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Gyno-Daktarin™

CREAM, VAGINAL CAPSULES, VAGINAL OVULES

NAME OF THE MEDICINAL PRODUCT

GYNO-DAKTARIN *CREAM*
Miconazole nitrate 20 mg/g cream
GYNO-DAKTARIN *VAGINAL CAPSULES*
Miconazole nitrate 200 mg, 400 mg, and 1200 mg vaginal capsules
GYNO-DAKTARIN *VAGINAL OVULES*
Miconazole nitrate 100 mg vaginal ovules

QUALITATIVE AND QUANTITATIVE COMPOSITION

GYNO-DAKTARIN Cream: Each gram contains 20 mg of the active substance miconazole nitrate.
GYNO-DAKTARIN Vaginal Capsules: Each vaginal capsule contains 200 mg, 400 mg or 1200 mg of the active substance miconazole nitrate.
GYNO-DAKTARIN Vaginal Ovules: Each vaginal ovule contains 100 mg of the active substance miconazole nitrate.
For excipients, see List of Excipients.

PHARMACEUTICAL FORM

GYNO-DAKTARIN Cream: White, homogenous cream for vulvar and vaginal use.
GYNO-DAKTARIN Vaginal Capsules: White to off-white, egg-shaped capsules for vaginal use.
GYNO-DAKTARIN Vaginal Ovules: White to beige colored, egg-shaped ovules for vaginal use.

CLINICAL PARTICULARS

Therapeutic Indications

Local treatment of vulvovaginal candidosis and superinfections due to gram-positive bacteria.
GYNO-DAKTARIN Cream may also be used for the treatment of mycotic balanitis.

Posology And Method Of Administration

GYNO-DAKTARIN Cream
Once daily before bedtime, administer the contents of 1 applicator (about 5 g of cream) deeply into the vagina (see Instructions for Use and Handling). Repeat this procedure for 7 days, even if symptoms (e.g. pruritus and leukorrhea) have disappeared or menstruation begins.
Treatment of concurrent symptoms of mycotic balanitis of the male partner: apply the cream twice daily on the glans penis. The treatment duration is the same as for the female partner.

GYNO-DAKTARIN Vaginal Capsules
200 mg capsules:
Once daily before bedtime, insert one vaginal capsule deeply into the vagina. This is best done in the reclining position. Repeat this procedure for 7 days. The treatment can be shortened by beginning with one vaginal capsule on the first day and continuing with two vaginal capsules (one in the morning, one before bedtime) for the next three days. Complete the entire treatment, even if symptoms (e.g., pruritus and leukorrhea) have disappeared or menstruation begins.

400 mg capsules:
Once daily before bedtime, insert one vaginal capsule deeply into the vagina. This is best done in the reclining position. Repeat this procedure for 3 days. The treatment can be repeated if necessary.
Complete the entire treatment even if symptoms (e.g., pruritus and leukorrhea) have disappeared or menstruation begins.
In case of severe infections it may be advisable to prescribe a 6-day treatment course right from the start.

1200 mg capsules:
Insert the vaginal capsule deeply into the vagina, preferably at bedtime. This is best done in the reclining position. The treatment may be repeated if necessary.
In case of severe infections it may be advisable to prescribe a longer treatment course right from the start.

GYNO-DAKTARIN Vaginal Ovules
Once daily before bedtime, insert one ovule deeply into the vagina. This is best done in the reclining position. Repeat this procedure for 14 days, even if symptoms (e.g., pruritus and leukorrhea) have disappeared or menstruation begins.

Contraindications

GYNO-DAKTARIN Cream, Vaginal Capsules, and Vaginal Ovules are contraindicated in individuals with a known hypersensitivity to miconazole nitrate or another ingredient of the formulations.

Special Warnings and Special Precautions for Use

Should local sensitization or an allergic reaction occur, the treatment should be discontinued.
Appropriate therapy is indicated when the sexual partner is also infected.
GYNO-DAKTARIN products do not stain skin or clothes.
The concurrent use of latex condoms or diaphragms with vaginal antiinfective preparations may decrease the effectiveness of latex contraceptive agents. Therefore, GYNO-DAKTARIN products should not be used concurrently with a latex condom or latex diaphragm.

Interactions with Other Medicinal Products and Other Forms of Interaction

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after vaginal application, clinically relevant interactions occur very rarely. In patients on oral anticoagulants, such as warfarin, caution should be exercised and the anticoagulant effect should be monitored. The effects and side effects of some other drugs (e.g., oral hypoglycemics and phenytoin), when co-administered with miconazole, can be increased and caution should be exercised.
Contact should be avoided between latex products such as contraceptive diaphragms or condoms and GYNO-DAKTARIN since the constituents of GYNO-DAKTARIN may damage the latex (see Special Warnings and Special Precautions for Use).

Pregnancy and Lactation

Use during pregnancy
Although intravaginal absorption is limited, GYNO-DAKTARIN Cream, Vaginal Capsules, and Vaginal Ovules should be used in the first trimester of pregnancy only if, in the judgement of the physician, the potential benefits outweigh the possible risks.

Use during lactation
It is not known whether miconazole nitrate is excreted in human milk. Caution should be exercised when using GYNO-DAKTARIN Cream, Vaginal Capsules, and Vaginal Ovules during lactation (see Interactions with Other Medicinal Products and Other Forms of Interaction).

Effects on Ability to Drive and Use Machines

Not applicable.

Undesirable Effects

Clinical trial data
The safety of GYNO-DAKTARIN was evaluated in a total of 537 women with microbiologically confirmed candidiasis and symptoms (e.g., vulvovaginal itching, burning/irritation), or signs of vulvar erythema, edema, excoriation, or vaginal erythema or edema who participated in 2 single-blind clinical trials. Subjects were treated with miconazole intravaginally, randomly assigned to either a single 1200 mg capsule, or a 7-day application of 2% vaginal cream.
Adverse Drug Reactions (ADRs) reported by ≥1% of GYNO-DAKTARIN-treated subjects in these trials are shown in Table 1.

Table 1 Adverse Drug Reactions Reported by ≥1% of GYNO-DAKTARIN-treated Subjects in 2 Single Blind Clinical Trials

System/Organ Class Preferred Term	Miconazole 1200 mg Capsule (n=272) %	Miconazole 2% Vaginal Cream 7 Days (n=265)%
Reproductive System and Breast Disorders		
Genital pruritus female	16.5	23
Vaginal burning sensation	22.8	22.6
Vulvovaginal discomfort	16.2	14.3
Dysmenorrhoea	3.3	3.4
Vaginal discharge	3.7	0.4
Vaginal haemorrhage	1.1	0.4
Vaginal pain	1.5	0.4
Nervous System Disorders		
Headache	9.6	13.6
Infections and Infestations		
Urinary tract infection	1.1	0.4
Gastrointestinal Disorders		
Abdominal pain	1.8	2.3
Abdominal pain upper	1.5	1.1
Nausea	1.5	1.1
Abdominal pain lower	1.5	0

Table 1 Adverse Drug Reactions Reported by ≥1% of GYNO-DAKTARIN-treated Subjects in 2 Single Blind Clinical Trials

System/Organ Class Preferred Term	Miconazole 1200 mg Capsule (n=272) %	Miconazole 2% Vaginal Cream 7 Days (n=265)%
Skin and subcutaneous Tissue Disorders		
Rash	1.1	0.4
Renal and Urinary Disorders		
Dysuria	1.1	0.4

Additional ADRs that occurred in <1% of GYNO-DAKTARIN-treated subjects (n = 537 women) in the single-blind clinical studies are listed in Table 2.

Table 2. Adverse Drug Reactions Reported by <1% of GYNO-DAKTARIN-treated Subjects in 2 Single Blind Clinical Trials

System/Organ Class Preferred Term	Miconazole 1200 mg Capsule (n=272) %	Miconazole 2% Vaginal Cream 7 Days (n=265) %
Skin and subcutaneous tissue disorders		
Rash pruritic	0	0.4
Rosacea	0.4	0
Swelling face	0.7	0
Urticaria	0.4	0

The majority of ADRs reported in clinical trials were mild to moderate in severity.

Postmarketing Data
Adverse drug reactions first identified during postmarketing experience with GYNO-DAKTARIN are included in Table 3. In each table, the frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1000 and <1/100
Rare	≥1/10000, <1/1000
Very rare	<1/10000, including isolated reports

In Table 3, ADRs are presented by MedDRA System organ class and frequency category based on spontaneous reporting rates.

Table 3. Adverse Drug Reactions Identified During Postmarketing Experience with GYNO-DAKTARIN by Frequency Category Estimated from Spontaneous Reporting Rates

Immune System Disorders	
Very Rare	Hypersensitivity including Anaphylactic and Anaphylactoid reactions, Angioedema
Skin and Subcutaneous Tissue Disorders	
Very Rare	Pruritis
Reproductive System and Breast Disorders	
Very rare	Vaginal irritation
General Disorders and Administrative Site Conditions	
Very Rare	Application site reaction

Overdose

GYNO-DAKTARIN products are intended for local application and not for oral use. In the event of accidental ingestion of large quantities of GYNO-DAKTARIN products, an appropriate method of gastric emptying may be used, if considered necessary. See also Interactions with Other Medicinal Products and Other Forms of Interaction.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic classification: (Antiinfectives and antiseptics, excl. combinations with corticosteroids, imidazole derivative)
ATC code: G01A F04
Miconazole combines a potent antifungal activity against common dermatophytes and yeasts with an antibacterial activity against certain gram-positive bacilli and cocci.
Miconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane, resulting in fungal cell necrosis.
In general, miconazole exerts a very rapid effect on pruritus, a symptom that frequently accompanies dermatophyte and yeast infections

Pharmacokinetic Properties

GYNO-DAKTARIN Vaginal Capsules
After the capsule has been inserted into the vagina, the outer covering rapidly disintegrates and the active suspension is almost instantaneously released.

GYNO-DAKTARIN Cream, Vaginal Capsules, and Vaginal Ovules
Absorption: Miconazole persists in the vagina for up to 72 hours after a single dose. Systemic absorption of miconazole after intravaginal administration is limited, with a bioavailability of 1 to 2% following intravaginal administration of a 1200 mg dose. Plasma concentrations of miconazole are measurable within 2 hours of administration in some subjects, with maximal levels seen 12 to 24 hours after administration. Plasma concentrations decline slowly thereafter and were still measurable in most subjects 96 hours post-dose. A second dose administered 48 hours later resulted in a plasma profile similar to that of the first dose.
Distribution: Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).
Metabolism and Excretion: The small amount of miconazole that is absorbed is eliminated predominantly in feces as both unchanged drug and metabolites over a four-day post-administration period. Smaller amounts of unchanged drug and metabolites also appear in urine. The mean apparent elimination half-life is 57 hours.

Preclinical Safety Data

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

PHARMACEUTICAL PARTICULARS

List of Excipients

GYNO-DAKTARIN Cream: The cream formulation consists of PEG-6 (and) PEG-32 (and) glycol stearate, oleoyl macrogolglycerides, liquid paraffin, benzoic acid, butylated hydroxyanisole and purified water.
GYNO-DAKTARIN Vaginal Capsules: The inactive ingredients of the vaginal capsules are liquid paraffin, white petrolatum. The 1200 mg vaginal capsules also contain lecithin. The capsule itself contains gelatin, glycerol, titanium dioxide, sodium ethylparahydroxybenzoate and sodium propylparahydroxybenzoate.
GYNO-DAKTARIN Vaginal Ovules: The inactive ingredient of the ovules is hard fat.

Incompatibilities

None Known

Shelf Life

Observe expiry date on the outer pack

Special Precautions for Storage

GYNO-DAKTARIN Cream: Store at 25°C or below.
GYNO-DAKTARIN Vaginal Capsules: Store between 15 and 30° C and in a dry place.
GYNO-DAKTARIN Vaginal Ovules: Store between 15 and 30° C.
Keep GYNO-DAKTARIN Cream, Vaginal Capsules, and Vaginal Ovules out of reach of children.

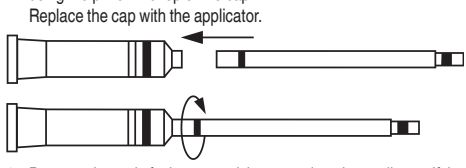
Nature and Contents of Container

GYNO-DAKTARIN Cream is supplied in tubes containing 40 g and 78 g and with 8 and 16 disposable applicators.
GYNO-DAKTARIN Vaginal Capsules 200 mg are supplied in boxes of 7, 400 mg in boxes of 3, 1200 mg in boxes of 1.
GYNO-DAKTARIN Vaginal Ovules are supplied in boxes of 8 or 15

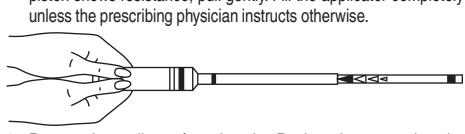
Instructions for Use and Handling <and Disposal>

GYNO-DAKTARIN Cream

1. To open the tube unscrew the cap. Then pierce the seal of the tube using the pin on the top of the cap.
   Replace the cap with the applicator.



2. Press on the end of tube to expel the cream into the applicator. If the piston shows resistance, pull gently. Fill the applicator completely unless the prescribing physician instructs otherwise.



3. Remove the applicator from the tube. Replace the cap on the tube instantly with care.
4. While lying down, knees bent and spread out, insert applicator into vagina as deeply as possible. Press piston completely to expel the cream. Remove the applicator and throw it away.

GYNO-DAKTARIN Vaginal Capsules
Not applicable.

GYNO-DAKTARIN Vaginal Ovules
Not applicable.

DATE OF REVISION OF THE TEXT

June 2007

JANSSEN-CILAG

Manufactured by: see outer pack
for Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse, Belgium