SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Finasteride 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg of finasteride.
Excipient(s):
Each tablet also contains 83.5mg of lactose and 6.6mg of sodium.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated -tablet
Blue, oval biconvex tablets marked with 'FIN' on one side and '5' on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride is indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with an enlarged prostate to:

- cause regression of the enlarged prostate, improve urinary flow and improve the symptoms associated with BPH.
- reduce the incidence of acute urinary retention and the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.

4.2 Posology and method of administration

The recommended adult dose is one 5mg tablet daily, with or without food. Finasteride can be administered alone or in combination with the alpha-blocker doxazosin (see section 5.1 'Pharmacodynamic properties').

Although early improvement in symptoms may be seen, treatment for at least six months may be necessary to assess whether a beneficial response has been achieved. Thereafter, treatment should be continued long term.

No dosage adjustment is required in the elderly or in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9ml/min).

There are no data available in patients with hepatic insufficiency.

Finasteride is contra-indicated in children.

4.3 Contraindications

Finasteride is not indicated for use in women or children.

Finasteride is contraindicated in the following:

- Hypersensitivity to any component of this product

- Pregnancy - Use in women when they are or may potentially be pregnant (see 4.6 Pregnancy and lactation, Exposure to finasteride - risk to male foetus).

4.4 Special warnings and precautions for use

General

To avoid obstructive complications it is important that patients with large residual urine and/or heavily decreased urinary flow are carefully controlled. The possibility of surgery should be an option.

Effects on PSA and prostate cancer detection

No clinical benefit has yet been demonstrated in patients with prostate cancer treated with 'Finasteride'. Patients with BPH and elevated serum prostate specific antigen (PSA) were monitored in controlled clinical studies with serial PSAs and prostate biopsies. In these BPH studies, 'Finasteride' did not appear to alter the rate of prostate cancer detection, and the overall incidence of prostate cancer was not significantly different in patients treated with 'Finasteride' or placebo.

Digital rectal examinations as well as other evaluations for prostate cancer are recommended prior to initiating therapy with 'Finasteride' and periodically thereafter. Serum PSA is also used for prostate cancer detection. Generally a baseline PSA >10 ng/mL (Hybritech) prompts further evaluation and consideration of biopsy; for PSA levels between 4 and 10 ng/mL, further evaluation is advisable. There is considerable overlap in PSA levels among men with and without prostate cancer. Therefore, in men with BPH, PSA values within the normal reference range do not rule out prostate cancer,

regardless of treatment with ‘Finasteride’. A baseline PSA <4 ng/mL does not exclude prostate cancer.

‘Finasteride’ causes a decrease in serum PSA concentrations by approximately 50% in patients with BPH, even in the presence of prostate cancer. This decrease in serum PSA levels in patients with BPH treated with ‘Finasteride’ should be considered when evaluating PSA data and does not rule out concomitant prostate cancer. This decrease is predictable over the entire range of PSA values, although it may vary in individual patients. In patients treated with ‘Finasteride’ for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. This adjustment preserves the sensitivity and specificity of the PSA assay and maintains its ability to detect prostate cancer.

Any sustained increase in PSA levels of patients treated with finasteride 5mg should be carefully evaluated, including consideration of non-compliance to therapy with‘Finasteride’.

Drug/laboratory test interactions

Effect on levels of PSA

Serum PSA concentration is correlated with patient age and prostatic volume, and prostatic volume is correlated with patient age. When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels decrease in patients treated with ‘Finasteride’. In most patients, a rapid decrease in PSA is seen within the first months of therapy, after which time PSA levels stabilise to a new baseline. The post-treatment baseline approximates half of the pre-treatment value. Therefore, in typical patients treated with ‘Finasteride’ for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men. For clinical interpretation, see 4.4 Special warnings and precautions for use, Effects on PSA and prostate cancer detection.

Percent free PSA (free to total PSA ratio) is not significantly decreased by ‘Finasteride’. The ratio of free to total PSA remains constant even under the influence of ‘Finasteride’. When percent free PSA is used as an aid in the detection of prostate cancer, no adjustment to its value is necessary.

Breast cancer in men

Breast cancer has been reported in men taking finasteride 5 mg during clinical trials and the post-marketing period. Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

Pediatric use

‘Finasteride’ is not indicated for use in children.

Safety and effectiveness in children have not been established.

Hepatic insufficiency

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 5 mg. Patients should be monitored for psychiatric symptoms and if these occur, the patient should be advised to seek medical advice.

Lactose

The tablet contains lactose monohydrate. Patients with any of the following genetic deficiencies should not take this drug: galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

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

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions of clinical importance have been identified. Finasteride is metabolized primarily via, but does not appear to affect significantly, 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. Compounds which have been tested in man have included propranolol, digoxin, glibenclamide, warfarin, theophylline, and phenazone and no clinically meaningful interactions were found.

4.6 Fertility, pregnancy and lactation

Pregnancy:

‘Finasteride’ is contra-indicated in women when they are or may potentially be pregnant (see 4.3 Contraindications).

Because of the ability of type II 5α-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including finasteride, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

In animal developmental studies, dose-dependent development of hypospadias were observed in the male offspring of pregnant rats given finasteride at doses ranging from 100 μg/kg/day to 100 mg/kg/day, at an incidence of 3.6% to 100%. Additionally, pregnant rats produced male offspring with decreased prostatic and seminal vesicular weights, delayed preputial separation, transient nipple development and decreased anogenital distance, when given finasteride at doses below the recommended human dose. The critical period during which these effects can be induced has been defined in rats as days 16-17 of gestation.

The changes described above are expected pharmacological effects of Type II 5 α-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 5 α-reductase. It is for these reasons that 'Finasteride' is contra-indicated in women who are or may potentially be pregnant.

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

Exposure to finasteride - risk to male foetus

Women should not handle crushed or broken tablets of 'Finasteride' when they are or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see 4.6 Pregnancy and Lactation '*Pregnancy'*). 'Finasteride' tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

Small amounts of finasteride have been recovered from the semen in subjects receiving finasteride 5 mg/day. It is not known whether a male foetus may be adversely affected if his mother is exposed to the semen of a patient being treated with finasteride. When the patient's sexual partner is or may potentially be pregnant, the patient is recommended to minimise exposure of his partner to semen.

Lactation:

'Finasteride' is not indicated for use in women. It is not known whether finasteride is excreted in human milk.

4.7 Effects on ability to drive and use machines

There are no data to suggest that 'Finasteride' affects the ability to drive or use machines.

4.8 Undesirable effects

The most frequent adverse reactions are impotence and decreased libido. These adverse reactions occur early in the course of therapy and resolve with continued treatment in the majority of patients.

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

Frequency of adverse reactions is determined as follows:

Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), not known (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.

System Organ Class	Frequency: adverse reaction
Immune system disorders	*Unknown:* hypersensitivity reactions including swelling of the lips, tongue, throat and face
Psychiatric disorders	*Common:* decreased libido *Unknown:* decreased libido that may continue after discontinuation of therapy, depression, anxiety, suicidal ideation
Cardiac disorders	*Unknown:* palpitation
Hepatobiliary disorders	*Unknown:* increased hepatic enzymes
Skin and subcutaneous tissue disorders	*Uncommon:* rash *Unknown:* pruritus, urticaria

Reproductive system and breast disorders	*Common:* impotence *Uncommon:* ejaculation disorder, breast tenderness, breast enlargement. *Unknown:* testicular pain, haematospermia, sexual dysfunction (erectile dysfunction and ejaculation disorder) which may continue after discontinuation of treatment; male infertility and/or poor seminal quality. Normalization or improvement of seminal quality has been reported after discontinuation of finasteride.
Investigations	*Common:* decreased volume of ejaculate

In addition, the following has been reported in clinical trials and post-marketing use: male breast cancer (see 4.4 Special warnings and precautions for use).

Medical Therapy of Prostate Symptoms (MTOPS)

The MTOPS study compared finasteride 5 mg/day (n=768), doxazosin 4 or 8 mg/day (n=756), combination therapy of finasteride 5 mg/day and doxazosin 4 or 8 mg/day (n=786), and placebo (n=737). In this study, the safety and tolerability profile of the combination therapy was generally consistent with the profiles of the individual components. The incidence of ejaculation disorder in patients receiving combination therapy was comparable to the sum of incidences of this adverse experience for the two monotherapies.

Other Long-Term Data

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' and 1147 (24.4%) men receiving placebo. In the 'Finasteride' group, 280 (6.4%) men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy vs. 237 (5.1%) men in the placebo group. Additional analyses suggest that the increase in the prevalence of high-grade prostate cancer observed in the 'Finasteride' group may be explained by a detection bias due to the effect of 'Finasteride' on prostate volume. 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' and tumours with Gleason scores 7-10 is unknown.

Laboratory Test Findings

When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels are decreased in patients treated with 'Finasteride' (see section 4.4 Special warnings and precautions for use). In most patients, a rapid decrease in PSA is seen within the first months of therapy, after which time PSA levels stabilise to a new baseline. The post-treatment baseline approximates half of the pre-treatment value. Therefore, in typical patients treated with 'Finasteride' for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men.

For clinical interpretation see 'Special warnings and precautions for use', *Effects on prostate-specific antigen (PSA) and prostate cancer detection.*

No other difference was observed in patients treated with placebo or 'Finasteride' in standard laboratory tests.

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 website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No specific treatment of overdosage with 'Finasteride' is recommended. Patients have received single doses of 'Finasteride' up to 400 mg and multiple doses of 'Finasteride' up to 80 mg/day for up to three months without any adverse effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Finasteride is a competitive inhibitor of human Type II 5-alpha reductase, an intracellular enzyme which metabolises testosterone into the more potent androgen, dihydrotestosterone (DHT). In benign prostatic hyperplasia (BPH), enlargement of the prostate gland is dependent upon the conversion of testosterone to DHT within the prostate. 'Finasteride' is highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor.

In clinical studies of patients with moderate to severe symptoms of BPH, an enlarged prostate on digital rectal examination and low residual urinary volumes, 'Finasteride' reduced the incidence of acute retention of urine from 7/100 to 3/100 over four years and the need for surgery (TURP or prostatectomy) from 10/100 to 5/100. These reductions were associated with a

2-point improvement in QUASI-AUA symptom score (range 0-34), a sustained regression in prostate volume of approximately 20% and a sustained increase in urinary flow rate.

Medical therapy of prostatic symptoms

The Medical Therapy of Prostatic Symptoms (MTOPS) Trial was a 4- to 6-year study in 3047 men with symptomatic BPH who were randomised to receive finasteride 5 mg/day, doxazosin 4 or 8 mg/day*, the combination of finasteride 5 mg/day and doxazosin 4 or 8 mg/day , or placebo. The primary endpoint was time to clinical progression of BPH, defined as a ≥4 point confirmed increase from baseline in symptom score, acute urinary retention, BPH-related renal insufficiency, recurrent urinary tract infections or urosepsis, or incontinence. Compared to placebo, treatment with finasteride, doxazosin, or combination therapy resulted in a significant reduction in the risk of clinical progression of BPH by 34(p=0.002), 39 (p<0.001), and 67% (p<0.001), respectively. The majority of the events (274 out of 351) that constituted BPH progression were confirmed ≥4 point increases in symptom score; the risk of symptom score progression was reduced by 30 (95% CI 6 to 48%), 46 (95% CI 25 to 60%), and 64% (95% CI 48 to 75%) in the finasteride, doxazosin, and combination groups, respectively, compared to placebo. Acute urinary retention accounted for 41 of the 351 events of BPH progression; the risk of developing acute urinary retention was reduced by 67(p=0.011), 31 (p=0.296), and 79% (p=0.001) in the finasteride, doxazosin, and combination groups, respectively, compared to placebo. Only the finasteride and combination therapy groups were significantly different from placebo.

Titrated from 1 mg to 4 or 8 mg as tolerated over a 3-week period

5.2 Pharmacokinetic properties

After 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. Two metabolites have been identified which possess only a small fraction of the Type II 5 alpha-reductase activity of finasteride.

The oral bioavailability of finasteride is approximately 80%, relative to an intravenous reference dose, and is unaffected by food. Maximum plasma concentrations are reached approximately two hours after dosing and the absorption is complete within 6-8 hours. Protein binding is approximately 93%. Plasma clearance and the volume of distribution are approximately 165 ml/min and 76 1, respectively.

In the elderly, the elimination rate of finasteride is somewhat decreased. Half-life is prolonged from a mean half-life of approximately 6 hours in men aged 18-60 years to 8 hours in men aged more than 70 years. This is of no clinical significance and does not warrant a reduction in dosage.

In patients with chronic renal impairment, whose creatinine clearance ranged from 9-55 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 which 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. Dosage adjustment in non-dialysed patients with renal impairment is not necessary.

There are no data available in patients with hepatic insufficiency.

Finasteride has been found to cross the blood-brain barrier. Small amounts of finasteride have been recovered in the seminal fluid of treated patients.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity, and carcinogenic potential. Reproduction toxicology studies in male rats have demonstrated reduced prostate and seminal vesicular weights, reduced secretion from accessory genital glands and reduced fertility index (caused by the primary pharmacological effect of finasteride). The clinical relevance of these findings is unclear.

As with other 5-alpha-reductase inhibitors, femininisation of male rat foetuses has been seen with administration of finasteride in the gestation period. Intravenous administration of finasteride to pregnant rhesus monkeys at doses up to 800 ng/day during the entire period of embryonic and foetal development resulted in no abnormalities in male foetuses. This dose is about 60-120 times higher than the estimated amount in semen of a man who have taken 5 mg finasteride, and to which a woman could be exposed via semen. In confirmation of the relevance of the Rhesus model for human foetal development, oral administration of finasteride 2 mg/kg/day (the systemic exposure (AUC) of monkeys was slightly higher (3x) than that of men who have taken 5 mg finasteride, or approximately 1-2 million times the estimated amount of finasteride in semen) 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Cellulose, Microcrystalline (E460)

Pregelatinised Maize Starch

Sodium Starch Glycolate (Type A)

Docusate Sodium

Magnesium Stearate (E470b)

Tablet coating:

Indigo Carmine (E132)

Hypromellose (E464)

Titanium dioxide (E171)

Macrogol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30ºC. Keep blister in the outer carton.

6.5 Nature and contents of container

Blister strips made of PVC/PE/PVdC or cold formable foil bases and lidded with aluminium foil. Available pack sizes are: 28, 30, 50 and 100 tablets, although not all pack sizes may be marketed.

6.6 Special precautions for disposal / Instructions for use/handling

Any unused product or waste material should be disposed of in accordance with local requirements and not via waste water or household waste. Pharmacists can advise of safe disposal to protect the environment.

Finasteride tablets have a film coating which prevents contact with the active ingredient provided that the tablets have not been broken or crushed.

Women should not handle crushed or broken finasteride Tablets when they are or may potentially be pregnant (see 'Contraindications', 'Pregnancy and lactation', *Exposure to finasteride – risk to male foetus*).

7 MARKETING AUTHORISATION HOLDER

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Milton Road, Cambridge,
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8 MARKETING AUTHORISATION NUMBER(S)

PL08553/0261

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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06/03/2024