IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0991/001/001
Case No: 2070878

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Transdermal Limited

35 Grimwade Avenue, **Croydon**, **Surrey CR0 5DJ**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Grisol 1% w/w Cutaneous Spray solution

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/12/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Grisol 1% w/w Cutaneous Spray solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.05 ml metered dose spray delivers 400 micrograms of griseofulvin.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous spray, solution.
Clear liquid with a characteristic odour of isopropyl alcohol.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The topical treatment of mycotic infections due to superficial dermatophytes of skin.

4.2 Posology and method of administration

Method of Administration

Cutaneous use: to be applied topically to the affected area.

A single spray should be applied, allowed to dry and a second spray delivered if necessary. Treatment should be applied once daily.

Children: Safety in children has not been established.

4.3 Contraindications

Hypersensitivity to griseofulvin or organic solvents.

4.4 Special warnings and precautions for use

Use with caution in patients with a family history of porphyria or those with hepatic dysfunction.
Grisol may cause irritation if introduced into the eyes.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

Safety in human pregnancy or lactation has not been established and therefore it should not be used unless the practitioner considers that the benefit of treatment outweighs the risk.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Application to deep cuts or fissures may cause stinging, local irritation, rash.

4.9 Overdose

If Grisol is accidentally ingested, overdosage from griseofulvin active ingredient is unlikely to require treatment. However the component solvents could give rise to symptoms of alcoholic intoxication and poisoning so that gastric lavage and emesis may be required. Any additional treatment should be symptomatic and supportive.

Grisol contains an alcohol base which will cause burning and irritation to the eyes. In the event that Grisol is accidentally sprayed into the eyes, the area should be bathed with large amounts of cool tap water.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The active ingredient of Grisol, Griseofulvin, is an antifungal agent which, when applied topically in this formulation, penetrates the skin in the tissues of which it remains active against dermatophyte infections even after subsequent evaporation of the solvent system.

Grisol is active against dermatophytes including *Microsporum canis*, *Trichophyton rubrum* and *Trichophyton verrucosum*.

5.2 Pharmacokinetic properties

Studies in humans have demonstrated no significant absorption.

When taken orally griseofulvin is metabolised by the liver mainly to 6-desmethylgriseofulvin which is excreted in the urine. A large amount of an oral dose of griseofulvin is excreted unchanged in faeces and a small amount in urine, some is excreted in sweat.

5.3 Preclinical safety data

Animal studies undertaken with respect to Grisol relate appropriately to local toxicity and absorption.

28 day studies of the effects of griseofulvin, benzyl alcohol, acetone and isopropyl alcohol on the skin of rabbits showed few signs of dermal irritation.

Systemic absorption after topical administration of Grisol to shaved rats is poor, being approximately 20% in 24 hours. The data suggest a reduced systemic absorption in man by the topical route and a much more favourable distribution between the dermis and the skin.

In human volunteer studies, serum concentrations after topical administration of high doses are too small to be measured.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetone
Benzyl Alcohol
Isopropyl alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25 °C.
Protect from direct light and heat. Highly flammable, keep away from naked flames. Store the container in an upright position.

6.5 Nature and contents of container

Clear glass bottles with a red outer PVC plastic lining of nominal volume 20 or 50 ml, each fitted with a spray pump assembly designed to deliver approximately 0.05 ml per actuation and fitted with a protective plastic cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Transdermal Ltd.
35 Grimwade Avenue
Croydon
Surrey CR0 5DJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 991/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th July 1992
Date of last renewal: 27th July 2007

10 DATE OF REVISION OF THE TEXT

June 2008