# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Minoxidil 5% w/v cutaneous spray, solution

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of cutaneous solution contains 50 mg of minoxidil.

Excipients with known effect:
Each millilitre contains 350 mg of propylene glycol and 510 mg of alcohol (ethanol).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Cutaneous spray, solution.

Clear, colourless to yellowish homogeneous solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Minoxidil 5% w/v cutaneous spray, solution 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 Minoxidil 5% w/v cutaneous spray, solution individual responses cannot be predicted.

### 4.2 Posology and method of administration

*Men aged 18-65:*

Posology

1 ml Minoxidil should be applied twice daily (morning and evening) to the affected areas of the scalp.

The daily amount applied of 2 x 1 ml solution should not be exceeded, regardless of the size of the affected scalp area.

*Too low dosage*
If too little minoxidil has been applied or a dose has been missed, the patient must not make up for the missing amount. In this case, treatment should be continued at the recommended dose.

*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 Minoxidil 5% w/v cutaneous spray, solution in children and adolescents below the age of 18 years or adults over 65 years has not been established.
Method of administration

Minoxidil should only be used on the scalp.

Each pack of Minoxidil solution contains 2 different pump spray applicators:

- pre-assembled applicator for large-area application
- separate applicator with extended tip for smaller areas

Both applicators can be swapped by detaching the one applicator and replacing it with the other.

Prior to applying minoxidil, it must be ensured that the scalp is dry.
Minoxidil should not be applied to other parts of the body.

Hands should be washed carefully after applying minoxidil, in order to avoid accidental contact with mucous membranes and eyes.

After applying minoxidil, the hair can be styled as normal. However, the scalp should not be moistened for about 4 hours. This will prevent minoxidil from being washed off.

*Instructions for use/application*

According to the affected area and the application device provided.

**A. Spray pump**

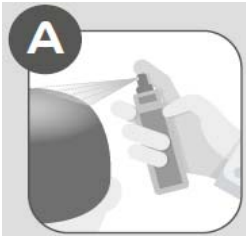


Fig. 1

1. The outer cap of the bottle should be removed.
2. 1 ml of solution should be applied, by pressing the spray pump 6 times (Fig. 1).

After each pumping action, the patient should spread the liquid over the affected area with their fingertips. At the same time, inhalation of the spray mist should be avoided.

For a more localised application (small areas of the scalp or under the hair), the applicator provided with the pack should be used.

**B. Applicator**

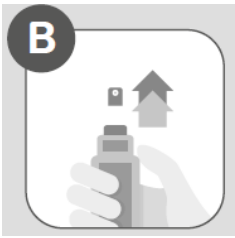


Fig. 2

Fig 3

Fig. 4

Fig. 5

1. The outer cap of the bottle should be removed.

2. The top part of the spray head (piece with the orifice) should be removed by pulling it up (Fig. 2), and the applicator should be inserted (Fig. 3 and 4).

3. 1 ml of solution should be applied by pressing the applicator 6 times (Fig. 5).

After each pumping action, the patient should spread the liquid over the affected area with their fingertips. At the same time, inhalation of the spray mist should be avoided.

Duration of use

The onset and extent of hair growth are different in individual patients.

In general, twice-daily treatment for 2 to 4 months is required before an effect is seen. In order to maintain the effect, it is recommended to continue the twice-daily application without interruption. Anecdotal reports indicate that regrown hair may disappear three to four months after stopping Minoxidil 5%

w/v cutaneous spray, solution application and the balding process will continue. Applying minoxidil in larger amounts or more frequently does not achieve better results. Regarding a possible therapeutic effect, there is sufficient clinical experience for a treatment period of up to one year.

If no effect is seen after 12 months, treatment should be discontinued.

## 4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1,
- in users with treated or untreated hypertension
- in women, due to occasional signs of cosmetically distressing, reversible, facial hair growth during treatment,
- use of occlusive dressings or other topical medical preparations on the scalp,
- sudden or uneven hair loss
- in patients with any scalp abnormality (including psoriasis, sunburn, shaved scalp or if the scalp is damaged by burns or scarring).

## 4.4 Special warnings and precautions for use

Prior to treatment with minoxidil, the patient should be thoroughly examined, and her/his medical history taken.

Endocrinological causes, underlying systemic diseases or malnutrition must be excluded. In these cases, if necessary, a specific treatment should be initiated.

The patient should have a normal, healthy scalp. Minoxidil should not be used if the cause of hair loss is not known, if the scalp is infected or if the scalp is red, inflamed or painful.

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. Minoxidil is intended only for external use on the scalp and should not be applied to other parts of the body.

There is no clinical experience to date with regard to efficacy for hair loss in the temporal region (receding hairline).

The patient should discontinue the medicinal product and consult a doctor if a reduction in blood pressure is detected, or if one or more of the following manifestations occur: chest pain, accelerated heartbeat, asthenia or dizziness, sudden unexplained weight gain, swollen hands or feet, persistent redness or

irritation of the scalp or if other not expected new symptoms appear (see section 4.8).

In some patients, a transient increase in the amount of hair shedding has been observed two to six weeks after the start of treatment. This effect is due to the fact that the resting phase (telogen phase) of the hair cycle is shortened in hair follicles treated with minoxidil and the growth phase (anagen phase) is reached more quickly. This stimulates new hair growth, which pushes the "old", no longer active hairs out of the scalp. This gives the initial impression of increased hair loss. However, it is accompanied by increased hair regrowth. This effect regresses within a few weeks and can be interpreted as a first sign of the minoxidil effect. Using more than the recommended dose or more often will not improve results. If shedding persists (>2 weeks), users should stop Minoxidil 5% w/v cutaneous spray, solution application and consult their doctor.

Unwanted hair growth may be caused by the transfer of the medicinal product to areas other than the scalp.

Treatment with minoxidil should not take place in patients with signs of cardiovascular disease or cardiac arrhythmias or in hypertensive patients, including patients on treatment with antihypertensives.

Isolated cases of slight changes in hair colour have been reported by patients with very fair hair upon concomitant use of hair care products or after swimming in heavily chlorinated water. Users should be aware that, whilst extensive use of Minoxidil 5% w/v cutaneous spray, solution 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.

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.

Inadvertent ingestion can cause severe cardiovascular adverse reactions. This product must therefore be kept out of the reach of children.

When treatment with minoxidil is stopped, shedding of the hairs will occur again.

Due to the ethanol and propylene glycol content in minoxidil, repeated spraying of minoxidil on the hair rather than the scalp might result in increased hair dryness and/or stiffness.

Inhalation of the spray mist should be avoided.

Minoxidil 5% w/v cutaneous spray, solution is flammable. It should not be used near an open flame, lit cigarettes or some devices (e.g. hairdryers).

Minoxidil 5% w/v cutaneous spray, solution contains ethanol 96%. It may cause burning sensation on damaged skin.
It can also cause eye stinging and irritation. In case of accidental contact with sensitive areas (eyes, skin abrasions, mucous membranes), these must be rinsed with plenty of water.

This medicine contains 350 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.

## 4.5 Interaction with other medicinal products and other forms of interaction

To date, no information is available on interactions between minoxidil and other medicinal products. Although not clinically proven, there is a theoretical possibility that absorbed minoxidil may potentiate orthostatic hypotension in patients concomitantly taking peripheral vasodilators.

Minoxidil should not be used on the scalp together with other dermatological products (or with agents that enhance skin absorption).

Pharmacokinetic drug interaction studies in humans showed that the percutaneous absorption of minoxidil is enhanced by tretinoin, corticosteroids, petrolatum and dithranol as a result of increased permeability of the stratum corneum. Betamethasone dipropionate increases the local tissue concentration of minoxidil and reduces the systemic absorption of minoxidil.

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

Minoxidil is indicated for use in male patients only and must not be used by pregnant women and breastfeeding mothers.

<u>Pregnancy</u>

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).

Breast-feeding
Systemically absorbed minoxidil is excreted in human milk. The effect of minoxidil on new-borns/infants is unknown.

Fertility
Minoxidil caused a dose-dependent decrease in the conception rate in rats. Due to the low systemic exposure following topical administration, the clinical relevance is probably limited.

## 4.7 Effects on ability to drive and use machines

This medicinal product may cause dizziness or hypotension (see section 4.8). If affected, patients should not drive or operate machinery.

## 4.8 Undesirable effects

The following frequencies are used for the evaluation of adverse reactions:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

The safety of topical minoxidil from clinical trial data is based on data from 7 placebo-controlled randomised clinical trials in adults evaluating either 20 mg/ml or 50 mg/ml minoxidil solution, and two placebo-controlled randomised clinical trials in adults evaluating a 50 mg/ml 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).

| System Organ Class (SOC) | Frequency | Adverse Drug Reaction (ADR) |
|---|---|---|
| Immune System Disorders | Not known | Allergic reactions including angioedema (with symptoms such as oedema of the lips, mouth, tongue and throat, swelling of the lips, tongue and oropharynx) |

| System Organ Class (SOC) | Frequency | Adverse Drug Reaction (ADR) |
|---|---|---|
| | Common | Hypersensitivity (including facial oedema, generalised skin rash, general pruritus, facial swelling and throat tightness) |
| Psychiatric Disorders | Not known | Depressed mood |
| Nervous System Disorders | Very common | Headache |
| | Uncommon | Dizziness |
| Eye disorders | Not known | Eye irritation |
| Cardiac disorders | Not known | Tachycardia, palpitations |
| | Common | Chest pain |
| Vascular disorders | Common | Hypertension |
| | Not known | Hypotension |
| Respiratory, thoracic and mediastinal disorders | Common | Dyspnoea |
| Gastrointestinal Disorders | Uncommon | Nausea |
| | Not known | Vomiting |
| Skin and subcutaneous tissue disorders | Common | Pruritus, hypertrichosis (including facial hair growth in women), dermatitis, dermatitis acneiform, skin rash,<br>local side effects on the scalp: stinging, burning, itching, dryness, scaling and folliculitis |
| | Not known | Symptoms at the administration site which may also affect the ears and face, such as pruritus, skin irritation, pain, redness, oedema, dry skin and inflammatory rash up to exfoliation, dermatitis, blisterin, bleeding and ulceration<br><br>Temporary hair loss (see section 4.4)<br><br>Changes in hair colour |
| | Rare | Changes in hair texture |
| | 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 |

| System Organ Class (SOC) | Frequency | Adverse Drug Reaction (ADR) |
|---|---|---|
| | | be more severe and include exfoliation, dermatitis, blistering, bleeding and ulceration) |
| General disorders and administration site conditions | Common | Peripheral oedema |
| | Not known | Chest pain |
| 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 Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Symptoms of intoxication
Application of minoxidil at higher than the recommended dosage and to relatively large body surfaces or areas other than the scalp may possibly lead to increased systemic absorption of minoxidil. To date, there have been no known cases where the topical use of minoxidil solution has resulted in intoxication.

After inadvertent swallowing, the concentration of the active compound minoxidil in this medicinal product may lead to systemic effects corresponding to the pharmacological action of the active substance (2 ml minoxidil 50 mg/ml contains 100 mg minoxidil, which is equivalent to the maximum recommended daily dose for the treatment of hypertension).

Due to the systemic effects of minoxidil, the following adverse reactions may occur:
Cardiac disorders: accelerated heartbeat, hypotension
General disorders: fluid accumulation and subsequent sudden weight gain
Nervous system disorders: dizziness

Treatment of intoxication
Clinically significant tachycardia can be controlled with β-blockers and oedema with diuretics.

An excessive decrease in blood pressure can be treated by intravenous infusion of physiological saline solution. Sympathomimetics such as adrenaline and noradrenaline are to be avoided due to their excessive cardiotonic effect.

Treatment of minoxidil overdosage should be symptomatic and supportive.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatological preparations; other dermatologicals
ATC code: D11AX01

Mechanism of action
The exact mechanism of action by which minoxidil stimulates hair growth is not fully known. However, minoxidil may stop hair loss in androgenetic alopecia by:

- increasing the diameter of the hair shaft,
- stimulating hair growth in the anagen phase,
- extending the anagen phase,
- shortening the telogen phase, whereby the anagen phase is reached more quickly.

Pharmacodynamic effects
As a peripheral vasodilator, minoxidil increases the microcirculation to hair follicles. Minoxidil stimulates vascular endothelial growth factor (VEGF) which is probably responsible for the increased capillary permeability and hence shows a high metabolic activity which can be observed during the anagen phase.

The following study data refer to the topical minoxidil-containing medicinal products of the originator MAH:
In clinical studies, a mean serum concentration of 1.6 ng/ml was measured in patients treated with minoxidil. In pharmacological studies on a haemodynamically sensitive population of subjects with low-grade untreated hypertension, minor effects on heart rate were measurable only at a serum concentration of 21.7 ng/ml or more.
If treatment is interrupted, within 3 to 4 months a condition will set in as would have been achieved without treatment with minoxidil.

## 5.2 Pharmacokinetic properties

Absorption
When minoxidil solution is topically applied, about 1-2% of the active substance is systemically absorbed, compared to 90-100% with oral formulations.

The following study data refer to the topical minoxidil-containing medicinal products of the originator MAH:
In a study on men, the mean minoxidil serum concentration AUC for the 2% solution was 7.54 ng*hr/ml, compared to a mean AUC of 35 ng*hr/ml for 2.5 mg of an oral formulation. The mean plasma concentration ($C_{max}$) for the topical solution was 1.25 ng/ml compared to 18.5 ng/ml following oral administration of 2.5 mg.

In another study on men, systemic absorption of a 50 mg/ml foam formulation was about half as much as that of a 50 mg/ml solution. The mean AUC (0-12 h) and $C_{max}$ for the 50 mg/ml foam, i.e. 8.81 ng*hr/ml and 1.11 ng/ml, respectively, were about 50% of AUC (0-12 h) and $C_{max}$ for the 50 mg/ml solution, i.e. 18.71 ng*hr/ml and 2.13 ng/ml, respectively.

For the 50 mg/ml foam, the time to peak plasma concentration ($t_{max}$) of 5.42 h was similar to the $t_{max}$ for the solution, i.e. 5.79 h. No haemodynamic effect of minoxidil is evident up to a mean serum concentration of 21.7 ng/ml.

Distribution
The volume of distribution after intravenous administration of 4.6 mg and 18.4 mg minoxidil was 73.1 L and 69.2 L, respectively.

Biotransformation
Following topical administration, about 60% of absorbed minoxidil is metabolised to glucuronides, primarily via the liver.

Elimination
The half-life of topical minoxidil is 22 hours, compared to 1.49 hours with oral dosage forms. 97% of minoxidil is excreted via the urine and 3% via the faeces.
Mean renal clearance of minoxidil and its glucuronides, based on data from oral dosage forms, is 261 ml/min and 290 ml/min, respectively.
Upon discontinuation of treatment, about 95% of the minoxidil absorbed after topical administration is excreted within 4 days.

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or carcinogenic potential.

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

Carcinogenicity

A high incidence of hormone-induced tumours was observed in rats and mice. These tumours were caused by a secondary hormonal effect (hyperprolactinaemia), which was observed only in rats at extremely high doses and was similar to the effect of reserpine.
The use of topical minoxidil has shown no effect on the hormonal status of women. Therefore, hormone-induced tumours do not pose a carcinogenic risk to humans.

Teratogenicity
Reproductive toxicity studies on rats and rabbits, with very high exposure rates compared to the anticipated exposure level in humans, have revealed signs of maternal toxicity and a risk to the foetus. There is a slight risk to the human foetus.

Fertility
Minoxidil doses of more than 9 mg/kg (at least 25 times the human exposure), administered subcutaneously in rats, were associated with a reduced rate of conception and implantation, as well as a reduction in the number of viable pups.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Propylene glycol
ethanol (96 per cent)

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

30 months

After first opening: 1 year.

## 6.4 Special precautions for storage

Do not refrigerate or freeze.

Keep the bottle tightly closed.

### 6.5 Nature and contents of container

The cutaneous solution is provided in red transparent polyethylene terephthalate (PET) bottles, closed with a red spray-pump.
The spray-pump is composed by a body, a diffusor and an outer cap made of several materials***, namely*** plastics [polyethylene (PE), polypropylene (PP) and polyoxymethylene (POM)] and stainless steel (SS).
A separate, white polypropylene applicator with extended tip is included in the box.

Pack sizes: 1 x 60 ml and 3 x 60 ml cutaneous solution.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Spray pump and applicator cleaning
The top part of the spray head or applicator should be removed and rinsed with isopropyl alcohol (70 per cent) after each use to clean the product residues and to avoid clogging. After cleaning, the removed parts (either the spray pump and outer cap or the spray-tip applicator) should be placed back.

## 7 MARKETING AUTHORISATION HOLDER

axunio Pharma GmbH
Van-der-Smissen-Straße 1
22767 Hamburg
Germany

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 47848/0022

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<to be completed nationally>

## 10 DATE OF REVISION OF THE TEXT

03/01/2025