NEOXIDIL

Minoxidil

FORM AND PRESENTATION

2% solution for topical application: Metred-dose aerosol spray bottle containing 60 ml. Unit packs containing 1 bottle or 3 bottles.

COMPOSITION

	per 100 ml.	*per bottle*	
		x1	x3
Minoxidil (INN)	2 g	1.2 g	3.6g

Excipient : ethyl alcohol (95% v/v), propylene glycol, purified water.

PROPERTIES

The topical application of minoxidil stimulates the growth of keratinocytes in vitro and in vivo and the growth of hair in some subjects presenting with androgenic alopecia. The onset of this phenomenon takes place after about 4 months (or more) of product usage and varies from one individual to another. Upon discontinuing treatment, re-growth ceases and a return to the original state may be expected within 3 or 4 months. The precise mechanism of action is not known. The topical application of minoxidil during clinical trials in normotensive or hypertensive, untreated patients, did not give rise to the observation of systemic effects linked to the absorption of minoxidil.

FATE OF THE DRUG

Minoxidil, when applied topically, is poorly absorbed; a mean of 1.4% (range: 0.3% to 4.5%) of the dose applied is detected systemically. By comparison, when it is administered orally in tablet form (in the treatment of certain forms of hypertension) minoxidil is practically entirely absorbed from the gastro-intestinal tract. A dose of 1 ml of solution, corresponding to an application to the skin of 20 mg minoxidil, would hence result in the absorption of approximately 0.280 mg minoxidil.

The influence on minoxidil absorption that concomitant dermal infections or occlusion techniques might have has not been determined.

Serum minoxidil levels following topical administration are dependent upon the rate of percutaneous absorption. After discontinuing topical application, approximately 95% of the minoxidil absorbed is eliminated in 4 days. The biotransformation of minoxidil absorbed following topical application is not fully understood.

INDICATIONS

Androgenic alopecia of moderate severity in the male and female. An increase in the number of hairs after 6 to 12 months of continous treatment has been observed in approximately 30% of patients.

CONTRA-INDICATIONS

- Known allergy to minoxidil, propylene glycol or ethanol
- The efficacy and safety in subjects aged under 18 years or over 65 years have not been studied.
- The effects in patients presenting concomitant dermatological infections or already treated with topical corticosteroids or other topical preparations have not been evaluated.
- It has not been clearly established whether or not, under occlusion, minoxil absorption is increased.

WARNINGS

Although the onset of systemic effects allied to minoxidil have not been observed during usage of the solution, the possibility of the occurrence of such effects cannot be excluded. It is advisable, as a precautionary measure, to monitor regularly any appearance of symptoms indicative of systemic effects such as lowering of blood pressure, tachycardia, signs of water and sodium retention. In the event of the appearance of systemic effects of severe dermatological reactions, the patient must cease treatment and consult the doctor.

PRECAUTIONS

- On contact with the eye, the solution may cause a burning sensation and irritation. In the event of contact with sensitive areas (eyes, irritated skin, mucous membranes), rinse abundantly with running water.
- Accidental ingestion may lead to severe side effects. Keep out of the reach of children.

Pregnancy: In the animal, studies carried out with minoxidil have not shown any evidence of a teratogenic effect; in the absence of clinical data, these experimental results are insufficient to permit evaluation of any likely malformation effect in the human species. Consequently, as a precaution, avoid prescribing during pregnancy as a precautionary measure.

Breast-feeding When administered systemically, minoxidil passes into the breast milk; consequently, the preparation should be avoided in the breast-feeding woman.

DRUG INTERACTIONS

- Although no clinical proof is available, the risk of onset of orthostatic hypotension cannot be excluded in patients undergoing guanethidine treatment.
- Particular prudence should be exercised in patients receiving specific treatment for cardiac conditions or hypertension; an interaction with the minoxidil absorbed after topical application cannot be excluded and demands the precise evaluation of the treatment prescribed.

MAJOR INCOMPATIBILITY

Incompatibility with oxidants and acids.

SIDE EFFECTS

The side effects most frequently encountered in clinical trials consist of minor skin reactions. The most frequently reported effect has been local irritation with, in particular, desquamation, erythema, dermatitis, dry skin, hypertrichosis (extended period), burning sensation and pruritus. More rarely, other reactions have been described, of an allergic type (sensitivity, rhinitis, eruption, generalised erythema, facial oedema), ear infection (particularly otitis externa), disturbed vision, ocular irritation. Finally, a few cases have been reported of alopecia, irregular hair growth, thoracic pain, changes in blood pressure and pulse rate, hepatitis and renal lithiasis.

It should be noted, however, that these events, in particular the most rarely reported ones, occurred without any formal imputability to treatment being established.

USE AND ADMINISTRATION

Apply twice a day a dose of 1 ml to the scalp, taking as starting point the centre of the area to be treated. This dose must be respected whatever the size of the area concerned. The total daily dose must not exceed 2 ml. A metred-dose applicator fits the bottle so that appropriate dosage may be followed.
Aafter application of the solution, wash the hands thoroughly. Do not apply the product to another part of the body.
Only apply when the hair and scalp are thorughly dry. Do not use a hair dryer to accelrate evaporation of the solution: this could diminish the activity of the product.
Metred-dose aerosol spray:
- Remove the cap from the bottle.
- Direct the nozzle towards the centre of the area to be treated, actuate once and spread the product with the fingertips so as to cover the whole area to be treated.
- Repeat the operation 10 times to apply a dose of 1 ml.
- Avoid inhalation of the aerosol spray.
- Replace the cap on the bottle after use.

Experience acquired during clinical trials demonstrates that 2 applications per day for a period of 4 months or more may be necessary before evidence is noted of stimulated hair-growth. The onset and degree of response vary from one individual to another. Some observations suggest that a return to the initial state may occucr within 3 to 4 months of ending treatment.

STORAGE PRECAUTIONS

Flammable preparation.

OVERDOSAGE

Accidental ingestion may provoke systemic effects due to the vasodilator action of minoxidil (5 ml of solution contain 100 mg of minoxidil, equivalent to the maximum dose taken orally by an adult under treatment for arterial hypertension.
The signs and symptoms of any possible overdose will be cardiovascular in nature, with a reduction in blood pressure, tachycardia and water and sodium retention. Water and sodium retention may be treated with an appropriate diuretic treatment, tachycardia and angina with a beta-blocker or other inhibitor of the sympathetic nervous system. Hypotension might be treated by intravenous administration of an isotonic sodium chloride solution. It is advisable to avoid using sympathomimetics such as noradrenaline and adrenaline in view of excessive cardiac stimulation.