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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINE

Sandoz finasterid 5mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 5 mg of finasteride. Excipient with known effect: One film-coated tablet contains 75 mg of lactose monohydrate. For list complete list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablet Sandoz finasterid tablets are white, rounded, biconvex, film-coated tablets with the inscriptions "F" and "5" on one side. They have a diameter of 7 mm.

4. CLINICAL DATA

4.1 Therapeutic indications

Sandoz finasterid is indicated for the treatment and control of benign prostatic hyperplasia (BPH) to:

• reduce prostate volume, improve urinary flow and reduce symptoms associated with benign prostatic hyperplasia (BPH)
• reduce the risk of acute urinary retention and the need for intervention surgery, including transurethral resection of the prostate (TURP) and prostatectomy.

Sandoz Finasterid 5 mg tablets should only be administered to patients with increased prostate volume (prostatic volume greater than approx. 40 ml).

4.2 Posology and method of administration

Dosage

The recommended dose is one 5 mg tablet per day, taken alone or with a meal. Although an improvement can be seen quickly, a treatment of at least six months can be necessary to objectively assess whether a satisfactory response to treatment has been obtained.

Patients with hepatic impairment

There are no data for patients with hepatic impairment (see section 4.4).

Patients with renal impairment

No dosage adjustment is necessary for patients with various degrees of renal impairment (when creatinine clearance is no more than 9 ml/min) since pharmacokinetic studies have not shown any modification in elimination of finasteride. The use of finasteride in patients undergoing hemodialysis has not been studied to date.

The elderly

No dosage adjustment is necessary although pharmacokinetic studies have indicated that the elimination of finasteride is slightly reduced in patients over 70 years of age.

Summary of product characteristics

Pediatric population

Sandoz finasterid is contraindicated in children (see section 4.3).

Administration mode

By mouth only.

The tablet should be swallowed whole and should not be split or crushed (see section 6.6).

4.3 Contraindications

Hypersensitivity to finasteride or to any of the excipients listed in section 6.1. Sandoz finasterid is contraindicated in women (see also sections 4.6 and 6.6) and in children.

Pregnancy

– Use in pregnant or possibly pregnant women (see section 4.6, Exposure to finasteride: risk to the male fetus).

4.4 Special warnings and precautions for use

General

In order to avoid constructive complications, it is important that patients with a large amount of residual urine and/or a significant decrease in urinary flow are closely monitored. The possibility of surgery should be an option. Consultation with a urologist should be considered for patients treated with finasteride.

Effects on PSA levels and prostate cancer screening

No clinical benefit has yet been demonstrated in patients with prostate cancer.

Prostate treated with finasteride 5 mg

Patients with BPH and elevated serum levels of specific antigen the prostate (PSA) have been followed during controlled clinical studies accompanied by the regular PSA measurements and prostate biopsies. During these studies carried out in patients with BPH, the administration of a dose of 5 mg of finasteride did not appear to alter the detection rate of prostate cancer, and the

incidence overall prostate cancer was not significantly different in treated patients by 5 mg finasteride or placebo.

Digital rectal examinations and other assessments for cervical cancer are recommended. prostate before initiating treatment with 5 mg finasteride, then periodically. The Measurement of serum PSA levels is also used for the detection of prostate cancer. In generally, PSA levels > 10 ng/ml (Hybritech) at baseline prompt an evaluation additional and to consider a biopsy; in the event of a PSA level between 4 and 10 ng/ml, it is advised to carry out an additional assessment. The PSA levels obtained in men with cancer of the prostate and in those who are not, are very much the same. Therefore, the presence of prostate cancer should not be excluded in men with BPH whose PSA levels are within normal limits, even though these men are treated with 5 mg of finasteride.

The measurement of PSA level < 4 ng/ml at the initial state does not exclude the existence of cancer of the prostate. Finasteride 5 mg causes an approximately 50% decrease in serum PSA levels in patients who have BPH, even in the presence of prostate cancer. This decrease in the rate serum PSA in patients with BPH who are treated with finasteride 5 mg should be taken into consideration in the interpretation of PSA values and does not exclude the concomitant presence of a Prostate cancer. This reduction is expected for all PSA levels, although it may vary from patient to patient.

Analysis of PSA values measured in more than 3,000 patients during the PLESS study, a 4-year, placebo-controlled, double-blind study evaluating the efficacy and safety at term of finasteride, confirmed that in typical patients treated with 5 mg of finasteride for six months or more, the value of the PSA level must be doubled in order to be able to compare it to the 2/10 Summary of product characteristics normal values observed in untreated men. Thanks to this correction, the PSA assay maintains its sensitivity and specificity as well as its reliability as a screening method for cancer of prostate. Any significant increase in PSA levels in patients treated with finasteride 5 mg should be carefully assessed taking into account the possibility of non-compliance with the treatment with 5 mg of finasteride.

The percentage of free PSA (the ratio of free PSA to total PSA) does not decrease significantly significant under the effect of 5 mg of finasteride. The ratio of the free PSA rate to the total rate of PSA remains constant even under the influence of 5 mg of finasteride. When the free PSA ratio is used for the detection of prostate cancer, no adjustment of the value is necessary.

Drug Interactions/Interactions with Biological Tests Effect on PSA Levels Serum

PSA concentrations correlate with patient age and volume of the prostate, and the volume of the prostate varies with the age of the patient. When interpreting the values PSA laboratory tests, take into account that PSA levels decrease in patients treated with 5 mg of finasteride. In most patients, a rapid decrease in PSA levels is seen at during the first months of treatment, then the PSA levels stabilize at a new value of base. The post-treatment baseline value is approximately half of the pre-treatment value. At the house of typical patients treated with 5 mg finasteride for six months or longer, PSA levels should therefore double to allow a comparison with the normal values observed in men untreated. For clinical interpretation of results, see section

4.4 Effects on PSA and detection of prostate cancer

Male breast cancer In clinical studies and in the post-marketing period, breast cancer in men treated with finasteride 5 mg has been reported. Physicians should instruct their patients to

immediately report any changes in breast tissue such as lumps, pain, swelling, gynecomastia or breast secretion.

Mood swings and depression

Mood changes, including depressed mood, depression and, less frequently, suicidal ideation has been reported in patients treated with finasteride 5 mg. The patients should be monitored for psychiatric symptoms and, if these appear, they should patients should be advised to seek medical advice.

Pediatric population

The use of finasteride is not indicated in children. Safety and effectiveness have not been established in children.

Hepatic insufficiency

The effect of hepatic impairment on the pharmacokinetics of finasteride has not been studied. Caution is advised in patients with impaired liver function as levels finasteride plasma concentrations may be higher in these patients (see section 4.2).

Lactose

Sandoz finasterid contains lactose monohydrate. Patients with hereditary problems rare cases of galactose intolerance (e.g. galactosemia) or glucose malabsorption syndrome and galactose should not take this medicine. This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, i.e. that it is essentially “sodium-free.”

Summary of product characteristics

4.5 Interactions with other medicinal products and other forms of interaction

No clinically significant drug interactions have been identified. Finasteride is primarily metabolized by the cytochrome P450 3A4 system but does not appear to significantly impact this system. Although it is believed that the risk of affecting the pharmacokinetics other drugs is weak for finasteride, it is likely that inhibitors and inducers cytochrome P450 3A4 will alter finasteride plasma concentrations. However, based on established safety margins, it is unlikely that any increase secondary to the concomitant use of these inhibitors is clinically significant. Compounds tested in humans included propranolol, digoxin, glibenclamide, warfarin, theophylline and phenazone and no clinically significant interaction was observed.

4.6 Fertility, pregnancy and lactation

Finasteride is contraindicated for use in women who are pregnant or possibly speakers (see section 4.3). Given the ability of type II 5-alpha-reductase inhibitors to inhibit the conversion of testosterone to dihydrotestosterone, these drugs, including finasteride, can cause abnormalities of the external genitalia in the male fetus when administered to a pregnant woman. Finasteride exposure – risk to male fetus. Women should not handle crushed or broken finasteride tablets when they are pregnant or potentially pregnant, due to the possibility of absorption of finasteride and the potential later risks for a male fetus (see “Pregnancy” above). The finasteride tablets are covered with a film that prevents contact with the substance active during normal use, if the

tablets are not broken or crushed. Small amounts of finasteride have been recovered from semen in subjects receiving 5 mg of finasteride per day. It is not known whether a male fetus may be adversely affected in the event of exposure of the mother to the semen of a patient treated with finasteride. In the case of a confirmed pregnancy or possible pregnancy in the patient's sexual partner, the latter is recommended to minimize your partner's exposure to semen.

Breastfeeding

The use of finasteride is not indicated in women. It is not known whether finasteride passes into breast milk.

4.7 Effects on ability to drive and use machines

There are no data to suggest that finasteride affects the ability to drive vehicles or to use machines.

4.8 Adverse reactions

The most common side effects are impotence and decreased libido. These effects side effects occur early in the course of treatment and resolve in the majority of patients continuing the treatment. Adverse reactions reported during clinical trials and/or the use of finasteride 5 mg and/or of finasteride at lower post-marketing doses are listed in the table below. The frequency of side effects is determined as follows: Very common (≥1/10), common (≥1/100, <1/10)>, uncommon (≥1/1,000, <1/100), rare (≥1/10,000, Summary of product characteristics <1/1,000), very rare (<1/10,000), frequency unknown (cannot be estimated from the available data available).

The frequency of adverse reactions reported during post-marketing use cannot not be determined, as these effects are from spontaneous reports.

System organ classes	Frequent (≥ 1/100, < 1/10)	Infrequent (≥ 1/1 000, < 1/100)	Rare (≥ 1/10,000, < 1/1,000)	Very rare (< 1/10,000)	Frequency not known (cannot be estimated from available data)
Immune system disorders					Hypersensitivity reactions such as angioedema, including swelling of the lips, tongue, throat and face
Psychiatric disorders	Loss of libido				Depression, decreased libido which persists after stopping treatment, anxiety
Heart conditions					Palpitations
Hepatobiliary disorders					Increased liver enzymes
Skin and subcutaneous tissue disorders		Eruptions			Pruritus, urticaria
Reproductive system and breast disorders	Impotence	Breast tenderness/ enlargement, ejaculation disorders			Testicular pain, erectile dysfunction that persists after stopping treatment; male infertility and/or poor sperm quality
Investigations	Reduced semen volume				

Additionally, clinical studies and post-marketing use have revealed the following: cancer male breast (see section 4.4).

Medical Therapy of Prostate Symptoms (MTOPS) study prostate

The MTOPS study compared treatment with 5 mg/day of finasteride (n=768), treatment with 4 or 8 mg/day of doxazosin (n=756), a combination treatment combining 5 mg/day of finasteride and 4 or 8 mg/day doxazosin (n=786), and placebo (n=737). During this study, the safety profiles and safety of the combined treatment were generally consistent with the component profiles individual. The incidence of ejaculation disorders in patients receiving combination therapy was comparable to the sum of the incidences of this adverse event for the two monotherapies.

Other long-term data

In a 7-year placebo-controlled trial that enrolled 18,882 men healthy, of which 9,060 had analysis results following a needle biopsy of the prostate, a prostate cancer was detected in 803 (18.4%) men receiving finasteride 5 mg and in 1,147 (24.4%) men receiving placebo. In the finasteride 5 mg group, 280 (6.4%) men had prostate cancer with Gleason scores ranging from 7 to 10 detected by needle biopsy, versus 237 (5.1%) men in the placebo group. Additional analyzes suggest that the increased incidence of high-grade prostate cancers seen in the finasteride 5 group mg may be explained by a detection bias due to the effect of finasteride 5 mg on the volume of the prostate. Of the total number of prostate cancer cases diagnosed in this study, approximately 98% were classified as intracapsular (clinical stage T1 or T2) at the time of diagnostic. The clinical significance of the 7-10 score data according to the Gleason scale is unknown.

Results of laboratory tests

When performing the PSA assay in the laboratory, it should be taken into consideration that the PSA levels are reduced in patients treated with finasteride (see section 4.4). No other differences were observed in the results of routine laboratory tests between the patients receiving placebo and those treated with finasteride.

Reporting of suspected adverse reactions

The reporting of suspected adverse reactions after authorization of the medicinal product is important as a means of continuously monitoring the benefit/risk profile 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 received single doses of finasteride up to 400 mg and multiple doses up to 80 mg/day for up to three months without side effects. No specific treatment of finasteride overdose is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 5-α-testosterone reductase inhibitors.

ATC code: G04CB01 Finasteride is a synthetic 4-azasteroid, a specific competitive inhibitor of the enzyme intracellular 5-alpha reductase type II. The enzyme converts testosterone into dihydrotestosterone (DHT), more potent androgen. The prostate gland, and therefore the hyperplastic prostatic tissue also, depend on the conversion of testosterone to DHT for their function and growth normal. Finasteride has no affinity for the androgen receptor. Clinical studies show a rapid reduction in serum DHT levels by 70%, leading to a reduction in the volume of the prostate. After 3 months, there is a reduction of approximately 20% of the volume of the gland, and this shrinkage continues and reaches about 27% after 3 years. A discount net

occurs in the periurethral area immediately around the urethra. Urodynamic measurements also confirmed a significant reduction in detrusor pressure following the reduction of obstruction. Compared to the start of treatment, significant improvements in maximum speed urine flow and symptoms were obtained within a few weeks. Differences with placebo were reported after 4 and 7 months of treatment, respectively. All efficacy parameters were maintained over a 3-year follow-up period. Effects of four years of treatment with finasteride on the incidence of acute urinary retention, need for surgery, symptom score and prostate volume In clinical studies in patients with moderate to severe symptoms benign prostatic hyperplasia, enlargement of the prostate on digital rectal examination and low residual urinary volumes, finasteride reduced the incidence of urinary retention acute 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 to 34), a sustained regression in the volume of the prostate by about 20% and a sustained increase in the velocity of urinary flow.

5.2 Pharmacokinetic properties

Absorption

The bioavailability of finasteride is approximately 80%. Peak plasma concentrations are reached approximately 2 hours after taking the drug, and absorption is complete 6 to 8 hours after the plug. Distribution Plasma protein binding is approximately 93%. Clearance and volume of distribution are approximately 165 ml/min (70 to 279 ml/min) and 76 L (44 to 96 l), respectively. An accumulation of small amounts of finasteride is observed after repeated administration. After a daily dose of 5 mg, the highest finasteride concentration low at steady state has been calculated as 8-10 ng/ml, which remains stable over time. Biotransformation Finasteride is metabolized in the liver. Finasteride does not significantly affect the cytochrome P 450 enzyme system. Two metabolites with weak inhibition effects of 7/10 Summary of product characteristics 5-alpha reductase have been identified.

Elimination

The plasma half-life is on average 6 hours (4 to 12 hours) (in men over 70: 8 hours, range from 6 to 15 hours). After administration of radioactively labeled finasteride, approximately 39% (32-46%) of the dose is excreted in the urine as metabolites. There is practically no trace of unmodified finasteride in urine. Approximately 57% (51-64%) of the total dose is excreted in faeces. In patients with renal insufficiency (creatinine clearance greater than 9 ml/min), no changes were observed in the elimination of finasteride (see section 4.2). Finasteride has been shown to cross the blood-brain barrier. Small amounts of finasteride have been recovered from the semen of treated patients. In 2 studies in subjects healthy subjects (n=69) receiving finasteride 5 mg/day for 6 to 24 weeks, Finasteride concentrations in semen ranged from undetectable (< 0.1 ng/ml) to 10.54ng/ml. In a previous study using a less sensitive assay, concentrations of finasteride in the semen of 16 subjects receiving finasteride 5 mg/day ranged from undetectable value (< 1.0 ng/ml) at 21 ng/ml. Thus, from an ejaculate volume of 5 ml, the

quantity of finasteride in the semen was estimated to be 50 to 100 times lower than the dose of finasteride (5 µg) showing no effect on circulating DHT levels in humans (see also section 5.3.)

5.3 Preclinical safety data

Non-clinical data from conventional repeated-dose toxicology studies, genotoxicity and carcinogenicity did not reveal any particular risk for humans. Reproductive toxicology studies in male rats have shown a reduction in weight of the prostate and seminal vesicles, a reduction in the secretion of the genital glands accessories, and a reduction in the fertility index (caused by the primary pharmacological effect finasteride). The clinical relevance of these results is unclear. As with other 5-alpha reductase inhibitors, feminization of male rat fetuses has been observed with administration of finasteride during gestation. Administration intravenous finasteride in pregnant rhesus monkeys at doses up to 800 ng/day during the entire period of embryonic and fetal development did not cause any abnormality in male fetuses. This dose is approximately 60-120 times higher than the estimated amount in semen of a man who took 5 mg of finasteride and to which a woman is likely to be exposed by the sperm. In order to confirm the relevance of the rhesus model for human fetal development, oral administration of finasteride at 2 mg/kg/day (systemic exposure (AUC) of monkeys was slightly higher (3x) than men who took 5 mg of finasteride, or about 1-2 million times the estimated amount of finasteride in semen) in pregnant monkeys resulted in external genital abnormalities in the male fetus. No other abnormalities were observed in the male fetus and no finasteride-related abnormalities were observed in the female fetus at one any dose.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Tablet core: Lactose monohydrate microcrystalline cellulose
Pregelatinized Corn Starch
Sodium Starch Glycolate (Type A)
Sodium laurilsulfate
Magnesium Stearate
Tablet coating: microcrystalline cellulose
Hypromellose Macrogol (8) stearate (type I)

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 precautions

6.5 Nature and contents of the outer packaging

PVC/PVDC/aluminum pads: 10, 15, 20, 28, 30, 50, 50 x 1, 60, 90, 98, 100, 100 x 1, 105 and 120 tablets. Bottles (HDPE) with PP caps: 30 or 100 tablets. Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

Women who are pregnant or may become pregnant should not handle tablets of broken or crushed finasteride due to the possibility of finasteride absorption and danger possible subsequently incurred by the male fetus (see section 4.6).

7. MARKETING AUTHORIZATION HOLDER

Sandoz Hungária Kft.
H-1114 Budapest, Bartók Béla út 43.-47
Hungary

8. MARKETING AUTHORIZATION NUMBERS

BE294262 (plate) BE294271 (bottle)

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of first authorization: March 22, 2005
Date of last renewal: Sept. 22, 2010

10. DATE OF REVISION OF THE TEXT

February 22, 2020