NEW ZEALAND DATA SHEET

MICREME

1. Product Name

MICREME, 2% w/w, vaginal cream.

2. Qualitative and Quantitative Composition

Each 1 g of cream contains 20 mg of miconazole nitrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

MICREME vaginal cream is a smooth white cream which contains the synthetic bactericidal and fungicidal broad-spectrum antifungal agent miconazole nitrate.

4. Clinical Particulars

4.1 Therapeutic indications

Local treatment of vulvovaginal candidiasis and superinfections due to Gram-positive bacteria.

MICREME vaginal cream may also be used for the treatment of mycotic balanitis.

4.2 Dose and method of administration

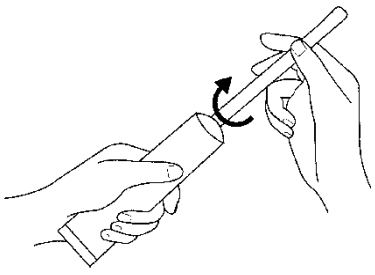
Dose

MICREME vaginal cream should be used once daily (before bedtime), the contents of one applicator (approximately 5 g of cream) should be squeezed deeply into the vagina, for seven days, even after pruritus and leukorrhoea has disappeared.

Method of administration

Patient instructions for use

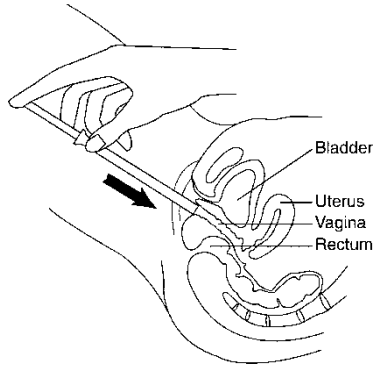
A) Filling the applicator



1. Wash your hands thoroughly.

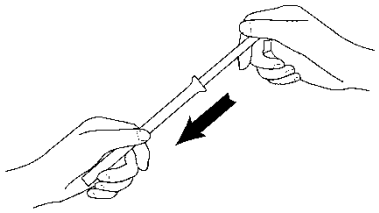
2. Remove the cap from the tube, and use the reverse side of the cap to pierce the tube nozzle.
3. Screw the applicator to the tube, and fill the applicator by squeezing the bottom of the tube until the plunger is fully extended.
4. Unscrew the applicator from the tube and replace the tube cap.

B) Inserting the applicator



1. Hold the filled applicator by the cylinder and carefully insert into the vagina, as far as is comfortably possible. This is best achieved by lying on your back with your knees bent.
2. Slowly press the plunger until it stops. This places the cream into the vagina.
3. Remove the applicator from the vagina with plunger still depressed.

C) Care of the applicator



After each use, wash the applicator thoroughly. It can be taken apart by firmly pushing the head of the plunger up inside the cylinder. Withdraw the plunger from the cylinder. Wash the parts in warm water, with a mild detergent, and rinse thoroughly. Reassemble by pushing the plunger into the cylinder.

4.3 Contraindications

MICREME vaginal cream is contraindicated in individuals who have shown hypersensitivity to miconazole, miconazole nitrate, other imidazole derivatives or any other components of this medicine (see section 6.1).

4.4 Special warnings and precautions for use

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with miconazole nitrate vaginal cream and with other miconazole formulations (see section 4.8).

If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

General hygienic measures should be observed to control sources of infection and reinfection.

Appropriate therapy is indicated when the sexual partner is also infected.

The concurrent use of latex condoms or diaphragms with vaginal anti-infective preparations may decrease the effectiveness of latex contraceptive agents. Therefore MICREME vaginal cream should not be used concurrently with a latex condom or latex diaphragm.

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 vaginal application, clinically relevant interactions occur very rarely. In patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored. The effects and side effects of other drugs metabolized by CYP2C9 (e.g. oral hypoglycemics and phenytoin) and also CYP3A4 (e.g. HMG-CoA reductase inhibitors such as simvastatin and lovastatin and calcium channel blockers such as dihydropyridines and verapamil), when co-administered with miconazole, can be increased and caution should be exercised.

Contact should be avoided between certain latex products such as contraceptive diaphragms or condoms and MICREME vaginal cream since the constituents of the cream may damage the latex (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Although intravaginal absorption is limited, MICREME vaginal cream should be used in the first trimester of pregnancy only if, in the judgement of the physician, the potential benefits outweigh the possible risks.

Breast-feeding

It is not known whether miconazole nitrate is excreted in human milk. Caution should be exercised when using MICREME vaginal cream during lactation.

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 nitrate vaginal cream was evaluated in a total of 537 women with microbiologically confirmed candidiasis and symptoms (e.g., vulvovaginal itching, burning/irritation), or signs of vulvar erythema, edema, excoriation, or vaginal erythema or edema who participated in 2 single-blind clinical trials. Subjects were treated with miconazole intravaginally, randomly assigned to either a single 1,200 mg capsule, or a 7 day application of 2% vaginal cream. Adverse Drug Reactions (ADRs) reported by ≥ 1% of miconazole nitrate vaginal cream -treated subjects in these trials are shown in Table 1.

In the table, the frequencies are provided according to the following convention:

Very common:	≥ 1/10
Common	≥ 1/100 and < 1/10
Uncommon	≥ 1/1000 and < 1/100
Rare	≥ 1/10,000 and < 1/1000
Very rare	< 1/10,000

Table 1. Adverse drug reactions reported by subjects treated with miconazole nitrate vaginal cream in 2 single blind clinical trials	
Body system/organ class Frequency category	**Undesirable effects**
Skin and subcutaneous tissue disorders	
Common	Rash
Uncommon	Rash pruritic, urticaria
Reproductive system and breast disorders	
Very common	Genital pruritus female, vaginal burning sensation, vulvovaginal discomfort
Common	Dysmenorrhoea

A range of additional reactions were reported during the clinical trials, such as: vaginal discharge, vaginal haemorrhage, vaginal pain, headache, dysuria, urinary tract infection, abdominal pain, rosacea, swelling of the face and nausea. However due to the design of these studies, a definitive causal relationship could not be established.

Table 2. Adverse drug reactions identified during post-marketing experience with miconazole nitrate vaginal cream by frequency category estimated from spontaneous reporting rates	
Immune system disorders	
Not known	Hypersensitivity including anaphylactic and anaphylactoid reactions, angioedema
Skin and subcutaneous tissue disorders	
Not known	Pruritus
Reproductive system and breast disorders	
Not known	Vaginal irritation, pelvic cramps

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

In case of accidental ingestion, no problems are expected.

Treatment

In the event of accidental ingestion of large quantities of this medicine, an appropriate method of gastric emptying may be used if considered appropriate.

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

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiinfectives and antiseptics, excl. combinations with corticosteroids, imidazole derivatives. ATC code: G01AF04

Mechanism of action

Miconazole combines a potent antifungal activity against common dermatophytes and yeasts with an antibacterial activity against certain Gram-positive bacilli and cocci. Miconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane, resulting in fungal cell necrosis.

In general, miconazole exerts a very rapid effect on pruritus, a symptom that frequently accompanies dermatophyte and yeast infections.

5.2 Pharmacokinetic properties

Absorption

Miconazole persists in the vagina for up to 72 hours after a single dose. Systemic absorption of miconazole after intravaginal administration is limited, with a bioavailability of 1 to 2% following intravaginal administration of a 1200 mg dose. Plasma concentrations of miconazole are measurable within 2 hours of administration in some subjects, with maximal levels seen 12 to 24 hours after administration. Plasma concentrations decline slowly thereafter and were still measurable in most subjects 96 hours post-dose. A second dose administered 48 hours later resulted in a plasma profile similar to that of the first dose.

Distribution

Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Biotransformation and 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. The apparent elimination half-life ranges from 15 to 49 hours in most subjects and likely reflects both absorption from the site of application and metabolism/excretion of the drug.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6. Pharmaceutical Particulars

6.1 List of excipients

MICREME 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

2 years.

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 40 g with 5 g applicator.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Restricted Medicine

8. Sponsor Details

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

9. Date of First Approval

28 October 1988

10. Date of Revision of the Text

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