SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Regaine for Men Extra Strength

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Minoxidil 50 mg/ml (5% w/v).

Contains propylene glycol 500 mg/ml and ethanol 280.53 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous Solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Regaine for Men Extra Strength is indicated for the treatment of alopecia androgenetica in men.

Onset and degree of hair regrowth may be variable among users. Although trends in the data suggest that those users who are younger, who have been balding for a shorter period of time or who have a smaller area of baldness on the vertex are more likely to respond to Regaine for Men Extra Strength, individual responses cannot be predicted.

4.2 Posology and method of administration

Men aged 18-65:

Hair and scalp should be thoroughly dry prior to topical application of Regaine for Men Extra Strength. A dose of 1 ml Regaine for Men Extra Strength cutaneous solution should be applied to the total affected areas of the scalp twice daily. The total dosage should not exceed 2 ml. If fingertips are used to facilitate drug application, hands should be washed afterwards.

It may take twice daily applications for 2 months or more before evidence of hair growth can be expected.

If hair re-growth occurs, twice daily applications of Regaine for Men Extra Strength are necessary for continued hair growth. Anecdotal reports indicate that re-grown hair may disappear three to four months after stopping Regaine for Men Extra Strength application and the balding process will continue.

Users should discontinue treatment if there is no improvement after one year.

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 in children and adolescents below the age of 18 years or adults over the age of 65 years has not been established.

Method of Administration

For topical use only.

The method of application varies according to the disposable applicator used:

Pump spray applicator: this is useful for large areas. Aim the pump at the centre of the bald area, press once and spread with fingertips over the entire bald area. Repeat for a total of 6 times to apply a dose of 1 ml. Avoid breathing spray mist.

Extended spray-tip applicator: this is useful for small areas, or under hair. The pump spray applicator must be in place in order to use this additional applicator. Use in the same way as the pump spray.

4.3 Contraindications

Regaine for Men Extra Strength is contraindicated:
- in women
- in users with a history of sensitivity to minoxidil, ethanol, or propylene glycol
- 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, 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 only indicated for the treatment of alopecia androgenetica and should not be used in other types of hair loss for example 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 and see a doctor if hypotension is detected or if the patient is experiencing chest pain, rapid heart beat, 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.

Some patients have experienced changes in hair colour and/or texture with use of Regaine for Men Extra Strength.

Regaine for Men Extra Strength 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 solution. Inhalation of the spray mist should be avoided.

Some consumers reported increased hair shedding upon initiation of therapy with Regaine for Men Extra Strength. 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 and consult their doctor.

Users should be aware that, whilst extensive use of Regaine for Men Extra Strength 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 (e.g. 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.

This medicine contains 280.53 mg of alcohol (ethanol) in each 1 ml. 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.

This medicine contains 500 mg of propylene glycol in each 1 ml. Propylene glycol may cause skin irritation. Because this medicine contains propylene glycol, do not use it on open wounds or large areas of broken or damaged skin (such as burns) without checking with your doctor or pharmacist.

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 and < 1/10
Uncommon ≥1/1,000 and <1/100
Rare ≥1/10,000 and <1/1,000
Very rare <1/10,000, including isolated reports
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	Common	Hypertrichosis

tissue disorders		(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 solution 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 Solution, accidental ingestion has the potential of producing systemic effects related to the pharmacological action of the drug (2 ml of Regaine for Men Extra Strength 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

The effect of Regaine for Men Extra Strength has been assessed in a phase III clinical trial conducted over a 48 week treatment period.

In this study Regaine for Men Extra Strength (5% minoxidil cutaneous solution) was compared to the product vehicle without the minoxidil active ingredient and also to 2% minoxidil cutaneous solution.

The primary efficacy criterion was non-vellus hair count in a 1.0cm^2 reference area of affected scalp. The mean changes observed in this parameter in these studies were significantly in favour of active treatment. A significant dose

effect was also demonstrated. The results are summarized in the following table:

Mean change in non-vellus hair count in reference 1cm^2 area of scalp compared with baseline				
	Regaine for Men Extra Strength (n=139) Minoxidil 5%	**(n=142) Minoxidil 2%**	**(n=71) Vehicle**	**Pairwise comparison**
Baseline	151.1	143.6	152.4	
	Mean change from baseline	Mean change from baseline	Mean change from baseline	
8 weeks	+29.7	+24.9	+14.3	5%>2%>vehicle
16 weeks	+35.3	+29.8	+15.3	5%>2%>vehicle
32 weeks	+29.0	+22.2	+7.7	5%>2%>vehicle
48 weeks	+18.6	+12.7	+3.9	5%>2%>vehicle

Efficacy was further assessed by comparing photographs taken at various timepoints with baseline.

Assessment was undertaken by patients using a 100 mm visual analogue scale and assessing scalp coverage where point 0 represented much less scalp coverage, 50 mm no difference and 100 mm much more scalp coverage. In addition, an assessment was undertaken by 2 blinded reviewers who compared photographs taken at baseline and after 48 weeks. Differences were assessed using a 7 point categorical scale viz:

Dense growth
Moderate growth
Minimal growth
No change
Minimal loss
Moderate loss
Dense loss

The results of these analyses were as follows:

Patient evaluation of change in scalp coverage				
	Regaine for			**Pairwise**

	Men Extra Strength (n=139) Minoxidil 5%	(n=142) Minoxidil 2%	(n=71) Vehicle	comparison
	mm	**mm**	**mm**	
16 weeks	63.5	58.2	51.4	5%>2%>vehicle
32 weeks	63.4	58.0	52.0	5%>2%>vehicle
48 weeks	62	56.9	51.0	5%>2%>vehicle

Photographic Evaluation of Clinical Response (Reviewer 1)						
	Dense Growth %	**Moderate Growth %**	**Minimal Growth %**	**No change %**	**Hair Loss %**	**Unable to rate**
Minoxidil 5%	2.2	37.4	22.3	31.7	5.0	1.4
Minoxidil 2%	2.8	19.7	21.1	50.0	2.8	3.5
Vehicle	0	7.0	22.5	60.0	9.9	0

Photographic Evaluation of Clinical Response (Reviewer 2)						
	Dense Growth %	**Moderate Growth %**	**Minimal Growth %**	**No change %**	**Hair Loss %**	**Unable to rate**
Minoxidil 5%	10.1	20.1	23.7	28.8	6.5	10.8
Minoxidil 2%	3.5	12.0	22.5	47.2	1.4	13.4
Vehicle	0	7.0	9.9	60.6	14.1	8.5

Based upon these photographic data, around 60% of the patients experienced an increased scalp coverage after 48 weeks treatment with Regaine for Men Extra Strength as defined by re-growth of hair; compared with around 23% as an average for those who received vehicle alone. Of these, around 35% treated with Regaine for Men Extra Strength experienced dense or moderate

re-growth compared with around 7% who received vehicle alone. In addition 30% of patients who received Regaine for Men Extra Strength were adjudged to have no change between the photographic assessments of hair growth compared with 60% who received vehicle alone. Stabilisation of hair loss (expressed both as re-growth of hair and no continuation of hair loss) can therefore be expected in about 4 out of 5 of patients using Regaine for Men Extra Strength compared with 3 out of 4 patients using vehicle alone.

Regaine for Men Extra Strength may therefore be considered by men who wish to achieve a faster onset and greater degree of hair re-growth than would be expected through the use of Regaine Regular Strength.

The mechanism by which minoxidil stimulates hair growth 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 telegon 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.

5.2 Pharmacokinetic properties

The failure to detect evidence of systemic effects during treatment with Regaine solution 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% solution formulation has been estimated in a pharmacokinetic study in subjects with androgenetic alopecia, which included 5% topical foam as a comparator. This demonstrated that in men, the systemic absorption of minoxidil from twice daily application of 5% minoxidil solution was about twice that, as observed with 5% minoxidil foam. The mean steady state $AUC_{(0\text{-}12\ h)}$ and C_{max} for 5% minoxidil foam, 8.81 ng·h/ml and 1.11 ng/ml, respectively, were both approximately 50% of $AUC_{(0\text{-}12\ h)}$ and C_{max} of the 5% solution, 18.71 ng·h/ml and 2.13 ng/ml, respectively. The time to maximum minoxidil concentration (T_{max}) for the 5% solution, 5.79 hours, was similar to T_{max} for the 5% foam, 5.42 hours.

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

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or carcinogenic potential.

Cardiac effects of minoxidil in dogs are species-specific in terms of the low doses that cause profound haemodynamic effects and associated changes in the heart. Available data indicate that similar cardiac effects do not occur in humans treated topically or orally with minoxidil.

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 (from 19 to 570-fold human exposure). A low, albeit remote, risk of foetal harm is possible in humans.

Fertility
Preclinical fertility studies in rats have shown minoxidil doses equal to or greater than 3 mg/kg/day (at least 8-fold human exposure) when administered orally and greater than 9 mg/kg/day (at least 25-fold human exposure) when administered subcutaneously were associated with reduced conception and implantation rates as well as a reduction in the number of live pups.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Propylene glycol, ethanol, water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4. Special precautions for storage

Regaine for Men Extra Strength is flammable. Store below 25°C.

6.5 Nature and contents of container

HDPE bottle with a child-resistant plastic or polypropylene overcap, containing 60 ml of solution. Packs contain either one or three bottles. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The solution is flammable. Do not use while smoking, or near any naked flame or strong heat source. Avoid exposure of the container and contents to naked flames during use, storage and disposal. Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

PL 15513/0148

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

28th June 2005

10 DATE OF REVISION OF THE TEXT

17/12/2024