AUSTRALIAN PRODUCT INFORMATION – FINASTERIDE VIATRIS 1 (finasteride) film-coated tablet

1 NAME OF THE MEDICINE

Finasteride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

FINASTERIDE VIATRIS 1 film-coated tablets contain 1 mg of finasteride.

List of excipients with known effects: lactose monohydrate.

For the full list of excipients, see **Section 6.1 List of Excipients**.

3 PHARMACEUTICAL FORM

FINASTERIDE VIATRIS 1 film-coated tablets are reddish-brown, round, biconvex, film-coated tablet, marked 'F1' on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

FINASTERIDE VIATRIS 1 is indicated for the treatment of male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss in men 18 years or older. Efficacy has not been demonstrated in men over the age of 41 years.

FINASTERIDE VIATRIS 1 is not indicated for use in women (see **Section 4.6 Fertility, Pregnancy and Lactation – Use in Pregnancy** and **Section 5.1 Pharmacodynamic Properties – Clinical Trials**) or children.

4.2 Dose and Method of Administration

The recommended dosage is one 1 mg tablet daily. FINASTERIDE VIATRIS 1 may be taken with or without food.

In general, daily use for 3 months or more is necessary before increased hair growth and/or prevention of further hair loss is observed. Continued use is recommended to obtain maximum benefit.

4.3 Contraindications

FINASTERIDE VIATRIS 1 is contraindicated in the following:

- Use in women when they are or may potentially be pregnant (see **Section 4.6 Fertility, Pregnancy and Lactation – Use in Pregnancy).**
- Hypersensitivity to any component of this product.

FINASTERIDE VIATRIS 1 is not indicated for use in women or children.

4.4 Special Warnings and Precautions for Use

In clinical studies with finasteride in men 18-41 years of age, the mean value of serum prostate-specific antigen (PSA) decreased from 0.7 ng/mL at baseline to 0.5 ng/mL at month 12. When finasteride is used for treatment of male pattern hair loss in older men who also have benign prostatic hyperplasia (BPH), consideration should be given to the fact that, in older men with BPH, PSA levels are decreased by approximately 50%.

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 (5 times the dose of FINASTERIDE VIATRIS 1) 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%) [See **Section 4.8 Adverse Effects (Undesirable Effects)**]. Similar results were observed in a 4-year placebo-controlled clinical trial with another 5α-reductase inhibitor (dutasteride). 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.

Use in renal impairment

See **Section 5.2 Pharmacokinetic Properties, Renal impairment.**

Use in the Elderly

Clinical studies with FINASTERIDE VIATRIS 1 have not been conducted in elderly men with male pattern hair loss.

Paediatric Use

FINASTERIDE VIATRIS 1 is not indicated for use in children.

Effects on Laboratory Tests

When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels decrease in patients treated with finasteride 1mg. For clinical interpretation (see Section 4.4 Special Warnings and Precautions for Use).

4.5 Interactions with Other Medicines and Other Forms of Interactions

No druginteractions of clinical importance have been identified. Compounds that have been tested in man have included antipyrine, digoxin, glyburide, propranolol, theophylline, and warfarin and no interactions were found. Increases in P450 drug-metabolising activity were observed in animal studies (in rats, mice and dogs) receiving doses of > 80, 250 and 45 mg/kg/day respectively. Finasteride is metabolised primarily via, but does not affect, the cytochrome P450 3A4 system.
Although the risk for finasteride to affect the pharmacokinetics of other drugs is estimated to be small, it is probable that inhibitors and inducers of cytochrome P450 3A4 will affect the plasma concentration of finasteride. However, based on established safety margins, any increase due to concomitant use of such inhibitors is unlikely to be of clinical significance.

Although specific interaction studies were not performed, in clinical studies finasteride doses of 1 mg or more were used concomitantly with ACE inhibitors, paracetamol, alpha blockers, benzodiazepines, beta blockers, calcium-channel blockers, cardiac nitrates, diuretics, H_2 antagonists, HMG-CoA reductase

inhibitors, prostaglandin synthetase inhibitors (NSAIDs), and quinolones, without evidence of clinically significant adverse interactions.

4.6 Fertility, Pregnancy and Lactation

Effects on Fertility

Oral treatment of male rabbits with finasteride up to 80 mg/kg/day (estimated exposure more than 4,000 times that in humans at the recommended dose) did not impair fertility. In male rats, oral treatment for up to 24 or 30 weeks with 80 mg/kg/day (estimated exposure approximately 440 times that in humans at the recommended dose) resulted in an apparent decrease in fertility associated with a significant decrease in weight of seminal vesicles and prostate. All of these effects were reversible within 6 weeks of discontinuation of treatment. This decrease in fertility in rats was secondary to the effect of finasteride on the accessory sex organs, resulting in failure to form a seminal plug, which is essential for fertility in rats, but is not relevant to man.

Use in Pregnancy

Category X

Drugs which have such a high risk of causing permanent damage to the foetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

FINASTERIDE VIATRIS 1 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 DHT in some tissues, these drugs, including finasteride, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

Women who are or may potentially be pregnant should not handle crushed or broken tablets of FINASTERIDE VIATRIS 1, or handle tablets with wet hands, because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus. Whole tablets are coated to prevent contact with the active ingredient during normal handling.

Developmental Studies

Hypospadias was observed in the male offspring of pregnant rats given finasteride at oral doses ranging from 100 µg/kg/day to 100 mg/kg/day (≥5 times the recommended human dose) at an incidence of 3.6 to 100%. Additionally, pregnant rats produced male offspring with decreased prostatic and seminal vesicular weights, delayed preputial separation, and transient nipple development when given finasteride at oral doses ≥30 µg/kg/day (≥1.5 times the recommended human dose), and decreased anogenital distance when given finasteride in oral doses ≥3 µg/kg/day (approximately one-fifth the recommended human dose). The critical period during which these effects can be induced has been defined in male rats as Days 16-17 of gestation.

The changes described above are expected pharmacological effects of Type II 5α-reductase inhibitors. Many of the changes, such as hypospadias, observed in male rats exposed in utero to finasteride are similar to those reported in male infants with a genetic deficiency of Type II 5α-reductase.

No effects were seen in female offspring exposed in utero to any dose of finasteride.

Administration of finasteride to rats during the late gestation and lactation period resulted in slightly decreased fertility in first generation male offspring (3 mg/kg/day). No developmental abnormalities have been observed in first generation male or female offspring resulting from mating finasteride-treated male rats (80 mg/kg/day) with untreated females.

No evidence of malformations has been observed in rabbit foetuses exposed to finasteride *in utero* from Days 6-18 of gestation at doses up to 100 mg/kg/day.

The *in utero* effects of finasteride exposure during the period of embryonic and foetal development were evaluated in the rhesus monkey (Gestation Days 20-100), a species more predictive of human development than rats or rabbits. Intravenous administration of finasteride to pregnant monkeys at doses up to 800 ng/day (at least 750 times the highest estimated amount, on a bodyweight basis, of finasteride in semen to which a pregnant woman might be exposed) resulted in no abnormalities in male foetuses. In confirmation of the relevance of the rhesus model for human foetal development, oral administration of a very high dose of finasteride (2 mg/kg/day; 100 times the recommended human dose or approximately 12 million times the highest estimated amount, on a bodyweight basis, of finasteride in semen to which a pregnant woman might be exposed) to pregnant monkeys resulted in external genital abnormalities in male foetuses. No other abnormalities were observed in male foetuses and no finasteride-related abnormalities were observed in female foetuses at any dose.

Use in Lactation

FINASTERIDE VIATRIS 1 is not indicated for use in women and should not be used by lactating women. It is not known whether finasteride is excreted in human milk.

4.7 Effects on Ability to Drive and Use Machines

The effects of this medicine on a person's ability to use and drive machinery were not assessed as part of its registration.

4.8 Adverse Effects (Undesirable Effects)

FINASTERIDE VIATRIS 1 is generally well tolerated. Side effects, which usually have been mild, generally have not required discontinuation of therapy.

Clinical Trial Data

Finasteride for male pattern hair loss has been evaluated for safety in clinical studies involving more than 3,200 men. In three 12-month, placebo-controlled, double-blind, multicentre studies of comparable design, the overall safety profiles of finasteride and placebo were similar.

Discontinuation of therapy due to any clinical adverse experience occurred in 1.7% of 945 men treated with finasteride and 2.1% of 934 men treated with placebo.

Table 1 presents the only clinical adverse reactions considered possibly, probably or definitely drug-related by the investigator, for which the incidence on finasteride was ≥ 1% and greater than placebo over the 12 months of the study.

Table 1: Drug-Related Adverse Reactions

	Treatment	Year 1 (%)
Decreased Libido	Placebo	1.3
	Finasteride	1.8
Erectile Dysfunction	Placebo	0.7
	Finasteride	1.3

In addition, in the 12-month controlled studies, decreased volume of ejaculate was reported in 0.8% of men treated with finasteride and 0.4% of men treated with placebo. Resolution of these side effects occurred in men who discontinued therapy with finasteride and in many who continued therapy. In a separate study, the effect of finasteride on ejaculate volume was measured and was not different from that seen with placebo.

The incidence of each of the above side effects decreased to ≤ 0.3% by the fifth year of treatment with finasteride.

Table 2 presents the other most common clinical adverse experiences reported in the initial 12-month phase III clinical studies occurring in ≥ 2% of men treated with finasteride or placebo. A causal relationship to treatment with finasteride has not been established.

Table 2: Other Adverse Experiences Incidence ≥ 2% in any Treatment Group Without Regard to Causality Phase III Controlled Studies

	Finasteride 1 mg (N = 945)	Placebo (N = 934)
Body as a Whole		
Trauma	17 (1.8)	21 (2.2)
Musculoskeletal Disorders		
Pain, back	24 (2.5)	23 (2.5)
Nervous System and Psychiatric Disorders		
Headache	114 (12.1)	96 (10.3)
Respiratory System Disorders		
Bronchitis	26 (2.8)	21 (2.2)
Infection, respiratory upper	139 (14.7)	145 (15.5)
Influenza	70 (7.4)	72 (7.7)
Pharyngitis	45 (4.8)	34 (3.6)
Sinusitis	36 (3.8)	26 (2.8)

Breast Cancer

Finasteride has also been studied in men with prostate disease at 5 times the dosage recommended for the treatment of male pattern hair loss. During the 4-to-6-year placebo and comparator-controlled Medical Therapy of Prostatic Symptoms (MTOPS) study that enrolled 3047 men, there were 4 cases of breast cancer in men treated with finasteride 5 mg, but no cases in men not treated with finasteride 5 mg. 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 5 mg. 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. There have been post-marketing reports of male breast cancer with the use of finasteride 1 mg and 5 mg. The relationship between long-term use of finasteride and male breast neoplasia is currently unknown.

Long-term studies with finasteride 5 mg

The PCPT trial was a 7-year randomised, 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 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), similar results for Gleason score 8-10 prostate cancer were observed. The clinical significance of these findings with respect to use of finasteride 1 by men is unknown.
No clinical benefit has been demonstrated in patients with prostate cancer treated with finasteride.

Post-Marketing Experience

The following additional adverse experiences have been reported in post-marketing use. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or established a casual relationship to drug exposure.

Immune system disorders: hypersensitivity reactions such as rash, pruritus, urticaria, and angioedema (including swelling of the lips, tongue, throat and face).

Psychiatric disorders: depression; decreased libido that continued after discontinuation of treatment; suicidal ideation.

Reproductive system and breast disorders: sexual dysfunction (erectile dysfunction and ejaculation disorders) that continued after discontinuation of treatment; breast tenderness and enlargement; male breast cancer; testicular pain; haematospermia; male infertility and/or poor seminal quality. Normalisation or improvement of seminal quality has been reported after discontinuation of finasteride.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

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 side effects.

No specific treatment for overdosage with FINASTERIDE VIATRIS 1 is recommended.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Mechanism of Action

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). Finasteride has no affinity for the androgen receptor and has no androgenic, antiandrogenic, oestrogenic, antioestrogenic, or progestational effects. Inhibition of this enzyme blocks the peripheral conversion of testosterone to the androgen dihydrotestosterone (DHT), resulting in significant decreases in serum and tissue DHT concentrations. Finasteride produces a rapid reduction in serum DHT concentration, reaching significant suppression within 24 hours of dosing.

Hair follicles contain Type II 5α-reductase. In men with male pattern hair loss, the balding scalp contains miniaturised hair follicles and increased amounts of DHT. Administration of finasteride decreases scalp and serum DHT concentrations in these men. In addition, men with a genetic deficiency of Type II 5α-reductase do not suffer from male pattern hair loss. These data and the results of the clinical studies confirm that finasteride inhibits the process responsible for miniaturisation of the scalp hair follicles, leading to reversal of the balding process.

Pharmacodynamics

Finasteride had no effect on circulating levels of cortisol, oestradiol, prolactin, thyroid-stimulating hormone, or thyroxine, nor did it affect the plasma lipid profile (eg. total cholesterol, low density lipoproteins, high density lipoproteins, and triglycerides) or bone mineral density. In studies with finasteride, no clinically meaningful changes in luteinising hormone (LH) and follicle-stimulating hormone (FSH) were detected. Gonadotropin-releasing hormone (GnRH) stimulated levels of LH or FSH were not altered, indicating that regulatory control of the hypothalamic-pituitary-testicular axis was not affected. There was no effect on semen parameters in men treated with finasteride 1 mg/day for 48 weeks.

Finasteride appeared to inhibit both C19 and C21 steroid metabolism and hence appeared to have an inhibitory effect on both hepatic and peripheral Type II 5α-reductase activity. The serum DHT metabolites androstenediol glucuronide and androsterone glucuronide were also significantly reduced. This metabolic pattern is similar to that observed in individuals with a genetic deficiency of Type II 5α-reductase who have markedly decreased levels of DHT and who do not suffer from male pattern hair loss.

Clinical Trials

Studies in Men

The efficacy of finasteride was demo nstrated in men (88% Caucasian) with mild to moderate androgenetic alopecia (male pattern hair loss) between 18 and 41 years of age. There were three double-blind, randomised, placebo-controlled studies of 12-month duration. The two primary endpoints were hair count and patient self-assessment; the two secondary endpoints were investigator assessment and ratings of photographs. The three studies were conducted in 1,879 men with mild to moderate, but not complete, hair loss. Two of the studies enrolled men with predominantly mild to moderate vertex hair loss (n = 1,553). The third enrolled men having mild to moderate hair loss in the anterior mid-scalp area with or without vertex balding (n = 326).

Two Studies on Vertex Baldness

Of the men who completed the first 12 months of the two vertex baldness trials, 1,215 elected to continue in double-blind, placebo-controlled, 12-month extension studies. There were 547 men receiving finasteride for both the initial study and first extension periods (up to 2 years of treatment) and 60 men receiving placebo for the same periods. The extension studies were continued for 3 additional years, with 323 men on finasteride and 23 on placebo entering the fifth year of the study.

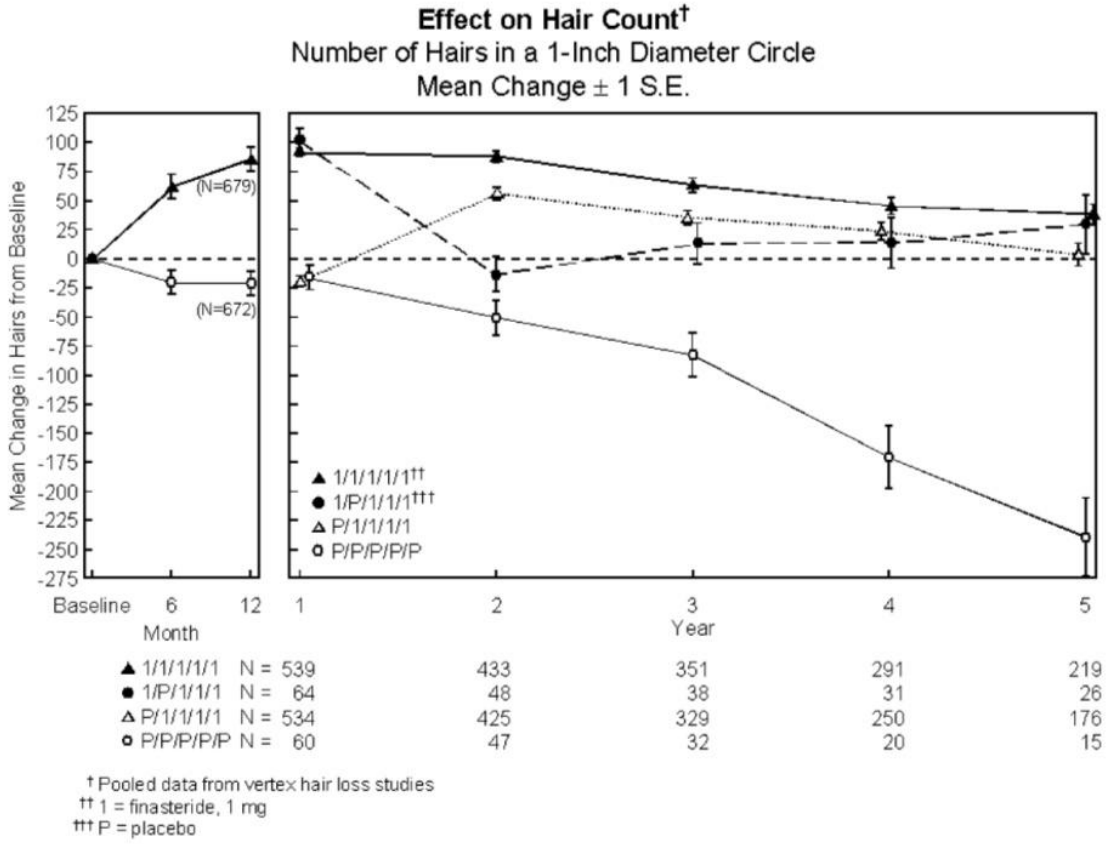
In order to evaluate the effect of discontinuation of therapy, there were 65 men who received finasteride for the initial 12 months followed by placebo in the first 12-month extension period. Some of these men continued in additional extension studies and were switched back to treatment with finasteride, with 32 men entering the fifth year of the study. Lastly, there were 543 men who received placebo for the initial 12 months followed by finasteride in the first 12-month extension period. Some of these men continued in additional extension studies receiving finasteride, with 290 men entering the fifth year of the study (see **Figure** below).

Hair counts were assessed by photographic enlargements of a representative area of active hair loss. In these two studies in men with vertex baldness, significant increases in hair count were demonstrated at 6 and 12 months in men treated with finasteride, while significant hair loss from baseline was demonstrated in those treated with placebo. At 12 months, there was a 107-hair difference from placebo ($p < 0.001$, finasteride [n = 679 evaluable men] vs placebo [n = 672 evaluable men]) within a 1-inch diameter circle (5.1 cm^2). Hair count was maintained in those men taking finasteride for up to 2 years resulting in a 138-hair difference between treatment groups ($p < 0.001$, finasteride [n = 433 evaluable men] vs placebo [n = 47 evaluable men]) within the same area. In men treated with finasteride, the maximum improvement in hair count compared to baseline was achieved during the first two years, and hair count was maintained above baseline throughout the 5 years of the studies. The difference between treatment groups also continued to increase throughout the studies, resulting in a 277-hair difference ($p < 0.001$, finasteride [n = 219 evaluable men] vs placebo [n = 15 evaluable men]) at 5 years. Thus, compared to baseline, hair loss did not progress further in the majority of men treated with finasteride; in contrast, hair loss progressively worsened in all men in the placebo group (see **Figure** below).

Patients who switched from placebo to finasteride (n = 426 evaluable men) had a decrease in hair count at the end of the initial 12-month placebo period, followed by an increase in hair count after 1 year of treatment with finasteride. This increase in hair count was less (56 hairs above original baseline) than the increase (91 hairs above original baseline) observed after 1 year of treatment in men initially randomised to finasteride. Although the increase in hair count, relative to when therapy was initiated, was comparable between these two groups, a higher absolute hair count was achieved in patients who were started on treatment with finasteride in the initial study. This advantage was maintained throughout the 5 years of the studies. A change of treatment from finasteride 1 mg tablets to placebo (n = 48 evaluable men) at the end of the initial 12 months resulted in reversal of the increase in hair count 12 months later, at 24 months (see **Figure -1** below).

At 12 months, 58% of men in the placebo group had further hair loss (defined as any decrease in hair count from baseline) compared with 14% of men treated with finasteride. In men treated for up to 2 years, 72% of men in the placebo group demonstrated hair loss, compared with 17% of men treated with finasteride 1 mg tablets. At 5 years, 100% of men in the placebo group demonstrated hair loss, compared with only 35% of men treated with finasteride.

Figure -1



Patient self-assessment was obtained at each clinic visit from a self-administered questionnaire, which included questions on their perception of hair growth, hair loss, and appearance. This self-assessment demonstrated an increase in amount of hair, a decrease in hair loss, and improvement in appearance in men treated with finasteride. Overall improvement compared with placebo was seen as early as 3 months ($p < 0.05$), with continued improvement over 5 years.

Investigator assessment was based on a 7-point scale evaluating increases or decreases in scalp hair at each patient visit. This assessment showed significantly greater increases in hair growth in men treated with finasteride compared with placebo as early as 3 months ($p < 0.001$). At 12 months, the investigators rated 65% of men treated with finasteride as having increased hair growth compared with 37% in the placebo group. At 2 years, the investigators rated 80% of men treated with finasteride 1 mg tablets as having increased hair growth compared with 47% of men treated with placebo. At 5 years, the investigators rated 77% of men treated with finasteride as having increased hair growth, compared with 15% of men treated in the placebo group.

An independent panel rated standardised photographs of the head in a blinded fashion based on increases or decreases in scalp hair, using the same 7-point scale as the investigator assessment. At 12 months, 48% of men treated with finasteride had an increase as compared with 7% of men treated with placebo. At 2 years, an increase in hair growth was demonstrated in 66% of men treated with finasteride compared with 7% of men treated with placebo. At 5 years, an increase in hair growth was demonstrated in 48% of men treated with finasteride compared with 6% of men treated with placebo. Based on this assessment, 10% of men treated with finasteride for 5 years were rated as having lost hair, compared with 75% of men in the placebo group. These results demonstrate that 90% of the men treated with finasteride had no further visible progression of hair loss, compared with 25% of men treated with placebo, based on ratings of either no change or increased hair growth.

In one of the two vertex baldness studies, patients were questioned on non-scalp body hair growth. Finasteride did not appear to affect non-scalp body hair.

Study on Hair Loss in the Anterior Mid-Scalp Area

A study of 12-month duration, designed to assess the efficacy of finasteride in men with hair loss in the anterior mid-scalp area, also demonstrated significant increases in hair count compared with placebo. Increases in hair count were accompanied by improvements in patient self-assessment, investigator assessment, and ratings based on standardised photographs. Hair counts were obtained in the anterior mid-scalp area, and did not include the area of bitemporal recession or the anterior hairline.

Phototrichogram Study

A 48-week, placebo-controlled study designed to assess the effect of finasteride on the phases of the hair-growth cycle (growing phase [anagen] and resting phase [telogen]) in vertex baldness enrolled 212 men with androgenetic alopecia. At baseline and 48 weeks, total, telogen, and anagen hair counts were obtained in a 1 cm^2 target area of the scalp. Treatment with finasteride led to improvements in anagen hair counts, while men in the placebo group lost anagen hair. At 48 weeks, men treated with finasteride showed net increases in total and anagen hair counts of 17 hairs ($p < 0.001$) and 27 hairs ($p < 0.001$), respectively, compared to placebo. This increase in anagen hair count, compared to total hair count, led to a net improvement in the anagen-to-telogen ratio of 47% ($p < 0.001$) at 48 weeks for men treated with finasteride, compared to placebo.

Summary of Clinical Studies

Clinical studies were conducted in men aged 18 to 41 with mild to moderate degrees of androgenetic alopecia. Clinical improvement was seen as early as 3 months in the patients treated with finasteride and led to a net increase in scalp hair count and hair regrowth. In clinical studies for up to 5 years, treatment with finasteride prevented the further progression of hair loss observed in the placebo group. In general, the difference between treatment groups continued to increase throughout the 5 years of the studies. There were no studies comparing finasteride with other medicines for androgenetic alopecia.

Ethnic Analysis of Clinical Data

In a combined analysis of the two studies on vertex baldness, mean hair count changes from baseline were 91 vs -19 hairs (finasteride vs placebo) among Caucasians (n = 1,185), 49 vs -27 hairs among North American blacks (n = 84), 53 vs -38 hairs among Asians (n = 17), 67 vs 5 hairs among North American Hispanics (n = 45) and 67 vs -15 hairs among other ethnic groups (n = 20). Patient self-assessment showed improvement across racial groups with finasteride treatment, except for satisfaction of the frontal hairline and vertex in North American black men, who were satisfied overall.

A sexual function questionnaire was self-administered by patients participating in the two vertex baldness trials to detect more subtle changes in sexual function. At Month 12, statistically significant differences in favour of placebo were found in 3 of 4 domains (sexual interest, erections, and perception of sexual problems). However, no significant difference was seen in the question on overall satisfaction with sex life.

Studies in Women

Lack of efficacy was demonstrated in postmenopausal women with androgenetic alopecia who were treated with finasteride in a 12-month, placebo-controlled study (n = 137). These women showed no

improvement in hair count, patient self-assessment, investigator assessment, or ratings based on standardised photographs, compared with the placebo group (see **Section 4.1 Therapeutic Indications).**

5.2 Pharmacokinetic Properties

Absorption

Relative to an intravenous reference dose, the oral bioavailability of finasteride is approximately 80%. The bioavailability is not affected by food. Maximum finasteride plasma concentrations are reached approximately two hours after dosing and the absorption is complete after 6-8 hours.

Distribution

Protein binding is approximately 93%. The volume of distribution of finasteride is approximately 76 litres.

There is a modest accumulation of finasteride in plasma after multiple dosing. At steady state following dosing with 1 mg/day, maximum finasteride plasma concentration averaged 9.2 ng/mL and was reached 1 to 2 hours post-dose; $AUC_{(0\text{-}24\ hr)}$ was 53 ng.hr/mL.

Finasteride has been recovered in the cerebrospinal fluid (CSF) but the drug does not appear to concentrate preferentially to the CSF. A very small amount of finasteride has also been detected in the seminal fluid of subjects receiving finasteride.

Metabolism

Finasteride is metabolised primarily via the cytochrome P450 3A4 enzyme subfamily. Following an oral dose of ^{14}C-finasteride in man, two metabolites of finasteride were identified that possess only a small fraction of the 5α-reductase inhibitory activity of finasteride.

Excretion

Following an oral dose of ^{14}C-finasteride in man, 39% of the dose was excreted in the urine in the form of metabolites (virtually no unchanged drug was excreted in the urine) and 57% of total dose was excreted in the faeces.

Plasma Clearance is approximately 165 mL/min.

The elimination rate of finasteride decreases somewhat with age. 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. These findings are of no clinical significance and hence, a reduction in dosage in the elderly is not warranted.

Renal Impairment

In patients with chronic renal impairment whose creatinine clearance ranged from 9 to 55 mL/min, the disposition of a single dose of ^{14}C-finasteride was not different from that in healthy volunteers. Protein binding also did not differ in patients with renal impairment. A portion of the metabolites that normally is excreted renally was excreted in the faeces. It therefore appears that faecal excretion increases commensurate to the decrease in urinary excretion of metabolites. No adjustment in dosage is necessary in non-dialysed patients with renal impairment.

An open label, balanced, randomised, two-treatment, two-period, two-sequence, single dose, two-way crossover, comparative oral bioavailability study of two formulations of finasteride 5 mg film-coated tablets was conducted in 30 healthy adult human male subject under fasting condition. The study compared finasteride 5 mg film-coated tablets with reference product Proscar® 5 mg tablets.

Statistical comparisons of geometric means for Test vs Reference for finasteride C_{max} and $AUC_{0-\infty}$ were as follows:

Parameters (units)	**Geometric Least Squares Mean**			**90% Confidence Interval (Parametric)**
	Test Product B	Reference Product A	Ratio B/A%	
C_{max} (ng/mL)	52.717	47.293	111.5	106.28-116.91%
$AUC_{0-\infty}$ (ng.h/mL)	427.803	395.307	108.2	101.48-115.41%

This comparison of test product with reference product finasteride met the predefined criteria for bioequivalence, as the calculated 90% CI for all ratios of pre-specified In-Transformed PK parameters fell within the range 80.00%-125.00%.

5.3 Preclinical Safety Data

Genotoxicity

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, when Chinese hamster ovary cells were treated with high concentrations (450-550 µmol) of finasteride, there was a slight increase in chromosome aberrations. These concentrations are in excess of the peak plasma concentrations in men given a total dose of 1 mg and are not achievable in a biological system. In an *in vivo* chromosome aberration assay in mice, no treatment-related increases in chromosome aberration were observed with finasteride at the maximum tolerated dose.

Carcinogenicity

In a 24-month carcinogenicity study in rats there was an increase in the incidence of thyroid follicular adenomas in male rats receiving 160 mg/kg/day finasteride (statistically significant trend test). This oral dose produced an exposure in rats of more than 800 times that observed in humans at the recommended dose (based on $AUC_{(0\text{-}24\ hrs)}$ values). The effect of finasteride on the thyroid in rats appears to be due to an increased rate of thyroxine clearance and not a direct effect of the drug. These observations seen in the rat are thought not relevant to man.

In a 19-month carcinogenicity study in mice, a statistically significant increase in the incidence of testicular Leydig cell adenoma was observed at an oral dose of 250 mg/kg/day (estimated exposure of more than 1,700 times that observed in humans at the recommended dose); no adenomas were seen in mice given 2.5 or 25 mg/kg/day.

In mice at an oral dose of 25 mg/kg/day (estimated exposure about 90 times that in humans at the recommended dose) and in rats at an oral dose of ≥ 40 mg/kg/day, (estimated exposure about 300 times that in humans at the recommended dose) an increase in the incidence of Leydig cell hyperplasia was observed. A positive correlation between the proliferative changes of the Leydig cells and the increase in serum luteinising hormone (LH) levels (2-3 fold above control) has been demonstrated in both rodent species treated with high doses of finasteride. This suggests the Leydig cell changes are secondary to elevated serum LH levels and not due to a direct effect of finasteride.

No drug-related Leydig cell changes were seen in either rats or dogs treated with finasteride for one year at respective oral doses of 20 mg/kg/day (estimated exposure more than 220 times that in humans at the recommended dose) and 45 mg/kg/day (estimated exposure more than 2,600 times that in humans at the recommended dose) or in mice treated for 19 months at an oral dose of 2.5 mg/kg/day (estimated exposure about 9 times that in humans at the recommended dose).

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

The tablets contain lactose monohydrate, microcrystalline cellulose, pregelatinised maize starch, lauroyl macrogolglycerides, sodium starch glycollate type A, magnesium stearate and OPADRY complete film coating system 03F34739 PINK (PI 12855).

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf Life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 25 ^{o}C.

6.5 Nature and Contents of Container

They are available in packs containing 28 tablets in Al/Al foil blisters.

Australian Registration Numbers

FINASTERIDE VIATRIS 1 mg film-coated tablets: AUST R 330151

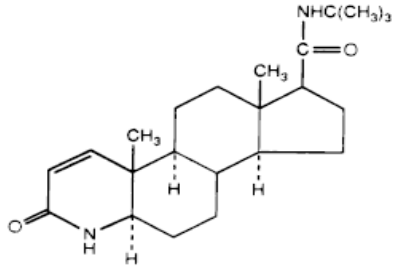
6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical Properties

Finasteride is a white, crystalline solid with a molecular weight of 372.55. It is freely soluble in chloroform and in lower alcohol solvents but is practically insoluble in water.

Chemical Structure



Chemical Name: N-(1,1-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide
Molecular Formula: $C_{23}H_{36}N_2O_2$
Molecular Weight: 372.55

CAS Number

98319-26-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 - Prescription Only Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

May 4, 2020

10 DATE OF REVISION

December 23, 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of New Information
All	MEC in line with innovator's PI of January 2025
4.4	Addition of "Increased risk of high-grade prostate cancer – PSA" in line with innovator's PI of January 2025
4.7	Update in line with innovator's PI of January 2025
4.8	Addition of "Breast Cancer" and "Long-term studies with Finasteride 5 mg – PSA". Update post marketing experience both in line with innovator's PI of January 2025