

# **Micanol**

## **Dithranol 1% w/w Topical Cream**

### **Presentation**

Micanol is a smooth white cream for topical application which contains 10 mg of dithranol per gram of cream.

### **Uses**

#### ***Actions***

Dithranol belongs to the family of hydroxyanthrones, which have been used in the treatment of psoriasis for more than a century. 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.

The unstable dithranol is oxidised to danthron, dianthrone (dithranol dimer) and further insoluble oxidation products. Exposure to sunlight increases the breakdown of diathranol to danthron. Danthron has been found in the urine of patients receiving dithranol therapy.

#### ***Pharmacokinetics***

##### **Absorption**

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

##### **Distribution**

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 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.

## **Clinical Trials**

Short contact treatment of psoriasis with Micanol 1% has been investigated using a randomised, within-patient comparison design and a composite sign severity score (CSSS). In a four week study, Micanol was compared to placebo (10 patients). The CSSS was reduced in all actively treated lesions, whereas no improvement was seen in lesions treated with vehicle.

In two six-week studies, Micanol 1% was compared to 1% dithranol in either a petrolatum (33 patients) or paraffin plus petrolatum (16 patients) vehicle. After six weeks, the reductions to CSSS were 79% and 92% in patients treated with Micanol and dithranol/petrolatum respectively, and 55% and 66% in patients treated with Micanol and dithranol/petrolatum plus petrolatum respectively.

Adverse effects such as burning and staining of skin and clothing were more prevalent with dithranol/petrolatum compared to Micanol.

## **Indications**

Treatment of stable chronic plaque-type psoriasis by the short contact therapy method

## **Dosage and Administration**

### ***Adults including the elderly***

#### **Use on the skin**

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

Hands should be thoroughly washed with soap and water after applying to affected areas.

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% dithranol 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.

Healing of the lesions is usually seen within 3 to 6 weeks.

### **Use on the scalp**

For use on the scalp, first wash the hair with shampoo, rinse and then apply Micanol cream while the hair is still damp. Leave in contact for up to 30 minutes and then rinse off using plenty of lukewarm water only. Further shampoo may be used after the cream has been removed.

### **Children**

Safety and efficacy of the use of Micanol in children have not been established.

### **Stains**

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.

## **Contraindications**

- Acute pustular psoriasis or presence of inflammation of skin, including folliculitis
- Erythroderma
- Hypersensitivity to dithranol or any other component of Micanol.

## **Warnings and Precautions**

### ***Topical steroids***

Use with caution if potent topical steroids have been applied recently.

### ***Face and eyes***

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.

### ***Mucous membranes and sensitive skin***

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

### ***Redness and burning***

A small proportion of patients are sensitive to any form of dithranol treatment. If the initial treatment produces excessive redness or burning, or if the lesions spread, reduce frequency of application. In extreme cases, stop treatment.

### ***Skin sensitivity***

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

### ***Scalp application***

Prior to application on the scalp, the hair must be washed thoroughly, so that grease is removed. Otherwise there is a risk of discolouration of the hair after treatment.

### ***Hands***

Hands should be thoroughly washed with soap and water after applying to affected areas to avoid contact with normal skin (see DOSAGE AND ADMINISTRATION).

### ***Stains***

Dithranol will cause staining and discolouration of the skin, clothing and bed linen. Staining of the skin is due to the formation of danthron, which is accelerated by sunlight. Exposure to sunlight following application of the cream should be avoided so as to minimise the formation of this hazardous substance (see Carcinogenicity, mutagenicity and impairment of fertility).

### ***Carcinogenicity, mutagenicity and impairment of fertility***

There are inadequate data in animals and no data in humans to assess dithranol's potential carcinogenicity. However, the drug is a potent tumour-promoting agent. At concentrations as low as 0.01%, dithranol produced papillomas in mice pretreated with a single application of 7,12-dimethylbenzanthracene (DMBA).

Dithranol was mutagenic in strain TA1537 of *Salmonella typhimurium*, with and without metabolic activation; caused increases in chromosome and chromatid gaps in a human peripheral blood lymphocyte clastogenesis assay; and inhibited DNA repair synthesis in human diploid fibroblasts damaged with N-acetoxy-s-acetylaminofluorene.

There are no animal or human data with which to assess the effect of dithranol on fertility.

Danthron is an impurity of Micanol cream. Danthron causes gene mutations in *Salmonella typhimurium* and mouse lymphoma cells *invitro*, and DNA damage in *Bacillus subtilis* and rodent hepatocytes. Carcinogenicity studies with danthron have shown an increased incidence of malignant liver tumours in mice, and benign and malignant intestinal tumours in rats after dietary administration for 16-18 months.

### ***Use during Pregnancy and Lactation***

Category B2

Animal reproduction studies have not been conducted with dithranol, and it is not known whether Micanol cream can damage the embryo or foetus when administered to pregnant women. Treatment of pregnant women with Micanol cream is not recommended.

Because it is not known whether dithranol is excreted in human milk and animal studies have not been done, use of Micanol cream in lactating women is not recommended. If breast-feeding mothers do use the cream, they should avoid accidental contamination of the skin or mouth of the baby.

### ***Effects on ability to drive and use machines***

Micanol is unlikely to have any effect on a person's ability to drive or operate machinery.

### ***Use in Children***

Safety and efficacy of the use of Micanol in children have not been established.

## **Adverse Effects**

### ***Clinical Trial Information***

The adverse event profile of dithranol is well recognised. Clinical trials of Micanol 1% in patients with psoriasis have documented the following mean incidences of adverse reactions.

Perilesional erythema (26%); perilesional burning (19%); lesional burning (24%). These reactions are generally mild to moderate and usually lessen after one or two weeks of treatment.

Lesional staining and perilesional staining are common, occurring with a mean incidence in clinical trials of 24% and 32% respectively. Staining disappears within 1 to 2 weeks after the end of the treatment.

Micanol cream may temporarily discolour fingernails or grey or white hair and may stain fabrics.

### ***Postmarketing Information***

Rare: Allergic reaction (skin rash).

## **Interactions**

### ***Photosensitising medications***

Concurrent use of these medications with dithranol may enhance their photosensitising effects.

### ***Propylene glycol-containing drugs***

Dithranol would be oxidised and inactivated.

### ***Steroids***

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.

## **Overdosage**

### ***Symptoms***

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

### ***Treatment***

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, advice should be sought from the National Poisons Centre (0800 764 766) or the nearest Hospital Emergency Department.

## **Pharmaceutical Precautions**

Store below 25 °C in a dry place.

## **Medicines Classification**

Pharmacist Only Medicine

## **Package Quantities**

Aluminium tube which contains 50 g of Micanol Cream.

## **Further Information**

Micanol Cream also contains purified water, glyceryl myristate, glyceryl monolaurate, citric acid and sodium hydroxide

## **Name and Address**

AFT Pharmaceuticals Ltd  
P.O. Box 33-203  
Takapuna  
Auckland  
Email:customer.service@aftpharm.com

## **Date of Preparation**

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