Composition

reEssence Vasodilator Formula contains Minoxidil 2% at a concentration of 20 mg minoxidil per mL in a solution composed of alcohol, propylene glycol and water.

Description

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 2 mg/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).

Pharmacology Pharmacodynamics

Minoxidil topical solution showed no systemic effects related to absorption when tested in controlled clinical trials in both normotensive and untreated hypertensive patients. Minoxidil does not interfere with vaso-motor 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 reEssence Vasodilator Formula 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.

Contraindications

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

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

Before starting on reEssence Vasodilator Formula 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 reEssence Vasodilator Formula 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 reEssence Vasodilator Formula. reEssence Vasodilator Formula 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 reEssence Vasodilator Formula should be monitored after starting therapy and periodically thereafter. If systemic effects should occur, discontinue use of reEssence Vasodilator Formula. 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.

reEssence Vasodilator Formula 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 reEssence Vasodilator Formula 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 reEssence Vasodilator Formula before covering the head.

Some patients have experienced changes in hair colour and/or texture with reEssence Vasodilator Formula.
**Carcinogenicity, Mutagenicity and Impairment of Fertility**

Carcinogenic activity of minoxidil has been investigated following dietary administration to mice at 10-64 mg/kg/day, and following topical administration to mice and rats at 8-80 mg/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 3-10 mg/kg/day and at 80 mg/kg/day SC.

**Use in Lactation**

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

Subcutaneous administration of minoxidil at 80 mg/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 reEssence Vasodilator Formula in patients under 20 years of age have not been established.

**Use in Elderly**

Safety and efficacy of reEssence Vasodilator Formula in patients over 80 years of age have not been established.

**Adverse Reactions**

In general reEssence Vasodilator Formula is well tolerated.

Most frequently reported adverse reactions with 2% 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).
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 reEssence Vasodilator Formula have been reported.

**Drug Interactions**

There are currently no known drug interactions associated with the use of reEssence Vasodilator Formula. Although it has not been clinically demonstrated, there exists the theoretical possibility of absorbed minoxidil potentiating orthostatic hypotension in patients currently taking peripheral vasodilators.

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.

**Dosage and Administration.** FOR EXTERNAL USE ONLY.

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

A total dose of 1 mL reEssence Vasodilator Formula should be applied twice per day to the frontal and temple hairline scalp. The total daily dose should not exceed 2 mL. After applying reEssence Vasodilator Formula, wash hands thoroughly.

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

At least two to four months of twice daily applications of reEssence Vasodilator Formula are generally required before evidence of wrinkle reduction 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.

reEssence Vasodilator Formula must only be used for application to the frontal and temple hairline scalp. Avoid contact with eyes, nose, mouth and broken skin. reEssence Vasodilator Formula must not be taken by mouth.

reEssence Vasodilator Formula should be applied to a dry scalp and the solution allowed to dry naturally. reEssence Vasodilator Formula should not be used 24 hours before or after hair treatments such as color or perm. Sunscreens should be applied at least two hours after the application of reEssence Vasodilator Formula, and shampooed off before the next application. Hats must not be worn for at least an hour after applying.

Patients should stop using reEssence Vasodilator Formula and seek immediate medical attention if experiencing any or the following: rapid heart rate, rapid weight gain, swelling or fluid retention, dizziness, chest or shoulder pains.