SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Finjuve for men 2.275 mg/mL cutaneous spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL solution contains 2.275 mg of finasteride.

Each actuation delivers 50 microlitres, which contain 114 micrograms of finasteride.

Excipient with known effect
One actuation of 50 microlitres solution contains 25 mg of ethanol (96 per cent).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous spray, solution.

Colourless, clear, slightly viscous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Finjuve is indicated for the topical treatment of adult men from 18 to 41 years of age with mild to moderate male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss.

4.2 Posology and method of administration

Posology
Finjuve should be applied once daily to bald areas of the scalp. Depending on the size of the baldness, 1 to 4 non-overlapping spray actuations (50 to 200 microlitres of solution) can be used.

The dose selected for the size of baldness should not be increased beyond the maximum of 4 actuations. Efficacy and duration of treatment should continuously be assessed by the treating physician. Generally, 3 to 6 months of once daily treatment are required before evidence of hair growth can be expected. Continuous use is recommended to sustain benefit. There is no clinical experience with Finjuve beyond 6 months.

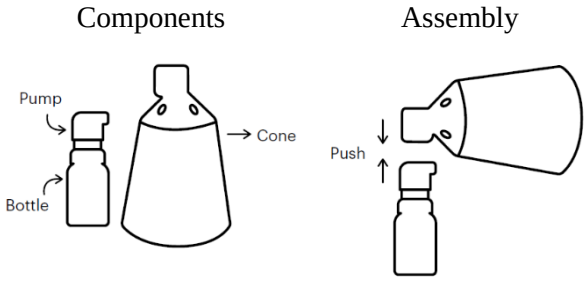
The bottle contains up to 180 actuations (delivering 50 microlitres each), which is sufficient for 45 days of treatment when the maximum dose of 4 actuations once daily is administered, 60 days of treatment for 3 actuations once daily, 90 days of treatment for 2 actuations once daily, and 180 days of treatment for 1 actuation once daily. The bottle should not be used beyond 180 actuations as it could result in the delivery of an insufficient dose. Patients should be advised accordingly.

Patients with renal or hepatic impairment
No dose adjustment is required in patients with renal or hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of Finjuve in children and adolescents under 18 years of age have not been established (see section 4.4).

Method of administration
Finjuve is for cutaneous use. It is only to be used on the scalp.

Assembly of the spray applicator
The presentation of Finjuve contains 2 separate components: a bottle with an attached metering pump, and a cone. These components require assembly prior to first use.



Before using Finjuve for the first time, the pump must be primed by means of 4 full actuations, directing the sprayed solution toward the bathroom sink (the sink must be rinsed afterwards). When Finjuve has not been used for at least 2 weeks the pump must be reprimed by means of 1 full actuation. Other than this, there is no need to shake or to prime the pump at each use.

Handling of the spray applicator
Finjuve should be administered by the patient himself. Hair and scalp should be fully dry prior to application of the solution. The solution should not be sprayed towards the face and should not come into contact with the hands or any part of the body other than the area to be treated on the scalp. In case of unintended contact with the solution, the affected body part should be washed thoroughly.

When spraying the scalp, the cone must be in contact with the scalp to avoid finasteride dispersion in the air. The bald scalp area covered by the cone limits the maximum treatment area for 1 actuation. To cover an area larger than the cone diameter 2, 3, or 4 actuations may be prescribed. In these cases, before applying the second, third, or fourth actuation, the cone should be moved to an area of the scalp next to, but not touching, the area of any previous actuations to avoid spray overlap.

Immediately after application the patient should avoid contact between the treated scalp and surfaces (e.g. pillows, helmets, hats etc.) until the solution has dried. Once applied, Finjuve should be left in place for at least 6 hours.

See section 4.4 for advice if the patient may be in contact with a pregnant woman or a woman who may become pregnant, or children and adolescents.

4.3 Contraindications

Finjuve is not intended for use by women.

Women who are pregnant or may become pregnant (see sections 4.4, 4.6 and 5.3).

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Possible transfer of Finjuve
Women who are pregnant or may become pregnant must not come into contact with Finjuve, or the scalp or surfaces exposed to Finjuve, because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see section 5.3). In case of unintended contact with the solution, the affected body part should be washed thoroughly.

Children and adolescents under 18 years of age must not come into contact with Finjuve, or the scalp or surfaces exposed to Finjuve, because of the possibility of absorption of finasteride and its potential adverse reactions (see section 5.1). In case of unintended contact with the solution, the affected body part should be washed thoroughly.

Effects on Prostate-Specific Antigen (PSA)
In clinical studies with oral finasteride 1 mg in men 18 to 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. Although there is very low systemic exposure to finasteride after topical administration compared to oral administration (see section 5.2), no data are available on the effect of Finjuve on PSA levels, and this should be considered when interpreting the results of PSA tests.

Effects on dihydrotestosterone (DHT) in serum
Dihydrotestosterone is an androgen, a metabolite, and the biologically most active form of testosterone. In the Phase III clinical study at week 24, there was a decrease of DHT in serum in the Finjuve group. The percentage decrease in mean DHT serum concentration from baseline was higher in the oral finasteride group but the decrease was clinically significant with both Finjuve (34.5%) and oral finasteride (55.6%), thus indicating the possibility of systemic adverse reactions of a sexual nature related to a decrease in DHT, though with less probability for Finjuve than with oral finasteride (see sections 4.8 and 5.1). The dosing scheme should be adhered to (see section 4.2).

Breast cancer
There were no reports of breast cancer in patients treated with Finjuve in clinical studies. However, as breast cancer in men is a known risk with oral finasteride, patients should be instructed to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

Mood alterations and depression
There were no reports of mood alterations or depression in patients treated with Finjuve in clinical studies. However, as mood alterations, including depressed mood, depression and, less frequently, suicidal ideation have been reported in patients treated with oral finasteride 1 mg, patients should be instructed to seek medical advice, if they experience any psychiatric symptoms.

Ethanol content
Finjuve contains 25 mg ethanol (96 per cent) in each actuation which is equivalent to 0.5 mg/microlitres (55 per cent). It may cause burning sensation on damaged skin.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with Finjuve. Topical finasteride results in low systemic levels of finasteride (see section 5.2), which is metabolised by cytochrome P450 3A4 (CYP3A4). A clinically relevant effect of concomitantly used CYP3A4 inducers or inhibitors on topical finasteride or of topical finasteride on other treatments metabolised by this enzyme is unlikely.

Concomitant use of Finjuve with other topical products, such as cosmetics, sunscreens or other topical medicinal products, on the same area has not been studied. Use of such products on areas treated with Finjuve should be avoided.

No data are available on the concomitant use of Finjuve and oral finasteride 1 mg or topical minoxidil in male pattern hair loss.

4.6 Fertility, pregnancy and lactation

Finjuve is not intended for use by women.

Pregnancy
Finjuve is contraindicated in women who are pregnant or may become pregnant due to the teratogenicity risk in pregnancy to male foetuses (see sections 4.3, 4.4 and 5.3).

Women who are pregnant or may become pregnant must not come into contact with Finjuve, or the scalp or surfaces exposed to Finjuve, because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see section 5.3). In case of unintended contact with the solution, the affected body part should be washed thoroughly.

Breast-feeding
Not applicable, as Finjuve is indicated for the topical treatment of adult men.

Fertility
Fertility in humans has not been studied with Finjuve.

4.7 Effects on ability to drive and use machines

Finjuve has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The safety profile of Finjuve is based on data from 229 patients with androgenetic alopecia and 97 healthy subjects who were exposed to Finjuve in the clinical development program. In the Phase III clinical study 181 patients were exposed to Finjuve for up to 6 months, 181 patients treated with placebo and 84 patients with oral finasteride. Pruritus and erythema, most of them occurring on the scalp, were reported in this study. Pruritus occurred in 5 (2.8%) and erythema in 4 (2.2%) of 181 patients with Finjuve.

Tabulated list of adverse reactions
The adverse reactions reported during the clinical development program are listed below using the following frequency categories: 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).

System Organ Class (SOC)	Frequency	Adverse reaction
Skin and subcutaneous tissue disorders	Common	Pruritus
	Common	Erythema
Investigations	Very common	Dihydrotestosterone decreased

Description of selected adverse reactions
For oral finasteride, adverse reactions of a sexual nature are listed (decreased libido, erectile dysfunction and ejaculation disorder [including decreased volume of ejaculate]). In the pivotal Phase III clinical study for Finjuve, such treatment-related adverse events of a sexual nature (loss of libido, libido decreased, erectile dysfunction, sexual dysfunction) were also reported and had an overall frequency of 2.8% in patients treated with Finjuve, 3.3% in patients treated with placebo, and 4.8% in patients treated with oral finasteride 1 mg. Please see also sections 4.4 and 5.1.

Further systemic adverse reactions reported in relation to oral finasteride during clinical trials and/or post-marketing may also be possible with Finjuve: hypersensitivity reactions, including rash, pruritus, urticaria, and angioedema; depression; anxiety; palpitations; increased hepatic enzymes; breast tenderness and enlargement; testicular pain; haematospermia; and infertility.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows for 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

There is very low absorption of topically applied finasteride. In case of overdose DHT serum levels are expected to decrease, which may result in an increased probability for systemic effects.

No specific treatment of overdose with Finjuve is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Dermatologicals; Other dermatologicals
ATC code: D11AX10

Mechanism of action
Finasteride is a competitive and specific inhibitor of Type II 5α–reductase, the isozyme that converts the androgen testosterone into its biologically most active metabolite, dihydrotestosterone (DHT). In men with male pattern hair loss, the balding scalp contains miniaturised hair follicles and increased amounts of DHT. Finasteride inhibits a process responsible for miniaturisation of the scalp hair follicles, which can lead to reversal of the balding process.

Pharmacodynamic effects
In the clinical pharmacology studies, the key pharmacodynamic endpoints were DHT concentrations in scalp as a surrogate marker for efficacy in the target tissue, and DHT concentrations in serum as a potential surrogate marker for safety, as decreased systemic concentrations of DHT have been associated with the adverse reactions profile of oral finasteride. Using these surrogate markers, the optimal dose of Finjuve was identified to be up to 200 microlitres once daily (4 actuations).

There is high interindividual variability in serum DHT concentrations. In the Phase III clinical study, at week 24 the percentage decrease in mean DHT serum concentration from baseline was higher in the oral finasteride group (55.6%) than with Finjuve (34.5%), but the decrease was clinically significant for both treatments. Of those patients who were within the normal range at baseline, a higher proportion of patients in the oral finasteride group (55.2%) compared to the Finjuve group (15.3%) developed DHT serum values that decreased to below the normal range (DHT serum <14 ng/dl) after 24 weeks of treatment, thus indicating the possibility for systemic adverse events related to decreased DHT in both groups, though with less probability for Finjuve than for oral finasteride.

Clinical efficacy and safety
The clinical efficacy and safety of Finjuve were assessed in one multi-centre, double-blind, double-dummy, randomised, controlled Phase III study in adult male patients with androgenetic alopecia (PM1541). Patients were to be treated once daily for 24 weeks, randomised in a ratio of 2:2:1 as follows: Finjuve group (up to 200 microlitres Finjuve + oral placebo), placebo group (topical placebo + oral placebo), and oral finasteride group (topical placebo + 1 mg oral finasteride). At baseline, a target 1 cm^2 circular balding area was identified with a small dot tattoo as a reference point for hair count measurements.

Efficacy was evaluated by the target area hair count (primary efficacy variable) and target area hair width as assessed by macrophotography, patient assessment based on the Male Hair Growth Questionnaire (which included questions on hair growth, hair loss, and hair appearance), and investigator's and blinded assessor's assessments of improvement (based on patient hair growth/loss).

Of 458 randomised patients, 446 patients (97.4%) received at least 1 dose of study treatment and were included in the safety population, and 323 (70.5%) completed the study. Premature discontinuation was high in all groups, and was 32.3% of the randomized patients in the Finjuve group and 29.4% of the oral finasteride group. Overall, only 250 patients (54.6%) had evaluable hair count measurements both at baseline and on treatment and were defined as meeting the criteria for inclusion in the intent-to-treat (ITT) population: 105 patients in the Finjuve group, 97 patients in the placebo group, and 48 patients in the oral finasteride group. Nearly all patients were Caucasian (98.0%), the overall mean age was approximately 32 years (range of 19 to 41 years) and the most common vertex pattern hair loss was Type III vertex (approximately 50% of patients) according to the modified Hamilton-Norwood scale. The baseline mean hair count in the Finjuve group was 201 hairs/cm² which was similar to the other groups.

Finjuve demonstrated moderate clinical efficacy that was superior to placebo and numerically similar to that of the oral finasteride group, which was included as an exploratory, descriptive comparator arm. The mean change in target area hair count from baseline at 24 weeks (primary endpoint) was statistically significantly greater for patients in the Finjuve group than in the placebo group and was numerically similar to the oral finasteride group in the ITT population. Similar results were observed in the safety population at 24 weeks, for the mean change in target area hair count from baseline at 12 weeks, and across all the sensitivity analyses performed using different methods for handling missing data.

Change from baseline in target area hair count (number of hairs) at 12 and 24 weeks of treatment (ITT Population)

Duration of treatment	**Finjuve (N=105)**	**Placebo (N=97)**	**Oral finasteride (N=48)**
12 weeks			
LS mean change from baseline (number of hairs)	19.4	7.4	22.3
LS mean difference versus placebo (95% CI)	12.0 (5.7, 18.3)		-
24 weeks			
LS mean change from baseline (number of hairs)	16.3	6.3	18.7
LS mean difference versus placebo (95% CI)	10.0 (2.2, 17.7)		-

Target area size (circular): 1 cm^2
CI=confidence interval; ITT=intent-to-treat; LS=least squares; N=total number of patients per treatment group
Note: Statistically significant differences in favour of Finjuve vs. placebo were observed after both 12 and 24 weeks of treatment ($p<0.001$ and $p=0.012$ respectively).

Secondary endpoints
For secondary endpoints, a post-hoc analysis was done assessing response by any degree of improvement. In the safety population (446 patients), differences were observed in favour of Finjuve compared to placebo in the proportion of patients showing any degree of improvement of hair growth based on the investigator's and blinded assessor's evaluation after 24 weeks of treatment. No difference was observed in the patient's self-assessment of overall change of hair growth at week 24. Overall, results in the Finjuve group were similar to those in the oral finasteride group for responder evaluations, but differences to placebo were generally small (see table below).

Percentage of responders[a] for secondary endpoints at week 24 (Safety Population)

Treatment group	N	% Responders				
		Investigator assessment	Blinded Assessor assessment	MHGQ - Patient Assessment		
				Hair appearance	Hair growth	Overall change
Finjuve	181	42.0[b]	26.0[c]	40.9[c]	39.8	26.5
Oral Finasteride	84	35.7	28.6	36.9	31.0	25.0
Placebo	181	27.6	16.0	28.7	32.0	19.9

MHGQ=Male Hair Growth Questionnaire
[a] Response for each parameter was defined as showing any degree of improvement.
[b] p-value <0.005 from a Chi-square comparison of Finjuve vs. placebo.
[c] p-value <0.05 from a Chi-square comparison of Finjuve vs. placebo.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with Finjuve in all subsets of the paediatric population in the treatment of androgenetic alopecia. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Absorption
The systemic absorption of finasteride following topical application of Finjuve on normal, intact scalp skin is minimal. After administration of Finjuve at the intended dose (i.e., up to 200 microlitres once daily), mean maximum plasma finasteride concentrations are >100-times lower than after 1 mg once daily oral finasteride administration (approximately <50 pg/mL vs. 7000 pg/mL) at all sampling times over 6 months of treatment. The relative bioavailability of finasteride after multiple-dose administration of Finjuve compared to oral finasteride is also minimal (approximately 2 to 3%).

Distribution
Protein binding is approximately 90%. The volume of distribution of finasteride is approximately 76 litres.

Biotransformation
Finasteride is metabolised primarily via the cytochrome CYP3A4 enzyme subfamily, but does not affect these enzymes. Following an oral dose of ^{14}C-finasteride in man, 2 metabolites were identified that possess only a small fraction of the 5α-reductase inhibitory activity of finasteride. Compared to oral finasteride, the plasma levels of these 2 metabolites (and any unchanged finasteride) are expected to be negligible following topical administration of Finjuve due to the significantly lower systemic exposure to finasteride with Finjuve.

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. Following topical administration of Finjuve, any unchanged finasteride and the derived metabolites will be eliminated from the body through faeces and urine, similar to an oral treatment.

Following cessation of dosing, approximately 95% of finasteride absorbed after topical administration of Finjuve will be eliminated within 24 to 36 h.

In men treated with oral finasteride, less than 0.001% of the 1 mg dose per ejaculation has been detected in the seminal fluid. As mean maximum plasma concentrations of finasteride are >100-times lower after topical administration of Finjuve compared to 1 mg oral finasteride, it is unlikely for any finasteride from Finjuve to be excreted in the seminal fluid.

Renal or hepatic impairment
Clinical studies with Finjuve have not been performed in patients with impaired renal or hepatic function. Due to the very low systemic absorption of finasteride by the topical route, no dosage adjustment is required.

5.3 Preclinical safety data

Repeat-dose toxicity studies
The toxicity findings recorded in repeat-dose toxicity studies with oral administration of finasteride were related to the pharmacological effects of finasteride resulting in hormonal imbalances. Dermal toxicity studies performed with Finjuve confirmed its safety profile and its overall tolerability following repeated daily application on the skin for up to 39 weeks.

Skin discolouration after topical treatment was seen in all groups in the 4- and 13-week, but in no group in the 39-week minipig studies. This was interpreted as a brownish composite of the contained non-volatile excipients. There were no reports of skin discolouration in the clinical development program.

Photosensitisation
4 of 10 treated guinea pigs showed a photosensitisation reaction (very slight erythema (score 1) up to 72 hours post dose) following dermal exposure to finasteride topical solution in association with UV light. However, in the clinical development program, no potential for photosensitisation was identified in 58 healthy subjects treated with Finjuve.

Reproductive toxicity
Intravenous administration of finasteride to pregnant Rhesus monkeys at doses as high as 800 ng once daily (resulting in an estimated maternal plasma concentration of 1.86 ng/mL) during the entire period of embryonic and foetal development resulted in no abnormalities in male foetuses (no observed adverse effect level [NOAEL]). With the higher dose of orally administered 2 mg/kg bw finasteride once daily (>200-times the maximum recommended topical daily dose of Finjuve) to pregnant monkeys, external genital abnormalities in male foetuses were observed. No other abnormalities were observed in male foetuses and no finasteride-related abnormalities were observed in female foetuses at any dose.

In clinical trials with human males, mean finasteride exposure following topical application of 0.2 mL Finjuve once daily over 24 weeks (corresponding to 0.445 mg finasteride once daily, the maximum recommended daily dose with mean maximum finasteride plasma concentrations of 48.0 pg/mL) was 39-times lower than the estimated exposure resulting from the NOAEL in pregnant Rhesus monkeys. Thus, the systemic finasteride levels that a pregnant woman could be exposed to by contact with a partner being treated with Finjuve would be even lower.

Rats given 20 to 80 mg/kg once daily orally showed mild to moderate reduction of fertility, but this was completely reversible when the treatment was stopped. This decrease in fertility is believed to be secondary to the effects on prostate and seminal vesicles, resulting in failure to form a seminal plug. However, plug formation is not relevant for human fertility.

Genotoxicity and carcinogenicity
Studies on genotoxicity and carcinogenicity have not revealed any hazards for humans at the intended dose of Finjuve.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96 per cent)
Propylene glycol
Hydroxypropyl chitosan
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years
After first opening the bottle: 6 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
Finjuve contains ethanol, which is flammable. Finjuve must not be sprayed near to open flames or while smoking.

6.5 Nature and contents of container

Polypropylene bottle containing 18 mL of solution, with a snap-on mechanical spray pump and a separate polypropylene cone. These components require assembly prior to first use.

Pack sizes:
1 bottle (corresponding to 180 actuations) with a spray pump and 1 separate cone.
3 bottles (corresponding to 3 x 180 actuations) with a spray pump and 3 separate cones.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Finjuve should not be used beyond 180 actuations.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]