SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Finasterid Actavis 5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg finasteride.

Excipient with known effect: Each film-coated tablet contains 90.96 mg lactose monohydrate.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet

Blue, round biconvex tablet marked “F5”. The diameter is 7 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasterid Actavis 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.

Finasterid Actavis 5 mg tablets should only 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 if 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 (with creatinine clearance down to 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.

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 above 70 years of age.

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

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 section 4.6)

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.

- Consultation with an urologist should be considered in patients treated 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. Patients with BPH and elevated 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. Generally, when PSA assays are performed 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 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 to its value is necessary.

Drug/laboratory test interactions

Effects 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 'Effects on prostate-specific antigen (PSA) and prostate cancer detection' in this section. No other difference was observed in patients treated with placebo or finasteride in standard laboratory tests.

Breast cancer in men

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

Paediatric 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.

Caution is advised in patients with impaired hepatic function, as finasteride is metabolised extensively in the liver and the plasma levels of finasteride may be increased in such patients (see section 4.2).

Mood alterations and depression

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

Excipients

Lactose

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 sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No significant interactions with other medicinal products 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. The following medicinal products have been investigated in humans and no clinically meaningful interactions have been identified: propranolol, digoxin, glibenclamide, warfarin, theophylline and phenazone.

4.6 Fertility, pregnancy and lactation

Pregnancy

Finasteride is contraindicated for use in women when they are or may potentially be pregnant (see section 4.3).

Because of the ability of type II 5α-reductase inhibitors to inhibit the 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 (see sections 5.3 and 6.6).

Exposure to finasteride – risk to male fetus
Pregnant women and women who may become pregnant should not handle crushed or broken tablets of finasteride, due to the risk of absorption of finasteride through the skin and the consequent potential risk to a male fetus (see 'Pregnancy' in this section).
Finaset 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.

Breastfeeding
Finasteride tablets are not indicated for use in women**.** It is not known whether finasteride is excreted in breast milk.

Fertility
Although animal studies did not show relevant adverse effects on fertility, there have been spontaneous reports of infertility and/or poor seminal quality after the launch of other finasteride-containing products. In some of these reports, patients had other risk factors that may have contributed to the infertility. Normalisation or improvement in seminal quality has been reported after discontinuation of finasteride.

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 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 (≥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 angioedema (including swelling of the lips, tongue, throat and face)
Psychiatric disorders	*Common*	Decreased libido

	Not known	Depression, decreased libido that continued after discontinuation of treatment, anxiety
Cardiac disorders	*Not known*	Palpitation
Hepatobiliary disorders	*Not known*	Increased hepatic enzymes
Skin and subcutaneous tissue disorders	*Uncommon*	Rash
	Not known	Pruritus, urticaria
Reproductive system and breast disorders	*Common*	Impotence
	Uncommon	Ejaculation disorder, breast tenderness, breast enlargement
	Not known	Testicular pain, haematospermia, erectile dysfunction that continued after discontinuation of treatment, ejaculatory dysfunction that continued after discontinuation of treatment, male infertility and/or poor seminal quality*.
Investigations	*Common*	Decreased volume of ejaculate

*Normalisation or improvement of seminal quality has been reported after discontinuation of finasteride (see section 4.6).

In addition, the following has been reported in clinical trials and post-marketing use; male breast cancer (see section 4.4).

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.

Laboratory test findings
When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels generally decrease in patients treated with finasteride (see section 4.4 Drug/laboratory test interactions).

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%) of men receiving finasteride 5 mg and in 1147 (24.4%) of men receiving placebo. In the finasteride group, 280 (6.4%) of men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy versus 237 (5.1%) 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.

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 national reporting system listed in Appendix V.

4.9 Overdose

Patients have taken single doses of finasteride up to 400 mg and multiple doses of up to 80 mg daily for three months without experiencing any adverse 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-inhibitors
ATC-Code: G04CB01

Finasteride is a synthetic 4-azasteroid, a specific competitive inhibitor of the intracellular enzyme Type-II-5α-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 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.

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 the cytochrome P 450 enzyme system. Two metabolites with low 5α-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 patients with renal impairment (creatinine clearance above 9 ml/min), no changes in the elimination of finasteride have been seen (see section 4.2).

Finasteride has been found to cross the blood-brain barrier. 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.)

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 fetuses 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 fetuses. 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 (3 x) 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 fetuses. No other abnormalities were observed in male fetuses and no finasteride-related abnormalities were observed in female fetuses at any dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Lactose monohydrate
Microcrystalline cellulose
Pregelatinised starch (maize)
Lauroyl macrogolglycerides
Sodium starch glycolate (Type A)
Magnesium stearate

Film-coating

Hypromellose
Macrogol
Titanium dioxide (E171)
Indigo carmine aluminium lake (E132)

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.

6.5 Nature and contents of container

Blister packs Aluminium/PVC or Aluminium/Aluminium: 7, 10, 14, 15, 20, 28, 30, 49, 50, 60, 98, 100 and 300 (10x30) tablets.

Plastic bottles (HDPE): 10, 30, 50, 100 and 300 tablets.

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 (see section 4.6).

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2024-02-22
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