Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Finasteride 5 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 5 mg finasteride

Excipient(s) with known effect: lactose monohydrate (90.95 mg)

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.

Blue, round biconvex, film-coated tablet with "F5" marking on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride 5 mg Tablets are indicated for the treatment and control of benign prostatic hyperplasia (BPH) 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 reduce need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.

Finasteride 5 mg tablets should be administered in patients with an enlarged prostate (prostate volume above ca. 40 ml).

4.2 Posology and method of administration

Posology
The recommended dosage is one 5 mg tablet daily with or without food. Even though improvement can be seen within a short time, treatment for at least 6 months may be necessary in order to determine objectively whether a satisfactory response to treatment has been achieved.

Dosage in the elderly
Dosage adjustments are not necessary although pharmacokinetic studies have shown that the elimination rate of finasteride is slightly decreased in patients over the age of 70.

Dosage in hepatic insufficiency
The effect of hepatic insufficiency on the pharmacokinetics of finasteride has not been studied. (See section 4.4).

Dosage in renal insufficiency
Dosage adjustments are not necessary in patients with varying degrees of renal insufficiency (starting from creatinine clearance as low as 9 ml/min) as in pharmacokinetic studies renal insufficiency was not found to affect the elimination of finasteride. Finasteride has not been studied in patients on hemodialysis.

Method of administration
For oral use only.

The tablet should be swallowed whole and not divided or crushed. The tablet can be taken with or without food.

4.3 Contraindications

Hypersensitivity to finasteride or to any of the excipients listed in section 6.1.

Contra-indicated in women and children (see sections 4.4, 4.6 and 6.6)
Pregnancy - Use in women when they are or may potentially be pregnant (see 4.6 Pregnancy and lactation, Exposure to finasteride - risk to male fetus).

4.4 Special warnings and precautions for use

General:

- Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy.
- Consultation of an urologist should be considered in patients treated with finasteride.
- Obstruction due to trilobular growth pattern of the prostate should be excluded before starting treatment with finasteride.
- There is no experience in patients with liver insufficiency. Since finasteride is metabolised in the liver (see section 5.2). Caution is advised in patients with decreased hepatic function as the plasma-levels of finasteride may be increased in such patients.
- This medicinal product contains lactose-monohydrate. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucosegalactose malabsorption should not take this medicine.
- 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 prostate-specific antigen (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 examination, and, if necessary, determination of prostate-specific-antigen (PSA) in serum should be carried out on patients prior to initiating therapy with finasteride and periodically during treatment to rule out prostate Cancer. 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. Analysis of PSA data from over 3000 patients in the 4-year, double-blind, placebo-controlled Proscar Long-Term Efficacy and Safety Study (PLESS) confirmed that in the average 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 or specificity of the PSA assay and maintains its ability to detect prostate Cancer.

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

Percent free PSA (free to total PSA ratio) is not significantly decreased by finasteride and 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 is necessary.

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. Finasteride tablets have a film

coating which prevents contact with the active ingredient provided that the tablets have not been broken or crushed (see sections 4.6 and 6.6).

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 stabilize 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.

Effects on fertility
See section 4.6

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.

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.

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

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

4.5 Interaction with other medicinal products and other forms of interaction

No clinically significant drug interactions have been identified. Finasteride does not appear to significantly affect the cytochrome P450-linked drug metabolizing enzyme 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.

The following medicinal products have been investigated in man, and no clinically significant interactions have been found: propanolol, digoxin, glibenclamide, warfarin, theophylline, phenazone and antipyrine 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 section 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.

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 section 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 *5* mg tablets are not indicated for use in women. It is not known whether finasteride is excreted in human milk.

Fertility
There are no long-term fertility data in humans, and no specific studies in subfertile men have been performed. Male patients who were planning to become fathers were initially excluded from clinical trials. Although animal studies have not shown any relevant adverse effects on fertility, there have been spontaneous post-marketing reports of infertility and/or poor semen quality. In some of these reports, patients had other risk factors that could have contributed to the infertility.
Normalization or improvement in semen quality has been reported after discontinuation of finasteride therapy.

4.7 Effects on ability to drive and use machines

There is no available information indicating that finasteride would have an influence on 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 with finasteride 5mg and/or finasteride at lower doses are listed in the table below.
Frequency of adverse reactions is determined as follows:
Very common (³1/10), 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**
Investigations	*Common:* decreased volume of ejaculate
Cardiac disorders	*Unknown:* palpitation
Skin and subcutaneous tissue disorders	*Uncommon:* rash
Immune system disorders	*Unknown:* hypersensitivity reactions including pruritus, urticaria and angioedema (swelling of lips, tongue, throat and face)
Hepatobiliary disorders	*Unknown:* increased hepatic enzymes
Reproductive system and breast disorders	*Common:* impotence *Uncommon:* ejaculation disorder, breast tenderness, breast enlargement *Unknown:* testicular pain, erectile dysfunction that continued after discontinuation of treatment; hematospermia, male infertility and/or poor seminal quality.
Psychiatric disorders	*Common:* decreased libido *Unknown:* decreased libido that continued after discontinuation of treatment,

	depression, anxiety, suicidal ideation.

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 prostatic 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 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 the placebo group. Additional analyses suggest that the increase in the prevalence of high-grade prostate cancer observed in the finasteride 5 mg group may be explained by a detection bias due to the effect of finasteride 5 mg on prostate volume. Of the total cases of prostate cancer diagnosed in this study, approximately 98% were classified as intracapsular (clinical stage T1 or T2) at diagnosis. The clinical significance of the Gleason 7-10 data 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).

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:
HPRA Pharmacovigilance,
Website: www.hpra.ie.

4.9 Overdose

Patients have received Single doses of finasteride up to 400 mg and multiple doses up to 80 mg/day without adverse effects. There is no specific recommended treatment of overdose of finasteride.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Testosteron-5α-reductase-inhibitors

ATC-Code: G04CB01

Finasteride is a synthetic 4-azasteroid, a specific competitive inhibitor of the intracellular enzyme Type-II-5a-reductase. The enzyme converts testosterone into the more potent androgen dihydrotestosterone (DHT). The prostate gland and, consequently, also the hyperplasic prostate tissue are dependent on the conversion, of testosterone to DHT for their normal function and growth. 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.

Clinical studies show a rapid reduction of the Serum DHT levels of 70%, which leads to a reduction on prostate volume. After 3 months, a reduction of approx. 20% in the volume of the gland occurs, and the shrinking continues and reaches approx. 27% after 3 years. Marked reduction takes place in the periurethral Zone immediately surrounding the Urethra. Urodynamic measurements have also confirmed a significant reduction of detrusor pressure as a result of the reduced obstruction.

Significant improvements in maximum urinary flow rate and symptoms have been obtained after a few weeks, compared with the stand of treatment. Differences from Placebo have been documented at 4 and 7 months, respectively.

All efficacy parameters have been maintained over a 3-year follow-up period.

Effects of four years treatment with finasteride on incidence of acute urine retention, need for surgery, symptom-Score and prostate volume:

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 7/1 00 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 QUASJ-AUA Symptom Score (range 0-34), a sustained regression in prostate volume of approximately 20% and a sustained increase in urinary flow rate.

Prostate volume as a predictor of therapeutic response
The degree of symptomatic response and of improvement in maximum urinary flow with Finasteride appears to be related to the size of the prostate at the start of treatment. Patients with an enlarged prostate (40 cc and larger) have a greater response to Finasteride.

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 ^{3} 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 ^{3} 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

In this study the safety and tolerability profile of combined treatment was broadly similar to the profile of each of the drugs taken separately. However, undesirable effects concerning the "nervous system" and "uro-genital system" organ classes were observed more frequently when the two drugs were used in combination (see section 4.8).

5.2 Pharmacokinetic properties

Absorption:
The oral bioavailability of finasteride is approx. 80%. Peak plasma concentrations are reached approx. 2 hours after drug intake, and absorption is complete after 6-8 hours.

Distribution:
Binding to plasma proteins is approx. 93%. Plasma clearance and volume of distribution are approx. 165 ml/min (70-279 ml/min) and 76 l(44-96 l), respectively. Accumulation of small amounts of finasteride is seen on repeated administration. After a daily dose of 5 mg the lowest steady-state concentration of finasteride has been calculated to be 8-10 ng/ml, which remains stable over time.

Finasteride has been found in the CSF of men treated with finasteride for 7-10 days, but the drug does not appear to preferentially concentrate in the CSF. Finasteride has also been found in the semen of men given 5 mg of Finasteride per day.

Biotransformation:
Finasteride is metabolised in the liver. Finasteride does not significantly affect the cytochrome P 450 enzyme system. Two metabolites with low 5α-reductase-inhibiting effects have been identified.

Elimination:
The plasma half-life averages 6 hours (4-12 hours) (in men >70 years of age, 8 hours, range 6-15 hours). After administration of radioactively labelled finasteride, approx. 39% (32-46%) of the given dose is excreted in the urine in the form of metabolites. Virtually no unchanged finasteride is recovered in the urine. Approximately 57% (51-64%) of the total dose is excreted in the faeces.

Small amounts of finasteride have been recovered in the seminal fluid of treated. In 2 studies of healthy subjects (n=69) receiving finasteride 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 finasteride 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 µg) that had no effect on circulating DHT levels in men (see also section 5.3.).

Renal impairment
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 (see section 4.2). 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. Plasma concentrations of metabolites were significantly higher in patients with renal impairment (based on a 60% increase in total radioactivity AUC). However, finasteride was well tolerated in BPH patients with normal renal function who received up to 80 mg/day for 12 weeks, and the exposure of these patients to metabolites was likely much higher. Therefore, in patients with renal insufficiency who are not on dialysis, no dosage adjustment is necessary because the therapeutic window of finasteride is sufficient and because a correlation between creatinine clearance and accumulation was not demonstrated.

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 to120 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 to 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),
Starch pregelatinised
Lauroyl macrogolglycerides,
Sodium starch glycolate (type-A),

Magnesium stearate (E572)

Film coating:
Hypromellose (E464)
Titanium dioxide (E 171)
Indigo carmine (E132)
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

An opaque white (PVC –PVdC /Aluminium) Blister

The Finasteride 5 mg tablets are packed in blister pack of 7, 10, 14, 15, 20, 28, 30, 50, 56, 60, 84, 90, 98, 100 or 120 tablets.

Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Women who are pregnant or may become pregnant should not handle finasteride tablets especially if crushed or broken because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see section 4.6). Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/089/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th November 2008
Date of last renewal: 1st April 2016

10 DATE OF REVISION OF THE TEXT

May 2026