

## Data Sheet

# ROGAINE®

*Topical Solution 2%, Topical Solution 5%*

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## FOR EXTERNAL USE ONLY

### Composition

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ROGAINE Topical Solution 2% contains minoxidil, at a concentration of 20mg minoxidil per mL in a solution composed of alcohol, propylene glycol and water.

WOMEN'S ROGAINE Topical Solution 2% contains minoxidil, at a concentration of 20mg minoxidil per mL in a solution composed of alcohol, propylene glycol and water.

ROGAINE Topical Solution 5% contains minoxidil, at a concentration of 50mg minoxidil per mL in a solution composed of alcohol, propylene glycol and water.

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### Description

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Minoxidil, a peripheral vasodilator, occurs as a white or off-white, odourless, crystalline solid which is readily soluble in propylene glycol or ethanol, soluble in water to the extent of 2mg/mL and is almost insoluble in acetone, chloroform or ethyl acetate. The chemical name for minoxidil is 2, 4-diamino-6-piperidino-pyrimidine-3-oxide (MW = 209.25).

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### Pharmacology

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#### *Pharmacodynamics*

When applied topically, ROGAINE (minoxidil) has been shown to stimulate hair growth in males and females with alopecia androgenetica; however, the exact mechanism of action of ROGAINE in the treatment of alopecia androgenetica is not known. The regrowth can be observed after approximately 4 or more months of use and is variable among patients. Upon discontinuation of treatment with ROGAINE, new hair growth stops and restoration of pretreatment appearance may occur within 3-4 months.

Topical application of ROGAINE showed no systemic effects related to absorption of minoxidil when tested in controlled clinical trials in both normotensive and untreated hypertensive patients.

Minoxidil administered orally for the treatment of hypertension has a direct peripheral vasodilator effect which reduces elevated systolic and diastolic blood pressure by decreasing peripheral vascular resistance. Reduction of peripheral arteriolar resistance and the associated fall in blood pressure induces sympathetic, vagal inhibitory, and renal homeostatic mechanisms, including an increase in renin secretion, which lead to increased heart rate and cardiac output, and salt and water retention. Minoxidil does not interfere with vasomotor reflexes and therefore does not produce orthostatic hypotension. In experimental animals, the drug does not enter the central nervous system (CNS) in significant amounts.

### ***Pharmacokinetics***

Following topical application, minoxidil is poorly absorbed from normal intact skin, with an average of approximately 1.7% of the total applied dose ultimately reaching the systemic circulation. In contrast, minoxidil is almost completely absorbed from the gastrointestinal tract following oral administration of minoxidil tablets. Following cessation of topical dosing of ROGAINE approximately 95% of systemically absorbed minoxidil is eliminated within 4 days. The effects of concomitant dermal diseases on absorption are unknown.

The metabolic biotransformation of minoxidil absorbed following topical application has not been fully determined. The active form of the drug appears to be a sulfated metabolite, minoxidil sulfate. Orally administered minoxidil is metabolised predominantly by conjugation with glucuronic acid at the N-oxide position in the pyrimidine ring but also by conversion to more polar products. Minoxidil does not bind to plasma proteins and its renal clearance corresponds to the glomerular filtration rate. Minoxidil does not cross the blood brain barrier. Minoxidil and its metabolites are haemodialysable, and are excreted principally in the urine.

### ***Clinical Studies***

In 2326 adults with early male pattern baldness who applied 1mL of 2% topical solution on the scalp twice daily for 12 months, cosmetically acceptable hair growth was observed in only a small % of individuals. Dense hair growth occurred in only 8% of individuals. Moderate hair growth was observed in a further 30% of subjects.

Two studies in healthy males aged 18-50 years with androgenetic alopecia showed statistically significant differences favouring 5% over 2% topical solution with regard to non-vellus hair counts. Compared to mean baseline counts of 103-106/cm<sup>2</sup>, at the end of 32 weeks treatment mean increases in non-vellus hair counts were 39/cm<sup>2</sup> in subjects who received 5% topical solution (N=163), 30/cm<sup>2</sup> in subjects who received 2% topical solution (N=79), and 5/cm<sup>2</sup> in subjects who received placebo (N=79). In the other study, compared to mean baseline counts of 144-152 /cm<sup>2</sup>, at the end of 48 weeks treatment mean increases in non-vellus hair counts were 19/cm<sup>2</sup> in subjects who received 5% topical solution (N=137), 13/cm<sup>2</sup> in subjects who received 2% topical solution (N=139), and 4/cm<sup>2</sup> in subjects who received placebo (N=70).

Two studies in healthy females aged 18 to 50 years with androgenetic alopecia showed statistically significant differences favouring 5% over placebo, but not over 2% topical solution with regard to non-vellus hair counts. Compared to mean baseline counts of 178-185 /cm<sup>2</sup>, at the end of 36 weeks treatment mean increases in non-vellus hair counts were 18/cm<sup>2</sup> in subjects who received 5% topical solution (N=64), 15/cm<sup>2</sup> in subjects who received 2% topical solution (N=74) and 3/cm<sup>2</sup> in subjects who received placebo (N=40). In the other study, compared to mean baseline counts of 138-150/cm<sup>2</sup>, at the end of 48 weeks treatment mean increases in non-vellus hair counts were 25/cm<sup>2</sup> in subjects who received 5% topical solution (N=97), 21/cm<sup>2</sup> in subjects who received 2% topical solution (N=106), and 9/cm<sup>2</sup> in subjects who received placebo (N=50).

Examination of efficacy data based on hair weight measurements demonstrated an overall clinical benefit of 5% topical solution and 2% topical solution in stimulating hair growth. Additionally, this study strongly demonstrated the stabilisation of hair loss over the 2 year treatment period.

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## Indications

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Treatment (regrowth) of androgenic alopecia in males and females and stabilisation of hair loss in patients with androgenic alopecia.

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## Contraindications

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Topical minoxidil is contraindicated in patients with a history of hypersensitivity to minoxidil, propylene glycol or ethanol.

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## Warnings and Precautions

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KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

Before starting on ROGAINE the patient should have a healthy, normal scalp.

Although extensive use of topical minoxidil has not revealed evidence that enough minoxidil is absorbed to have systemic effects, greater absorption because of misuse or individual variability or unusual sensitivity could lead, at least theoretically, to a systemic effect, and patients need to be aware of this.

Accidental ingestion of ROGAINE could lead to serious adverse effects. The following adverse effects may be observed as a result of systemic absorption:

- salt and water retention,
- generalised and local oedema,
- pericardial effusion,

- pericarditis,
- tamponade,
- tachycardia,
- increased frequency of angina or new onset of angina, or
- the potentiation of the orthostatic hypotension produced by guanethidine.

Patients with known cardiovascular disease or cardiac arrhythmias should contact a physician before using ROGAINE. ROGAINE is recommended for use only in healthy adults with normal cardiovascular status. The safety is unknown in patients with cerebrovascular disease, ischaemic heart disease, cardiac arrhythmias or congestive heart failure. Patients with a history of underlying heart disease should be aware that adverse effects in them might be especially serious. The consumer should stop using the product and see a doctor if hypotension is detected or if 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.

Patients treated with ROGAINE should be monitored after starting therapy and periodically thereafter. If systemic effects should occur, discontinue use of ROGAINE. If necessary, fluid retention and oedema can be managed with diuretic treatment. Tachycardia and angina can be controlled by administration of beta-adrenergic blocking drugs or other sympathetic nervous system suppressants.

Topical minoxidil therapy should be stopped if hair regrowth is not evident after 12 months of treatment.

ROGAINE contains an alcohol base which will cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin, mucous membranes), the area should be bathed with copious amounts of cool tap water. Inhalation of the spray mist should be avoided.

The effects of ROGAINE in patients with concomitant skin diseases, or in those using topical corticosteroids or other dermatological preparations, are unknown. There is a possibility that an increase in bioavailability, of topically administered minoxidil, may occur in the presence of inflammatory conditions of the scalp and such situations are to be avoided.

If a patient wishes to wear any form of protective headgear, he should be instructed to allow 1 hour to elapse after using ROGAINE before covering the head.

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

### ***Carcinogenicity, Mutagenicity and Impairment of Fertility***

Carcinogenic activity of minoxidil has been investigated following dietary administration to mice at 10-64mg/kg/day, and following topical administration to mice and rats at 8-80mg/kg/day. Minoxidil treatment was associated with the development of benign pituitary tumours and malignant mammary tumours in female mice, hepatic adenomas and splenic haemangiosarcomas in male mice, and adrenal medullary and clitoral gland adenomas in

female rats. The hepatic tumours were only observed at high dose levels. The development of mammary adenocarcinomas in mice may be related to stimulation of prolactin release. Tumour development in the pituitary, preputial and clitoral glands may also involve endocrine mechanisms, while the vascular wall tumours in mouse spleen and adrenal medullary tumours in rats may be related to the vasodilator activity of the drug.

In a 12-month photocarcinogenicity study in hairless mice, topical minoxidil did not accelerate the development of dermal tumours initiated by ultraviolet light.

Genetic toxicology studies showed that minoxidil does not cause gene mutation in bacterial cells, but gene mutation studies in mammalian cells have not been reported. Minoxidil had weak clastogenic activity in a cytogenetics assay in Chinese hamster lung cells *in vitro*, but there was no evidence of similar effects in cultured human lymphocytes, or in an *in vivo* assay (micronucleus test in mice). Minoxidil did not cause DNA damage in an alkaline elution assay in Chinese hamster fibroblasts or unscheduled DNA synthesis in rat hepatocytes.

In fertility studies in rats, minoxidil decreased live litter size at oral doses of 3-10mg/kg/day and at 80mg/kg/day SC.

### ***Use in Pregnancy***

Animal studies have shown a risk to the foetus at exposure levels that in comparison to levels obtained in humans are very high and showing signs of maternal toxicity. The risk of foetal harm is low if topical minoxidil is administered as directed during pregnancy.

There are no adequate and well-controlled studies in pregnant women. Minoxidil should be used during pregnancy only if the potential benefit justifies the risk to the foetus.

### ***Use in Lactation***

Systemically-absorbed minoxidil is secreted in human milk. ROGAINE should not be used by nursing women.

Subcutaneous administration of minoxidil at 80mg/kg/day to lactating rats suppressed postnatal growth and increased postnatal mortality of the offspring. These effects may have been due to interference with nursing behaviour rather than to ingestion of drug-related material by the offspring.

### ***Use in Children***

Safety and efficacy of ROGAINE in patients under 18 years of age have not been established.

### ***Use in Elderly***

Safety and efficacy of ROGAINE in patients over 65 years of age have not been established.

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## Adverse Reactions

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In general ROGAINE is well tolerated.

The dermatologic events were of similar type and severity in the 5% and 2% groups. Most frequently reported adverse reactions with 2% and 5% topical minoxidil in commercial marketing experience are dermatological reactions and include: local erythema, itching, and dry skin/scalp flaking, skin irritation, rash, and dermatitis. Increased hair shedding can occur due to minoxidil's action of shifting hairs in the resting telogen phase to the growing anagen phase (old hairs fall out as new hairs grow in their place). This temporary increase in shedding generally occurs two to six weeks after beginning treatment and subsides within a couple of weeks (first sign of action of minoxidil).

Rare cases of hypotension have been reported.

Rare cases of hypertrichosis (unwanted non-scalp hair including facial hair growth in women) upon initiation of therapy with ROGAINE have been reported.

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## Drug Interactions

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There are currently no known drug interactions associated with the use of ROGAINE. Although it has not been clinically demonstrated, there exists the theoretical possibility of absorbed minoxidil potentiating orthostatic hypotension in patients currently taking peripheral vasodilators. *In vitro* studies have shown that paracetamol and diethylcarbamazine may inhibit the stimulation of hair growth by minoxidil.

Drugs for cutaneous use, e.g., tretinoin and anthralin/dithranol, which alter the stratum corneum barrier, could result in increased absorption of cutaneously used minoxidil if applied concurrently.

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## Dosage and Administration

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### ***FOR EXTERNAL USE ONLY.***

Use ROGAINE only as directed. Do not apply ROGAINE to any area of the body other than the scalp.

A total dose of 1mL ROGAINE should be applied twice per day to the scalp, beginning at the centre of the affected area. This dose should be used regardless of the size of the

affected area. The total daily dose should not exceed 2mL. After applying ROGAINE, wash hands thoroughly.

Apply ROGAINE when the hair and scalp are thoroughly dry. Do not use a hairdryer to speed the drying of ROGAINE, because blowing air on the scalp may decrease the effectiveness of ROGAINE. ROGAINE must remain in contact with the scalp for several hours (up to 4 hours).

At least four months of twice daily applications of ROGAINE are generally required before evidence of hair regrowth can be expected. Onset and degree may be variable among patients.

**Note: Following discontinuation of medication, relapse to pretreatment appearance has been reported to occur within 3-4 months.**

### ***Directions for Use***

Make sure the scalp is dry and that the skin is healthy and intact. The method of application depends on the type of disposable applicator used:



#### **A. Pump spray applicator:**

1. This applicator works best for applying ROGAINE to large areas of the scalp.
2. Remove large outer cap; remove small inner cap and discard it.
3. Insert the pump spray applicator into bottle and screw on firmly.
4. After aiming the pump toward the center of the bald area of the scalp, press the pump once and spread ROGAINE with fingertips to cover all of the bald area. Repeat for a total of 6 times, to apply a dose of 1mL of solution. Avoid breathing spray mist. Place large outer cap on bottle when not in use.



### **B. Extended spray-tip applicator:**

1. This applicator works best for applying ROGAINE to small areas of the scalp, or under hair.
2. The pump spray applicator must be on the bottle to use the extended tip applicator. Follow steps A.2 and A.3.
3. Remove small spray head from top of pump spray applicator; fit the extended spray tip applicator onto the spray shaft and push down firmly. Remove the small cap on the end of the extended tip.
4. After aiming the applicator toward the center of the bald area of the scalp, press the pump once and spread ROGAINE with fingertips to cover all of the bald area. Repeat for a total of 6 times, to apply a dose of 1mL of solution. Avoid breathing spray mist. If desired, replace the small cap on end of extended tip when not in use.



### **C. Rub-on applicator:**

1. This applicator works best for applying ROGAINE to small areas of the scalp.
2. Remove large outer cap; remove small inner cap and discard it.
3. Insert the rub-on applicator into bottle and screw on firmly.
4. Holding the bottle upright, squeeze the bottle once to fill the upper chamber to the black line. The chamber now contains one full dose (1mL of solution).

5. Holding the bottle upside down, rub the applicator on the scalp to cover all of the bald area, until the chamber is completely empty. Place large outer cap on bottle when not in use.

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## **Overdosage and Accidental Ingestion**

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Accidental ingestion has the potential of producing systemic effects related to the action of the drug. Signs and symptoms of minoxidil overdosage would most likely be cardiovascular effects associated with hypotension, sudden weight gain, rapid heart beat, faintness or dizziness. If encountered, the consumer should see a physician. Fluid retention can be managed with appropriate diuretic therapy. Tachycardia can be controlled by administration of a beta-adrenergic blocking agent. Symptomatic hypotension should be treated by intravenous administration of normal saline. Sympathomimetic drugs, such as noradrenaline and adrenaline should be avoided because of their excessive cardiac stimulating activity.

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## **Package Quantities**

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ROGAINE Topical Solution 2%, containing 20mg minoxidil per mL is available in a 60mL bottle.

WOMEN'S ROGAINE Topical Solution 2%, containing 20mg minoxidil per mL is available in a 60mL bottle.

ROGAINE Topical Solution 5%, containing 50mg minoxidil per mL is available in a 60mL bottle, in single packs and packs of 3.

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## **Medicine Classification**

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Pharmacy Medicine

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## **Name and Address**

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Johnson & Johnson (New Zealand) Ltd  
Ground Floor, Tonkin & Taylor House  
105 Carlton Road  
Newmarket  
Auckland

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## **Date of Preparation**

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20 January 2010