

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Micanol 1% Cream

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dithranol 10mg/g cream (1% w/w).

For excipients see section 6.1

#### 3 PHARMACEUTICAL FORM

Cream.  
Smooth and yellow in colour.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

For the topical treatment of sub-acute and chronic psoriasis, by the short contact therapy method.

##### 4.2 Posology and method of administration

Cutaneous Use

###### Recommended Dosage Schedules

###### Adults including the elderly

Apply Micanol cream only to the affected areas being careful to avoid contact with normal skin. Use only a small amount, rubbing it in gently and thoroughly until it no longer smears.

Micanol cream should be applied once every 24 hours and removed by washing off usually no more than 30 minutes after application. The cream must be washed off using plenty of lukewarm water only. This may be easiest in a bath or shower, particularly if the treated area is extensive.

When removing the cream, it is important that the water is not too hot and soap is not used, as these can damage the Micanol cream base and cause increased staining of the skin. Soap may be used for washing after the Micanol cream has been rinsed off.

The treatment should start with 1% cream on a limited surface. Where the response to dithranol has not been previously established contact with 1% cream should initially be not greater than 10 minutes. This may gradually be increased to 30 minutes over a period of about seven days depending on the individual response.

**Missed Application:** Apply as soon as you remember but not near the time for next dose. Do not apply two doses simultaneously.

After 1-2 weeks patients may progress to Micanol 3% if necessary provided they do not show any sign of skin irritation.

If the skin is irritated, patients should revert to 1% cream. Treatment should be continued until the skin is clear of

psoriasis.

Micanol 1% cream should always be used under medical supervision.

Micanol cream may cause staining of clothing and bed linen. To remove staining on clothing or bed linen rinse in lukewarm water only (not more than 30°C). To prevent the possibility of discolouration to the bath or shower always rinse with lukewarm water. Should any deposit be left on the surface a suitable cleanser may be used.

### Children

Micanol is not suitable for the treatment of infants and young children.

## 4.3 Contraindications

Hypersensitivity to Dithranol or any other component of Micanol or presence of inflammation of skin, including; Erythroderma; vesiculo-bullous dermatoses such as acute eczematous dermatoses

Acute pustular psoriasis,

Folliculitis;

Wounds and ulcers;

Psoriasis of the face and flexures and intertriginous psoriasis.

Although it is not known whether dithranol has the potential to induce renal damage, the compound may not be used in patients with renal insufficiency.

## 4.4 Special warnings and special precautions for use

For external use only. Use with caution if potent steroids have been administered recently (within the last 7 days).

Do not apply to the face and keep away from eyes; if accidentally applied to the eyes, severe conjunctivitis, keratitis, or corneal opacity may result. If accidental contact occurs, wash with plenty of lukewarm water and contact an eye specialist.

Do not apply to mucous membrane, genitalia or intertriginous skin, do not apply to blistered, raw or oozing areas of the skin.

When excessive redness or burning is observed, reduce frequency or concentration, or discontinue application. Such irritation is more likely with higher concentrations.

If sensitivity reactions occur, especially on the normal skin surrounding the plaque site, discontinue use.

Wash hands thoroughly after use.

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

**Do not use with** photosensitising medications (concurrent use of these medications with Dithranol may enhance their photosensitising effects).

Concurrent use of topical preparations containing coal tar, zinc oxide and starch during therapy with Micanol may diminish treatment results. Concomitant use of topical preparations containing salicylic acid or urea enhance the effect of Micanol. The absorption of other substances applied concomitantly during treatment with Micanol is increased.

**Do not use with** propylene glycol containing drugs (Dithranol would be oxidised and inactivated).

Withdrawal of long term steroids in psoriasis may cause a rebound phenomenon. An interval of one to two weeks should therefore be left between stopping long term steroids and starting Micanol treatment. A bland emollient may be used in the intervening period.

## 4.6 Pregnancy and lactation

There is no experimental evidence to support the safety of dithranol in pregnancy. Micanol cream should be given to pregnant women only if clearly needed.

No animal studies with respect to effects on pregnancy, embryonal-fetal development, parturition and postnatal development have been conducted. Therefore, during pregnancy, the cream must neither be applied to a large area of the skin (not more than 30% of body surface) nor repeatedly; especially if skin absorption were increased for any reason.

### Lactation

The cream must not be applied to the breast of lactating mothers.

## 4.7 Effects on ability to drive and use machines

None reported and none expected.

## 4.8 Undesirable effects

Frequent undesirable effects ( $>1/100$ ) include: perilesional erythema and burning, lesional burning (usually mild or moderate). These reactions usually lessen after one or two weeks of treatment.

Rare undesirable effects ( $>1/1,000$ ) include: Allergic reaction (Skin rash).

Contact allergy reactions to dithranol have been reported but seem to be extremely rare ( $\leq 1/10,000$ ) and are difficult to differentiate from the regular delayed reactions.

Staining of the treated and surrounding skin may appear. It will disappear within 1 to 2 weeks after the end of the treatment.

May temporarily discolour fingernails or hair or may stain fabrics.

## 4.9 Overdose

Excessive application of the cream and prolonged usage causes burning and deep staining of the skin.

The skin should be rinsed firstly with water only and then washed, never wash at a temperature exceeding 30°C. Dithranol is a cathartic (laxative) and if accidentally swallowed, should be removed by gastric lavage.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

#### Pharmacotherapeutic classification (ATC-Code: DO5A COA)

Dithranol is a synthetic anthracene derivative which has antipsoriatic effects. The therapeutic action of dithranol has been linked to its ability to generate free radicals

Dithranol has been shown to accumulate in the mitochondria where it induces morphological and functional changes. This affects the cellular energy supply which, in turn, results in inhibition of energy dependent process such as DNA replication which slows down excessive cell division as seen in psoriasis plaque. Cyclic nucleosides are important in the regulation of epidermal cell division.

The psoriatic hyperproliferative epidermis contains elevated levels of cyclic guanosine monophosphate. As dithranol has been shown to reduce the elevated level of cGMP back to normal, this could represent an additional mechanism of action.

### 5.2 Pharmacokinetic properties

#### Absorption and distribution:

It has been demonstrated that dithranol penetration depends on skin integrity: penetration is faster in diseased skin than in healthy skin.

When the time of contact is short (<30mn) penetration of the drug is maintained in diseased skin but significantly decreased in healthy perilesional skin. Therefore, the short contact therapy method significantly reduces the risk for local side effects in perilesional skin.

In vitro studies with human skin showed more dithranol penetrates into skin with impaired stratum corneum barrier in 30 minutes than into intact skin during about 16 hours. The concentration reaches its maximum after 30-60 minutes contact time and remains rather constant thereafter. In intact skin, however, the concentration continues to increase with time.

The highest concentration of unchanged dithranol is found in the horny layer where it can be detected for 24-48 hours, even after the skin has been washed. In deeper dermal layers relatively small amounts of unoxidised dithranol are detected whereas higher concentrations of the dithranol dimer are found.

#### Metabolism

The unstable dithranol is oxidised to danthron, to dithranol dimer and to further insoluble polymerisation products.

#### Elimination:

There are no studies which indicate that unchanged dithranol is absorbed through the human skin. However, small quantities of oxidation products have been detected in the urine of patients after topical application.

### 5.3 Preclinical safety data

Tumour-promoting properties of dithranol have been observed in animal experiments.

As yet, dithranol was not subject to extensive mutagenicity testing. Present investigations do not indicate a mutagenic potential. For the dithranol metabolite dantron, small amounts of which are found in the epidermis following epicutaneous application, there are also indications of a genotoxic effect in addition to negative findings. In long-term studies in mice and rats dantron was found to be carcinogenic, albeit at high oral doses.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Glyceryl monolaurate  
Glyceryl monomyristate  
Anhydrous citric acid  
Sodium hydroxide  
Purified water

### 6.2 Incompatibilities

Oxidants e.g. propylene glycol.

### 6.3 Shelf Life

2 years.  
Shelf life after first opening: 28 days.

### 6.4 Special precautions for storage

Do not store above 25°C.  
Store in the original package in order to protect from moisture.

### 6.5 Nature and contents of container

Micanol 1% Cream is packed into aluminium tubes lined internally with a protective lacquer and sealed at the nozzle end with an aluminium membrane, and fitted with polypropylene caps.

### 6.6 Instructions for use and handling

Micanol can be washed away by means of water only. In order to avoid lasting stains on clothes and fittings, washing should be performed as soon as possible. Rinse first with water only before washing. Never wash at a temperature exceeding 30°C (lukewarm).

## 7 MARKETING AUTHORISATION HOLDER

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## 8 MARKETING AUTHORISATION NUMBER

PA 469/17/1

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

Date of first authorisation: 13<sup>th</sup> November 1995  
Date of last renewal: 6<sup>th</sup> August 2003

**10 DATE OF REVISION OF THE TEXT**

January 2005

