SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Minoxidil 50 mg/g (5% w/w)

Contains butylhydroxytoluene (BHT), stearyl alcohol, cetyl alcohol and ethanol 536.3 mg/g.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous foam
White to off-white foam

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam is indicated for the treatment of alopecia androgenetica in men.

4.2 Posology and method of administration

Men aged 18-49:

Hair and scalp should be thoroughly dry prior to topical application of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam. A dose of 1 g (equivalent to the volume of half a capful) Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam should be applied to the total affected areas of the scalp twice daily. The total daily dosage should not exceed 2 g.

It may take twice-daily applications for 8 weeks or more before evidence of hair growth can be expected. Users should discontinue treatment if there is no improvement seen after 16 weeks.

If hair regrowth occurs, twice daily applications of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam are necessary for continued hair growth.

Clinical Trials have not investigated the efficacy of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam beyond 16 weeks.

Special populations
There are no specific recommendations for use in patients with renal or hepatic impairment

Paediatric and Elderly Populations
Not recommended. The safety and effectiveness of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam in children and adolescents below the age of 18 years or adults over 49 years old has not been established.

Method of administration

For topical use only.

Hold can upside down and press nozzle to dispense foam onto the hand. Spread with fingertips over entire bald area. Hands should be washed thoroughly after application.

4.3 Contraindications

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam is contraindicated:

- in women
- in users with a history of sensitivity to Minoxidil or any of the other ingredients
- in users with treated or untreated hypertension
- in users with any scalp abnormality (including psoriasis and sunburn)
- in users with a shaved scalp
- if occlusive dressings or other topical medical preparations are being used.

4.4 Special warnings and precautions for use

Before using Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam, the user should determine that the scalp is normal and healthy. Topical minoxidil should not be applied to inflamed, infected, irritated or painful scalp skin (see section 4.3).

Topical minoxidil is not indicated when there is no family history of hair loss, hair loss is sudden and/or patchy, hair loss is due to childbirth, or the reason for hair loss is unknown.

The patient should stop using Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam and see a doctor if hypotension is detected or if the patient is experiencing chest pain, rapid heartbeat, faintness or dizziness, sudden unexplained weight gain, swollen hands or feet or persistent redness or irritation of the scalp or other unexpected new symptoms occur (see section 4.8).

Patients with known cardiovascular disease or cardiac arrhythmia should contact a physician before using Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam.

Some patients have experienced changes in hair colour and/or texture with this product use.

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam is for external use only. Do not apply to areas of the body other than the scalp.

Using more than the recommended dose or more often will not improve results.

Unwanted hair growth may be caused by the transfer of the product to areas other than the scalp.

Hands should be washed thoroughly after applying the foam.

Some consumers reported increased hair shedding upon initiation of therapy with Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam. This is most likely due to minoxidil's action of shifting hairs from the resting telogen phase to the growing anagen phase (old hairs fall out as new hairs grow in their place). This temporary increase in hair shedding generally occurs two to six weeks after beginning treatment and subsides within a couple of weeks. If shedding persists (> 2 weeks), users should stop using Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam and consult their doctor.

Users should be aware that, whilst extensive use of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam has not revealed evidence that sufficient minoxidil is absorbed to have systemic effects, greater absorption because of misuse, individual variability, unusual sensitivity or decreased integrity of the epidermal barrier caused by inflammation or disease processes

in the skin (eg. excoriations of the scalp, or scalp psoriasis) could lead, at least theoretically, to systemic effects.

Accidental ingestion may cause serious cardiac adverse events. Therefore this product has to be kept out of the reach of children.

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam contains 536.3 mg of alcohol (ethanol) in each 1 g. It may cause burning sensation on damaged skin. Ethanol may cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin and mucous membranes) the area should be bathed with large amounts of cool tap water.

Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam also contains butylated hydroxytoluene, which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes or mucous membranes, and cetyl and stearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

Hypertrichosis in children following inadvertent topical exposure to minoxidil:

Cases of hypertrichosis have been reported in infants following skin contact with minoxidil application sites of patients (caregivers) using topical minoxidil. Hypertrichosis was reversible, within months, when infants were no longer exposed to minoxidil. Contact between children and minoxidil application sites should therefore be avoided.

4.5 Interaction with other medicinal products and other forms of interaction

This product should not be used concomitantly with other medications applied topically on the scalp (see section 4.3).

Topical drugs, such as corticosteroids, tretinoin,dithranol or petrolatum, which alter the stratum corneum barrier, could result in increased absorption of minoxidil if applied concurrently. Although it has not been demonstrated clinically, there exists the theoretical possibility of absorbed minoxidil potentiating orthostatic hypotension caused by peripheral vasodilators.

Guanethidine has been reported to interact with oral formulations of minoxidil resulting in rapid and pronounced lowering of blood pressure.

There is a theoretical possibility that topical minoxidil may also interact with guanethidine.

4.6 Fertility, pregnancy and lactation

This product should not be used during pregnancy or lactation.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Studies in animals have shown a risk to the foetus at exposure levels that are very high compared to those intended for human exposure. There is potentially a risk of foetal harm in humans (see section 5.3).

Lactation
Systemically absorbed minoxidil is secreted in human milk. The effect of minoxidil on newborns/infants is unknown.

4.7 Effects on ability to drive and use machines

This product may cause dizziness or hypotension (see section 4.8). If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The safety of topical minoxidil from clinical trial data is based on data from 7 placebo-controlled randomised clinical trials in adults evaluating either 2% or 5% minoxidil solution, and two placebo-controlled randomised clinical trials in adults evaluating a 5% foam formulation. Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with minoxidil are included in the table below by System Organ Class (SOC).
The frequencies are provided according to the following convention:

Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available, or 2) when incidence cannot be estimated, frequency category is listed as 'Not known'

Body System (SOC)	**Frequency**	**Adverse Drug Reaction (Preferred Term)**
Immune System Disorders	Common	Hypersensitivity reactions *(*including: face oedema, generalised

		erythema, pruritus generalised, swelling face, and throat tightness)
	Not known	Angioedema (including: lip oedema, lip swelling, oedema mouth, oropharyngeal swelling, pharyngeal oedema, swollen tongue and tongue oedema)
Psychiatric Disorders	Not known	Depressed mood
Nervous System Disorders	Very common	Headache
	Uncommon	Dizziness
Eye disorders	Not known	Eye irritation
Cardiac disorders	Common	Chest pain
	Uncommon	Palpitations
	Not known	Heart rate increased
Vascular disorders	Not known	Hypotension
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
Gastrointestinal Disorders	Uncommon	Nausea
	Not known	Vomiting
Skin and subcutaneous tissue disorders	Common	Hypertrichosis (unwanted non-scalp hair including facial hair growth in women) Pruritus (including rash pruritic generalised and eye pruritus) Rash (including pustular, papular, generalised,

		vestibular and macular rash) Dermatitis (including contact, allergic, atopic and seborrhoeic dermatitis)
	Rare	Changes in hair texture
	Not known	Dry skin Skin exfoliation (including exfoliative rash and dermatitis exfoliative) Acne (acneiform rash) Temporary hair loss (see section 4.4) Changes in hair colour
General disorders and administration site conditions	Common	Oedema peripheral
	Not known	Application site reactions (These sometimes involve nearby structures like the ears and face and typically consist of pruritus, irritation, pain, rash, oedema, dry skin, erythema and rash erythematous but can sometimes be more severe and include exfoliation, dermatitis, blistering, bleeding and ulceration).
Investigations	Common	Weight increased

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 Yellow Card scheme at:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Increased systemic absorption of minoxidil may potentially occur if higher-than-recommended doses of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam are applied to larger surface areas of the body or areas other than the scalp.

Because of the concentration of minoxidil in Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam, accidental ingestion has the potential of producing systemic effects related to the pharmacological action of the drug (2 g of Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam contains 100 mg minoxidil; the maximum recommended adult dose for oral minoxidil administration in the treatment of hypertension). Signs and symptoms of minoxidil overdosage would primarily be cardiovascular effects associated with sodium and water retention. Tachycardia, hypotension, dizziness and lethargy can also occur.

Treatment

Treatment of minoxidil overdosage should be symptomatic and supportive.

Fluid retention can be managed with appropriate diuretic therapy. Clinically significant tachycardia can be controlled by administration of a beta-adrenergic blocking agent.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatologicals, ATC code: D11AX.

Minoxidil stimulates hair growth in persons with early and moderate stages of hereditary hair loss (alopecia androgenetica). This hair loss appears in men as a receding hairline and balding in the vertex area. The exact mechanism of action of minoxidil for topical treatment of alopecia is not fully understood, but minoxidil can reverse the hair loss process of androgenetic alopecia by the following means:

- increasing the diameter of the hair shaft
- stimulating anagen growth
- prolonging the anagen phase
- stimulating anagen recovery from the telegen phase

As a peripheral vasodilator minoxidil enhances microcirculation to hair follicles. The Vascular Endothelial Growth Factor (VEGF) is stimulated by minoxidil and VEGF is presumably responsible for the increased capillary fenestration, indicative of a high metabolic activity, observed during the anagen phase.

The efficacy of 5% minoxidil foam has been assessed in a Phase 3 clinical trial conducted over a 16-week treatment period. In this study 5% minoxidil foam was compared to the product vehicle without the minoxidil active ingredient.

The primary efficacy endpoints were a) mean change in non-vellus hair count within the target region between Baseline and Week 16, as determined by validated computer-assisted dot-mapping technique; and b) subject rating of treatment benefit via use of global photographs of the vertex region, assessed as an overall improvement from baseline, collected on a subject questionnaire.

The active treatment showed a statistically significant greater increase in hair count than the vehicle foam group (21.0 versus 4.3 hairs cm^2) at week 16. A clear difference between treatment groups was already evident at week 8, increasing at week 12 and again at week 16. The subject`s rating of treatment benefit was statistically significantly better for the 5% minoxidil foam treatment group than placebo (1.4 vs 0.5) at week 16.

The secondary efficacy endpoints were a) expert panel review (EPR) of hair regrowth when comparing global photographs obtained at baseline with photographs obtained at Week 16 and b) percent change from baseline in non-vellus hair counts within a pre-specified area of clipped hair.
The 5% minoxidil foam group showed a better score in the expert panel review (EPR) than the placebo foam group (adjusted mean 0.5 vs 0.1, $p<0.0001$).

At weeks 8, 12 and 16, the difference in adjusted means for percent change in non-vellus hair counts between vehicle foam and minoxidil foam were statistically significant ($p<0.0001$ at all 3 visits).

<u>Regaine Foam Data: Mean change in non-vellus hair count in reference $1cm^2$ area of scalp compared with baseline</u>

	Regaine for Men Extra Strength Foam (n=180)	**Placebo (n=172)**	**Difference (p-value)**
Baseline haircount	170.8	168.9	
	Mean change from baseline	Mean change from baseline	
8 weeks	16.0	4.9	11.1 (<0.0001)

12 weeks	19.9	4.5	15.4 (<0.0001)
16 weeks	21.0	4.3	16.7 (<0.0001)

5.2 Pharmacokinetic properties

The failure to detect evidence of systemic effects during treatment with Regaine Foam reflects the poor absorption of topically applied minoxidil from normal intact skin. Systemic absorption of minoxidil from topically applied solution ranges between 1% and 2% of the total applied dose.

The systemic absorption of minoxidil from a 5% foam formulation has been estimated in a pharmacokinetic study in subjects with androgenetic alopecia, which included 5% topical solution as a comparator. This demonstrated that in men, the systemic absorption of minoxidil from twice daily application of 5% minoxidil foam was about half of that observed with 5% minoxidil solution. The mean steady state AUC (0-12 hr) and Cmax for 5% minoxidil foam, 8.81 ng·hr/mL and 1.11 ng/mL, respectively, were both approximately 50 % of AUC (0-12 hr) and Cmax of the 5% solution, 18.71 ng·hr/mL and 2.13 ng/mL, respectively. The time to maximum minoxidil concentration (Tmax) for the 5% foam, 5.42 hr, was similar to Tmax for the 5% solution, 5.79 hr.

There is some evidence from *in vitro* studies that minoxidil reversibly binds to human plasma proteins. However, since only 1 – 2% of topically applied minoxidil is absorbed, the extent of plasma protein binding occurring *in vivo* after topical application would be clinically insignificant. The volume of distribution of minoxidil after intravenous administration has been estimated at 70 litres.

Approximately 60% minoxidil absorbed after topical application is metabolised to minoxidil glucuronide, primarily in the liver. Minoxidil and its metabolites are excreted almost entirely in the urine, with a very minor degree of elimination via the faeces. Following cessation of dosing, approximately 95% of topically applied minoxidil will be eliminated within four days.

5.3 Preclinical safety data

Mutagenicity

Minoxidil showed no evidence of mutagenic/genotoxic potential in a number of *in vitro* and *in vivo* assays.

Carcinogenicity

A high incidence of hormone-mediated tumours was observed in mice and rats. These tumours are due to the secondary hormonal (hyperprolactinemia) effects observed only in the rodents at extremely high doses by a mechanism similar to that seem with reserpine. Application of topical minoxidil has not demonstrated any effect on hormonal status in women. Therefore, hormonally mediated tumour promotion by minoxidil does not represent a carcinogenic risk to humans.

Teratogenicity

Animal reproduction toxicity studies in rats and rabbits have shown signs of maternal toxicity and a risk to the foetus at exposure levels that are very high compared to those, intended for human exposure. A low, albeit remote, risk of foetal harm is possible in humans.
Fertility

Minoxidil doses greater than 9 mg/kg (at least 25-fold human exposure) administered subcutaneously in rats were associated with reduced conception and implantation rates as well as reduction in the number of live pups.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol, Anhydrous
Purified Water
Butylated hydroxytoluene (E321)
Lactic acid
Citric acid anhydrous
Glycerol
Cetyl alcohol
Stearyl Alcohol
Polysorbate 60
Propane/n-Butane/Iso-butane (as propellant)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C.
Regaine for Men Extra Strength Scalp Foam 5% w/w Cutaneous Foam is extremely flammable.

6.5 Nature and contents of container

A lined aluminium pressurised container with a child-resistant plastic or polypropylene overcap, containing 60 gram of product.

Packs contain either one or three cans. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Precautions during use, storage and disposal:
Pressurized container: May burst if heated. Protect from sunlight and do not expose to temperatures above 50°C. Do not pierce or burn, even after use. Do not spray on a naked flame or any incandescent material. Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. Do not use near or place container on polished or painted surfaces.

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

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
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High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0366

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2024

10 DATE OF REVISION OF THE TEXT

17/12/2024