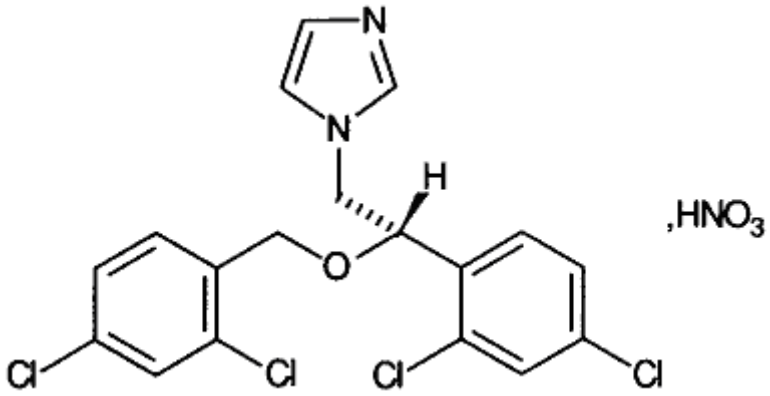
Monistat 1

Miconazole nitrate Soft Gel Vaginal Ovule and External Cream

Description

Miconazole nitrate is 1-[2,4-dichloro-β-(2,4-dichlorobenzyloxy) phenethyl] imidazole nitrate and is a synthetic 1-phenethylimidazole derivative. It is a white, microcrystalline powder, very slightly soluble in water and in ether, soluble in 140 parts of ethanol (96%) and slightly soluble in chloroform.



CAS-22832-87-7 $C_{18}H_{14}C_{l4}N_2O.HNO_3$ MW: 479.16

MONISTAT® 1 contains two components: one MONISTAT® soft gel vaginal ovule containing 1200 mg of miconazole nitrate together with gelatin, glycerol, lecithin, liquid paraffin, titanium dioxide and soft white paraffin, and 9 grams of MONISTAT® antifungal cream, containing 2 % w/w of miconazole nitrate together with benzoic acid, cetyl alcohol, isopropyl myristate, polysorbate 60, potassium hydroxide, propylene glycol, purified water and stearyl alcohol.

Pharmacology

Pharmacodynamics

Miconazole is an antifungal which exhibits *in vitro* fungistatic activity against species of the genus *Candida.* Miconazole appears to act on the fungal cell wall and membranes inducing permeability changes which alter the ionic macromolecular composition of the affected cells. Depending on the concentration and duration of exposure *in vitro*, the yeast cells show progressive cytoplasmic deterioration and prominent shape change,

finally resulting in complete cell necrosis. *In vivo* imidazole antifungal agents exert mainly a fungistatic effect.

Pharmacokinetics

Human Absorption and Metabolism: Following intravaginal administration of miconazole nitrate, small amounts are absorbed. After the ovule has been inserted into the vagina, the outer covering rapidly disintegrates and the active suspension is almost instantaneously released. Systemic absorption after intravaginal administration is limited.

Following intravaginal administration of a single MONISTAT® soft gel vaginal ovule to 10 healthy females, plasma miconazole concentrations were detectable at two hours and peaked at 12-24 hours, with an average T_{max} at 18.4 hours. The mean (range) plasma concentrations at 24, 48, 72, and 96 hours are summarised in the following table:

Hours post-dose	**24**	**48**	**72**	**96**
Mean conc (ng/mL)	9.22	4.51	2.95	1.84
Range	4.53 - 16.78	1.25 -10.06	0.57 -7.78	0.29 - 6.31

The average (range) peak plasma concentration, C_{max}, was 10.71 (5.78 - 18.33) nanograms/mL while the AUC_{0-96} was 477.3 (244.8 - 774.8) nanograms.h/mL.

Indications

For the treatment of candidal infections of the vagina and vulvovagina.

Contraindications

MONISTAT® 1 is contraindicated in patients with known hypersensitivity to miconazole nitrate or other imidazoles, or any ingredient in this product.

Precautions

Treatment should be discontinued if irritation or sensitisation occurs during use.

If there is a lack of response to miconazole nitrate vaginal therapy, appropriate investigations should be performed to confirm the diagnosis and rule out other pathogens, such as *Trichomonas* and *Haemophilus vaginalis (Gardnerella)*.

Recurrent vulvovaginal candidiasis rarely may be caused by resistant strains of *C. albicans* or, more commonly, by other *Candida* with reduced susceptibility to azole antifungals (e.g. *C. glabrata).* Repeated or prolonged use many favour selection of resistant organisms.

Intractable candidiasis may be the presenting symptom of unrecognised diabetes. Therefore, appropriate urine/blood investigations may be indicated in patients not responding to treatment.

During treatment, it is recommended that the patient refrains from sexual intercourse or that the male partner wears a condom. It may also be necessary for the male partner to be treated at the same time as the patient.

The base contained in MONISTAT® 1 may interact with latex products. The effectiveness and safety of certain latex products, such as condoms and diaphragms may be reduced.

Use in pregnancy

Category A (Drugs which have been used by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed). Patients who are pregnant should be advised to exercise caution when inserting the vaginal applicator provided with MONISTAT® 1, especially during the third trimester.

Use in lactation

It is not known whether miconazole nitrate is excreted in human milk, therefore, caution should be exercised when miconazole nitrate is administered to a woman who is breast feeding.

Use in children

Vaginal products should only be used in children under 12 years on medical advice.

Interactions with other drugs

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after vaginal application of miconazole, clinically relevant interactions are unlikely to occur. However, in patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored as these patients may be at risk of increased bleeding or bruising.

Adverse Reactions

Clinical studies show that miconazole nitrate cream and ovule formulations are generally well tolerated. Most frequently reported reactions (mainly mild to moderate) in clinical trials included local irritation (16-25%), pruritus (16-22%), discharge (9-12%), headache (12.5-23.1%) and a burning sensation (24-28%), especially at the start of the treatment. Complaints of pelvic cramping, hives and skin rash have also been reported rarely.

Dosage and Administration

MONISTAT® 1:

Ovule: The ovule should be inserted intravaginally once at bedtime.

Cream: The cream is used in the management of candidal vulvovaginitis or infection of the peri-anal area. The partner may be treated with the external cream to treat cutaneous candidiasis in the genital area.

Apply a small amount of the cream to the external vaginal area twice a day until symptoms disappear. The partner may apply a small amount of cream to the affected genital area twice a day until symptoms disappear.

During treatment, it is recommended that the patient refrains from sexual intercourse or that the male partner wears a condom. The base contained in MONISTAT® 1 may interact with latex products. The effectiveness and safety of certain latex products, such as condoms and diaphragms may be reduced.

Overdosage

Overdosage of miconazole nitrate in humans has not been reported to date. In mice and guinea pigs, the oral LD_{50} values were found to be 578 and 276 mg/kg respectively. If accidentally ingested it is not likely to be harmful; however a Poisons Information Centre should be contacted - Phone 0800 764 766.

Storage

MONISTAT® 1 should be stored below 25°C.

Medicine Classification

Pharmacist-Only medicine

Presentation

MONISTAT® 1 contains two components: one MONISTAT® 1200 mg ovule in a plastic blister pack with a plastic plunger-type applicator and a 9 g tube of 2% MONISTAT® external cream.

Name and Address

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