SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Finasteride 1 mg Film-coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 1 mg of Finasteride.

Excipient(s): Lactose monohydrate 95.58 mg.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet.

Reddish brown, round, biconvex, film coated tablets, marked 'F1' on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride 1 mg is indicated for treatment of the first stage of the hair loss (androgenetic alopecia) in males. Finasteride 1 mg stabilizes the process of the androgenetic alopecia in the 18-41 year old males. Its effectiveness in bitemporary recession nor in the loss of hair has not been determined.

Finasteride is not indicated for use in women or children and adolescents.

4.2 Posology and method of administration

Posology

For oral use only.

The recommended dosage is one 1 mg tablet daily. Finasteride Accord 1mg may be taken with or without food. The tablet should be swallowed whole and must not be divided or crushed (See section 6.6).

There is no evidence that an increase in dosage will result in increased efficacy.

Efficacy and duration of treatment should continuously be assessed by the treating physician. Generally, three to six months of once daily treatment are required before evidence of stabilization of hair loss can be expected. Continuous use is recommended to sustain benefit. If treatment is stopped, the beneficial effects begin to reverse by six months and return to baseline by 9 to 12 months.

Method of administration

For oral use only.

Dosage in renal insufficiency
No dosage adjustment is required in patients with renal insufficiency.

Dosage in hepatic insufficiency
There are no data available in patients with hepatic insufficiency

4.3 Contraindications

Finasteride should not be used in children / adolescents.
Contraindicated in women and children (see section 4.4 'special warning and precaution for use', 4.6 'pregnancy and lactation', and 5.1 'pharmacodynamic properties'). Should not be taken by men who are taking Finasteride 5 mg Tablets or any other 5α-reductase inhibitor for benign prostatic hyperplasia or any other condition.
Hypersensitivity to finasteride or to any of the excipients listed in 6.1.

4.4 Special warnings and precautions for use

Paediatric population

Finasteride must not be used in children / adolescents (< 18 years). There are no data demonstrating efficacy or safety of finasteride in children under the age of 18.

Effects on Prostate Specific Antigen (PSA)

In clinical studies with Finasteride 1 mg Tablets in men 18-41 years of age, the mean value of serum prostate-specific antigen (PSA) decreased from 0.7 ng/ml at baseline to 0.5 ng/ml at month 12. This decrease in serum PSA concentrations needs to be considered, if during treatment with Finasteride Tablets 1mg, a patient requires a PSA assay. In this case it should be considered to double PSA value before making a comparison with the results from untreated men.

Effects on fertility

See 4.6 Fertility, pregnancy and lactation

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, gynaecomastia or nipple discharge.

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

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

Mood alterations and depression

Mood alterations including depressed mood, depression and, less frequently, suicidal ideation have been reported in patients treated with finasteride 1 mg. Patients should be monitored for psychiatric symptoms and if these occur, treatment with finasteride should be discontinued and the patient advised to seek medical advice.

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 affect the cytochrome P450-linked drug metabolizing 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. Compounds which have been tested in man have included antipyrine, digoxin, glibenclamide, propranolol, theophylline and warfarin and no interactions were found.

Due to lacking data for the concomitant use of finasteride and topical minoxidil in male pattern hair loss the combination is not recommended.

Interaction studies have only been performed in adults

4.6 Fertility, pregnancy and lactation

Use during pregnancy

Finasteride is contra-indicated in women due to the risk in pregnancy (see section 4.3).
Because of the ability of type II 5α-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone (DHT) in some tissues, these drugs, including Finasteride, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman (see section 5.3 and section 6.6).

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).

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 (e. g. by using condoms).

Breast-feeding Finasteride 1 mg are not indicated for use in women. It is not known whether finasteride is excreted in breast milk**.**

Fertility

Long-term data on fertility in humans are lacking, and specific studies in subfertile men have not been conducted. The male patients 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. Normalisation or improvement of seminal quality has been reported after discontinuation of finasteride. Patients who are planning to father a child should consider to stop treatment.

4.7 Effects on ability to drive and use machines

Finasteride 1 mg has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

The adverse reactions during clinical trials and / or post-marketing use are listed in the table below.

The frequencies of undesirable effects are following: 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.

Immune system disorders:	*Not known:* Hypersensitivity reactions, including rash, pruritus, urticaria and angioedema (swelling of the lips, tongue, throat, and face).
Cardiac disorders:	*Not known:* Palpitation
Psychiatric disorder:	*Uncommon*[$]*:* Decreased libido, depression *Not known:* Anxiety
Hepatobiliary disorders:	*Not known:* Increased hepatic enzymes.
Reproductive system and breast disorders:	*Uncommon*[$]*:* Erectile dysfunction, ejaculation disorder (including decreased volume of ejaculate) *Not known:* Breast tenderness and enlargement (gynecomastia), Testicular pain, infertility*

* See section 4.4
[$] incidences presented as difference from placebo in clinical studies at Month 12

In addition, the following have been reported in post-marketing use: Persistent sexual dysfunction (decreased libido, erectile dysfunction and ejaculation disorder) after discontinued treatment with finasteride; Male breast cancer (see section 4.4 Special warnings and precautions for use)

Drug-related sexual undesirable effects were more common in the finasteride-treated men than the placebo-treated men, with frequencies during the first 12 months of 3.8% vs 2.1%, respectively. The incidence of these effects decreased to 0.6% in finasteride-treated men over the following four years. Approximately 1% of men in each treatment group discontinued due to drug related sexual adverse experiences in the first 12 months, and the incidence declined thereafter.

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 ADR ReportingWebsite: www.medicinesauthority.gov.mt//adrportal

4.9 Overdose

In clinical studies, single doses of finasteride up to 400 mg and multiple doses of finasteride up to 80 mg/day for three months (n=71) did not result in dose related side effects. No specific treatment of overdose with finasteride Tablets 1mg is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatologicals
ATC-Code: D11 AX10

Mechanism of action

Finasteride is a 4-azasteroid, which inhibits human Type 2 5α-reductase (present within the hair follicles) with greater than 100-fold selectivity over human Type 1 5α-reductase, and blocks the peripheral conversion of testosterone to the androgen dihydrotestosterone (DHT). In men with male pattern hair loss, the balding scalp contains miniaturized hair follicles and increased amounts of DHT. Finasteride inhibits a process responsible for miniaturization of the scalp hair follicles, which can lead to reversal of the balding process.

Clinical efficacy
Studies in men:

The efficacy of finasteride 1mg tablets was demonstrated in three studies in 1879 men 18 to 41 years of age with mild to moderate, but not complete, vertex hair loss and frontal/mid-area hair loss. In these studies, hair growth was assessed using four separate measures including hair count, ratings of photographs of the head by an expert panel of dermatologists, investigator assessment, and patient self-assessment. In the two studies in men with vertex hair loss, treatment with finasteride 1mg tablets was continued for 5 years, during which time patients improved compared to baseline in men treated with finasteride 1mg tablets were generally greatest at 2 years and gradually declined thereafter (e.g., hair count in a representative 5.1 cm2 area was increased 88 hairs from baseline at 2 years and 38 hairs from baseline at 5 years), hair loss in the placebo group progressively worsened compared to baseline (decrease of 50 hairs at 2 years and 239 hairs at 5 years). Thus, although improvement compared to baseline in men treated with finasteride 1mg tablets did not increase further after 2 years, the difference between treatment groups continued to increase throughout the 5 years of the studies. Treatment with finasteride 1mg tablets for 5 years resulted in stabilization of hair loss in 90% of men based on photographic assessment and in 93% based on investigator assessment.

In addition, increased hair growth was observed in 65% of men treated with finasteride 1mg tablets based on hair counts, in 48% based on photographic assessment, and in 77% based on investigator assessment. In contrast, in the placebo group, gradual hair loss over time was

observed in 100% of men based on hair counts, in 75% based on photographic assessment, and in 38% based on investigator assessment. In addition, patient self-assessment demonstrated significant increases in hair density, decreases in hair loss, and improvement in appearance of hair after treatment over 5 years with finasteride 1mg tablets (see Table below).

Percent of Patients Improved as Assessed by Each of the 4 Measures

	Year 1†		Year 2††		Year 5††	
	FINASTERIDE 1MG TABLETS	Placebo	FINASTERIDE 1MG TABLETS	Placebo	FINASTERIDE 1MG TABLETS	Placebo
Hair Count	(N=679) 86	(N=672) 42	(N=433) 83	(N=47) 28	(N=219) 65	(N=15) 0
Global Photographic Assessment	(N=720) 48	(N=709) 7	(N=508) 66	(N=55) 7	(N=279) 48	(N=16) 6
Investigator Assessment	(N=748) 65	(N=747) 37	(N=535) 80	(N=60) 47	(N=271) 77	(N=13) 15
Patient Self-Assessment: Satisfaction with appearance of hair overall	(N=750) 39	(N=747) 22	(N=535) 51	(N=60) 25	(N=284) 63	(N=15) 20

† Randomization 1:1 FINASTERIDE 1MG TABLETS to placebo
†† Randomization 9:1 FINASTERIDE 1MG TABLETS to placebo

In a 12-month study, in men with frontal/mid-area hair loss, hair counts were obtained in a representative 1 cm2 area (approximately 1/5 the size of the area sampled in the vertex studies). Hair counts, adjusted to a 5.1 cm2 area, increased by 49 hairs (5%) compared to baseline and by 59 hairs (6%) compared to placebo. This study also demonstrated significant improvements in patient self-assessment, investigator assessment, and ratings of photographs of the head by an expert panel of dermatologists. Two studies of 12 and 24 weeks duration showed that a dose 5-fold the recommended dose (finasteride 5 mg daily) produced a median decrease in ejaculate volume of approximately 0.5 mL (-25%) compared with placebo. This decrease was reversible after discontinuation of treatment. In a study of 48 weeks of duration, Finasteride 1 mg daily produced a median decrease in ejaculate volume of 0.3 mL (-11%) compared with a 0.2 mL (-8%) decrease for placebo. No effect was observed on sperm count, motility or morphology. Longer-term data are not available. It has not been feasible to undertake clinical studies, which directly elucidate possible negative effects on fertility. However, such effects are judged as very unlikely (see also 5.3 Preclinical safety data).

Studies in women

Lack of efficacy was demonstrated in post-menopausal women with androgenetic alopecia who were treated with finasteride 1 mg tablets in a 12-month, placebo-controlled study (n=137). These women did not show any improvement in hair count, patient self-assessment, investigator assessment, or ratings based on standardized photographs, compared with the placebo group.

5.2 Pharmacokinetic properties

Absorption

Relative to an intravenous reference dose, the oral bioavailability of finasteride is approximately 80%. The bioavailability is not affected by food. Maximum finasteride plasma concentrations are reached approximately two hours after dosing and the absorption is complete after six to eight hours.

Distribution

Protein binding is approximately 93%. The volume of distribution of finasteride is approximately 76 liters.
At steady state following dosing with 1 mg/day, maximum finasteride plasma concentration averaged 9.2 ng/ml and was reached 1 to 2 hours post dose; $AUC_{(0\text{-}24\ hr)}$ was 53 ng•hr/ml.

Finasteride has been recovered in the cerebrospinal fluid (CSF), but the drug does not appear to concentrate preferentially to the CSF. A small amount of-finasteride has also been detected in the seminal fluid of subjects receiving the drug.

Biotransformation

Finasteride is metabolized primarily via but does not affect the cytochrome P450 3A4 system. Following an oral dose of ^{14}C-finasteride in man, two metabolites of finasteride were identified that possess only a small fraction of the 5α-reductase inhibitory activity of finasteride.

Elimination

Following 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.
Plasma clearance is approximately 165 ml/min.

The elimination rate of finasteride decreases somewhat with age. Mean terminal half-life is approximately 5-6 hours in men 18-60 years of age and 8 hours in men more than 70 years of age. These findings are of no clinical significance and hence, a reduction in dosage in the elderly is not warranted.

Characteristics in patients

No adjustment in dosage is necessary in non-dialyzed patients with renal impairment.

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 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 foetuses. 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. The reproductive toxicity is believed to be mediated via the intended inhibition of 5α-reductase. Taken into account the species enzyme difference in sensitivity to finasteride inhibition the margin of pharmacological exposure would be about 4 times. 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 below or in the range of that of men who have taken 5 mg finasteride, or approximately 1 to 2 million times the estimated mount 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
Cellulose, microcrystalline (E460)
Starch, pregelatinised (maize)
Sodium starch glycolate (type A)
Lauroyl macrogolglycerides
Magnesium stearate (E572)

Film coating:

Hypromellose (E464)
Titanium dioxide (E 171)
Macrogol 6000
Iron oxide red (E172)
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

Alu-Alu Blister

Finasteride Accord 1 mg tablets are packed in blister pack of 28, 30, 84 and 98 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 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 product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Limited,
7-8 Euro House
Euro Business Park
Little Island, Co. Cork
T45K857, Ireland

8 MARKETING AUTHORISATION NUMBER(S)

MA 1269/00701

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 1st April 2011
Renewal of the authorization: 25th June 2016

10 DATE OF REVISION OF THE TEXT

26/02/2019