# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Fintrid 5 mg Film-Coated Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 5 mg finasteride.

*Excipient with known effect:* Contains lactose monohydrate 90.0 mg

For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Film-coated tablet

Blue, round, biconvex, film-coated tablet, plain on both sides. Diameter approx. 8 mm.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Treatment and control of benign prostatic hyperplasia (BPH) to cause regression of the enlarged prostate, improve urinary flow and symptoms associated with BPH, reduce the incidence of acute urinary retention and reduce need for surgery.

Fintrid 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 hepatic insufficiency
There are no data available in patients with hepatic insufficiency (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.

Dosage in older people
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.

*Method of administration*
Oral use
The tablet should be swallowed whole and must not be divided or crushed (see section 6.6).

Finasteride can be taken with or without food with sufficient liquid.

## 4.3 Contraindications

Finasteride is not indicated for use in women or children.

Finasteride is contraindicated in the following:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- 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. The possibility of surgery should be an option.
- 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.

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 5 mg. 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 5 mg 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 5 mg or placebo.

Digital rectal examinations as well as other evaluations for prostate cancer are recommended prior to initiating therapy with finasteride 5 mg 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 5 mg. A baseline PSA <4 ng/mL does not exclude prostate cancer.
Finasteride 5 mg 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 5 mg 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 finsteride Long-Term Efficacy and Safety Study (PLESS) confirmed that in typical patients treated with finasteride 5 mg 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 5 mg should be carefully evaluated, including consideration of non-compliance to finasteride 5 mg 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.

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 5 mg. 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 5 mg for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men. For clinical interpretation, see section 4.4, Effects on PSA and prostate cancer detection.

*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 population*
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.

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

## 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, glibencamide, warfarin, theophylline, and phenazoneand no clinically meaningful interactions were found.

## 4.6 Fertility, pregnancy and lactation

Pregnancy
Finasteride is contraindicated for use 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 fetus when administered to a pregnant woman.

*Exposure to finasteride - risk to male fetus*
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 fetus (see 4.6 Pregnancy and lactation). Fintrid 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 fetus 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.

Breast-feeding
Fintrid 5 mg tablets are 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 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 | *Not known:* hypersensitivity reactions including swelling of the lips and face |
| Psychiatric disorders | *Common:* decreased libido<br>*Not known*: depression, decreased libido that continued after discontinuation of treatment |
| Cardiac disorders | *Not known:* palpitation |
| Hepatobiliary disorders | *Not known:* increased hepatic enzymes |
| Skin and subcutaneous tissue disorders | *Uncommon:* rash<br>*Not known:* pruritus, urticaria |
| Reproductive system and breast disorders | *Common:* impotence<br>*Uncommon:* ejaculation disorder, breast tenderness, breast enlargement<br>*Not known:* testicular pain, erectile dysfunction that continued after discontinuation of treatment; male infertility and/or poor seminal quality |
| 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 5 mg and 1147 (24.4%) men receiving placebo. In the finasteride 5 mg group, 280 (6.4%) of men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy versus 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 (stage T1 or T2). 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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

## 4.9 Overdose

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

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Testosteron-5a-reductase-inhibitors
ATC-Code: G 04 CB 01

Mechanism of action
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. Finasteride has no affinity for the androgen receptor.

Clinical efficacy and safety
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 start 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 7/100 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.

## 5.2 Pharmacokinetic properties

Absorption
The 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%. 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.

Biotransformation
Finasteride is metabolised in the liver. Finasteride does not significantly affect the cytochrome P 450 enzyme system. Two metabolites with low 5a-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.

In patients with impaired renal function (creatinine clearance as low as 9 ml/min), no changes in the elimination of finasteride have been seen (see section 4.2).

## 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.

Reproduction toxicity studies
Dose-dependent development of hypospadias was 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-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. It is for these reasons that finasteride is contraindicated in women who are or may potentially be pregnant. No effects were seen in female offspring exposed in utero to any dose of finasteride.

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 foetusus. This dose is about 60-120 times higher than the estimated amount in semen of a man who has 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

Microcrystalline cellulose
Povidone
Docusate sodium
Magnesium stearate
Talc
Sodium starch glycolate (type A)

Film coating
Hypromellose
Propylene glycol
Titanium dioxide (E 171)
Talc
Indigo carmine lake (E 132)

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

2 years.

## 6.4 Special precautions for storage

Do not store above 25 °C.

## 6.5 Nature and contents of container

Blister PVC/Aluminium

Package sizes:
10, 15, 30, 50, 60, 100, 120 tablets in standard blister
14, 28 and 56 tablets in weekly blister
50 tablets (50 x 1) in single dose blister

Not all pack sizes may be marketed.

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

## 7 MARKETING AUTHORISATION HOLDER

Rowex Ltd
Bantry
Co. Cork
Ireland

## 8 MARKETING AUTHORISATION NUMBER

PA 0711/073/001

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

Date of first authorisation: 7 June 2005

Date of last renewal: 17 January 2010

## 10 DATE OF REVISION OF THE TEXT

January 2015