

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Finasteride 1 mg film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 1 mg of finasteride.

Excipient(s) with known effect:

Each film-coated tablet contains 90.77 mg lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Round biconvex, reddish brown tablets 7mm in diameter, marked "F1

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride is indicated for the treatment of the early stages of androgenetic alopecia in men. Finasteride stabilises the process of androgenic alopecia in men 18–41 years of age. Efficacy in bitemporal recession and end-stage hair loss has not been established.

Finasteride is **not** indicated for use in women or children and adolescents.

4.2 Posology and method of administration

Posology

The recommended dose is 1 mg daily. Finasteride may be taken with or without food.

There is no evidence that an increase in dose will result in increased efficacy. Efficacy and duration of treatment should continuously be assessed by the treating physician. Generally, three to six months of once daily treatment are

required before evidence of stabilisation of hair loss can be expected. Continuous use is recommended to sustain benefit. If treatment is stopped, the beneficial effects begin to reverse by six months and return to baseline by 9 to 12 months.

Renal impairment

No adjustment in dose is required in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 ml/min), as pharmacokinetic studies did not indicate any change in the disposition of finasteride.

Hepatic impairment

There are no data available in patients with hepatic insufficiency (see section 4.4).

Paediatric population

Finasteride should not be used in children. There are no data demonstrating efficacy or safety of finasteride in children under the age of 18.

Method of administration

For oral use only.

The tablet should be swallowed whole and must not be divided or crushed (see section 6.6).

Crushed or broken tablets of Finasteride should not be handled by women when they are or may potentially be pregnant because of the possibility of absorption of finasteride and subsequent potential risk to a male foetus (see section 4.6). Finasteride tablets are coated and will prevent contact with the active substance during normal handling, provided that the tablets are not broken or crushed.

4.3 Contraindications

Contraindicated for use in women (see sections 4.6 and 5.1) and in patients with hypersensitivity to finasteride or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Paediatric population

Finasteride should not be used in children. There are no data demonstrating efficacy or safety of finasteride in children under the age of 18.

Effects on prostate-specific antigen (PSA)

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. Doubling the PSA level in men taking finasteride should be considered before evaluating this test result.

Effect on fertility

See section 4.6

Breast cancer

Breast cancer has been reported in men taking finasteride 1 mg during the post-marketing period. Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynecomastia or nipple discharge.

Hepatic impairment

The effect of hepatic insufficiency on the pharmacokinetics of finasteride has not been studied.

Mood alterations and depression

Mood alterations including depressed mood, depression and, less frequently, suicidal ideation have been reported in patients treated with finasteride 1 mg. Patients should be monitored for psychiatric symptoms and if these occur, treatment with finasteride should be discontinued and the patient advised to seek medical advice.

Finasteride contains lactose and sodium

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

This medicinal product contains less than 1 mmol (23 mg) sodium per film-coated tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Finasteride is metabolized 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.

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Finasteride is contraindicated for use in women due to the risk in pregnancy. Because of the ability of finasteride to inhibit conversion of testosterone to dihydrotestosterone (DHT) finasteride may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman (see section 6.6).

Breast-feeding

It is not known whether finasteride is excreted in human milk.

Fertility

Long-term data on fertility in humans are lacking, and specific studies in subfertile men have not been conducted. The male patients who were planning to father a child were initially excluded from clinical trials. Although, animal studies did not show relevant negative effects on fertility, spontaneous reports of infertility and /or poor seminal quality were received post-marketing. In some of these reports, patients had other risk factors that might have contributed to infertility. Normalisation or improvement of seminal quality has been reported after discontinuation of finasteride.

4.7 Effects on ability to drive and use machines

Finasteride has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The adverse reactions during clinical trials and/or post-marketing use are listed in the table below.

Frequency of adverse reactions is determined as follows:

Very Common ($\geq 1/10$);

Common ($\geq 1/100$ to $< 1/10$);

Uncommon ($\geq 1/1,000$ to $< 1/100$);

Rare ($\geq 1/10,000$ to $1/1,000$);

Very rare ($< 1/10,000$);

Not known (frequency cannot be estimated from the available data).

The frequency of adverse reactions reported during post-marketing use cannot be determined as they are derived from spontaneous reports.

Table 1. Frequency of adverse reactions

Immune system disorders	Not known: Hypersensitivity reactions, including rash, pruritus, urticaria and angioedema (including swelling of the lips, tongue, throat and face).
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Psychiatric disorders	Uncommon*: Decreased libido. Uncommon: Depression [†] . Not known: Anxiety
Cardiac disorders	Not known: Palpitation
Hepatobiliary disorders	Not known: Increased hepatic enzymes.
Reproductive system and breast disorders	Uncommon*: Erectile dysfunction, ejaculation disorder (including decreased volume of ejaculate). Not known: Breast tenderness and enlargement, testicular pain, infertility**. **See section 4.4.

12. *Incidences presented as difference from placebo in clinical studies at Month

† This adverse reaction was identified through post-marketing surveillance but the incidence in randomized controlled Phase III clinical trials (Protocols 087, 089, and 092) was not different between finasteride and placebo.

Side effects, which usually have been mild, generally have not required discontinuation of therapy.

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.

In these studies, the following drug-related adverse experiences were reported in >1% of men treated with finasteride: decreased libido (finasteride, 1.8% vs. placebo, 1.3%) and erectile dysfunction (1.3%, 0.7%). In addition, 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. The effect of finasteride on ejaculate volume was measured in a separate study and was not different from that seen with placebo.

By the fifth year of treatment with finasteride, the proportion of patients reporting each of the above side effects decreased to <0.3%.

Finasteride has also been studied for prostate cancer risk reduction at 5 times the dose recommended for male pattern hair loss. In a 7-year placebo-controlled trial that enrolled 18,882 healthy men, of whom 9060 had prostate needle biopsy data available for analysis, prostate cancer was detected in 803 (18.4%) men receiving finasteride 5 mg and 1147 (24.4%) men receiving placebo. In the finasteride 5 mg group, 280 (6.4%) men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy vs. 237 (5.1%) men in placebo group. Of the total cases of prostate cancer diagnosed in this study,

approximately 98% were classified as intracapsular (stage T1 or T2). The relationship between long-term use of finasteride 5 mg and tumours with Gleason scores of 7-10 is unknown.

In addition, the following have been reported in post-marketing use: persistence of sexual dysfunction (decreased libido, erectile dysfunction and ejaculation disorder) after discontinuation of treatment with finasteride; male breast cancer (see section 4.4).

Drug-related sexual undesirable effects were more common in the finasteride 1 mg-treated men than the placebo-treated men, with frequencies during the first 12 months of 3.8% vs 2.1%, respectively. The incidence of these effects decreased to 0.6% in finasteride 1 mg-treated men over the following four years. Approximately 1% of men in each treatment group discontinued due to drug related sexual adverse experiences in the first 12 months, and the incidence declined thereafter.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the Yellow Card Scheme (www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 (n=71) did not result in dose-related undesirable effects.

No specific treatment of overdose with finasteride is recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatological preparations, other dermatologicals
ATC-Code: D11AX10

Mechanism of action

Finasteride is a 4-azasteroid, which inhibits human Type 2 5 α -reductase (present within the hair follicles) with greater than 100-fold selectivity over

human Type 1 5 α -reductase, and blocks the peripheral conversion of testosterone to the androgen dihydrotestosterone (DHT). In men with male pattern hair loss, the balding scalp contains miniaturised hair follicles and increased amounts of DHT. Finasteride inhibits a process responsible for miniaturization of the scalp hair follicles, which can lead to reversal of the balding process.

Clinical efficacy and safety

Studies in men

The efficacy of finasteride was demonstrated in three studies in 1879 men 18 to 41 years of age with mild to moderate, but not complete, vertex hair loss and frontal/mid-area hair loss. In these studies, hair growth was assessed using four separate measures including hair count, ratings of photographs of the head by an expert panel of dermatologists, investigator assessment, and patient self-assessment.

In the two studies in men with vertex hair loss, treatment with finasteride was continued for 5 years, during which time patients improved compared to both baseline and placebo beginning at 3 to 6 months. While hair improvement measures compared to baseline in men treated with finasteride were generally greatest at 1-2 years and gradually declined thereafter (e.g., hair count in a representative 5.1 cm² area was increased 88 hairs from baseline at 2 years and 38 hairs from baseline at 5 years), hair loss in the placebo group progressively worsened compared to baseline (decrease of 50 hairs at 2 years and 239 hairs at 5 years). Thus, although improvement compared to baseline in men treated with finasteride did not increase further after 2 years, the difference between treatment groups continued to increase throughout the 5 years of the studies. Treatment with finasteride for 5 years resulted in stabilization of hair loss in 90% of men based on photographic assessment and in 93% based on investigator assessment. In addition, increased hair growth was observed in 65% of men treated with finasteride based on hair counts, in 48% based on photographic assessment, and in 77% based on investigator assessment. In contrast, in the placebo group, gradual hair loss over time was observed in 100% of men based on hair counts, in 75% based on photographic assessment, and in 38% based on investigator assessment. In addition, patient self-assessment demonstrated significant increases in hair density, decreases in hair loss, and improvement in appearance of hair after treatment over 5 years with finasteride (see Table below).

Table 2. Percent of Patients Improved as Assessed by Each of the 4 Measures

	Year 1*		Year 2**		Year 5**	
	Finasteride 1 mg	placebo	Finasteride 1 mg	placebo	Finasteride 1 mg	placebo
Hair Count	(N=679) 86	(N=672) 42	(N=433) 83	(N=47) 28	(N=219) 65	(N=15) 0
Global Photographi c Assessment	(N=720) 48	(N=709) 7	(N=508) 66	(N=55) 7	(N=279) 48	(N=16) 6
Investigator	(N=748)	(N=747)	(N=535)	(N=60)	(N=271)	(N=13)

Assessment	65	37	80	47	77	15
Patient Self-Assessment: Satisfaction with appearance of hair overall	(N=750) 39	(N=747) 22	(N=535) 51	(N=60) 25	(N=284) 63	(N=15) 20

* Randomization 1:1 Finasteride 1 mg to placebo

** Randomization 9:1 Finasteride 1 mg to placebo

In a 12-month study, in men with frontal/mid-area hair loss, hair counts were obtained in a representative 1 cm² area (approximately 1/5 the size of the area sampled in the vertex studies). Hair counts, adjusted to a 5.1 cm² area, increased by 49 hairs (5%) compared to baseline and by 59 hairs (6%) compared to placebo. This study also demonstrated significant improvements in patient self-assessment, investigator assessment, and ratings of photographs of the head by an expert panel of dermatologists.

Two studies of 12 and 24 weeks duration showed that a dose 5-fold the recommended dose (finasteride 5 mg daily) produced a median decrease in ejaculate volume of approximately 0.5 mL (-25%) compared with placebo. This decrease was reversible after discontinuation of treatment. In a study of 48 weeks of duration, finasteride 1 mg daily produced a median decrease in ejaculate volume of 0.3 mL (-11%) compared with a 0.2 mL (-8%) decrease for placebo. No effect was observed on sperm count, motility or morphology. Longer-term data are not available. It has not been feasible to undertake clinical studies which directly elucidate possible negative effects on fertility. However, such effects are judged as very unlikely (see also section 5.3).

Studies in women

Lack of efficacy was demonstrated in post-menopausal women with androgenetic alopecia who were treated with finasteride in a 12 month, placebo-controlled study (n=137). These women did not show any improvement in hair count, patient self-assessment, investigator assessment, or ratings based on standardised photographs, compared with the placebo group.

5.2 Pharmacokinetic properties

Absorption

The oral bioavailability of finasteride is approximately 80% and is not affected by food. Maximum finasteride plasma concentrations are reached

approximately 2 hours after dosing and the absorption is complete after 6 to 8 hours.

Distribution

Protein binding is approximately 93%. The volume of distribution of finasteride is approximately 76 litres (44-96 l).

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 postdose; $AUC_{(0-24\text{ h})}$ was 53 ng x hr/ml.

Finasteride has been recovered in the cerebrospinal fluid (CSF), but the active substance 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. Studies in rhesus monkeys showed that this amount is not considered to constitute a risk to the developing male foetus (see sections 4.6 and 5.3).

Biotransformation

Finasteride is metabolised primarily via but does not affect the cytochrome P450 3A4 enzyme system. 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.

Elimination

Following an oral dose of ^{14}C -finasteride in man, approximately 39% (32-46%) of the dose was excreted in the urine in the form of metabolites. Virtually no unchanged drug was excreted in the urine) and 57% (51-64%) of total dose was excreted in the faeces.

Plasma clearance is approximately 165 ml/min (70-279 ml/min).

The elimination rate of finasteride decreases somewhat with age. Mean terminal plasma half-life is approximately 5-6 hours (3-14 hours) (in men more than 70 years of age 8 hours (6-15 hours)). These findings are of no clinical significance and hence, a reduction in dose in the elderly is not warranted.

Hepatic impairment

The effect of hepatic impairment on the pharmacokinetics of finasteride has not been studied.

Renal impairment

In patients with chronic renal impairment, with creatinine clearances ranging from 9-55 ml/min, area under the curve, maximum plasma concentrations, half-life, and protein binding of unchanged finasteride after a single dose of ^{14}C -finasteride were similar to values obtained in healthy volunteers.

5.3 Preclinical safety data

Mutagenicity/carcinogenicity: Studies on genotoxicity and carcinogenicity have not revealed any hazards for humans.

Reproduction disturbing effect including fertility: The effects on embryonal and foetal development have been studied in rats, rabbits and rhesus monkeys. In rats treated with 5-5,000 times the clinical dose, a dose-related occurrence of hypospadias has been observed in male foetuses. In rhesus monkeys, treatment with oral doses of 2 mg/kg/day has also resulted in external genital abnormalities. Intravenous doses of up to 800 ng/day in rhesus monkeys have not shown any effects in male foetuses. This represents at least 750 times the highest estimated exposure of pregnant women to finasteride from semen of men taking 1 mg/day (see 5.2 Pharmacokinetic properties). In the rabbit study the foetuses were not exposed to finasteride during the period critical for genital development.

Neither ejaculation volume, sperm count nor fertility were affected in the rabbit after treatment with 80 mg/kg/day, a dose that in other studies is shown to have pronounced weight lowering effect of accessory sexual glands. In rats treated for 6 and 12 weeks with 80 mg/kg/day (approx. 500 times the clinical exposure) no effect on fertility was observed. After 24-30 weeks treatment some reduced fertility and pronounced weight reduction of prostate and seminal vesicle were seen. All changes were reversible within a 6-week period. The reduced fertility has been shown to be due to impaired seminal plug formation, an effect that has no relevance to man. The development of the newborns and their reproduction capacity at the age of sexual maturation were without remark. After insemination of female rats with epididymis sperms from rats treated for 36 weeks with 80 mg/kg/day no effect was seen on a number of fertility parameters.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Lactose monohydrate

Microcrystalline cellulose

Starch, pregelatinised

Lauroyl Macrogolglycerides

Sodium starch glycolate – Type A

Magnesium stearate

Tablet Coating

Hypromellose 6 cps.
Titanium dioxide (E171)
Iron oxide yellow E 172
Iron oxide red E 172
Macrogol 6000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister packs: Aluminium/PVC or Aluminium/Aluminium. Pack size 28 tablets.

Plastic bottles (HDPE) with cap. Pack size 28 tablets.

6.6 Special precautions for disposal and other handling

Women who are pregnant or may become pregnant should not handle crushed or broken finasteride tablets because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see section 4.6)

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Sandoz Limited
Frimley Business Park
Frimley

Camberley
Surrey
GU16 7SR
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 04416/1055

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

Date of first authorisation: 06/06/2008

Date of latest renewal:

10 DATE OF REVISION OF THE TEXT

05/09/2019