is metabolized extensively in the liver.

Renal Impairment

No dosage adjustment is necessary in patients with renal impairment. In patients with chronic renal impairment, with creatinine clearances ranging from 9.0 to 55 mL/min, AUC, maximum plasma concentration, half-life, and protein binding after a single dose of 14C-finasteride were similar to values obtained in healthy volunteers. Urinary excretion of metabolites was decreased in patients with renal impairment. This decrease was associated with an increase in fecal excretion of metabolites. Plasma concentrations of metabolites were significantly higher in patients with renal impairment (based on a 60% increase in total radioactivity AUC). However, finasteride has been well tolerated in BPH patients with normal renal function receiving up to 80 mg/day for 12 weeks, where exposure of these patients to metabolites would presumably be much greater.

6. Nonclinical properties

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No evidence of a tumorigenic effect was observed in a 24-month reported study in Sprague-Dawley rats receiving doses of finasteride up to 160 mg/kg/day in males and 320 mg/kg/day in females. These doses produced respective systemic exposure in rats of 111 and 274 times those observed in man receiving the recommended human dose of 5 mg/day. All exposure calculations were based on calculated AUC (0-24 hr) for animals and mean AUC (0-24 hr) for man (0.4 μg•hr/mL).

In a 19-month carcinogenicity reported study in CD-1 mice, a statistically significant ($p \leq 0.05$) increase in the incidence of testicular Leydig cell adenomas was observed at 228 times the human exposure (250 mg/kg/day). In mice at 23 times the human exposure, estimated (25 mg/kg/day) and in rats at 39 times the human exposure (40 mg/kg/day) 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- to 3-fold above control) has been demonstrated in both rodent species treated with high doses of finasteride. No drug-related Leydig cell changes were seen in either rats or dogs treated with finasteride for 1 year at 30 and 350 times (20 mg/kg/day and 45 mg/kg/day, respectively) or in mice treated for 19 months at 2.3 times the human exposure, estimated (2.5 mg/kg/day).

Mutagenesis

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 an in vitro chromosome aberration assay, using Chinese hamster ovary cells, there was a slight increase in chromosome aberrations. These concentrations correspond to 4000-5000 times the peak plasma levels in man given a total dose of 5 mg. In an in vivo chromosome aberration assay in mice, no treatment-related increase in chromosome aberration was observed with finasteride at the maximum tolerated dose of 250 mg/kg/day (228 times the human exposure) as determined in the carcinogenicity studies.

Impairment of Fertility

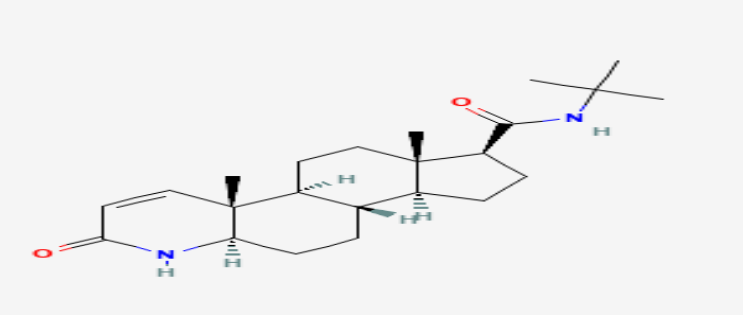
In sexually mature male rabbits treated with finasteride at 543 times the human exposure (80 mg/kg/day) for up to 12 weeks, no effect on fertility, sperm count, or ejaculate volume

was seen. In sexually mature male rats treated with 61 times the human exposure (80 mg/kg/day), there were no significant effects on fertility after 6 or 12 weeks of treatment; however, when treatment was continued for up to 24 or 30 weeks, there was an apparent decrease in fertility, fecundity and an associated significant decrease in the weights of the seminal vesicles and prostate. All these effects were reversible within 6 weeks of discontinuation of treatment. No drug-related effect on testes or on mating performance has been seen in rats or rabbits. This decrease in fertility in finasteride-treated rats is secondary to its effect on accessory sex organs (prostate and seminal vesicles) resulting in failure to form a seminal plug. The seminal plug is essential for normal fertility in rats and is not relevant in man.

7. Description

Finasteride

Finasteride is a 17 /3-(N-tert-butylcarbamoyl)-4-aza-5a-androst-l-en-3-one. Its empirical formula is $C_{23}H_{36}N_2O_2$ and its structural formula is:



Finasteride is a white or almost white, crystalline powder. With a molecular weight of 372.6.

Finast

White coloured, round, biconvex, film coated tablets with FIN debossing on one side, plain surface on other side.

The excipients are Lactose Monohydrate, MCC, Starch -1500 LM Grade Sodium Starch Glycolate, Docusate Sodium, Magnesium Stearate HydroxyPropyl Methylcellulose, Propylene Glycol, Titanium Dioxide, Talc Methylene Chloride, and Isopropyl Alcohol

8. Pharmaceutical particulars

8.1 Incompatibilities

None Stated

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

Available in Blister strip pack of 30 tablets.

8.4 Storage and handing instructions

Store protected from Light & Moisture, at a temperature not exceeding 30°C,

9. Patient Counselling Information

Package leaflet: Information for the user

FINAST

FINASTERIDE TABLETS I.P. 5 MG

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet?

9.1 What FINAST is and what it is used for

FINAST is film coated tablet, contains Finasteride 5mg. and It is use in treatment of benign prostatic hypertrophy only.

9.2 What you need to know before you use FINAST Do not take

- If you are allergic to any of the ingredients of this medicine. Do not take this medicine and talk to your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking FINAST

General

Effects on Prostate Specific Antigen (PSA) and the Use of PSA in Prostate Cancer Detection

In reported studies, FINAST reduced serum PSA concentration by approximately 50% within six months of treatment. This decrease is predictable over the entire range of PSA values in patients with symptomatic BPH, although it may vary in individuals.

For interpretation of serial PSAs in men taking FINAST, a new PSA baseline should be established at least six months after starting treatment and PSA monitored periodically thereafter. Any confirmed 3 increase from the lowest PSA value while on FINAST may signal the presence of prostate cancer and should be evaluated, even if PSA levels are still within the normal range for men not taking a 5α- reductase inhibitor. Non-compliance with FINAST therapy may also affect PSA test results. To interpret an isolated PSA value in patients treated with FINAST for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. These adjustments preserve the utility of PSA to detect prostate cancer in men treated with FINAST.

FINAST may also cause decreases in serum PSA in the presence of prostate cancer. The ratio of free to total PSA (percent free PSA) remains constant even under the influence of FINAST. If clinicians elect to use percent free PSA as an aid in the detection of prostate cancer in men undergoing finasteride therapy, no adjustment to its value appears necessary.

Increased Risk of High-Grade Prostate Cancer

In reported study men aged 55 and over with a normal digital rectal examination and PSA ≤3.0 ng/mL at baseline taking finasteride 5 mg/day in the 7-year Prostate Cancer Prevention Trial (PCPT) had an increased risk of Gleason score 8-10 prostate cancer (finasteride 1.8% vs placebo 1.1%). Similar results were observed in a 4-year placebo-controlled clinical trial with another 5α-reductase inhibitor (dutasteride, AVODART) (1% dutasteride vs 0.5% placebo). 5α- reductase inhibitors may increase the risk of development of high-grade prostate cancer. Whether the effect of 5α-reductase inhibitors to reduce prostate volume, or study-related factors, impacted the results of these studies has not been established.

Exposure of Females — Risk to Male Fetus

FINAST is contraindicated in pregnant females and in females who may potentially be pregnant and not indicated for use in females. Based on animal studies and the mechanism of action, FINAST may cause abnormal development of external genitalia in a male fetus if administered to a pregnant female. Females who are pregnant or may potentially be pregnant should not handle crushed or broken FINAST tablets. FINAST tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed. If a pregnant female comes in contact with crushed or broken FINAST tablets, the contact area should be washed immediately with soap and water.

Pediatric Patients and Females

FINAST is not indicated for use in pediatric patients or females.

Effect on Semen Characteristics

Treatment with FINAST for 24 weeks to evaluate semen parameters in healthy male volunteers revealed no clinically meaningful effects on sperm concentration, mobility, morphology, or pH. A 0.6 mL (22.1%) median decrease in ejaculate volume with a concomitant reduction in total sperm per ejaculate was observed. These parameters remained within the normal range and were reversible upon discontinuation of therapy with an average time to return to baseline of 84 weeks.

Consideration of Other Urological Conditions

Prior to initiating treatment with FINAST, consideration should be given to other urological conditions that may cause similar symptoms. In addition, prostate cancer and BPH may coexist. Patients with large residual urinary volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy. These patients may not be candidates for finasteride therapy.

9.3 How to use FINAST

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much to take and when

The amount of **FINAST** people have to take varies depending on their condition. Your

doctor will tell you exactly how many tablets of **FINAST** to take.

How to take FINAST

Swallow the tablets whole with some water.

How long to take FINAST

Take FINAST every day for as long as your doctor tells you.

Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you take more FINAST than you should

If you take too many FINAST tablets, or if someone else has taken your medicine, talk to your doctor straight away. Medical attention may be needed. If you need to see a doctor or go to the hospital, take the pack with you.

If you forget to take FINAST

If you forget to take a dose of this medicine, take it as soon as you remember. Then take your next dose at the usual time. If it is almost time for your next dose, skip the dose you missed. Do not take a double dose to make up for a forgotten tablet.

If you stop taking FINAST

Do not stop taking FINAST unless your doctor tells you to. If you have questions about how long to take this medicine, talk to your doctor.

9.4 Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects may happen with this medicine:

- Hypersensitivity reactions, such as pruritus, urticaria, and angioedema (including swelling of the lips, tongue, throat, and face)

- Testicular pain

- Hematospermia

- Sexual dysfunction

That continued after discontinuation of treatment, including erectile dysfunction, decreased libido and ejaculation disorders (e.g. reduced ejaculate volume).

- Breast Enlargement
- Breast Tenderness
- Asthenia
- Headache
- Hypotension
- Postural Hypotension
- Peripheral Edema
- Dizziness
- Depression
- Somnolence

- Dyspnea
- Rhinitis
- Gynecomastia
- Sexual Function Abnormal
- Male breast cancer
- Orgasm disorders.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

9.5 How to store FINAST

Store protected from Light & Moisture, at a temperature not exceeding 30°C.

9.6 Contents of the pack and other information

FINAST contain: Lactose Monohydrate, MCC, Starch -1500 LM Grade Sodium Starch Glycolate, Docusate Sodium, Magnesium Stearate HydroxyPropyl ethyl Cellulose, Propylene Glycol, Titanium Dioxide, Talc Methylene Chloride, Isopropyl Alcohol

FINAST Available in Blister strip pack of 30 tablets.

10 Details of manufacturer

TORRENT PHARMACEUITICAL PVT.LTD.

At: plot no. 16, vardhman industrial estate.

Village bahadarpur Saini NH-58, haridwar-247667,

Uttarakhand.

11 Details of permission or licence number with date

Mfg Lic No.: 24//UA/LL/2022 issued on 05.08.2021

12 Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/FINAST/JUNE-2022/01/PI