

NEW ZEALAND DATA SHEET

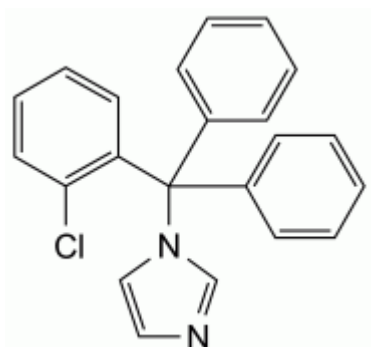
1. PRODUCT NAME

Clotrimazole Vaginal Cream + Applicator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name and strength of the active substance

Clotrimazole BP 10 mg/g (1% w/w)



C₂₂H₁₇ClN₂ 344.8 23593-75-1

Clotrimazole is a White or pale yellow, crystalline powder. Practically insoluble in water, soluble in ethanol (96%) and in methylene chloride. Melting point 141°C to 145°C

Excipient(s) with known effect

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream, topical

Presentation

A white, smooth homogeneous cream.

One pack contains a tube containing 35 g of vaginal cream, plus six single-use disposable applicators.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clotrimazole Vaginal Cream + Applicator, is indicated for the topical treatment of vulvovaginal candidiasis. Application of the cream to the glans penis of the partner may help prevent re-infection of the female.

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4.2 Dose and method of administration

Once daily, preferably in the evening for six successive days, one applicator should be filled with cream (approx. 5 g) and inserted as deeply as possible into the vagina with the patient lying on her back. The 35 g tube of cream for vaginal use provides for six such doses.

See your doctor if symptoms persist for more than 7 days or do not improve within 4 day or if the problem returns within 2 months

The treatment can be repeated if necessary, however recurrent infections may indicate an underlying medical cause, including diabetes or HIV infection. Patients should seek medical advice if they have had 3 or more infections within 6 months.

If the labia and adjacent areas are simultaneously infected, local treatment with an external cream should also be given in addition to the intravaginal treatment (combination treatment). The sexual partner should also undergo local treatment if symptoms e.g. pruritis, inflammation, etc. are present.

Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation.

Do not use tampons, intravaginal douches, spermicides or other vaginal products while using this product.

Avoidance of vaginal intercourse is recommended in case of vaginal infection and while using this product as the partner could become infected.

Clotrimazole vaginal products are for use by adults aged 18 – 60 years, unless use is advised by a doctor.

4.3 Contraindications

Hypersensitivity to the active substance, clotrimazole, or to any of the excipients as listed under Section 6.1.

4.4 Special warnings and precautions for use

If the patient has a fever (temperature of 38°C or above), lower abdominal pain, back pain, foul smelling vaginal discharge, nausea, vaginal haemorrhage and/or associated shoulder pain the patient should consult a doctor.

Keep the medicine out of reach of children. Avoid contact with eyes. Do not swallow.

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Clotrimazole cream may reduce the effectiveness and safety of latex products such as condoms and diaphragms when applied to the genital area (women: intravaginally, labia and adjacent area of the vulva; men: prepuce and glans of the penis). The effect is temporary and occurs only during treatment.

Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicines and other forms of interaction

Concomitant medication with vaginal clotrimazole and oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus plasma levels, and similarly with sirolimus. Patients should thus be thoroughly monitored for symptoms of tacrolimus or sirolimus overdose, if necessary by determination of the respective plasma levels

4.6 Fertility, pregnancy and lactation

Fertility:

No human studies of the effects of clotrimazole on fertility have been performed, however animal studies have not demonstrated any effects of the medicine on fertility.

Use in Pregnancy and Lactation:

Pregnancy (Category A)

Data from the use of clotrimazole in pregnant women is limited. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see Preclinical Safety Data). As a precautionary measure, it is preferable to avoid the use of clotrimazole during the first trimester of pregnancy.

Lactation

There is no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and is unlikely to lead to systemic effects. Clotrimazole may be used during lactation

4.7 Effects on ability to drive and use machines

The medication has no or negligible influence on the ability to drive or use machinery.

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4.8 Undesirable effects

Frequency not known. The following adverse reactions have been identified during post-approval use of clotrimazole. Because these reactions are reported voluntarily from a population of uncertain size, frequency cannot be estimated from the available data.

Immune system disorders

Anaphylactic reaction, angioedema, hypersensitivity

Vascular disorder

Syncope, hypotension

Respiratory, thoracic and mediastinal disorders

Dyspnea

Reproductive system and breast disorders

Vaginal exfoliation, vaginal discharge, vulvovaginal pruritis, vulvovaginal erythema, vulvovaginal discomfort, vulvovaginal burning sensation, vulvovaginal pain, vaginal haemorrhage.

Gastrointestinal disorders

Abdominal pain, nausea.

Skin and subcutaneous tissue disorders

Rash, urticaria

General disorders and administration site conditions

Application site irritation, oedema, pain

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

No risk of acute intoxication is seen as it is unlikely to occur following a single vaginal or dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.

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

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5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic Group

Antifungals for topical use – imidazole and triazole derivatives.

ATC Code: D01A C01

5.1 Pharmacodynamic properties

ATC Code: G01AF02, antifungals for vaginal use – imidazole and triazole derivatives.

Mechanism of Action

Azoles (e.g. clotrimazole) are usually recommended for the local treatment of vulvovaginal candidosis that is characterised by vulvovaginal symptoms such as itching, burning, discharge, redness, swelling and soreness.

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane.

Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062 – 8.0 µg/mL substrate.

The mode of action of clotrimazole is primarily fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. In vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

In addition to its antimycotic action, clotrimazole also acts on gram-positive micro-organisms (Streptococci / Staphylococci / Gardnerella vaginalis) and gram-negative micro-organisms (Bacteroides).

In vitro clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci (with the exception of Enterococci) in concentrations of 0.5 – 10 µg/mL substrate.

Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

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5.2 Pharmacokinetic properties

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3 – 10%) is absorbed. Due to the rapid hepatic metabolism of absorbed clotrimazole into pharmacologically inactive metabolites the resulting peak plasma concentrations of clotrimazole after vaginal application of a 500 mg dose were less than 10 ng/mL, suggesting that clotrimazole applied intravaginally is unlikely to lead to measurable systemic effects or side effects.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

The local and systemic tolerance of clotrimazole in different dosage forms was assessed in intravaginal studies in dogs and monkeys and in subacute dermal studies in rabbits. There was no evidence of treatment-related local or systemic adverse effects in any of these studies.

The oral toxicity of clotrimazole has been well-studied.

Following a single oral administration, clotrimazole was slight-to-moderately toxic in experimental animals, with LD50 values of 761 to 923 mg/kg bw for mice, 95 to 114 mg/kg bw for new born rats and 114 to 718 mg/kg bw for adult rats, > 1000 mg/kg bw for rabbits and > 2000 mg/kg bw for dogs and cats.

In repeated dose oral studies conducted in rats and dogs, the liver was found to be the primary target organ for toxicity. This was evidenced by an increase in serum transaminase activities and the appearance of liver vacuolation and fatty deposits starting at 50 mg/kg in the chronic (78-week) rat study and at 100 mg/kg in the subchronic (13-week) dog study.

Clotrimazole has been extensively studied in in vitro and in vivo mutagenicity assays, and no evidence of mutagenic potential was found. A 78-week oral dosing study of clotrimazole in rats did not show any carcinogenic effect.

In a rat fertility study, groups of FB30 rats received oral doses of clotrimazole up to 50 mg/kg bw for 10 weeks prior to mating and either throughout a 3-week mating period (for males only) or, for females, until day 13 of gestation or 4-week postpartum. Neonatal survival was reduced in the 50 mg/kg bw group. Clotrimazole at doses up to 25 mg/kg bw did not impair the development of the pups. Clotrimazole at all doses did not affect fertility.

No teratogenicity effects were demonstrated in studies in mice, rabbits and rats, given oral doses of up to 200, 180 and 100 mg/kg respectively.

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A study with 3 lactating rats administered 30 mg/kg clotrimazole intravenously showed that the medicine was secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hours after administration, followed by a decline to a factor of 0.4 by 24 hours.

Given the limited absorption of clotrimazole after vaginal application (estimated to be 3% – 10%) no hazard is expected from the use of vaginal clotrimazole.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Cetostearyl alcohol
Cetyl esters wax
Octyl Dodecanol
Polysorbate 60
Disodium Hydrogen Phosphate
Sodium Dihydrogen Phosphate Dihydrate
Sorbitan monostearate
Water purified

6.2 Incompatibilities

Unknown

6.3 Shelf life

36 months from date of manufacture.

6.4 Special precautions for storage

Store below 25 °C

6.5 Nature and contents of container

One tube containing 35 g of vaginal cream, 10 mg clotrimazole per gram (1% w/w) packed with six single-use disposable applicators.

6.6 Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste. Ask a pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

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7. MEDICINE SCHEDULE

Pharmacist Only Medicine

8. SPONSOR

Noumed Pharmaceuticals Limited
Auckland, New Zealand

Freephone 0800 527 545

9. DATE OF FIRST APPROVAL

N/A

10. DATE OF REVISION OF THE TEXT

18 August 2024

SUMMARY TABLE OF CHANGES

Section changes	Summary of new information
All sections	New