Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Finocar 5mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg finasteride.
Excipient(s): Each film-coated tablet contains 79mg lactose monohydrate.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
Coated light blue spherical biconvex tablets with 7 mm diameter.

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 (prostate volume above ca. 40 ml) 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

Oral use.

The recommended dose is one 5 mg tablet daily (with or without food). The tablet should be swallowed whole and must not be divided or crushed (see section 6.6).

Even if improvement can be seen within a short time, treatment for at least 6 months may be necessary in order to assess whether a beneficial response has been achieved. Thereafter, treatment should be continued long term. The risk of acute urinary retention is reduced within four months of treatment.

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

Use in renal insufficiency
Dosage adjustments are not necessary in patients with varying degrees of renal insufficiency (with 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 haemodialysis.

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

4.3 Contraindications

Finocar is not indicated in women or children.
Finocar is contraindicated in the following situations:

- Hypersensitivity to finasteride or to any of the excipients.
- Pregnancy - Use in women when they are or may potentially be pregnant (see section 4.6 Fertility, pregnancy and lactation, *"Exposure to finasteride - risk to male fetus"*).

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.

Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy.
Consultation with 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 hepatic insufficiency. Caution is advised in patients with impaired hepatic function as the plasma levels of finasteride may be increased in such patients (see section 4.2).

Effect on the 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, finsteride 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 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. Analysis of PSA data from over 3000 patients in the 4-year, double-blind, placebo-controlled finasteride Long-Term Efficacy and Safety Study (PLESS) confirmed that in typical 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 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. 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 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. 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.

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
Finocar is not indicated for use in children.
Safety and effectiveness in children have not been established.

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.

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

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 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. Finasteride does not appear to affect significantly the cytochrome P450-linked drug metabolizing enzyme system. 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 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", "*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 5mg/day (see sections 5.2 and 5.3). 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.

Lactation
Finocar is not indicated for use in women. It is not known whether finasteride is excreted into human breast milk.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The most frequent adverse reactions are impotence and reduced 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
Investigations	*Common:* decreased volume of ejaculate
Cardiac disorders	*Unknown:* palpitation
Skin and subcutaneous tissue disorders	*Uncommon:* rash *Unknown:* pruritus, urticaria
Immune system disorders	*Unknown:* hypersensitivity reactions including swelling of the lips 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
Psychiatric disorders	*Common:* decreased libido

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 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 (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").

4.9 Overdose

Single doses of finasteride up to 400 mg and multiple doses of up to 80 mg daily for 3 months did not produce any dose related undesirable effects.

No specific treatment in connection with overdosing of finasteride can be recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Testosterone, 5α reductase inhibitor, ATC code: G04CB01

Finasteride is a competitive inhibitor of human 5α reductase type II with which it gradually forms a stable enzyme complex. The conversion of this complex is very slow ($t_{1/2}$ = 30 days). *In vitro* and *in vivo* it has been found that finasteride is a specific type II 5α reductase inhibitor. 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 studies show a rapid reduction of the serum DHT levels of 70%, which leads to a reduction of 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 couple of 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.

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

Absorption
The bioavailability of finasteride is approx. 80%. Peak plasma concentrations are reached approx. 2 hours after 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 cytochrome P 450 enzyme system. Two metabolites with low 5a-reductase-inhibiting effects have been identified.

Elimination
The plasma half life is a mean of 6 hours (4-12 hours) (in men > 70 years: 8 hours, range 6 – 15 hours).

Following administration of radioactively labelled finasteride, approx. 39% (32 – 46%) of the dose was excreted in the urine in the form of metabolites. Virtually no unchanged finasteride was recovered in the urine. Approx. 57% (51 – 64%) of the total dose was excreted in the faeces.

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 renal impairment (creatinine clearance above 9 ml/min), no changes in the elimination of finasteride have been seen (see section 4.2). Protein binding also did not differ in patients with renal impairment. A portion of the metabolites which is normally 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

Current studies relating to general toxicity, genotoxicity and carcinogenicity did not demonstrate any special risks to humans.

Reproduction toxicology studies on male rats have not revealed decreased prostatic and seminal vesicular weights, reduced secretion from accessory sex glands and a reduction of fertility index (caused by the pharmacological effects of finasteride). The clinical relevance of these findings is unknown.

As with other 5-alpha-reductase inhibitors, feminisation of male rat foetuses has been observed with administration of finasteride during pregnancy. When finasteride was administered to primates during pregnancy, no evidence of feminisation of male foetuses was observed with exposure in blood well in excess of expected levels via human seminal fluid. It is unlikely that male foetuses will be negatively affected by transference of finasteride via seminal fluid.

In animal developmental studies, dose-dependent 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 alpha-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 alpha-reductase.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Lactose monohydrate
Cellulose microcrystalline
Maize starch, pre-gelatinised
Docusate sodium
Sodium starch glycolate (type A)
Silica, colloidal anhydrous
Sodium stearyl fumarate

Film-coating
ALBUM OPADRY II 31F58914 white (hypromellose, lactose monohydrate, titanium dioxide (E 171), macrogol 4000, sodium citrate dihydrate (E 331))
Indigocarmine (E 132).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Transparent PVC/PVDC/Al blister
Size of box: 10, 15, 28, 30, 50, 100 tablets
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Pregnant women or women who could potentially be pregnant may not touch the crushed or broken tablets of the preparation Finocar (cf. Item 4.3 Contraindications and 4.6 Fertility, pregnancy and lactation).

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 585/27/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th October 2007

Date of last renewal: 18th February 2011

10 DATE OF REVISION OF THE TEXT

July 2012