

MICREME H



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## 1. Product Name

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MICREME H, miconazole nitrate 2% w/w and hydrocortisone 1% w/w, topical cream.

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## 2. Qualitative and Quantitative Composition

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Each 1 g of cream contains 20 mg of miconazole nitrate and 10 mg of hydrocortisone.

For the full list of excipients, see section 6.1.

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## 3. Pharmaceutical Form

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A smooth, white cream containing miconazole nitrate 2 % w/w and hydrocortisone 1 % w/w.

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## 4. Clinical Particulars

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### 4.1 *Therapeutic indications*

MICREME H is indicated for the treatment of skin infections caused by yeast, dermatophytes or Gram-positive bacteria, in which inflammatory symptoms are predominant. MICREME H may also be used for mycotic infections with bacterial superinfection.

### 4.2 *Dose and method of administration*

MICREME H should be applied topically to the lesion once to twice daily. Squeeze 1 cm of cream (or more, according to the size of the lesion) onto the lesion and rub in gently until the cream has been completely absorbed by the skin. The treatment with MICREME H (or subsequently with a miconazole-containing cream) should be continued without interruption until the lesion has completely disappeared (usually after 2 to 5 weeks). MICREME H is particularly indicated for the initial stages of treatment.

Discontinue MICREME H cream on disappearance of the inflammatory symptoms (or after a maximum treatment period of 2 weeks) and continue treatment with an antifungal cream only until complete disappearance of the lesion (usually 2 to 5 weeks).

### 4.3 *Contraindications*

Hypersensitivity to miconazole/miconazole nitrate, other imidazole derivatives, hydrocortisone or to any of the excipients (see section 6.1). Tubercular or viral infections of the skin or those caused by Gram-negative bacteria.

### 4.4 *Special warnings and precautions for use*

When miconazole and hydrocortisone cream is used by patients taking oral anticoagulants, the anticoagulant effect should be carefully monitored.

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Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with miconazole topical formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued. Miconazole and hydrocortisone cream must not come into contact with the mucosa of the eyes.

As with any topical corticosteroid, caution is advised with infants and children when miconazole and hydrocortisone cream is to be applied to extensive surface areas or under occlusive dressings including baby napkins; similarly, application to the face should be avoided.

In infants, long term continuous topical corticosteroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

Natural thinning of the skin occurs in the elderly, hence corticosteroids should be used sparingly and for short periods of time.

Because of its corticosteroid content avoid long-term treatment with miconazole and hydrocortisone cream. Once the inflammatory symptoms have disappeared treatment may be continued with miconazole nitrate cream or powder.

Miconazole and hydrocortisone cream can damage certain synthetic materials. Therefore, it is recommended that cotton underwear be worn where clothing contacts the affected area.

#### **4.5 Interaction with other medicines and other forms of interaction**

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application (see section 5.2), clinically relevant interactions are rare. However, in patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored.

Miconazole is a CYP3A4 inhibitor that can decrease the rate of metabolism of hydrocortisone. Serum concentrations of hydrocortisone may be higher with the use of miconazole and hydrocortisone cream compared with topical preparations containing hydrocortisone alone.

#### **4.6 Fertility, pregnancy and lactation**

##### **Pregnancy**

Clinical data on the use of miconazole and hydrocortisone cream in pregnancy are limited. In animals corticosteroids are known to cross the placenta and consequently can affect the foetus (see section 5.3). Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to humans has not been established.

As a precautionary measure, it is preferable to avoid the use of miconazole and hydrocortisone cream during pregnancy. Treatment of large surfaces and the application under occlusive dressing is not recommended.

##### **Breast-feeding**

There are no adequate and well-controlled studies on the topical administration of miconazole and hydrocortisone cream during breastfeeding. It is not known whether concomitant topical administration of miconazole and hydrocortisone cream to the skin could result in sufficient systemic absorption to produce detectable quantities of hydrocortisone and miconazole in breast milk in humans. A risk to the newborn child cannot be excluded.

A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from miconazole and hydrocortisone cream therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. Treatment of large surfaces and the application under occlusive dressing is not recommended.

##### **Fertility**

No data available. For pre-clinical fertility data refer to section 5.3.

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

None known

#### **4.8 Undesirable effects**

The safety of miconazole and hydrocortisone cream was evaluated in 480 patients who participated in 13 clinical trials (six double-blind and seven open-label trials). These studies examined patients from 1 month to 95 years of age with infections of the skin caused by dermatophytes or candida species in which inflammatory symptoms were prominent.

##### **All patients**

No adverse drug reactions (ADRs) were reported by  $\geq 1\%$  of the 480 miconazole and hydrocortisone cream-treated patients (adult and paediatric patients combined).

The frequency categories use the following convention: very common ( $>1/10$ ); common ( $>1/100$  to  $<1/10$ ); uncommon ( $>1/1,000$  to  $<1/100$ ); rare ( $>1/10,000$  to  $<1/1,000$ ); very rare ( $<1/10,000$ ); and not known (cannot be estimated from the available clinical trial data).

Of the three ADRs identified from the 13 clinical trials of miconazole and hydrocortisone cream, skin irritation was reported in one clinical trial that included patients aged 17 to 84 years, skin burning sensation in two clinical trials that included patients aged 13 to 84 years, and irritability in one clinical trial of infants aged 1 to 34 months.

##### **Paediatric population**

The safety of miconazole and hydrocortisone cream was evaluated in 63 paediatric patients (1 month to 14 years of age) who were treated with miconazole and hydrocortisone cream in 3 of the 13 clinical trials noted above. One ADR term (irritability) was reported in these 3 trials. The frequency of irritability in miconazole and hydrocortisone cream-treated paediatric patients was common (3.2%).

All events of irritability occurred in one clinical trial of infants (aged 1 to 34 months) with napkin (diaper) dermatitis. The frequency, type, and severity of other ADRs in paediatric patients are expected to be similar to those in adults. ADRs were reported by  $\geq 1\%$  of the 480 miconazole and hydrocortisone cream-treated patients (adult and paediatric patients combined).

##### **Adverse drug reactions in adult and paediatric patients treated with miconazole and hydrocortisone cream.**

System organ class	Adverse drug reactions	
	Frequency category	
	Uncommon ( $\geq 1/1,000$ to $< 1/100$ )	Not known
Immune system disorders		Anaphylactic reaction, hypersensitivity
Skin and subcutaneous tissue disorders	Skin irritation, skin burning sensation, urticaria, pruritus	Angioedema, rash, contact dermatitis, erythema, skin inflammation, skin hypopigmentation, application site reaction

<b>General disorders and administration site conditions</b>	Irritability	
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## Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

## 4.9 Overdose

### Symptoms

Prolonged and excessive use can result in skin irritation, which usually disappears after discontinuation of therapy. Topically applied, corticosteroids can be absorbed in sufficient amounts to produce systemic effects.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

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## 5. Pharmacological Properties

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Imidazole and triazole derivatives, combinations, ATC code: D01AC20.

Miconazole nitrate is active against dermatophytes and pathogenic yeasts and many Gram-positive bacteria.

Hydrocortisone is an anti-inflammatory steroid. Its anti-inflammatory action is due to reduction in the vascular component of the inflammatory response, suppression of migration of polymorphonuclear leukocytes, and reversal of increased capillary permeability. The vasoconstrictor action of hydrocortisone may also contribute to its anti-inflammatory activity.

MICREME H combines the broad spectrum anti-fungal and antibacterial activity of miconazole with the anti-inflammatory and antipruritic action of hydrocortisone. It acts very rapidly on pruritus, which frequently accompanies dermatophyte and yeast infections. Symptomatic improvement is seen before the first signs of healing are observed. However, treatment is symptomatic and pruritus may flare up again after discontinuation of steroid treatment.

### 5.2 Pharmacokinetic properties

#### Absorption

Miconazole remains in the skin after topical application for up to 4 days. Systemic absorption of miconazole is limited, with a bioavailability of less than 1% following topical application of miconazole. Plasma concentrations of miconazole and/or its metabolites were measurable 24 and 48 hours after application. Approximately 3% of the dose of hydrocortisone is absorbed after application on the skin.

#### Distribution

Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%). More than 90% of hydrocortisone is bound to plasma proteins.

#### Biotransformation

The half-life of hydrocortisone is about 100 minutes. Metabolism takes place in the liver and tissues and the metabolites are excreted with the urine, mostly as glucuronides, together with a very small fraction of unchanged hydrocortisone.

## **Elimination**

The small amount of miconazole that is absorbed is eliminated predominantly in faeces as both unchanged drug and metabolites over a four-day post-administration period. Smaller amounts of unchanged drug and metabolites also appear in urine.

### **5.3 Preclinical safety data**

Preclinical data on the drug product (miconazole nitrate + hydrocortisone) revealed no special hazard for humans based on conventional studies of ocular irritation, dermal sensitization, single dose oral toxicity, primary dermal irritation toxicity, and 21 - day repeat dose dermal toxicity. Additional preclinical data on the individual active ingredients in this drug product reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and for miconazole toxicity to reproduction. Miconazole has shown no teratogenic effects but is fetotoxic at high oral doses. Reproductive effects (fetotoxicity, reduced weight gain) and developmental abnormalities specifically craniofacial effects including cleft palate have been reported with hydrocortisone in various animal models.

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## **6. Pharmaceutical Particulars**

### **6.1 List of excipients**

MICREME H also contains octyldodecanol, cetostearyl alcohol, cetyl esters wax, sorbitan monostearate, polysorbate 60, benzyl alcohol and purified water.

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

30 months.

### **6.4 Special precautions for storage**

Store at or below 25°C.

### **6.5 Nature and contents of container**

Aluminium tube with HDPE/[LLDPE](#) cap. Pack-size of 15 g.

### **6.6 Special precautions for disposal**

Not applicable.

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## **7. Medicines Schedule**

Restricted Medicine

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## **8. Sponsor Details**

Mylan New Zealand Ltd  
PO Box 11183  
Ellerslie  
AUCKLAND  
Telephone 09-579-2792

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## **9. Date of First Approval**

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18 November 1988

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## **10. Date of Revision of the Text**

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11 August 2017      Revise to SmPC format. Change to section 6.5.