

PRODUCT MONOGRAPH

CANESTEN® 6 DAY Internal Cream
1% Clotrimazole Vaginal Cream, Bayer Std.

CANESTEN® 3 DAY Internal Cream
2% Clotrimazole Vaginal Cream, Bayer Std.

CANESTEN® 1 DAY Internal Cream
10% Clotrimazole Vaginal Cream, Bayer Std.

CANESTEN® COMBI 1 DAY Internal + External Creams
10% & 1% Clotrimazole Vaginal Cream, Bayer Std.

CANESTEN COMFORTAB 1
500mg Clotrimazole Vaginal Tablet, BP Std.

CANESTEN COMFORTAB 3
200mg Clotrimazole Vaginal Tablets, BP Std.

CANESTEN® COMBI 1 DAY ComforTAB™ + External Cream
500mg Clotrimazole Vaginal Tablet, BP Std.
1% Clotrimazole Cream, Bayer Std.

CANESTEN® COMBI 3 DAY ComforTAB™ + External Cream
200mg Clotrimazole Vaginal Tablets, BP Std.
1% Clotrimazole Cream, Bayer Std.

CANESTEN® EXTERNAL CREAM
1% Clotrimazole Cream, Bayer Std.

CANESTEN® EXTERNAL ANTIFUNGAL CREAM
1% Clotrimazole Cream, Bayer Std.

CANESTEN® EXTRA STRENGTH EXTERNAL ANTIFUNGAL CREAM
2% Clotrimazole Cream, Bayer Std.

(Clotrimazole) Bayer Standard
Antifungal Agent

Bayer Inc.
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Mississauga, Ontario
L4W 5R6

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Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION	3
SUMMARY PRODUCT INFORMATION.....	3
INDICATIONS AND CLINICAL USE	3
CONTRAINDICATIONS.....	3
WARNINGS AND PRECAUTIONS	3
ADVERSE REACTIONS	4
DRUG INTERACTIONS	5
DOSAGE AND ADMINISTRATION	5
OVERDOSAGE.....	7
ACTION AND CLINICAL PHARMACOLOGY.....	7
STORAGE AND STABILITY	8
DOSAGE FORMS, COMPOSITION AND PACKAGING.....	8
PART II: SCIENTIFIC INFORMATION	10
PHARMACEUTICAL INFORMATION	10
CLINICAL TRIALS.....	10
MICROBIOLOGY	11
TOXICOLOGY	13
REFERENCES.....	15
PART III: CONSUMER INFORMATION	17

CANESTEN®

(Clotrimazole)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Vaginal	Cream 1%, 2%, 10%	<i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>
Vaginal	Tablet 200mg, 500mg	Lactose. <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

INDICATIONS AND CLINICAL USE

CANESTEN® 6 DAY Internal Cream (clotrimazole) is indicated for the 6-day treatment of vaginal candidiasis.

CANESTEN® 3 DAY Internal Cream (clotrimazole) is indicated for the 3-day treatment of vaginal candidiasis

CANESTEN® 1 DAY Internal Cream (clotrimazole) is indicated for the 1-day treatment of vaginal candidiasis

CANESTEN® Combi 3 DAY ComforTAB™ +External Cream(clotrimazole) is indicated for the 3-day treatment of vaginal candidiasis

CANESTEN® Combi 1 DAY ComforTAB™ +External Cream(clotrimazole) is indicated for the 1-day treatment of vaginal candidiasis

CANESTEN® Combi 1 DAY Internal+External Creams(clotrimazole) are indicated for either 3-day or 1-day treatment of vaginal candidiasis

CANESTEN® Extra Strength External Antifungal Cream (clotrimazole), CANESTEN® External Antifungal Cream (clotrimazole) and CANESTEN® External Cream (clotrimazole) are indicated for the topical treatment of external irritation cause by vulvovaginal candidiasis.

CONTRAINDICATIONS

Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

WARNINGS AND PRECAUTIONS

General

CANESTEN® Vaginal Tablets are not for oral use

CANESTEN® External Cream and CANESTEN® Vaginal Cream are not for ophthalmic use.

Patients should seek medical advice if they have frequent vaginal infections or if their yeast infection returns in less than 2 months.

Patients should seek medical advice if they suffer from diabetes mellitus, or have underlying immunodeficiency disease (such as HIV-AIDS)

As with all topical agents, skin sensitization may result. Use of CANESTEN® topical preparations should be discontinued should such reactions occur, and appropriate therapy instituted.

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

While sexual relation may be had during treatment with CANESTEN®, most couples wait until treatment has finished as the partner could become infected.

Effects on Fertility:

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

Special Populations

Pregnant Women:

There are limited amounts of data from the use of clotrimazole in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see ‘Reproduction and Teratology’). Although intravaginal application of clotrimazole has shown negligible absorption from both normal and inflamed human vaginal mucosa, CANESTEN® Vaginal Tablets and CANESTEN® Vaginal Cream should not be used in the first trimester of pregnancy unless the physician considers it essential to the welfare of the patient. The use of applicators may be undesirable in some pregnant patients and digital insertion of the vaginal tablets may be considered.

Nursing Women:

Available pharmacodynamics / toxicological studies in animals have shown excretion of clotrimazole / metabolites in milk. Breastfeeding should be discontinued during treatment with clotrimazole.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Experimental, therapeutic, and large scale clinical studies have shown CANESTEN® to be well tolerated after topical application.

For CANESTEN® External Antifungal Cream and CANESTEN® Extra Strength External Antifungal Cream:

Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticarial)

Skin and subcutaneous skin disorders: blisters, discomfort/pain, edema, erythema, irritation, peeling/exfoliation, pruritis, rash, stinging/burning

For CANESTEN® 6 DAY Internal Cream, CANESTEN® 3 DAY Internal Cream, CANESTEN® 1 DAY Internal Cream, CANESTEN® Combi 1 DAY Internal + External Creams, CANESTEN® Combi 1 DAY ComforTAB™ + External Cream and CANESTEN® Combi 3 DAY ComforTAB™ + External Cream:

Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticaria)

Reproductive system disorders and breast disorders: genital peeling, pruritis, edema, erythema, stinging, blistering, discomfort, general irritation of the skin and pelvic pain, vaginal hemorrhage

Gastrointestinal disorder: abdominal pain

Two of 419 (0.5%) patients treated with the 1% vaginal cream experienced adverse reactions judged to be possibly drug related. These were intercurrent cystitis and vaginal burning. Neither necessitated discontinuation of treatment. None were of serious consequence and no complications occurred.

The 100 mg vaginal tablets were also well tolerated. Only a few cases consisting primarily of burning sensation and mild skin reactions were reported. In studies comparing the 3- and 7-day regimen, four of 212 patients (1.9%) in the 7 day group reported adverse reactions possibly related to treatment. These included: irritation, burning, cramping, itching, redness, abdominal bloating, bleeding and rash. In an additional nine double-blind comparative studies, 5 out of 219 patients on the 7-day regimen with the 100 mg vaginal tablet experienced similar types of adverse reactions, none of which necessitated discontinuation of treatment. In a large open multicentre and two double-blind studies employing the 100 mg vaginal tablet in a 6-day regimen, 11 out of 595 (1.8%) patients complained of possible drug-related side effects. Mild burning occurred in 4 patients while other reactions such as skin rash, lower abdominal cramps, slight urinary frequency and burning or irritation in the sexual partner occurred rarely. In no case was it necessary to discontinue treatment.

In clinical trials involving 200 mg clotrimazole vaginal tablets, 24/832 patients (2.9%) experienced an adverse reaction. 2/217 patients (0.9%) who received 2% clotrimazole vaginal cream in clinical trials experienced an adverse reaction. In clinical trials involving 500 mg clotrimazole vaginal tablets, 12/515 patients (2.3%) experienced an adverse reaction. 26/796 (3.3%) of patients in clinical trials involving 10% clotrimazole vaginal cream experienced an adverse reaction. Most adverse reactions involved local itching and burning. Only rarely was it necessary to discontinue treatment.

DRUG INTERACTIONS

Overview

Drug-Drug Interactions

Concomitant medication with vaginal Clotrimazole and oral tacrolimus/sirolimus (immunosuppressants) might lead to increased tacrolimus/sirolimus plasma levels. Patients should thus be thoroughly monitored for symptoms of tacrolimus/sirolimus overdose.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Vaginal Candidiasis may be accompanied by irritation in the vaginal area. Therefore, concomitant local treatment with CANESTEN® Vaginal Cream (or CANESTEN® External Cream) applied to the irritated vaginal area and as far as the anal region twice a day is advisable. CANESTEN® External Cream (or CANESTEN® Vaginal Cream) applied on the glans penis may prevent re-infection by the partner.

N.B.: The cream or vaginal tablet should be inserted deep intravaginally by means of the applicator (See PRECAUTIONS). The plunger should then be depressed slowly.

CANESTEN® Vaginal Tablets need moisture in the vagina to dissolve completely. Otherwise, undissolved pieces of the vaginal tablet might crumble out of the vagina. To prevent this it is important that the vaginal tablet is inserted deep into the vagina, preferably at bedtime. If the vaginal tablet does not dissolve completely within one night, the use of a vaginal cream should be considered.

General hygienic measures such as twice daily tub baths and avoidance of tight underclothing are important in vaginal infections.

Recommended Dose and Dosage Adjustment

Vaginal Candidiasis

CANESTEN® 6 DAY Internal Cream

The recommended daily dose is ONE full applicator intravaginally for SIX consecutive days, preferably at bedtime.

CANESTEN® 3 DAY Internal Cream

The recommended daily dose is ONE full applicator intravaginally for THREE consecutive days, preferably at bedtime.

CANESTEN® 1 DAY Internal Cream

The recommended daily dose is ONE full applicator intravaginally (as a single dose therapy), preferably at bedtime.

CANESTEN® Combi 1 DAY Internal + External Creams

The recommended dose is ONE full applicator intravaginally (as a single dose therapy) preferably at bedtime. The external cream should be spread onto the irritated area once or twice a day as needed, for up to seven consecutive days.

CANESTEN® ComforTAB 1

The recommended daily dose is ONE vaginal tablet intravaginally for ONE day, preferably at bedtime.
[Sold as part of CANESTEN® Combi 1 DAY ComforTAB™ + External Cream]

CANESTEN® Combi 1 DAY ComforTAB™ + External Cream

The recommended dose is ONE vaginal tablet intravaginally for ONE day, preferably at bedtime. The cream should be spread onto the irritated area once or twice a day as needed, for up to seven consecutive days.

CANESTEN® ComforTAB 3

The recommended daily dose is ONE vaginal tablet intravaginally for THREE consecutive days, preferably at bedtime.
[Sold as part of CANESTEN® Combi 3 DAY ComforTAB™ + External Cream]

CANESTEN® Combi 3 DAY ComforTAB™ + External Cream

The recommended dose is ONE vaginal tablet intravaginally for THREE consecutive days, preferably at bedtime. The cream should be spread onto the irritated area once or twice a day as needed, for up to seven consecutive days.

CANESTEN® Extra Strength External Antifungal Cream, CANESTEN® External Cream or CANESTEN® External Antifungal Cream

Use only in conjunction with Canesten Vaginal Tablets, Creams (internal treatments) or CanesOral capsule. The cream should be spread onto the irritated area once or twice daily as needed, for up to seven consecutive days.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

CANESTEN® acts primarily by damaging the permeability barrier in the cell membrane of fungi. CANESTEN® brings about inhibition of ergosterol biosynthesis, an essential constituent of fungal cell membranes. If ergosterol synthesis is completely or partially inhibited, the cell is no longer able to construct an intact cell membrane. This leads to death of the fungus.

Exposure of *Candida albicans* to clotrimazole causes leakage of intracellular phosphorus compounds into the ambient medium with a concomitant breakdown of cellular nucleic acids and potassium efflux. The onset of these events is rapid and extensive after exposure of the organism to the drug, and causes a time-dependent and concentration-dependent inhibition of fungal growth.

Pharmacokinetics

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3-10%) is absorbed. Due to the rapid hepatic metabolization of absorbed clotrimazole into pharmacologically active 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.

Metabolism studies performed after oral or intravenous administration have shown that in most species studied, levels of clotrimazole in tissue and serum are low. The majority of the drug is excreted as metabolites in the feces, with small amounts excreted in the urine. Human studies indicate slow excretion following oral administration of ¹⁴C-labelled clotrimazole (greater than 6 days). After intraperitoneal and subcutaneous administration, very low levels have been observed in the urine. The absorption and organ distribution of the drug is very poor when administered parenterally.

The pharmacokinetics of topically applied clotrimazole in human subjects have been evaluated by Duhm et al. who reported on the penetration of radioactive clotrimazole 1% cream and 1% solution into intact and acutely inflamed skin. Six hours after application of the drug, the concentration of clotrimazole found in skin layers varied from 100 µg/cm³ in the stratum corneum to 0.5 to 1.0 µg/cm³ in the stratum reticulare and <0.1 µg/cm³ in the subcutis. No measurable amount of radioactivity (0.001 µg/mL) was found in the serum within 48 hours after application of 0.5 mL of the solution or 0.8 g of the cream.

Intravaginal application of ¹⁴C-labelled clotrimazole vaginal tablets containing 100 mg of active substance in human subjects has shown that the amount absorbed is less than 1/200 of that absorbed after the oral administration of 1.5 g of clotrimazole. The maximum serum concentration values were between 0.016 and 0.05 µg/mL from one to three days after intravaginal application. Intravaginal application in human subjects of 5 mL ¹⁴C-labelled

clotrimazole vaginal cream containing 50 mg of active substance has shown that the systemic absorption of clotrimazole from the Vaginal Cream is quantitatively proportional to that from the Vaginal Tablets.

In animal experiments, clotrimazole exerts an in vitro and in vivo, dose-dependent, stimulating effect on certain microsomal enzyme systems which is approximately equal to that of phenobarbital in its inductive potential. However, this stimulating effect subsides rapidly when treatment is discontinued. The enzyme-inductive effect of clotrimazole has been found to be intact in adrenalectomized animals.

STORAGE AND STABILITY

Store between 15 °C -30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

CANESTEN® 6 DAY Internal Cream is supplied in a 50 g tube of 1% vaginal cream in a carton containing 6 disposable plastic applicators and patient instructions. 50 g of CANESTEN® 6 Cream is sufficient for 6 intravaginal applications with additional cream for extravaginal use if required.

CANESTEN® 3 DAY Internal Cream is supplied in a 25 g tube of 2% vaginal cream in a carton containing 3 disposable plastic applicators and patient instructions. 25 g of CANESTEN® 3 Cream is sufficient for 3 intravaginal applications with additional cream for extravaginal use if required.

CANESTEN® 1 DAY Internal Cream is supplied in a box containing one 5 g pre-filled applicator with a plunger of CANESTEN® 10% vaginal cream in a blister pack and patient instructions.

CANESTEN® Combi 1 DAY Internal + External Creams is supplied in a box containing one 5 g pre-filled applicator with plunger of CANESTEN® 10% vaginal cream and one 10 g tube of CANESTEN® 1% External Cream.

CANESTEN® Combi 1 DAY ComforTAB™ + External Cream is supplied in a box containing one strip of one CANESTEN® 500 mg vaginal tablet and one 10 g tube of CANESTEN® 1% External Cream.

CANESTEN® Combi 3 DAY ComforTAB™ + External Cream is supplied in a box containing one strip of three CANESTEN® 200 mg vaginal tablets and one 10 g tube of CANESTEN® 1% External Cream.

CANESTEN® External Antifungal Cream is supplied in a box containing a 15 g tube of 1% external cream.

CANESTEN® Extra Strength External Antifungal Cream is supplied in a box containing a 15 g tube of 2% external cream.

Composition

CANESTEN® 6 DAY Internal Cream contains 10 mg/g of clotrimazole in a vanishing cream base of sorbitan monostearate, polysorbate 60, cetyl esters wax, cetostearyl alcohol, octyldodecanol, purified water, and benzyl alcohol 1% as preservative.

CANESTEN® 3 DAY Internal Cream contains 20 mg/g of clotrimazole in a vanishing cream base of sorbitan monostearate, polysorbate 60, cetyl esters wax, cetostearyl alcohol, octyldodecanol, purified water, and benzyl alcohol 1% as preservative.

CANESTEN® 1 DAY Internal Cream contains 100 mg/g of clotrimazole in a vanishing cream base of sorbitan monostearate, polysorbate 60, cetyl esters wax, cetostearyl alcohol, isopropyl myristate, purified water, and benzyl alcohol 1% as preservative.

CANESTEN® ComforTAB 1 contains 500 mg of clotrimazole per vaginal tablet, in a formulation containing lactose, maize starch, microcrystalline cellulose, lactic acid, crospovidone, calcium lactate, magnesium stearate, colloidal silicon dioxide and hydroxypropyl methylcellulose.

CANESTEN® ComforTAB 3 contains 200 mg of clotrimazole per vaginal tablet in a formulation containing lactose monohydrate, maize starch, microcrystalline cellulose, lactic acid, crospovidone, calcium lactate, magnesium stearate, colloidal silicon dioxide and hydroxypropyl methylcellulose.

CANESTEN® External Cream and CANESTEN® External Antifungal Cream contains 10 mg/g of clotrimazole in a vanishing cream base of sorbitan monostearate, polysorbate 60, cetyl esters wax, cetostearyl alcohol, octyldodecanol, purified water, and benzyl alcohol

CANESTEN® Extra Strength External Antifungal Cream contains 20 mg/g of clotrimazole in a vanishing cream base of sorbitan monostearate, polysorbate 60, cetyl esters wax, cetostearyl alcohol, octyldodecanol, purified water, and benzyl alcohol 1% as preservative.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: clotrimazole

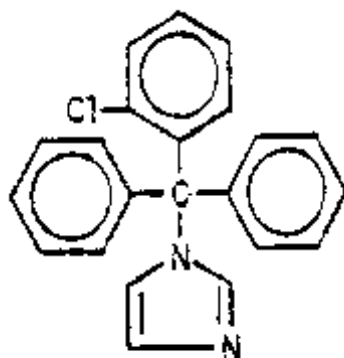
Chemical name: 1-(o-chloro- $\alpha\alpha$ -diphenylbenzyl) imidazole

Molecular formula $C_{22}H_{17}ClN_2$

Molecular mass: 344.84

Structural formula:

Physicochemical properties: Clotrimazole is a white to pale yellow, crystalline, weakly alkaline substance,



M.P. 145°C, soluble in acetone, chloroform and ethanol, and practically insoluble in water. It forms stable salts with both inorganic and organic acids. It is not photosensitive but slightly hygroscopic and may be hydrolyzed in acid media.

CLINICAL TRIALS

In 11 double-blind and one large multicentre open study, treatment of 814 patients with the 100 mg vaginal tablet for 6 to 7 days resulted in an average mycological cure rate of 79% (range of 67 - 91%). In studies comparing the 3- and 7-day regimen, 168 patients were treated with one clotrimazole vaginal tablet (100 mg) daily for 7 days. Overall and mycological cure rates were 67 and 70%, respectively.

In 8 double-blind studies and one single-blind study involving 432 patients using the 1% cream for 7 days, the average mycological cure rate was 72% with a range of 55 - 90%.

Oral contraceptives did not significantly alter mycological cure rates and overall success. In a limited number of pregnant women, both the 1% cream and the 100 mg tablet appeared to be effective, although the cure rates seemed to be somewhat lower.

In clinical trials involving 200 mg clotrimazole vaginal tablets, 498/611 patients (82%) had a negative culture for Candida sp. four weeks following treatment.

In clinical trials with clotrimazole 2% vaginal cream, 266/303 patients (88%) had a negative culture for Candida sp. four weeks following treatment.

In clinical trials with clotrimazole 500 mg vaginal tablets, 158/231 patients (68%) had a negative culture for Candida sp. four weeks following treatment.

In clinical trials with clotrimazole 10% vaginal cream, 592/726 patients (82%) had a negative culture for Candida sp. four weeks following treatment.

MICROBIOLOGY

CANESTEN® is an antifungal agent with a broad spectrum of activity. In general, the in vitro activity of CANESTEN® corresponds to that of tolnaftate, griseofulvin, and pyrrolnitrin against dermatophytes (Trichophyton, Microsporum and Epidermophyton species) and to that of the polyenes, amphotericin B and nystatin, against budding fungi (Candida and Histoplasma species).

In vitro, CANESTEN® is fungistatic for most isolates of pathogenic fungi at concentrations of 0.02 to 10 µg/mL. The drug is fungicidal for many isolates of Trichophyton, Microsporum, Epidermophyton and Candida species at concentration of 0.1 to 2 µg/mL.

No one-step or multiple-step secondary resistance to CANESTEN® has developed during successive passages of C. albicans, C. krusei, C. pseudotropicalis, T. mentagrophytes, T. rubrum, Cryptococcus neoformans, Aspergillus niger, and A. nidulans. Only a few isolates have been designated as having primary resistance to CANESTEN®: a single isolate of C. guilliermondii, six isolates of C. neoformans, three isolates of Paracoccidioides brasiliensis and two isolates of Blakeslea trispora.

Topical application of CANESTEN® has been effective in the treatment of skin infections experimentally induced in the guinea pig with T. mentagrophytes and T. quinckeanum.

Clinical studies conducted as double-blind trials with mycological control have shown that CANESTEN® is effective in the treatment of tinea cruris, tinea corporis, tinea pedis, tinea versicolor and cutaneous candidiasis. Mycological examinations have proven its efficacy against Trichophyton rubrum, T. mentagrophytes, Malassezia furfur and Candida albicans. Griseofulvin-resistant dermatophytes show no cross resistance to CANESTEN®. It may be assumed, therefore, that the site of action of this drug is different from that of other antimycotics.

Consequently, there is no cross resistance between these agents.

Antifungal Activity in Vitro

Minimum inhibitory concentrations (MICs) of clotrimazole were determined in serial dilution in broth or agar and in agar diffusion tests using the punched hole procedure. Conventional culture substrates, incubation times, and incubation temperatures were used. At concentrations less than 2 µg/mL, clotrimazole was fungicidal for many isolates of C. albicans, Trichophyton sp., Microsporum sp., and Epidermophyton sp., tested, and at concentrations less than 5 µg/mL, Clotrimazole was fungistatic for other isolates of these species. Addition of bovine serum to the culture media at a final concentration of 30% resulted in somewhat higher MICs of clotrimazole.

The in vitro antifungal activity of clotrimazole was comparable to that of pyrrolnitrin; either compound at 0.78 µg/mL was fungicidal for most strains of Trichophyton sp., Microsporum sp. and Epidermophyton sp., tested.

The type of action of clotrimazole was determined in the Warburg apparatus by measuring the oxygen consumption of proliferating organisms exposed to varying concentrations of the drug. Additional studies were performed using a classical subculture technique with organism counts made after 16, 24 and 48 hours of exposure to the drug. These experiments showed that the primary action of clotrimazole at concentrations up to 20 µg/mL is fungistatic and affects only proliferating organisms. At concentrations greater than 20 µg/mL, clotrimazole was fungicidal for some organisms.

The determinations of MICs of clotrimazole for budding fungi and for biphasic fungi in the yeast phase have been shown to be dependent on the size of the inoculum and the length of incubation time. MICs for several isolates of Candida albicans and Torulopsis glabrata were higher when the inoculum size or incubation time or both were increased.

The effects of inoculum size has been attributed to binding of clotrimazole to the surface of the fungal cells. This was established in a study of turntable cultures of C. albicans. After 24 hours, the amount of clotrimazole in a nutrient substrate was reduced from 1 µg/mL to 0.7 µg/mL by an inoculum of 1 to 5 x 10⁵ cells/mL.

A larger inoculum, 1 x 10⁸ cells/mL, reduced the drug concentration from 1 µg/mL to 0.3 µg/mL. When the cultures were centrifuged and the cell sediment was washed with physiological saline solution, the wash solutions contained clotrimazole in concentrations of 0.2 µg/mL to 0.4 µg/mL.

The effect of incubation time on the determination of MIC values is thought to be related to the mechanism of action of clotrimazole. Initial studies indicated that clotrimazole acted as an antimetabolite upon the amino acid and protein metabolism of the fungi, causing a gradual inhibition of fungal growth.

However, recent studies using C. albicans as the test organism have shown that the primary mode of action of clotrimazole is damage to the permeability of the cell membrane. Exposure of C. albicans to clotrimazole caused leakage of intracellular phosphorus compounds into the ambient medium with a concomitant breakdown of cellular nucleic acids. The onset of these events was rapid and extensive after exposure of C. albicans to the drug and caused a time-dependent and concentration-dependent inhibition of fungal growth.

Resistance Development

Only a few isolates have been designated as having primary resistance to clotrimazole; a single isolate of Candida guilliermondii, six isolates of Cryptococcus neoformans, three isolates of Paracoccidioides brasiliensis, and two isolates of Blakeslea trispora. The potential for development of secondary resistance to clotrimazole was determined for several organisms by successive passages in a liquid medium, successive passages on a solid medium, or the Warburg proliferation test. Growth of dermatophytes and yeasts on Szybalski plates was also used as a method for determining the development of secondary resistance.

No change in sensitivity was detected for C. albicans in any of the tests for secondary resistance, and no change in sensitivity was detected for Trichophyton mentagrophytes, T. rubrum, C. krusei, C. pseudotropicalis, C. neoformans, Aspergillus niger, or A. nidulans after successive passages on liquid and solid media. Possible resistance development was noted in successive passages of Torulopsis glabrata and other Torulopsis species. Data obtained from Szybalski plate growth and from other tests indicated that dermatophytes and yeasts do not develop one-step or oligo-step secondary resistance.

TOXICOLOGY

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenic potential. Effects in nonclinical studies, such as the effects on the liver (elevation of transaminases and alkaline phosphatase, liver cell hypertrophy) in the repeat-dose toxicity studies, the effects on the survival of the neonate in a rat fertility study, the species-specific indirect effects on the growth/survival of the fetus in a rat teratology study were observed with oral administration but only at exposures in excess of the maximum human exposure indicating little relevance to clinical use. Given the limited absorption of clotrimazole following a topic application, the potential for toxicity with the occasional use of Canesten 1% cream is further limited.

Carcinogenicity of clotrimazole was evaluated in a 78-week oral dosing study in rats and the results did not show any carcinogenic effect of clotrimazole.

Clotrimazole has been extensively studied in in vitro and in vivo mutagenicity assays, and no evidence of genotoxic potential was found. In an Ames test, an in vitro biological assay to detect the mutagenicity of chemical compounds, clotrimazole showed no evidence of mutagenic activity. Clotrimazole was found to be non-mutagenic in two additional in vitro studies, a gene mutation test in V79 cell lines and an Unscheduled DNA Synthesis (UDS) in primary rat hepatocytes. Studies evaluating the mutagenicity of clotrimazole in germ cells did not demonstrate mutagenic effects in a spermatogonia test in male hamsters, or in a dominant lethal test in male mice. Additionally, in mice, clotrimazole was not clastogenic in a micronucleus test.

Acute Toxicity

Animal

Species	LD ₅₀ mg/kg
Mouse	761-923
Rat	708-718
Rabbit	>1000
Cat	>1000; vomiting from 100 mg/kg
Dog	>2000; vomiting from 100 mg/ kg

Multiple Local Tolerance

1. Primary skin irritation (patch test): no detectable reddening on the intact rabbit skin at either 24 or 72 hours with 1% solution or cream of clotrimazole. Very slight erythema formation after 24 hours in the scarified rabbit skin.
2. Primary irritation on conjunctival mucosa: clotrimazole solution or cream produced a transient conjunctival irritation in rabbits, consisting in low-grade reddening and a slight increase in secretion. No grossly detectable alterations were present in either the cornea or the iris of any of the treated animals. Both the cream and solution produced a transient, very slight reddening of the conjunctival mucosa. No alterations occurred on the cornea.
3. Subacute (up to 13 weeks) dermal tolerance: the application of 1% clotrimazole solution or 1% cream was systemically well tolerated; no edema was seen on the treated skin, although mild erythema was observed sporadically. The animals in all groups with abraded skin manifested a slight healing tendency.
4. Subacute (dogs: 14 days; monkeys: 13 weeks) local vaginal tolerance: the repeated application of clotrimazole vaginal tablets showed a satisfactory local and systemic tolerance. There were no detectable adverse effects, and the cytological examination in monkeys indicated variations consistent with normal estrus cycles.
5. Subacute (5 dogs: 30 days; 4 monkeys: 13 weeks; 10 healthy human volunteers: 28 days) local vaginal tolerance. The repeated application of Vaginal Cream showed a satisfactory local and systemic tolerance

without adverse effects or abnormalities in vaginal cytology in all species.

Human

In 453 cases under treatment which were evaluated with respect to photosensitivity and phototoxicity, no reactions were encountered.

Twenty normal subjects were tested in a controlled study for sensitivity to ultraviolet radiation. Areas of skin treated with clotrimazole were irradiated for 30 seconds on the first day, and for one-half minute longer each time on every second day thereafter. One of the 20 subjects was irradiated once only; 9 subjects three times, and 10 subjects four times. One subject developed papule formation after the first exposure to ultraviolet radiation.

The topical tolerance of CANESTEN® Vaginal Tablets was studied in 462 patients with Candida or Trichomonas infections of the vagina. Five patients reported irritation (itching and burning after insertion) not necessitating the treatment to be discontinued.

There were undesirable effects in three (0.5%) of 653 patients treated with CANESTEN® Vaginal Cream which were possibly related to treatment. Discontinuation of treatment was necessary in a patient with a sensation of vaginal burning and in another patient with a possible allergic reaction, manifested by vaginal burning, local irritation and erythema. Treatment was, however, continued in a patient with intercurrent cystitis.

REPRODUCTION AND TERATOLOGY

At dosages up to 100 mg/kg (oral), clotrimazole was well tolerated by pregnant mice, rats and rabbits, and it had no embryotoxic or teratogenic effect.

When given to pregnant rats at oral doses of 100 mg/kg from day 6 through day 15 of gestation, the number of resorptions was higher and the fetal weights were lower than the controls, but the number of fetal malformations did not differ significantly from that of the control group.

Rats treated with clotrimazole for 10 weeks at dosage up to 50 mg/kg/day did not show any difference from the control group in the duration of estrus, fertility, duration of pregnancy, or in the number of implantations and resorptions. The dose of 50 mg/kg/day impaired the development of the young, and dams receiving this dose level raised fewer offspring.

The intravaginal administration of 100 mg/kg clotrimazole from the sixth to the fifteenth day of gestation was well tolerated by pregnant rats, and there were no harmful effects on the fertilization rate, the resorption rate, the mean fetal weight, and the frequency of stunted forms and of fetuses with slight bone alterations. No malformations were produced by this dose.

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PART III: CONSUMER INFORMATION

Canesten® 6 DAY Internal Cream 1% Clotrimazole vaginal cream - Antifungal

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® 6 DAY Internal Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® 6 DAY Internal Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

CANESTEN® 6 DAY Internal Cream is used to treat vaginal yeast infections. CANESTEN® can cure most vaginal yeast infections. Even though the symptoms of an infection may be relieved in only a few hours or days, you should use CANESTEN® for a full 6 days. This will decrease the chance of the infection returning.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

CANESTEN® is an antifungal that kills the overgrowth of yeast organisms that cause the infection.

When it should not be used:

Do not use CANESTEN® 6 DAY Internal Cream:

- if you are allergic to clotrimazole or any ingredient in the formulation.
- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 1% w/w

What the important nonmedicinal ingredients are:

Benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Cream: 1%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® 6 DAY Internal Cream talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- you are pregnant, think you are, or are nursing

CANESTEN® cream is for vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens, rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® 6 DAY Internal Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

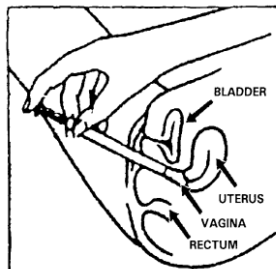
CANESTEN® is inserted high into the vagina once a day (preferably at bedtime) for 6 consecutive days. Sufficient cream is provided for 6 intravaginal applications. Extra cream is supplied for use in relieving the external itching and burning sometimes associated with a vaginal yeast infection. CANESTEN® is only for use in the vagina and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

Filling the Applicator:

Remove the cap from the tube of CANESTEN® and reverse it to puncture the safety seal over the end of the tube. To fill the applicator, screw the open end of the applicator on the end of the tube. Gently squeeze the tube. The plunger will rise as cream enters the applicator. When the plunger stops, the proper amount of CANESTEN® has been pushed into the applicator and the applicator may be removed. Replace the cap and roll up the tube from the bottom so that the tube will be ready for the next use.

Inserting the Medication:

CANESTEN® 6 DAY Internal Cream is inserted into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the filled applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.



Using the Cream Externally:

A small amount of CANESTEN® cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated vaginal area. Use the cream once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor.

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® 6 DAY Internal Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.bayer.ca
This leaflet was prepared by Bayer Inc., Mississauga ON L4W 5R6

Last Revised: October 23, 2018

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PART III: CONSUMER INFORMATION**CANESTEN® 3 DAY Internal Cream
2% Clotrimazole vaginal cream - Antifungal**

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® 3 DAY Internal Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® 3 DAY Internal Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

CANESTEN® 3 DAY Internal Cream is used to treat vaginal yeast infections.

CANESTEN® can cure most vaginal yeast infections. Even though the symptoms of an infection may be relieved in only a few hours or days, you should use CANESTEN® for a full 3 days. This will decrease the chance of the infection returning.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

CANESTEN® is an antifungal that kills the overgrowth of yeast organisms that cause the infection.

When it should not be used:

Do not use CANESTEN® 3 DAY Internal Cream:

- if you are allergic to clotrimazole or any ingredient in the

formulation

- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 2% w/w

What the important nonmedicinal ingredients are:

Benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Cream: 2%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® 3 DAY Internal Cream talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- If you have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- you are pregnant, think you are, or are nursing

CANESTEN® cream is for vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. . Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® 3 DAY Internal Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

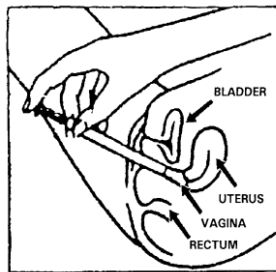
CANESTEN® cream is inserted high into the vagina once a day (preferably at bedtime) for 3 consecutive days. Sufficient cream is provided for 3 intravaginal applications. Extra cream is supplied for use in relieving the external itching and burning sometimes associated with a vaginal yeast infection. CANESTEN® is only for use in the vagina and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

Filling the Applicator:

Remove the cap from the tube of CANESTEN® and reverse it to puncture the safety seal over the end of the tube. To fill the applicator, screw the open end of the applicator on the end of the tube. Gently squeeze the tube. The plunger will rise as cream enters the applicator. When the plunger stops, the proper amount of CANESTEN® has been pushed into the applicator and the applicator may be removed. Replace the cap and roll up the tube from the bottom so that the tube will be ready for the next use.

Inserting the Medication:

CANESTEN® cream is inserted into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the filled applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.



Using the Cream Externally:

A small amount of CANESTEN® cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated vaginal area. Use the cream once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor-

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® 3 DAY Internal Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON K1A 0K9 Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.bayer.ca>

This leaflet was prepared by Bayer Inc.

Mississauga ON L4W 5R6

Last Revised: October 23, 2018

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PART III: CONSUMER INFORMATION**CANESTEN® 1 DAY Internal Cream
10% Clotrimazole vaginal cream - Antifungal**

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® 1 DAY Internal Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® 1 DAY Internal Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

CANESTEN® 1 DAY Internal Cream (pre-filled applicator) is used to treat vaginal yeast infections. CANESTEN® can cure most vaginal yeast infections and symptomatic relief can occur in a few hours or days.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

CANESTEN® is an antifungal that kills the overgrowth of yeast organisms that cause the infection.

When it should not be used:

Do not use CANESTEN® 1 DAY Internal Cream:

- if you are allergic to clotrimazole or any ingredient in the formulation

- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 10% w/w

What the important nonmedicinal ingredients are:

Benzyl alcohol, cetostearyl alcohol, cetyl esters wax, isopropyl myristate, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Cream: 10%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® 1 DAY Internal Cream talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often.
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- you are pregnant, think you are, or are nursing.

CANESTEN® cream is for vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

There is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® 1 DAY Internal

Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment

PROPER USE OF THIS MEDICATION

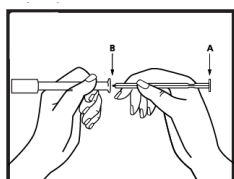
Usual dose:

CANESTEN® cream is inserted high into the vagina once (preferably at bedtime). Sufficient cream is provided for 1 intravaginal application. CANESTEN® cream is only for use in the vagina and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

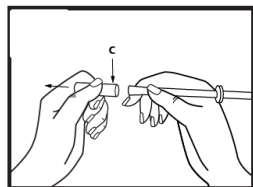
Using the Applicator:

The applicator supplied with this package should be used to ensure proper placement of the vaginal cream high in the vagina preferably at bedtime, where it will provide the most benefit. To use the applicator:

1. Remove the applicator from the package. Keeping the cap in place, insert plunger A into barrel of cream applicator B.

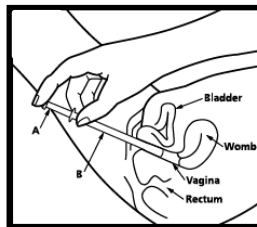


2. Twist and pull to remove cap C. Be careful not to press the plunger in any further before you have inserted the applicator into the vagina.



Inserting the Medication:

CANESTEN® cream (pre-filled applicator) is inserted into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the pre-filled applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.



Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor-

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® 1 DAY Internal Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
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Health Canada, Postal Locator 1908C
Ottawa, ON K1A 0K9 Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

www.bayer.ca

This leaflet was prepared by Bayer Inc., Mississauga ON L4W

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Last Revised: October 23, 2018

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PART III: CONSUMER INFORMATION

CANESTEN® Combi 1 DAY Internal + External Creams 10% Clotrimazole vaginal cream + 1% Clotrimazole External Cream- Antifungal

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® Combi 1 DAY Internal + External Creams was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® Combi 1 DAY Internal + External Creams. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

CANESTEN® can cure most vaginal yeast infections. The applicator filled with CANESTEN® cream is used to treat the vaginal yeast infection while the tube of CANESTEN® cream is used to externally relieve the itching associated with your vaginal yeast infection. The external cream should only be used during the time when external symptoms are present and for no longer than 7 days.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

CANESTEN® is an antifungal that kills the overgrowth of yeast organisms that cause the infection.

When it should not be used:

Do not use CANESTEN® Combi 1 DAY Internal + External Creams:

- if you are allergic to clotrimazole or any ingredient in the formulation
- in girls less than 12 years of age unless advised by a physician

What the medicinal ingredient is:

The prefilled applicator contains Clotrimazole 10% w/w

The tube contains Clotrimazole 1% w/w

What the important nonmedicinal ingredients are:

Prefilled Applicator: benzyl alcohol, cetostearyl alcohol, cetyl esters wax, isopropyl myristate, polysorbate 60, sorbitan monostearate, water.

External Cream: benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Cream: 10%

External Cream: 1%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® Combi 1 DAY Internal + External Creams talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- You are pregnant, think you are, or are nursing.

CANESTEN® cream is for vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. . Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® Combi 1 DAY Internal + External Creams include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

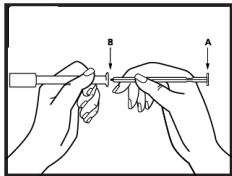
Usual dose:

CANESTEN® cream (pre-filled applicator) is placed high into the vagina once (preferably at bedtime). CANESTEN® vaginal and CANESTEN® external cream are only for use in the vagina and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

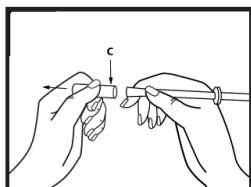
Using the Applicator:

The applicator supplied with this package should be used to ensure proper placement of the vaginal cream high in the vagina preferably at bedtime, where it will provide the most benefit. To use the applicator:

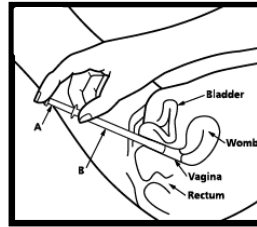
1. Remove the applicator from the package. Keeping the cap in place, insert plunger A into barrel of cream applicator B.



2. Twist and pull to remove cap C. Be careful not to press the plunger in any further before you have inserted the applicator into the vagina.



Inserting the Medication:



CANESTEN® cream (pre-filled applicator) is inserted into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the pre-filled applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.

Using the External Cream:

A small amount of Canesten external cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated area of the vulva. Use only once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor-

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® Combi 1 DAY Internal + External Creams, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

www.bayer.ca

This leaflet was prepared by Bayer Inc., Mississauga ON L4W 5R6

Last Revised: October 23, 2018

® TM see www.bayer.ca/tm-mc

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PART III: CONSUMER INFORMATION

CANESTEN® Combi 1 DAY ComforTAB® + External Cream
500 mg Clotrimazole Vaginal Tablet + 1% Clotrimazole External Cream- Antifungal

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® Combi 1 DAY ComforTAB® + External Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® Combi 1 DAY ComforTAB® + External Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

CANESTEN® can cure most vaginal yeast infections. The CANESTEN® vaginal tablet is used to treat the vaginal infection while the CANESTEN® cream is used externally to relieve the itching associated with your vaginal yeast infection. The cream should be used only during the time when external symptoms are present and for no longer than 7 days.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

CANESTEN® is an antifungal that kills the overgrowth of yeast organisms that cause the infection-

When it should not be used:

Do not use CANESTEN® Combi 1 DAY ComforTAB® + External Cream:

- if you are allergic to clotrimazole or any ingredient in the formulation
- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 500mg
 Clotrimazole 1% w/w

What the important nonmedicinal ingredients are:

Vaginal Tablet: calcium lactate, colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, lactic acid, lactose, magnesium stearate, microcrystalline cellulose, maize starch
 Cream: benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Tablet: 500mg
 External Cream: 1%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® Combi 1 DAY ComforTAB® + External Cream talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- You are pregnant, think you are, or are nursing.

CANESTEN® vaginal tablet is for vaginal use only.
 CANESTEN® cream is for external vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal

yeast infection. . Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® Combi 1 DAY ComforTAB® + External Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

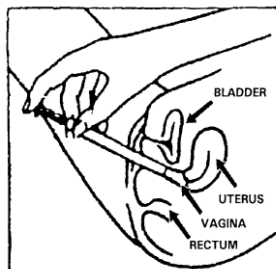
The CANESTEN® vaginal tablet is placed high into the vagina once (preferably at bedtime). CANESTEN® vaginal tablets and CANESTEN® cream are only for use in the vagina and irritated vaginal area and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

Using the Applicator:

The applicator supplied with this package should be used to ensure proper placement of the vaginal tablet high in the vagina, where it will provide the most benefit. To use the applicator, first remove the CANESTEN® vaginal tablet from its protective foil wrapper. Next, pull the applicator's plunger outward until it stops. The vaginal tablet is then placed into the end of the applicator and is ready for use.

Inserting the Medication:

The CANESTEN® vaginal tablet is placed into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the loaded applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.



Using the Cream:

A small amount of Canesten cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated vaginal area. Use once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor-

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® Combi 1 DAY ComforTAB® + External Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:

- Fax to 1-866-678-6789 (toll-free), or
- Mail to: Canada Vigilance Program

Health Canada,
Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
www.bayer.ca

This leaflet was prepared by Bayer Inc. Mississauga, ON L4W 5R6
Last revised: October 23, 2018

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www.bayer.ca/tm-mc

PART III: CONSUMER INFORMATION

CANESTEN® Combi 3 DAY ComforTAB™ + External Cream 200 mg Clotrimazole Vaginal Tablet + 1% Clotrimazole External Cream- Antifungal

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® Combi 3 DAY ComforTAB™ + External Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® Combi 3 DAY ComforTAB™ + External Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

CANESTEN® vaginal tablet is used to treat the vaginal infection while the CANESTEN® cream is used externally to relieve the itching associated with your vaginal yeast infection. The cream should be used only during the time when external symptoms are present and for no longer than 7 days. CANESTEN® can cure most vaginal yeast infections. Even though the symptoms of an infection may be relieved in only a few hours or days, you should use CANESTEN® as directed for a full 3 days. This will decrease the change of the infection returning.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

To cure a "yeast infection", it is necessary to kill the overgrowth of yeast organisms that cause the infection.

When it should not be used:

Do not use CANESTEN® Combi 3 DAY ComforTAB™ + External Cream:

- if you are allergic to clotrimazole or any ingredient in the formulation
- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 200mg
Clotrimazole 1% w/w

What the important nonmedicinal ingredients are:

Vaginal Tablet: calcium lactate, colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, lactic acid, lactose monohydrate, magnesium stearate, microcrystalline cellulose, maize starch

Cream: benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

Vaginal Tablet: 200mg
External Cream: 1%

WARNINGS AND PRECAUTIONS

BEFORE you use CANESTEN® Combi 3 DAY ComforTAB™ + External Cream talk to your doctor or pharmacist if:

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- You are pregnant, think you are, or are nursing.

CANESTEN® vaginal tablet is for vaginal use only.

CANESTEN® cream is for external vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. . Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with Combi 3 DAY ComforTAB™ + External Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

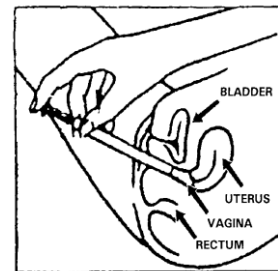
One CANESTEN® vaginal tablet is placed high into the vagina once a day (preferably at bedtime) for 3 consecutive days. CANESTEN® vaginal tablets and CANESTEN® cream are only for use in the vagina and irritated vaginal area and should never be taken by mouth. Treatment during the menstrual period should not be performed. The treatment should be finished before the onset of menstruation. While you may have sexual relations during treatment with CANESTEN®, most couples wait until treatment has finished as your partner could become infected.

Using the Applicator:

The applicator supplied with this package should be used to ensure proper placement of the vaginal tablet high in the vagina, where it will provide the most benefit. To use the applicator, first remove the CANESTEN® vaginal tablet from its protective foil wrapper. Next, pull the applicator's plunger outward until it stops. The vaginal tablet is then placed into the end of the applicator and is ready for use.

Inserting the Medication:

CANESTEN® vaginal tablets are placed into the vagina in much the same way as a tampon. Stand, squat, or lie on your back in a comfortable position. Insert the loaded applicator into the vagina as far as it will comfortably go. Holding the barrel of the applicator steady, gently depress the plunger until it stops. This will release the medication high in the vagina where it will be most effective. Remove the applicator.



Using the Cream:

A small amount of Canesten cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated vaginal area. Use once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Disposing of the Applicator:

The CANESTEN® vaginal applicator is recyclable where facilities exist.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor.

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® Combi 3 DAY ComforTAB™+ External Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:

- Fax to 1-866-678-6789 (toll-free), or
- Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.bayer.ca>

This leaflet was prepared by Bayer Inc., Mississauga ON L4W 5R6

Last Revised: October 23, 2018

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PART III: CONSUMER INFORMATION**CANESTEN® External Antifungal Cream
1% Clotrimazole External Cream- Antifungal**

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® External Antifungal Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® External Antifungal Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

CANESTEN® External Antifungal Cream is used externally to relieve the itching associated with your vaginal yeast infection. The cream should be used only during the time when external symptoms are present and for no longer than 7 days. Use only in conjunction with CANESTEN® Internal Treatments or CanesOral® Capsules.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

Relieves external vaginal itching, burning and discomfort.

When it should not be used:

Do not use CANESTEN® External Antifungal Cream:

- if you are allergic to clotrimazole or any ingredient in the

formulation

- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 1% w/w

What the important nonmedicinal ingredients are:

benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

External Cream: 1%

WARNINGS AND PRECAUTIONS**BEFORE you use CANESTEN® External Antifungal Cream talk to your doctor or pharmacist if:**

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- you are pregnant, think you are, or are nursing.

CANESTEN® cream is for external vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® External Antifungal Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

A small amount of Canesten cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated vaginal area. Use once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor.

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® External Antifungal Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator
1908C
Ottawa, ON
K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](#).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
www.Bayer.ca

This leaflet was prepared by Bayer Inc. Mississauga, ON L4W 5R6

Last revised: December 5, 2018

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PART III: CONSUMER INFORMATION**CANESTEN® Extra Strength External Antifungal Cream
2% Clotrimazole External Cream - Antifungal**

This leaflet is part III of a three-part "Product Monograph" published when CANESTEN® Extra Strength External Antifungal Cream was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CANESTEN® Extra Strength External Antifungal Cream. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

CANESTEN® Extra Strength External Antifungal Cream is used externally to relieve the itching associated with your vaginal yeast infection. The cream should be used only during the time when external symptoms are present and for no longer than 7 days. Use only in conjunction with CANESTEN® internal treatments or CanesOral®.

What is a "yeast infection"?

A "yeast infection" may occur any time there is an overgrowth of yeast organisms in the vagina. The vagina normally has bacteria and yeast organisms present. Under some conditions, the number of yeast organisms rises, irritating the delicate tissues of the vagina and vaginal opening. Conditions that make this more likely to occur are illness and the use of antibiotics (antibiotics do not affect the yeast organism). Changes in hormone levels may also increase the risk of a yeast infection. Changes that can occur during pregnancy, with the use of oral contraceptive pills, or just before a woman's period, may all increase the risk of a vaginal yeast infection. Some diseases, such as diabetes, can also make a person more susceptible. Even such things as hot humid weather, continuous use of panty liners, or tight, non-breathing clothing may increase a woman's chances of developing a yeast infection. These infections are not usually transmitted through sexual relations, even though a small percentage of male partners do have infections at the same time.

How do I know if I have a "yeast infection"?

When a "yeast infection" occurs, the body responds with an increase in vaginal secretions. These secretions are generally thick and sticky, but odourless. These are often referred to as "cheesy" or "curd-like" because of their similarity to cottage cheese. These secretions are irritating to the tissues of the vaginal area, causing intense itching, redness, and swelling. Sometimes red spots or sores may develop, especially if the area has been scratched in response to the itching. Soreness in the vagina, discomfort when passing urine and pain during sexual relations is common.

What it does:

Relieves external vaginal itching, burning and discomfort.

When it should not be used:

Do not use CANESTEN® Extra Strength External Antifungal Cream:

- if you are allergic to clotrimazole or any ingredient in the formulation
- in girls less than 12 years of age unless advised by a physician.

What the medicinal ingredient is:

Clotrimazole 2% w/w

What the important nonmedicinal ingredients are:

benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, polysorbate 60, sorbitan monostearate, water.

What dosage forms it comes in:

External Cream: 2%

WARNINGS AND PRECAUTIONS**BEFORE you use CANESTEN® Extra Strength External Antifungal Cream talk to your doctor or pharmacist if:**

- You are at increased risk for sexually transmitted diseases (e.g. HIV-AIDS), have multiple sexual partners or change partner often
- You have diabetes
- This is your first yeast infection
- You have frequent vaginal infections, or if your yeast infection returns in less than 2 months
- You are pregnant, think you are, or are nursing.

CANESTEN® cream is for external vaginal use only.

Do not use CANESTEN® if you have abdominal pain, fever or a foul-smelling vaginal discharge. If these symptoms are present, you could have a more serious condition and should consult your physician immediately.

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

Yeast infections do not cause fevers, chills, nausea, vomiting, diarrhoea, back pain, shoulder pain or vaginal haemorrhaging. If these symptoms are present, or if the vaginal discharge is foul-smelling, a more serious condition may be present and you should consult your physician immediately.

If there is no improvement in your symptoms in 3 days or if they have not disappeared within 7 days, you might not have a vaginal yeast infection. Discontinue treatment and contact your physician.

Contact your physician if symptoms worsen.

Avoid contact with eyes; if this happens rinse thoroughly with water.

If CANESTEN® is accidentally swallowed, contact your local emergency room or Poison Control Centre immediately.

If you have any questions about CANESTEN® or vaginal infections, contact your pharmacist or physician.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with CANESTEN® Extra Strength External Antifungal Cream include:

- tacrolimus/sirolimus (immunosuppressant)

CANESTEN® may reduce the effectiveness of some birth control methods, such as condoms, diaphragms, or vaginal spermicides. This effect is temporary and occurs only during treatment.

PROPER USE OF THIS MEDICATION

Usual dose:

A small amount of Canesten cream may be applied to the opening of the vagina to help provide extra relief of external symptoms. Squeeze a small amount of cream onto your finger and gently spread over the irritated external vaginal area. Use once or twice a day and only during the period when external symptoms are present, to a maximum of 7 days.

Overdose:

In case of drug overdose, call a poison control centre or get medical help right away even if there are no symptoms

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you experience a rash or new irritation while using the product, discontinue use and contact your doctor.

This is not a complete list of side effects. For any unexpected effects while taking CANESTEN® Extra Strength External Antifungal Cream, contact your doctor or pharmacist.

HOW TO STORE IT

Keep CANESTEN® and all other medications out of the reach of children.

Store at room temperature between 15°C and 30°C

REPORTING SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

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<http://www.bayer.ca>

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