# HEADWAY
# 2.0% TOPICAL SOLUTION

## Minoxidil 2.0% Topical Solution

## Submission for Reclassification

**October 2001**

**Pacific Pharmaceuticals Limited**

# BACKGROUND TO THE SUBMISSION

This submission is made in response to the Medicines Classification Committee's decision to decline a previous application for reclassification of minoxidil 2% topical solution to a General Sales Medicine. At this meeting in November 1999 the committee recommended that the company should be invited to make concurrent submissions to the MCC and the NDPSC for reclassification to Pharmacy Medicine classification

## Australian Schedule

Currently minoxidil topical solution has a Restricted Medicine classification in Australia. However it should be noted that these products have only been available for a limited period in Australia, whereas they have been marketed in New Zealand for well over 10 years. It should also be noted that Pacific Pharmaceutical Limited's product is not registered in Australia and there is no intention to seek registration, therefore an application to the NDPSC is deemed unnecessary.

## Benefits of Reclassification

This resubmission has been prepared to re-emphasise the benefits to the consumer of minoxidil 2% topical solution being scheduled as a Pharmacy Medicine. From this, it can be clearly demonstrated that there are no safety or other issues that should preclude this reclassification.

# SUMMARY OF RECLASSIFICATION SUBMISSION

The classification sought is for minoxidil 2% topical solution is **Pharmacy Medicine**. Currently there are no minoxidil 2% topical solutions available as the market is dominated by minoxidil 5% topical solution, which is a Restricted Medicine. The reclassification of minoxidil 2% topical solution as a Pharmacy Medicine will permit reintroduction of this product onto the market.

Treatment for hair loss can consist of oral finasteride, available only on prescription, minoxidil 2% or 5% topical solution, which are currently only available as Restricted Medicines or a raft of herbal remedies, dietary supplements and cosmetics etc., which are available without restriction. Many of these unregistered remedies are untested and unproven and are already available through hair salons and herbal medicine outlets.

The effectiveness of minoxidil on hair loss is greatly enhanced in younger people and where intervention can be made early in the balding process. Therefore hair care professionals are in a unique position to recommend early treatment whist minoxidil treatment would be at its most effective. Alopecia is also known to be notoriously slow to respond to treatment and a period of up to 6 months may be required for benefits to be shown. Consumers should be encouraged constantly to persevere with treatment..

Minoxidil 2% topical solution, as a first line treatment, provides consumers with a safe and effective hair loss treatment with an excellent, and extremely well researched, safety profile, well within that of established general sale products. In the USA, minoxidil 2% is an open selling product available through supermarkets, petrol stations and general sales outlets.

The current classification as Restricted Medicine provides a barrier to consumer awareness and access due to legislation and the Pharmaceutical Society code of practice. Control through a Pharmacy Medicine classification would permit sale of this product by the shop assistant.

In summary we contend that minoxidil 2% topical solution is an ideal candidate for reclassification as a Pharmacy Medicine in that it has an excellent safety profile demonstrated over more than 10 years use in New Zealand and its availability in the USA as a General Sales Medicine. Further hair loss is an easily recognisable condition not requiring the input of a health care professional. Availability of this product through pharmacy assistants will improve consumer access.

# PART A

## International Non-proprietary Name of the medicine

Minoxidil

## Proprietary name(s)

HEADWAY 2

## Name of company/organisation/individual requesting reclassification

Pacific Pharmaceuticals Ltd
P.O. Box 11183
Ellerslie
Auckland
New Zealand

## Dose form(s) and strength(s) for which a change is sought

Topical Solution 2.0 % w/v

## Pack size and other qualifications

HEADWAY Topical Solution 2.0% containing 20mg Minoxidil per mL is available as 60mL of solution in a white HDPE bottle. Included in each pack are metered disposable applicators consisting of pump spray and extended tip assemblies together with a comprehensive consumer information booklet.

## Indications for which change is sought

HEADWAY Topical Solution 2.0% is indicated for the treatment of alopecia androgenetica (male and female pattern baldness) and the stabilisation of hair loss. There is no proposed change to the indications for a Pharmacy Medicine classification.

## Present classification of medicine

Restricted Medicine

## Classification sought

Pharmacy Medicine.

## Classification status in other countries (especially Australia, UK, USA, Canada)

| | |
|---|---|
| United States of America | General Sales Medicine |
| Australia | Pharmacy Medicine |
| Canada | Prescription Medicine (non-prescription classification application pending) |
| France | Pharmacy Medicine |

OTC in many other countries

**Extent of usage in NZ and elsewhere (e.g. sales volumes) and dates of original consent to distribute.**

Date of Consent to Distribute Headway 2%: 4 July 1991

Table 1: Annual New Zealand sales figures (1998-1999)

| **Products** | **2%** | **5%** |
|---|---|---|
| Headway | - | 20 000 units |
| Regaine | - | 13 000 units |

Currently no minoxidil 2% products are actively marketed in New Zealand.

**Labelling or draft labelling for the proposed new presentation(s)**

The label, carton and patient information leaflet are attached.

**Proposed warning statements if applicable**

No additional warnings are proposed for the Minoxidil 2.0% strength of Headway when classified as a Pharmacy Medicine.

**Other products containing the same active ingredient(s) and which would be affected by the proposed change**

Currently no minoxidil 2% solution is marketed in New Zealand. Headway 2 Topical Solution will only be launched in New Zealand as a Pharmacy Medicine. Pharmacia & Upjohn have a minoxidil 2% solution registered in New Zealand but this product is not currently marketed.

Both Pacific Pharmaceuticals Ltd and Pharmacia & Upjohn market minoxidil 5% topical solutions in New Zealand. These presentations are unaffected by this application and remain Restricted Medicines.

# PART B

**A statement of the benefits to both the Consumer and to the public expected from the proposed change.**

- Availability from pharmacy assistants will improve consumer access

Minoxidil 2% topical solution, as a first line treatment, provides consumers with a safe and effective hair loss treatment with an excellent, and extremely well researched, safety profile, well within that of established general sale products. In the USA, minoxidil 2% is an open selling product available through supermarkets, petrol stations and general sales outlets. General sales status has enabled many more consumers access to minoxidil 2% as control through prescription was a barrier to sale.

Currently minoxidil 2% is classified as Restricted Medicine, which provides a barrier to consumer awareness and access due to legislation and the Pharmaceutical Society code of practice.

Presently it is a requirement of the Medicines Act that the sale of Restricted Medicines be conducted only by the pharmacist and that certain particulars are recorded in the Sale of Medicines Register. Additionally, the Medicines Regulations stipulate that no person shall put a Restricted Medicine in a place where unauthorised persons have ready access. This is interpreted by the Pharmaceutical Society to mean that Restricted Medicines should be kept either in the dispensary or in an area where the general public does not have direct access to them (e.g. behind the counter).

These requirements impose unnecessary restrictions to consumer access in two ways:

Firstly, minoxidil 2% topical solution is unable to be displayed along with other hair care products on shelving where the general public can self-select. Secondly, the requirement that only the pharmacist can conduct the sale and that certain particulars must be recorded often means that the sales transaction can take a considerable time, particularly if the pharmacist is busy in the dispensary.

Another aspect for sales of product within a pharmacy is the availability of a pharmacist to answer consumer's concerns. We accept that this availability of consultation is important where the medicine has potential interactions or there are precautions in its use to be followed. However for minoxidil 2% topical solution, which has an extremely good safety profile this would not be necessary. We also note the Medicines Classification Committee's willingness to review an application for a Pharmacy Medicine classification. Such a classification would permit sale of this product by the shop assistant. We support this view.

It is also apparent that the intent of the current requirements for the sale of Restricted Medicines are being circumvented by internet sales through retail pharmacy. A quick internet search of New Zealand pharmacies offering sale of medicines through the internet indicate that minoxidil 5% topical solution is being commonly offered for sale.

The Restricted Medicine category has been provided as a stepping stone between Prescription Medicine and wider availability, or where some OTC medicines have some safety concerns. As there are no safety concerns associated with the use of minoxidil 2% topical solution it is appropriate that it be available, along with other hair care products for self-selection by customers.

**Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated.**

- Suitable indications for self-medication
- Symptoms recognisable without medical attention
- Pharmacists are not asked to diagnose the fact that someone is losing their hair. Generally, both male and female hair loss sufferers make the decision to treat the condition before seeking purchase
- Label & leaflet instructions are clearly presented to ensure safe & effective use of the product
- In the USA, the diagnosis is made by the purchaser prior to making the decision to use the product.

Hair loss is readily self-diagnosed and there is little chance of misdiagnosis. The wider availability of minoxidil 2% topical solution through hair salons will enable hair care professionals to assist in the diagnosis.

**Relevant comparative data for like compounds**

Treatment for hair loss can consist of oral finasteride, available only on prescription, minoxidil 2% or 5% topical solution, which are currently only available as Restricted Medicines or a raft of herbal remedies, dietary supplements and cosmetics etc., which are available without restriction. Many of these unregistered remedies are untested and unproven and are already available in hair salons. The availability of minoxidil 2% topical solution through hair salons will provide hair care professionals with an alternative to these unproven remedies.

Minoxidil 2% is no longer available from pharmacy. This is due to the current availability of minoxidil 5% topical solution as a Restricted Medicine, which has improved efficacy. The reclassification of minoxidil 2% topical solution as a Pharmacy Medicine will permit reintroduction of this product onto the market.

Minoxidil 2% solution has had extensive use in New Zealand (> 10 years) and its safety and efficacy profiles are well established with no significant side effects.

**Safety**

Finasteride 1 mg Tablets (Propecia®) are recently approved and classified as prescription medicines. Clinical monitoring is necessary due to the nature & potential adverse effects of the product. In accordance with USP DI 1999, examples of possible side effects are potential risk of abnormal external genitalia development

in male foetuses, gynecomastia, hypersensitivity reaction, abdominal pain, decreased libido, etc[1].

In contrast, the safety & efficacy profiles of minoxidil topical solution are well established. The percutaneous absorption of minoxidil following topical application of the solution to an intact scalp is minimal. The amount absorbed is about 1.6% to 3.9% of the applied dose. Applying a 5 µl per $cm^2$ dose to the entire scalp is expected to yield a systemic dose of 1.2 mg for the 1% topical solution & 2.7 mg for the 5%. Applying a 1 or 2% topical concentration of minoxidil to up to 50% of the scalp is unlikely to cause systemic side effects, since the average absorbed dose is less than 1.2 mg of minoxidil[1].

Individuals who received 2 to 8 applications daily of 1.0 ml minoxidil topical solution in concentrations of 0.01 to 3% demonstrated that increasing the concentrations or the frequency of applications did not produce proportional increases in absorption, suggesting that saturation of the stratum corneum with drug occurred after the initial dose[2].

Side effects of topical minoxidil appear to consist entirely of cutaneous reactions such as transient mild irritation or pruritis. In a placebo-control clinical trial with 3857 patients, other than local dermatologic events, no individual reaction or systemic side effects were increased in the minoxidil group as compared to the placebo group[3].

According to the prescribing information provided by Upjohn, an effort was made to investigate the potential for systemic effects of topical minoxidil (1, 2 & 5%) applied twice daily. The results were compared to oral doses (2.5 & 5 mg given once daily) & placebo in hypertensive patients. The results showed detectable blood pressure decrease only in the group taking 5 mg oral dose. The failure to detect evidence of cardiovascular effects reflects the poor absorption of topically applied minoxidil, which averages about 1.4% (range 0.3 to 4.5%) from normal, intact scalp[4]. Since it requires a concentration of 20 nanograms/ml to cause even minimal haemodynamic effects in the body, there is approximately a 16-fold safety margin in the use of 5% topical minoxidil[3].

Minoxidil solution is not well absorbed through the scalp except when the stratum corneum is damaged; under these conditions application of the solution is painful & thus unlikely to be used. The bioavailability of minoxidil following twice-daily applications of one ml of minoxidil to normal, intact scalp is 1.4% (range 0.3-4.5%)[4], said to be 10 times less than that required to see just measurable cardiovascular effects[5].

Following extensive use of the drug for well over a decade, there has been no evidence that topical minoxidil is associated with any significant cardiovascular phenomenon.

**Efficacy**

89 healthy men with male pattern baldness completed a 6-month double-blind, placebo-controlled study of 0.01%, 0.1%, 1% & 2% topical minoxidil. Subjects on 2% topical minoxidil had a statistically significant increase in mean total target area hair count over baseline compared to the placebo, 0.01% and 0.1% topical minoxidil groups (p=0.04). The results indicate that 1 % topical minoxidil is the lowest

effective concentration for male pattern baldness of those tested. Because of the more impressive changes in hair counts and the cosmetic preference for the 2% versus 1% topical minoxidil, 2% topical minoxidil is recommended as the standard treatment for male pattern baldness[6].

It is also documented that minoxidil may be more effective in retarding the progression of male-pattern baldness than in reversing it[4].

A group of 308 women suffering from androgenic alopecia were randomised to receive either topical minoxidil 2% or placebo for 32 weeks. Objective evaluation at the end of the study period showed moderate hair growth in 13% of the minoxidil-treated group, with minimal growth in 50%. In the placebo group the figures were 6 & 33% respectively. No significant side effects were reported[7].

**Local data or special considerations relating to New Zealand**

- Over 10 years experience of usage as an over-the-counter medicine
- Very low incidence of side effects
- User compliance is good
- Users read consumer medicine information (CMI)
- 98% of New Zealand sales of minoxidil topical solution are for the 5% strength (Restricted Medicine)
- There are currently numerous herbal/homeopathic treatments available as open sellers to the general public in New Zealand

**Interactions with other medicines**

Minoxidil 2.0% Solution, being a topically applied solution is unlikely to be involved in interactions with other medications. The patient information leaflet provided in each pack clearly advises consultation with your doctor if any side affects manifest themselves.

**Contraindications**

Minoxidil 2.0% Solution should not be used in persons who have shown hypersensitivity to any of the ingredients of this formulation namely Minoxidil, propylene glycol or alcohol

**Resistance**

Not applicable

**Adverse events – nature, frequency**

Very low incidence. Scalp irritation, rash, dryness …in less than 1.5% of patients[8]

**Potential for abuse or misuse**

## Abuse

No evidential reports following more than 10 years usage

## Misuse

It is very unlikely that Headway 2% topical solution will be misused. The use of hair-loss treatments is well established in the minds of consumers as evident by the wide range of largely ineffective products, which have been available direct to the consumer for decades

In line with the labelling requirements for medicines, consumers will receive comprehensive directions for the product's safe and effective use. See coloured artwork provided.

## References

1. USPDI 1999. Drug Information for the Healthcare Professional: p1465-8, 2021-3.

2. Thiers BH. The Therapeutic Use of Topical Minoxidil. Dermatologic Clinics Apr 1990; 8(2): 367-75

3. 5% Topical Minoxidil Solution in the Treatment of Alopecia Androgenetica. (www.minoxidil.com)

4. Martindale – The Extra Pharmacopoeia 30th Ed. 1993.

5. Scrip 1964 page 22.

6. Olsen EA, DeLong ER, Weiner MS. Dose-response Study of Topical Minoxidil in Male pattern Baldness. J Am Acad Dermatol 1986 Jul; 15(1): 30-7 (www.follicle.com)

7. Dollery C. Therapeutic Drugs 2nd Ed. 1999: M190-3

8. Regaine Patient Information Leaflet