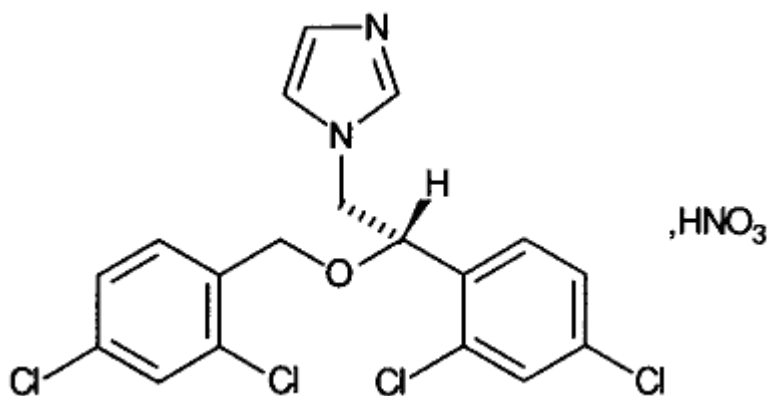


Monistat 3 Day Cream

Miconazole nitrate 40 mg/g Vaginal Cream Tube (25g) with 3 Disposable Applicators

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 $\text{C}_{18}\text{H}_{14}\text{Cl}_4\text{N}_2\text{O}\cdot\text{HNO}_3$ MW: 479.16

MONISTAT[®] 3 Day Cream contains one cream tube with 3 disposable applicators. The MONISTAT[®] 3 Day Cream contains miconazole nitrate 4% w/w as the active ingredient. The vehicle contains 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

Systemic absorption after intravaginal administration is limited. However, results of a clinical study reveal that miconazole nitrate levels were detectable at 2 hours and peaked at approximately 12 hours after initial dose. The systemic absorption after a single dose and at the end of therapy of miconazole nitrate 4% vaginal cream are approximately 4-fold higher than those with the 2% vaginal cream. While AUC and C_{max} increased, the T_{max} values for the 4% vaginal cream were comparable with the 2% vaginal cream. At the end of therapy, the value of AUC was 365.64 ug/L.h and the value of C_{max} was 12.678 ug/L. The plasma half-life for miconazole is approximately 24 hours.

Indications

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

Contraindications

MONISTAT[®] 3 Day Cream 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 may 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® 3 Day Cream 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® 3 Day Cream, 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 is generally well tolerated. Most frequently reported reactions (mainly mild to moderate) in clinical trials included local irritation (16-21%), pruritus (23-27%), discharge (3-4%), headache (18-19%) and a burning sensation (24-26%), especially at the start of the treatment. Complaints of pelvic cramping, hives and skin rash have also been reported rarely. A higher incidence and severity of adverse reactions were found with miconazole 4% vaginal cream than with miconazole 2% vaginal cream.

Dosage and Administration

MONISTAT® 3 Day Cream:

One applicator full of cream should be inserted into the vagina at bedtime for 3 consecutive days.

For external vaginal itch or irritation: A small amount of cream should be squeezed onto the finger and applied twice daily to the skin outside of the vagina 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® 3 Day Cream 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 LD₅₀ 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® 3 Day Cream should be stored below 25°C.

Medicine Classification

Pharmacist-Only medicine

Presentation

MONISTAT® 3 Day Cream contains a 25 g tube of 40 mg/g (4%) miconazole nitrate cream and 3 disposable applicators.

Name and Address

Johnson & Johnson Pacific (NZ) Ltd
Ground Floor, Ericsson House
105 Carlton Gore Road

Newmarket
Auckland

Date of Preparation

6 June 2006