Summary of Product Characteristic

1. Trade Name of the Medicinal Product

Minoxin Plus Solution

2. Qualitative and Quantitative Composition

Each ml contains:

Minoxidil USP……50 mg For excipients, see 6.1

3. Pharmaceutical Form

Topical Solution

4. Clinical Particulars

4.1 Therapeutic Indications

It is indicated for the treatment of androgenetic alopecia, expressed in males as baldness of the vertex of the scalp and in females as diffuse hair loss or thinning of front parietal area. At least, 4 (four) months of twice daily application of Minoxin plus solution are generally required before evidence of hair growth can be expected.

4.2. Posology and method of administration

For external use only. Use Minoxin only as directed. Do not apply to any other area of the body. A total dose of 1ml Minoxin should be applied twice daily on the scalp, beginning at the center of the affected area. This dose should be used regardless of the size of the affected area. Six pumps of the applicator release approx. 1ml of Minoxin. The total daily dose should not exceed 2ml. To avoid any systemic absorption, wash hands thoroughly after applying Minoxin. Apply Minoxin when the hair and scalp are thoroughly dried. Don't use a hairdryer to speed the drying of Minoxin solution because blowing air on the scalp may decrease the effectiveness of Minoxin.

4.3 Contraindications

It is contraindicated in those patients with a history of hypersesitivity to any component of preparation

4.4 Special warnings and precautions for use

Although the following effects have not been associated with the topical use of Minoxidil solution there is some absorption (on average 1.4 %) from the scalp. The potential exists for systemic effects such as tachycardia, angina, oedema and potentiation of orthostatic hypotension produced by guanethidine. Patients should be observed periodically for any such systemic effects. In the event of systemic side-effect or severe dermatologic reaction discontinue administration of the drug.

Minoxin (Minoxidil Topical Solution USP) will cause burning and irritation to the eye. In the event of accidental contact with sensitive surface (eye, abraded skin, mucous membranes), the area should be bathed with copious amounts of cool tap water. Minoxin (Minoxidil Topical Solution USP) should not be used in conjunction with other topical agents including corticosteroids, retinoids and petrolatum or agents that are known to enhance cutaneous drug absorption.

4.5 Interaction with other medicinal products and other forms of interaction

There are currently no known interactions associated with the use of Minoxidil Topical solution.

4.6 Pregnancy and lactation

Minoxin like other drugs should not be used by pregnant and nursing women.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamic and overall safety profile of minoxidil, it is not expected that would interfere with the ability to drive or operate machinery.

4.8 Undesirable effects

In placebo-controlled trials, the overall frequency of adverse events in females in all body system categories was approximately five times that of males.

Several thousand patients have used topical minoxidil in clinical trials where a comparison with an inactive solution was made. Dermatological reactions (e.g. irritation, itching) occurred in patients using both solutions. This has been explained by the presence of propylene glycol in both the active and inactive solution.

Data from 7 placebo-controlled trials are available with a population of 1,197 males and females treated with topical minoxidil solution (2% and 5% combined) where adverse events were assessed. Additionally,

adverse events reported in post-marketing are included.
The frequency of adverse reactions to topical minoxidil solution is defined using 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).

Body system	**Incidence**	**Reported adverse event**
Nervous system disorders	Common	Headache
Vascular disorders	Uncommon:	Hypotension
Cardiovascular Disorders	Rare:	Palpitations Heart Rate Increased Chest Pain
Respiratory, thoracic and mediastinal disorders	Uncommon:	Dyspnoea
Skin and subcutaneous tissue disorders	Common:	Hypertrichosis (unwanted non-scalp hair including facial hair growth in women), pruritus (including rash pruritic and application site, generalized and eye pruritus)

	Uncommon:	Temporary hair loss (see section 4.4), changes in hair texture and hair colour, skin exfoliation (including application site, exfoliative rash and dermatitis exfoliative), rash (including application site, pustular, papular, generalized vestibular and macular rash), acne (acne form rash), dermatitis (including contact, application site, allergic, atopic and seborrhoeic dermatitis) and dry skin (including application site dryness)
General disorders and administration site Conditions	Uncommon:	Oedema peripheral, Application site irritation (including skin irritation), application site erythema (including erythema and rash erythematous)

Users should stop using solution if they experience chest-pain, tachycardia, faintness, dizziness, sudden unexplained weight gain, swollen hands or feet or persistent redness or irritation of the scalp.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https:// pv.pharmacyboardkenya.org.

4.9 Overdose

Accidental ingestion may produce systemic effects related to vasodilatory action of minoxidil.Signs and symptoms of drugs over

usage would most likely be cardiovascular effects associated with fluid retention,lowered blood pressure and tachycardia.Tachycardia can be controlled by administration of beta adrenergic blocking agent.
Hypotension should be treated by intravenous administration of normal saline.Sympathomimetic drugs,such as norepinephrine and epinephrine should be avoided because of their excess cardiac stimulating activity.

Treatment
Treatment of minoxidil over dosage should be symptomatic and supportive.

5.Pharmacological properties

5.1 Pharmacodynamic properties

The effect of has been assessed in a phase III clinical trial conducted over a 48 week treatment period.
In this study (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

	(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 time points 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

	(n=139) Minoxidil 5%	**(n=142) Minoxidil 2%**	**(n=71) Vehicle**	**Pairwise 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 increased scalp coverage after 48 weeks treatment with 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 experienced dense or moderate re-growth compared with around 7% who received vehicle alone. In addition, 30% of patients who received 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 compared with 3 out of 4 patients using vehicle alone.
It 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 Minoxin Plus.
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 Minoxin Plus 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 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 liters.
Approximately 60% minoxidil absorbed after topical application is metabolized 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 feces. 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.

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

Teratogenicity
Animal reproduction toxicity studies in rats and rabbits have shown signs of maternal toxicity and a risk to the fetus 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 fetal 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:

- Ethanol
- Propylene glycol
  Injectable grade

- Purified water Q.S

6.2 Incompatibilities

None stated

6.3 Shelf Life

3 years

6.4 Special Precautions for Storage

Keep all medicines out of reach of children. Do not store above 30°C.Protect from light.

6.5 Nature and Contents of Container:

Samples are stored as per the recommended packaging, i.e. in 60ml white opaque bottle made of H.D.P.E, sealed with P.E lined aluminium seal, having plastic cap further covered with Royal Blue cosmetic cap packed in unit carton, having another carton for spray pump, booklet, insert and dermaroller.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorization holder

Brookes Pharma Private Limited.
Karachi – Pakistan

8. Marketing authorization number

2105

9. Date of first / latest renewal of the authorization

Date of first authorization: 25th March 2005 Date of renewal of authorization: 20th Jan 2020

10. Date of revision of the text

31/03/2026