Gyno-Daktarin® (miconazole nitrate) Cream

NAME OF THE MEDICINAL PRODUCT

GYNO-DAKTARIN® cream

Miconazole nitrate 20 mg/g cream

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 20 mg of the active substance miconazole nitrate.

PHARMACEUTICAL FORM

White, homogenous cream for vulvar and 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

Pediatrics (below 18 years old): The safety and efficacy of GYNO-DAKTARIN Cream in children and adolescents has not been studied.

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.

CONTRAINDICATIONS

GYNO-DAKTARIN Cream is contraindicated in individuals with a known hypersensitivity to miconazole/miconazole nitrate, another ingredient of the formulations or other imidazole derivatives.

Warnings and Precautions for Use

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with GYNO-DAKTARIN Cream and other miconazole topical formulations (see Adverse Reactions). If a reaction suggesting sensitivity or irritation occurs, the treatment is to 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 anti-infective 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

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 Breast-feeding

Pregnancy

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

Breast-feeding

It is not known whether miconazole nitrate is excreted in human milk. Caution should be exercised when using GYNO-DAKTARIN Cream during breast-feeding.

Effects on Ability to Drive and Use Machine

Not applicable.

Adverse Reactions

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 reactions reported by ≥1% of GYNODAKTARIN-treated subjects in these trials are shown in Table 1.

Table 1 Adverse Reactions Reported by ≥1% of GYNODAKTARIN- 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
Skin and subcutaneous Tissue Disorders		
Rash	1.1	0.4
Renal and Urinary Disorders		
Dysuria	1.1	0.4

Additional adverse reactions 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 Reactions Reported by <1% of GYNODAKTARIN-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 adverse reactions reported in clinical trials were mild to moderate in severity.

Postmarketing Data

In addition to the adverse reactions reported during clinical studies and listed above, the following adverse reactions have been reported during postmarketing experience (Tables 3). 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 and <1/1000
Very rare	< 1/10000 including isolated reports

In Table 3, adverse reactions are presented by frequency category based on spontaneous reporting rates.

Table 3. Adverse 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
Skin and Subcutaneous Tissue Disorders	
Very Rare	Angioedema, 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.

Treatment: In the event of accidental ingestion of large quantities of GYNO-DAKTARIN products, use appropriate supportive care. (See also Interactions with Other Medicinal Products and Other Forms of Interaction).

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: Antiinfectives and antiseptics, excl. combinations with corticosteroids, imidazole derivative. ATC code: G01A F04.

Mechanism of Action: Miconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane, resulting in fungal cell necrosis.

Pharmacodynamic effect: In general, miconazole exerts a very rapid effect on pruritus, a symptom that frequently accompanies dermatophyte and yeast infections.

Microbiology: Miconazole combines a potent antifungal activity against common dermatophytes and yeasts with an antibacterial activity against certain gram-positive bacilli and cocci.

Pharmacokinetic Properties

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 apparent elimination half-life ranges from 20 to 45 hours in most subjects and likely reflects both absorption from the site of application and metabolism/excretion of the drug.

Non-Clinical Information: 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

Shelf Life

Observe expiry date on the outer pack

Special Precautions for Storage

Do not store above 30°C.

Keep all medicines out of reach of children.

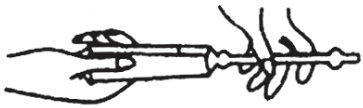
Protect from light and moisture.

Nature and Contents of Container

Gyno-Daktarin 20mg/g (miconazole nitrate) is supplied in tube of 20g with an applicator.

Instructions for Use and Handling:

The applicator consists of an outer part and an inner part.



1) To open the tube unscrew the cap. Then pierce the seal of the tube by means of he pin on the top of the cap. Replace the cap by the applicator.

2) Push on the end of the tube to bring the cream into applicator if the piston shows resistance, pull gently. The applicator should completely be filled, unless the practicing physician prescribes otherwise.

3) Remove applicator from tube. Close tube instantly with care.

4) While lying down, knees bent and spread out, insert applicator into vagina as deeply as possible. Press piston completely. Then remove applicator without touching the piston.

Directions for cleaning the applicator

Pull the 2 parts and wash them with lukewarm water and soap. Dry them and assemble the applicator by pushing the inner part back into the outer part. If the doctor specially recommends sterilisation of the applicator, his directions for use should be followed. Never use water that is hotter than 50°C and never use ether. Keep applicator in a case or another clean housing.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو روشنی اور نمی سے بچائیں۔

Manufactured by:

Aspin Pharma (Pvt) Ltd.,

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Gyno-Daktarin, TM of JANSSEN PHARMACEUTICA, Beerse, Belgium.

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