Public Assessment Report

Pharmacy to General Sales List Reclassification

Regaine for Women Once a Day Scalp Foam 5% w/w Cutaneous Foam

Minoxidil 5% w/w

PL 15513/0135 – 0020

McNeil Products Ltd

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The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for regulating medicines and medical devices. We continually review the safety of medicines and vaccines in the UK, and inform healthcare professionals and the public of the latest updates through several means, including public reclassification reports. Suspected side-effects to any drug or vaccine can be reported to MHRA by both healthcare professionals and members of the public via the Yellow Card Scheme (http://www.mhra.gov.uk/yellowcard).

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Alternative format versions of this report are available on request from reclassification@mhra.gov.uk
1. Background on deciding where medicines are available

The role of MHRA
MHRA regulates medicines and medical devices in the UK, on behalf of the UK Licensing Authority. This means that MHRA decides whether medicines are available:

- on prescription only - ‘prescription only medicine’ (POM)
- bought from pharmacies - ‘pharmacy medicine’ (P)
- bought from other shops - ‘general sales list medicine’ (GSL)

What is re-classification of a medicine?
Making a change on where a medicine is available is called ‘re-classification’. This is sometimes referred to as ‘switching’. To decide on this change, MHRA may:

- take advice from the Commission on Human Medicines and its Expert Advisory Groups
- take advice from a group (‘stakeholder group’) of health professionals and representatives of people affected by the classification change
- run a public consultation

To be reclassified from P to GSL, a medicine must be a medicine which can, with reasonable safety, be sold or supplied otherwise than by, or under the supervision of a pharmacist.

"Reasonable safety" has been defined as: "where the hazard to health, the risk of misuse, or the need to take special precautions in handling is small, and where wider sale would be a convenience to the purchaser."

These conditions are set out in the Human Medicines Regulations 2012, regulation 62(5)

What evidence is needed?
A company or organisation can ask MHRA for a medicine to be available as a pharmacy medicine or a general sale medicine. To do this, they need to get together evidence to show that the medicine
a) is likely to be used appropriately, and
b) with relatively little danger to the public.

This evidence needs to focus on the risk to the public. This includes evidence on the possible abuse or misuse of the medicine. The evidence may include:

- clinical studies
- evidence showing acceptable level of side effects
- advice of experts
- views of relevant health professionals and their professional bodies
- views of relevant public associations and individuals with an interest in the medicine under consideration.

Who makes the final decision?
The final decision on whether to approve a change is made by the MHRA, on behalf of the UK Licensing Authority.

2. About Regaine for Women Once a Day Scalp Foam
Regaine for Women Once a Day Scalp Foam Scalp Foam 5% w/w Cutaneous Foam is a treatment for female pattern hair loss in women aged 18 – 65 years. Female pattern hair loss is a distinctive

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1 The Commission on Human Medicines (CHM) is an advisory non-departmental public body, sponsored by the Department of Health. The CHM advises ministers on the safety, efficacy and quality of medicines. The CHM is supported in its work by Expert Advisory Groups (EAGs), covering various areas of medicine. The CHM’s views are sought on reclassifications when more complex or new reclassifications of medicines are being proposed.
form of hair loss that occurs in women. There is a thinning of hair on the scalp due to increased hair shedding or a reduction in hair volume or both.

Each gram (g) of the product consists of 50 mg (5%) minoxidil.

The full name of the medicine is Regaine for Women Once a Day Scalp Foam 5% w/w Cutaneous Foam— in this document, we will call it ‘Regaine for Women Once a Day Scalp Foam’

This report outlines the evidence that the MHRA reviewed which led to the decision to approve this application.

What is Regaine for Women Once a Day Scalp Foam used for?
Minoxidil is used either as tablets or capsules for the treatment of high blood pressure, or as a solution or foam to be put on the scalp for the treatment of male and female pattern baldness.

Preparations of minoxidil for use on the scalp have been licensed in the UK since 1988. They are the only licensed medicinal products available without prescription for the treatment of female pattern hair loss.

A 2% scalp solution of minoxidil, called Regaine for Women Regular Strength, has been available as a GSL medicine since 2002 in a maximum pack size of 60ml (equivalent to 1.2g minoxidil). Regaine for Women Once a Day Scalp Foam has been available as a Pharmacy (P) medicine since 2015 in a maximum pack size of 2 x 73ml (equivalent to 6g minoxidil).

Who has made the proposal?
The licence-holder² for Regaine for Women Once a Day Scalp Foam, McNeil Products Limited, applied to make this product available as a GSL medicine.

3. Proposed terms of reclassification
Regaine for Women Once a Day Scalp Foam will be made available through shops under the following conditions:

   a) For external use
   b) Maximum strength 5%
   c) For the treatment of alopecia androgenetica (also known as female pattern hair loss) in women between 18 and 65
   d) With a maximum dose of 1g (equivalent to 50mg minoxidil) to be applied daily
   e) With a maximum pack size of 2 x 73mls (equivalent to 2 x 60g product providing 120 days’ supply)

The proposed SmPC³ and patient leaflet are identical to that of the current P product that was reclassified from POM to P in 2015.

Two proposed additional warnings have been added to the label, which will be referred to in section 5 below (Risk Management Plan).

This reclassification will increase the strength of minoxidil for women available as GSL from 2% solution to 5% foam for use on the scalp. However, in the application to reclassify this product from POM to P in 2015, the Applicant⁴ demonstrated that a daily dose for women of 1g of 5% minoxidil

² A Licence Holder or Marketing Authorisation Holder is the company with legal authorisation to make the medicine available to patients

³ SmPC stands for Summary of Product Characteristics. The SmPC is a legal document describing a medicine’s properties and how it can be used. SmPCs are available online via the MHRA.

⁴ The Applicant is the company that has submitted the application to reclassify a medicine.
Topical foam, equivalent to 50mg minoxidil daily, was therapeutically equivalent to a twice daily dose of 1ml of 2% minoxidil topical solution, equivalent to 40mg minoxidil daily, both in terms of efficacy and safety. Moreover, despite the daily dosage from use of the 5% foam resulting in putting a higher amount of minoxidil (50mg) on the scalp compared to the 2% solution (40mg), the Applicant had satisfactorily demonstrated that this did not present a higher safety risk over the 2% solution since there is a similar degree of systemic absorption between a twice daily dose of the 2% solution and a daily dose of 5% foam. Therefore, the higher strength of Women Once a Day Scalp Foam 5% w/w Cutaneous Foam compared to the 2% scalp solution is not clinically significant.

The reclassification will also increase the maximum length of treatment for a GSL product for women from 30 days to 120 days.

4. How the proposal was assessed

Under the provisions of The Human Medicines Regulations 2012, regulation 62(5), General Sales List is appropriate for medicines which can, with reasonable safety, be sold or supplied by someone other than a pharmacist. The term “with reasonable safety” has been defined as: “where the hazard to health, the risk of misuse, or the need to take special precautions in handling is small and where wider sale would be a convenience to the purchaser.”

Assessment of suitability for General Sales List availability

The MHRA assessed the application against this criterion for reclassification.

Hazard to Health

Safety profile

During the safety assessment for the application to reclassify this product from POM to P in 2015 it was noted that there was a potentially higher rate of cardiovascular (CV) adverse events in women than in men. While this was resolved to enable approval of the POM to P reclassification the Applicant was asked specifically to provide evidence of the safety in use of Regaine for Women Once a Day Scalp Foam since it was reclassified as a P medicine in the UK, particularly in relation to CV events.

The applicant therefore provided:

- an overview of CV events reported with the use of Regaine for Women Once a Day Scalp Foam in the United Kingdom
- A Safety and Efficacy Summary for minoxidil containing once a day scalp foam products for women, (including data from the USA)

Overall the analysis of adverse events concerning minoxidil foam products for both men and women since the product for women was reclassified to P indicated that there did not appear to be a higher rate of CV adverse events in women than in men. Also, analysis of all adverse events reported for minoxidil foam products demonstrated that cardiac and vascular disorders adverse events were infrequent and a small proportion of all adverse events.

An evaluation of the adverse events profile of minoxidil 5% foam for women in the USA from September 2014 (when the product became available in that country as a GSL) to 31 January 2017 provided reassurance of the safety of minoxidil in the GSL setting.

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5 Two medicines are therapeutically equivalent if they have the same clinical effect and safety profile when administered to patients under the conditions specified in the labelling.

6 Systemic absorption means absorption of a drug into the blood stream.
Risk of Misuse
The MHRA considers that there is no reason to believe that there is a higher risk of misuse of Regaine for Women Once a Day Scalp Foam compared to the 2% solution that has already been available in the UK as a GSL since 2002. Instructions about who should not use the product and warnings and precautions for when using it, including a warning not to use the product if pregnant or breastfeeding, are on the product label. The use of “Once a day” in the name of the product and clear labelling instructions will ensure it is not used twice a day like the 2% solution.

Self-diagnosis
minoxidil for use on the scalp has been available as a GSL medicine for women since 2002. Therefore, women’s ability to self-diagnose female pattern hair loss has already been established. Also, over the past 16 years, the pack design of this product range has improved. There is a clear statement on the front of the pack stating that the product is “For female pattern hair loss”, there are pictures illustrating female pattern hair loss in women, and there is information about when the product should not be used, as well as warnings and precautions to follow when using it.

Incorrect Use
The MHRA considers that the risk of incorrect use can be managed through the label and patient leaflet, as is currently the case for 2% GSL solution for women.

Dependence and Abuse
From the safety and efficacy data provided there is no evidence of dependence in patients using minoxidil. There is also no potential for misuse of this product for illegal purposes. The potential for dependence and abuse is no different to that of the existing 2% GSL solution for women.

Overdose
There is a potential for increased absorption of minoxidil into the blood stream if excessive amounts are applied to larger areas of the body or areas other than the scalp. However, due to the nature of the product the MHRA considers it unlikely that women would wish to apply this to areas of the body other than the scalp.

The label and leaflet clearly state that it should be applied only to the scalp; that no more than one measured application should be applied; that the product should not be used more than once a day; and that hair will not re-grow any more quickly if the product is used more than recommended.

The Applicant stated that accidental ingestion may cause serious cardiac events, particularly in children. Apart from the product being contraindicated7 in children, the label also carries a warning to keep the product out of sight and reach of children and it is manufactured with a child resistant cap. The MHRA considers these measures to be acceptable for managing the risk of overdose in children if the product becomes more widely available as a GSL medicine.

Special Precautions in handling
The Applicant stated that foam preparations for men have been available as GSL medicines since 2010 and as there is no difference in storage requirements for the product for women, no special precautions are required in handling of Regaine for Women Once a Day Scalp Foam. However, as an extra precaution the Applicant was asked to make the flammable warnings on the label and in the leaflet more prominent.

Wider sale would be a convenience
The MHRA accepts that the wider availability of the foam in addition to the solution would be beneficial, providing the option of a once a day treatment (vs twice daily for the 2% solution) and a more cosmetically acceptable formulation. Moreover, treatment success relies upon regular use over a long period, so wider availability would be beneficial.

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7 Contraindications are the situations and circumstances under which a medicinal product should not be used. They are set out in the terms of a product’s licence
Consideration of the role of the pharmacist
With the addition of a warning on the label about not to use in pregnancy of if breast feeding the MHRA accepts that women can choose the product safely without the need for advice from a pharmacist. The risk of a woman choosing the wrong product or applying the wrong dose is managed satisfactorily by the instructions on the label and using “once a day” in the product name. Therefore, the MHRA accepts that the product can be selected and used correctly without a pharmacist’s advice.

Efficacy
Efficacy has already been addressed when the product was licensed; there were no other issues related to efficacy that needed to be considered as part of this application.

5. Further details on the application

Risk Management Plan
The application contained a risk management plan (RMP). RMPs are documents that contain information on a medicine’s safety profile and one or more of the following:

- How any risks identified in the safety profile will be prevented or minimised in patients
- Plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine
- Risk factors for side effects
- Measuring the effectiveness of measures taken to prevent or minimise risks.

The RMP for this product considered the main risks associated with the product and proposed additional warnings on the labelling about not to use in pregnancy and breast feeding or if a woman is sensitive to any of the ingredients. The MHRA considers that apart from this, no further risk minimisation measures are need for this application.

6. Reasons for not seeking advice from the Commission on Human Medicines or carrying out a public consultation

Overall, no new issues of concern were raised in relation to the GSL availability of Regaine for Women Once a Day Scalp Foam based on the following reasons:

- Female pattern baldness is well established as a condition that can be treated with a GSL medicine. Therefore, the risk of misdiagnosis without help from a doctor or a pharmacist is low
- The product has been demonstrated to have equivalent efficacy and safety to, and has the same systemic absorption as, the 2% minoxidil solution which has been available as GSL for 16 years
- The only difference between this product and existing minoxidil scalp preparations classified as P or GSL is that it has a once daily, rather than a twice daily dose. Satisfactory measures have been put in place to manage the risk of a women mistakenly using the product twice a day. These include the use of “once a day” in the name of the product, and information on the label and leaflet
- Analysis of UK safety data on CV for the 5% foam in women compared to men since the product for women was reclassified to P, and USA data on all minoxidil scalp preparations, where they are available as GLS did not reveal any safety concerns
- In view of the clinical similarity between the GSL 2% minoxidil solution for women, and the proposed 5% foam for women, apart from the longer length of treatment provided with the proposed maximum pack size for the 5% foam, which has resulted from the once daily dose, there is nothing new for CHM to consider

7. Conclusion
The MHRA has taken the decision to approve GSL classification of Regaine for Women Once a Day Scalp Foam under the following conditions:
a) For external use
b) Maximum strength 5%
c) For the treatment of alopecia androgenetica (also known as female pattern hair loss) in women between 18 and 65
d) With a maximum dose of 1g (equivalent to 50mg minoxidil) to be applied daily
e) With a maximum pack size of 2 x 73mls (equivalent to 2 x 60g product providing 120 days’ supply)

Medicines and Healthcare products Regulatory Agency,
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