SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Finasteride Aristo 5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg of finasteride.

Excipient with known effect:

Contains 80 mg lactose (as lactose monohydrate)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.
Blue colour, round shaped film coated tablets with a diameter of 6.5 mm, debossed with 'H' on one side and '37' on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride is indicated for the treatment and control of benign prostatic hyperplasia (BPH). To reduce the incidence of acute urinary retention and reduce need for surgery including transurethral resection of the prostate (TURP) and prostatectomy. Finasteride 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.

Finasteride can be administered alone or in combination with the alpha-blocker-doxazosin (see section 5.1).

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

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 haemodialysis.

Paediatric population

Finasteride is not indicated for use in children (see section 4.3). The safety and efficacy of finasteride in children under 18 years have not yet been established.

No data are available.

Method of administration

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

The duration of administration is decided by the treating physician.

4.3 Contraindications

Finasteride is not indicated for use in women or children (see sections 4.4 and 4.6).

Finasteride is contraindicated in the following situations:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- Pregnancy - in women who are pregnant or may become pregnant (see section 4.6).

4.4 Special warnings and precautions for use

General information

Treatment with finasteride should be initiated in consultation with an urologist.

Urinary obstruction due to a trilobulary pattern of prostate enlargement should be excluded before initiation of therapy.
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 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.

The 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. The analysis of data obtained during a 4 years placebo-controlled, double-blind study (Proscar Long-Term efficacy and Safety Study, PLESS) which was conducted in 3,000 men confirmed that in 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 therapy with Finasteride.

The 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 to its value is necessary.

Drug/laboratory test interactions

Effect on levels of PSA

The 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 stabilise 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, Effects on PSA and prostate cancer detection.

Breast cancer in men

Breast cancer has been reported in men taking finasteride 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.

Paediatric population

Finasteride is not indicated for use in children (see section 4.3). The safety and efficacy of finasteride in children under 18 years have not yet 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. Patients should be monitored for psychiatric symptoms and if these occur, the patient should be advised to seek medical advice.

Hepatic Insufficiency

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

Finasteride Aristo contains Lactose

Patients with any of the following genetic deficiencies should not take this drug: galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

Finasteride Aristo contains Sodium

This medicine 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 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 that have been tested in man included propranolol, digoxin, glibenclamide, warfarin, theophylline, and phenazone and no clinically meaningful interactions were found.

4.6 Fertility, pregnancy and lactation

Fertility

Long-term data on fertility in humans are lacking and specific studies in subfertile men have not been conducted. The male patiens who were planning to father a child were initially excluded from clinical trials. Although, animal studies did not show relevant negative effects on fertility, spontaneous reports of infertility and/or poor seminal quality were received post-marketing. In some of these reports, patients had other risk factors that might have contributed to infertility. Normalization or an improvement in sperm quality was reported upon discontinuation of finasteride (see section 4.8).

Pregnancy

Finasteride is contra indicated in women when they are or may potentially be pregnant (see section 4.3). Because of the ability of 5α-Reductase-inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including finasteride, might cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

Exposure to finasteride - risk to male foetus

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 6.6).

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.

Breastfeeding

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

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 usually occur early in the course of therapy resolve with continued treatment in the majority of patients.

Tabulated list of adverse reactions

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**
Immune system disorders	*Unknown:* hypersensitivity reactions such as angioedema (including swelling of lips, tongue, throat and face)
Psychiatric disorders	*Common:* libido decreased *Unknown:* depression, anxiety, suicidal ideation
Cardiac disorders	*Unknown*: palpitation
Hepatobiliary disorders	*Unknown:* hepatic enzymes increased
Skin and subcutaneous tissue disorders	*Uncommon:* rash *Unknown:* pruritus, urticaria
Reproductive system and breast disorders	*Common:* impotence *Uncommon:* ejaculation disorder, breast tenderness, breast enlargement. Isolated cases of nipple discharge have been reported and lumps in the breast as part of gynecomastia have been reported, which has been surgically removed in individual patients. *Unknown:* after discontinuation of treatment continued decreased libido, testicular pain and sexual dysfunction (erectile dysfunction and ejaculation disorders); male infertility and/or poor sperm quality. A normalization or improvement in sperm quality was reported after discontinuation of finasteride.
Investigations	*Common:* decreased volume of ejaculate

Description of selected adverse reactions

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

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).

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 received single doses of finasteride up to 400 mg and multiple doses to 80 mg/day for every 3 months up without adverse effects. There is no specific recommended treatment of overdose of finasteride.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Testosterone-5-alpha reductase inhibitors, medicinal product for the treatment of benign prostate hyperplasia. ATC-Code: G04CB 01

Mechanism of action/Pharmacodynamic effects

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 efficacy and safety

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 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 (MTOPS)

The Medical Therapy of Prostatic Symptoms (MTOPS) Trial was a 4-to 6-year study in 3047 men with symptomatic BPH who were randomized to receive finasteride 5 mg/day (n = 768), doxazosin 4 or 8 mg/day* (n = 756), the combination of finasteride 5 mg/day and Doxazosin 4 or 8 mg/day* (n = 786), or placebo (n = 737). The primary endpoint was time to clinical progression of BPH, defined as a $\geq$ 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 procression were confirmed $\geq$ 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.
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

* Titrated from 1 mg to 4 or 8 mg as tolerated over a 3-week period.

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.

5.2 Pharmacokinetic properties

Absorption

Maximum plasma concentrations are reached approximately two hours after dosing and the absorption is complete within 6-8 hours. The oral bioavailability of finasteride is approximately 80%, relative to an intravenous reference dose, and is unaffected by food.

Distribution

Protein binding for medicinal product is approximately 93%. The volume of distribution is approximately 76 liters.

A multiple-dose study demonstrated a slow accumulation of small amounts of finasteride over time. After daily dosing of 5 mg/day, trough plasma concentrations of finasteride of about 8-10 ng/mL were reached and these remained stable over time.

Finasteride has been recovered in the cerebrospinal fluid (CSF) of patients treated with a 7-10 day course of finasteride, but the medicine does not appear to concentrate preferentially in the CSF.

Finasteride has also been recovered in the seminal fluid of subjects receiving 5 mg of finasteride daily.

Biotransformation

Finasteride undergoes oxidative metabolism in the liver.

After an oral dose of ^{14}C-finasteride in man, 39% of the dose was excreted in the urine in the form of metabolites (virtually no unchanged drug was excreted in the urine), and 57% of total dose was excreted in the faeces. Two metabolites have been identified which possess only a small fraction of the Type II 5 α-reductase activity of finasteride.

Elimination

Finasteride displays a mean plasma elimination half-life of six hours. Plasma clearance of finasteride is approximately 165 mL/min.

In the elderly, the elimination rate of finasteride is somewhat decreased. Half-life is prolonged from a mean half-life of approximately six hours in men aged 18-60 years to eight 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 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. 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.

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 fetal development resulted in no abnormalities in male fetuses. 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 fetal 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 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 (E460)
Microcrystalline cellulose (PH 102)
Maize starch, pregelatinized (1500)
Sodium starch glycolate (Type A)
Docusate Sodium
Magnesium Stearate (E572)

Film –Coating

Hypromellose, type 2910 6cP (E464)
Titanium dioxide (E171)
Indigo carmine aluminium lake (E132)
Talc (E553b)
Iron oxide yellow (E172)

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

Blister Pack: Aluminium-PVC/PE/PVDC

Pack sizes 15, 28, 30, 50, 56, 60 or 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Women who are pregnant or may potentially be 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 medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Aristo Pharma GmbH
Wallenroder Straße 8-10
13435 Berlijn
Duitsland

8. MARKETING AUTHORISATION NUMBER(S)

Finasteride Aristo 5 mg filmomhulde tabletten RVG 129166

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 13 juni 2023

10. DATE OF REVISION OF THE TEXT

Laatste gedeeltelijke wijziging betreft rubriek 4.8; 3 september 2025