# CENTER FOR DRUG EVALUATION AND RESEARCH

**Approval Package for:**

**Application Number: 020968**

**Trade Name: MONISTAT SOFT GEL VAGINAL INSERT and MONISTAT EXTERNAL VULVAR CREAM 2%**

**Generic Name: MICONAZOLE NITRATE VAGINAL INSERT and MICONAZOLE NITRATE CREAM**

**Sponsor: ADVANCED CARE PRODUCTS**

**Approval Date: 06/30/99**

**INDICATION(s): TREATMENT OF VULVOVAGINAL CANDIDIASIS.**

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION: 020968

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| Approval Letter | X | | | |
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| Printed Labeling | X | | | |
| Medical Review(s) | X | | | |
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| Pharmacology Review(s) | X | | | |
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| Microbiology Review(s) | X | | | |
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# CENTER FOR DRUG EVALUATION AND RESEARCH

**Application Number: 020968**

## APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-968

JUN 30 1999

Advanced Care Products
Attention: Diane Herron
Director, Regulatory Affairs
691 Highway 1
North Brunswick, NJ 08902-0724

Dear Ms. Herron:

Please refer to your June 30, 1998 new drug application, NDA 20-968 for MONISTAT® DUAL-PAK™, containing MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert, 1200 mg, and MONISTAT® (miconazole nitrate cream) External Vulvar Cream, 2%, received June 30, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act. The User Fee goal date for this application is June 30, 1999.

We acknowledge receipt of your submissions and amendments dated:

| | | |
|---|---|---|
| September 16, 1998 | March 30, 1999 | June 2, 1999 |
| September 30, 1998 | April 19, 1999 | June 7, 1999 |
| October 8, 1998 | April 27, 1999 | June 9, 1999 |
| January 12, 1999 | May 3, 1999 | June 11, 1999 |
| January 13, 1999 | May 4, 1999 (2) | June 15, 1999 |
| February 18, 1999 | May 7, 1999 | June 23, 1999 |
| March 1, 1999 (2) | May 18, 1999 | June 29, 1999, |
| March 16, 1999 | | |

as well as your faxes dated August 11, 1998; May 25, June 17, 18, and 30, 1999.

This new drug application provides for the use of MONISTAT® DUAL-PAK™ for the treatment of vulvovaginal candidiasis.

We have completed the review of this application, as amended, and we have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved, effective on the date of this letter.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to

contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We are waiving the pediatric study requirement for this application, because the Agency believes adult clinical trial data can be extrapolated to demonstrate safety and effectiveness in postmenarchal girls, and it is unlikely that premenarchal girls would need to use this medication.

In addition, we remind you of 21 CFR 201.56 (b) which states that labeling shall not be promotional in tone.

The final printed labeling (FPL) must be identical to the submitted draft labeling (text for the physician package insert, text for the patient package insert, blister pack, immediate container of the cream, and carton labels submitted June 29, 1999, as amended by your fax of June 30, 1999). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-968." Approval of this submission by FDA is not required before the labeling is used.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:
Christina H. Chi, Ph.D.,
Regulatory Project Manager,
Phone: (301) 827-2127.

Sincerely yours,

/S/

Mark J. Goldberger, M.D., M.P.H.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

APPEARS THIS WAY ON ORIGINAL

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER: 020968

## PRINTED LABELING

PHYSICIAN PACKAGE INSERT

# MONISTAT® DUAL-PAK™

*[mon' ih stat dool pack]*

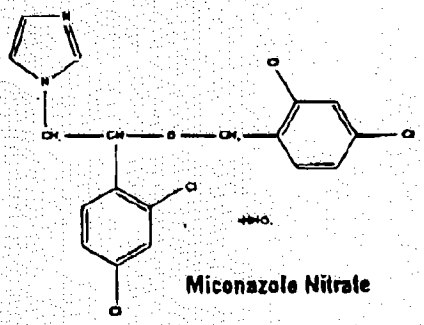
(miconazole nitrate vaginal insert) Soft Gel Vaginal Insert, 1200 mg
and (miconazole nitrate cream) External Vulvar Cream, 2%

**Rx only**

## DESCRIPTION

MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert is an off-white soft gelatin capsule containing the antifungal agent, miconazole nitrate, 1-[2,4-Dichloro-β-[(2,4-dichlorobenzyl) oxy]phenethyl]-imidazole mononitrate, 1200 mg, in a petrolatum base containing liquid paraffin, white petrolatum, and lecithin.

MONISTAT® (miconazole nitrate cream) External Vulvar Cream is a white to off-white oil-in-water emulsion base that contains miconazole nitrate, 1-[2,4-Dichloro-β-[(2,4-dichlorobenzyl) oxy]phenethyl]-imidazole mononitrate, 2%, purified water, propylene glycol, stearyl alcohol, cetyl alcohol, polysorbate 60, isopropyl myristate, benzoic acid, and potassium hydroxide.



Miconazole Nitrate

## CLINICAL PHARMACOLOGY

Following intravaginal administration of a single MONISTAT® Soft Gel Vaginal Insert in 10 healthy females, plasma miconazole concentrations were detectable at 4 hours and peaked at 12-24 hours, with an average Tmax at 18.4 hours. The mean (range) plasma miconazole concentrations at 24, 48, 72, and 96 hours are summarized in the following table:

| Hours Post-Dose | 24 | 48 | 72 | 96 |
|---|---|---|---|---|
| Mean Conc (ng/mL) | 9.22 | 4.51 | 2.95 | 1.84 |
| Range | 4.53 – 16.78 | 1.25 – 10.06 | 0.57 – 7.78 | 0.29 – 6.31 |

The average (range) peak plasma concentration, Cmax, was 10.71 (5.78-18.33) ng/mL while the AUC 0-96 was 477.3 (244.8-774.8) ng•h/mL. These results demonstrated that overall systemic exposure to miconazole nitrate is similar between MONISTAT® 3 (miconazole nitrate 4%) Vaginal Cream and MONISTAT® Soft Gel Vaginal Insert.

**Microbiology**

Mechanism of Action: Miconazole nitrate inhibits the biosynthesis of ergosterol, an essential component of the fungal cell wall. Miconazole nitrate has also been shown to interact with the synthesis of triglycerides and fatty acids, and to inhibit fungal oxidative and peroxidase enzymes.

*In vitro* and *in vivo* activity: *In vitro* miconazole nitrate is active against a variety of yeasts and moulds. Miconazole nitrate has demonstrated *in vitro* and *in vivo* activity against susceptible strains of *Candida albicans* and the dermatophytes including *Trichophyton* spp., *Microsporum* spp. and *Epidermophyton* spp.

Susceptibility testing: Miconazole nitrate susceptibility testing has been performed using numerous testing methods. Minor modifications to laboratory test conditions can alter the minimum inhibitory concentration (MIC) for azole antifungals. In one study where the National Committee for Clinical Laboratory Standards (NCCLS) antifungal susceptibility testing methodology M27-T was employed, 177 *Candida* isolates obtained from 50 patients with recurrent vulvovaginal candidiasis were tested. Most strains of *Candida albicans* exhibited miconazole MICs of <0.01 µg/mL.[1] Breakpoints to determine whether clinical isolates of *Candida albicans* or other *Candida* spp. are susceptible or resistant to miconazole nitrate have not been established using the National Committee for Clinical Laboratory Standards (NCCLS) antifungal susceptibility testing methodology M27-A.[2]

Data from clinical isolates have shown that the more common non-*albicans* strains of *Candida* producing vulvovaginal candidiasis have substantially higher MICs for the antifungal azoles, including miconazole, than *C. albicans* strains, suggesting that these pathogens may be more difficult to treat. However, the relevance of miconazole *in vitro* susceptibility data to clinical outcome remains to be defined.

Resistance: *In vitro* studies have shown that some *Candida* strains that demonstrate reduced susceptibility to one antifungal azole may also exhibit reduced susceptibility to other azole compounds, including miconazole. Clinical cases have shown that *Candida albicans* strains can develop antifungal azole resistance. Cross-resistance between azole compounds has been observed. The finding of cross-resistance is dependent upon a number of factors including the species evaluated, its clinical history, the particular azole compounds compared and the type of susceptibility test that is performed. The exact mechanism of action producing azole resistance and cross-resistance to other antifungal azoles, including miconazole, is not fully understood at this time.

**INDICATIONS AND USAGE**

**MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert:** One MONISTAT® Soft Gel Vaginal Insert is indicated for the topical treatment of vulvovaginal candidiasis (moniliasis). As MONISTAT® is effective only for candidal vulvovaginitis, the diagnosis should be confirmed by KOH smear and/or cultures. Other pathogens commonly associated with vulvovaginitis (*Trichomonas vaginalis* and *Haemophilus vaginalis*) should be ruled out by appropriate laboratory methods.

**MONISTAT® (miconazole nitrate cream) External Vulvar Cream:** MONISTAT® External Vulvar Cream is indicated for the relief of external vulvar itching and irritation associated with a yeast infection.

**CONTRAINDICATIONS**

Patients known to be hypersensitive to miconazole nitrate or any component of the vaginal insert or external vulvar cream. There is limited information regarding cross-hypersensitivity between miconazole and other azole antifungal agents. Caution should be used in prescribing MONISTAT® DUAL-PAK™ to patients with hypersensitivity to other azoles.

**WARNINGS**

The base contained in the vaginal insert and the external vulvar cream may interact with certain latex products, such as those used in vaginal contraceptive diaphragms or condoms. Therefore, condoms and diaphragms should not be relied upon to prevent sexually transmitted diseases or pregnancy until 3 days after last use of the vaginal insert and the external vulvar cream.

Tampons, douches or spermicides may remove the product from the vagina. Therefore, use of tampons, douches or spermicides should not be resumed until 7 days after last use of the vaginal insert and external vaginal cream.

## PRECAUTIONS

**General:** Discontinue drug if sensitization or irritation is reported during use.

**Carcinogenesis:** Studies to determine the carcinogenic potential of miconazole nitrate have not been performed.

**Mutagenesis:** Miconazole nitrate was not genotoxic when tested *in vitro* for induction of microbial point mutations (Ames test) or *in vivo* for dominant lethal mutation in mouse germ cells or structural chromosome aberrations in mouse or rat bone marrow cells following high oral or intraperitoneal doses (equivalent to a human dose of 52 mg/kg based on body surface area conversions).

**Impairment of Fertility:** No impairment of fertility occurred when female rats were administered miconazole nitrate orally at doses equivalent to a human dose of 53 mg/kg/day based on body surface area conversions.

**Pregnancy:** Pregnancy Category C

There are no adequate and well-controlled studies of MONISTAT® DUAL-PAK™ in pregnant women. Intravaginal administration of miconazole nitrate in rabbits 1 hour prior to mating did not affect reproductive performance or the offspring of these dams. Miconazole crosses the placenta and produces maternal and fetotoxicity when administered orally to rats and rabbits. Decreased food consumption and decreased pup survival were observed in rats and rabbits at or above doses equivalent to oral human doses of 13 mg/kg/day (rats) or 26 mg/kg/day (rabbits) based on body surface area conversions. Oral administration of miconazole nitrate has been reported to produce prolonged gestation in rats but not rabbits.

**Nursing Mothers:** It is not known whether miconazole nitrate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when miconazole nitrate is administered to a nursing woman.

**Pediatric Use:** The safety and efficacy of MONISTAT® DUAL-PAK™ in the treatment of vulvovaginal candidiasis in post-menarchal females have been established based on the extrapolation of clinical trial data from adult women. When a post-menarchal adolescent presents to a health professional with vulvovaginal symptoms, a careful evaluation for sexually transmitted diseases and other risk factors for vulvovaginal candidiasis should be considered. The safety and efficacy of MONISTAT® DUAL-PAK™ in pre-menarchal females have not been established.

**Geriatric Use:** Clinical studies of MONISTAT® DUAL-PAK™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

## ADVERSE REACTIONS

In controlled clinical studies, 272 patients with vulvovaginal candidiasis were treated with MONISTAT® DUAL-PAK™. MONISTAT® DUAL-PAK™ reactions most frequently involved the genital area:

| Drug-Related Adverse Reactions (frequency ≥ 1%) in Clinical Studies | | | | |
|---|---|---|---|---|
| Adverse Experience | Treatment Group: MONISTAT® DUAL-PAK™ (N=272) | | MONISTAT® 7 Vaginal Cream (N=265) | |
| | n | % | n | % |
| **Genital Reproductive System** | | | | |
| Burning, female genitalia | 48 | 18 | 49 | 18 |
| Irritation, female genitalia | 33 | 12 | 29 | 11 |
| Pruritus, external female genitalia | 32 | 12 | 45 | 17 |
| Discharge, female genitalia | 11 | 4 | 2 | 1 |
| Edema, female genitalia | 3 | 1 | 3 | 1 |
| Pain, female genitalia | 3 | 1 | 1 | <1 |
| **Gastrointestinal System** | | | | |
| Cramps, GI | 5 | 2 | 0 | 0 |
| Nausea | 3 | 1 | 0 | 0 |
| **Nervous System** | | | | |
| Headache | 4 | 1 | 1 | <1 |

MONISTAT® DUAL-PAK™ drug-related adverse events with a frequency <1% in clinical trials included: genital erythema, vaginal tenderness, dysuria, allergic reaction, dry mouth, flatulence, perianal burning, pelvic cramping, rash, urticaria, skin irritation, periorbital edema, and conjunctival pruritus.

The drug-related adverse event dropout rate was 1% in the MONISTAT® DUAL-PAK™ treatment group and 2% in the comparator arm. The adverse experiences most frequently causing study discontinuation were vulvovaginal burning and irritation for both the MONISTAT® DUAL-PAK™ and the comparator agent.

## OVERDOSAGE

Overdosage of miconazole nitrate in humans has not been reported to date. In mice, rats, guinea pigs, and dogs the oral minimum lethal dose values were equivalent to oral human doses between 26 and 204 mg/kg.

## DOSAGE AND ADMINISTRATION

MONISTAT® Soft Gel Vaginal Insert: One insert (miconazole nitrate, 1200 mg) is inserted intravaginally once at bedtime. Before prescribing another course of therapy, the diagnosis should be reconfirmed by smears and/or cultures to rule out other pathogens.

MONISTAT® External Vulvar Cream: Sufficient external vulvar cream should be applied to cover affected areas twice daily (morning and evening) for up to 7 days as needed.

## HOW SUPPLIED

MONISTAT® DUAL-PAK™ includes the following two components:

MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert, 1200 mg, is available as a 3.3 g (weight of one insert) elliptically shaped off-white vaginal insert packaged in a blister pack accompanied by a vaginal applicator.

MONISTAT® (miconazole nitrate cream) External Vulvar Cream, 2%, is supplied in a 9 g blind-end tube.

Important Information: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Avoid heat over 30°C (86°F). Avoid high humidity.
See end of carton for the lot number and expiration date.

## REFERENCES

1. Lynch et. al., 1996. Role of Antifungal Drug Resistance in the Pathogenesis of Recurrent Vulvovaginal Candidiasis. J. Med. Vet. Mycology 34:337-339.

2. National Committee for Clinical Laboratory Standards, 1997. Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts. Approved Standard M27-A. NCCLS, Wayne PA.

BARCODE

Distributed by: Personal Products Company
Division of McNeil-PPC, Inc., Skillman, NJ 08558-9148


XXX-XX-XXX-X

PATIENT PACKAGE INSERT

BARCODE

# MONISTAT® DUAL-PAK™

*[mon' ih stat dool pack]*

(miconazole nitrate vaginal insert) Soft Gel Vaginal Insert, 1200 mg
and (miconazole nitrate cream) External Vulvar Cream, 2%

**For prescription use only**

**What is the MONISTAT® DUAL-PAK™?**

The MONISTAT® DUAL-PAK™ is medicine to treat vaginal yeast infections and relieve itching and irritation of the skin outside the vagina (vulva) that is associated with a yeast infection.

The MONISTAT® DUAL- PAK™ contains two types of medicines to treat vaginal yeast infections:

1. one Soft-Gel Vaginal Insert that you put inside your vagina using the applicator
2. the External Vulvar Cream that is used on the skin outside the vagina

**Who should not use the MONISTAT® DUAL- PAK™?**

**You should not use the MONISTAT® DUAL-PAK™ if you are allergic to the active ingredient miconazole nitrate or any of the inactive ingredients in the medicine.** (See ACTIVE INGREDIENT and INACTIVE INGREDIENTS.)

**What is a vaginal yeast infection (Candidiasis)?**

A vaginal yeast infection is a common condition caused by an overgrowth of yeast *(Candida)* that may normally live in the vagina. Your health professional may call this infection "monilia" or "candidiasis." Some women may have a yeast infection on the skin outside the vagina at the same time that they have the vaginal infection.

**Who can get a vaginal yeast infection?**

Any woman can get a vaginal yeast infection. It is most common during the childbearing years. Women who are pregnant or diabetic, taking antibiotics, birth control pills or steroids, or who have a weakened immune system, are more likely to get repeated yeast infections that may not easily clear up with proper treatment.

Some medical conditions can weaken the body's normal ability to fight infection. One of the most serious of these conditions is infection with the human immunodeficiency virus (HIV – the virus that causes AIDS). The HIV virus causes the body to be more likely to get infections, including vaginal yeast infections that may not easily clear up with proper treatment. If you may have been exposed to HIV and get repeated vaginal yeast infections, see your health professional right away. For more information on HIV infection, please contact your health professional or the Centers for Disease Control and Prevention (CDC) National AIDS HOTLINE. The CDC phone numbers are: 1-800-342-AIDS (English), 1-800-344-7432 (Spanish), or 1-800-243-7889 (hearing impaired, TDD).

**What are the symptoms of a vaginal yeast infection?**

When you have a vaginal yeast infection, you may have one or more of the following symptoms:

- vaginal discharge that may be thick, white, and lumpy like cottage cheese
- vaginal itching
- vaginal soreness, irritation, or burning
- rash or redness on the skin outside the vagina
- burning on urination

Vaginal yeast infections do not cause fever, abdominal pain, or foul-smelling vaginal discharge. If you have these symptoms, you should call your health professional right away.

Your health professional can diagnose a yeast infection by evaluating your symptoms and looking at a sample of the discharge from your vagina under a microscope.

**Are vaginal yeast infections sexually transmitted?**

Yeast infections are usually not spread by having vaginal intercourse (sex). However, if your partner gets a rash or begins to itch in his genital area after having sexual contact with you, he should contact his health professional to find out the cause of his symptoms. He should tell the health professional that you recently treated yourself with the MONISTAT® DUAL- PAK™ for a vaginal yeast infection.

**Why do women get repeated vaginal yeast infections?**

Women may get repeated vaginal yeast infections that do not clear up easily with proper treatment. Listed below are some of the causes of repeated yeast infections:

- **hormonal changes** occurring a few days before the monthly period
- **use of antibiotics**
- **use of some** birth control pills
- **pregnancy**
- **diabetes** ("sugar" or "high blood sugar")
- **clothing** - wearing many tight layers or moist clothing in the genital area
- **weakened immune system** - some drugs (such as chemotherapy for cancer treatment or steroids) and medical conditions can weaken the body's normal ability to fight infection. One of the most serious of these conditions is infection with the human immunodeficiency virus (HIV- the virus that causes AIDS). Infection with HIV causes the person to be more likely to get infections, including vaginal yeast infections.

**If you get repeated vaginal yeast infections (such as once a month or 3 in 6 months), you should talk to your health professional.**

**How can I help prevent repeated vaginal yeast infections?**

To lower your chances of getting another yeast infection:

- try to keep the genital area cool and dry. Yeast grow well in warm, moist areas.

The following suggestions may be helpful:

(1) Wear cotton underwear and loose-fitting clothes.

(2) Change out of damp clothes or a wet bathing suit as soon as possible.

(3) If you use minipads when you are not having a menstrual period, change the minipads often.

- **talk with your health professional.** Your health professional may need to see you to make sure that you do not have other medical conditions such as diabetes or a weakened immune system.

**When can I expect symptom relief?**

While the MONISTAT® DUAL- PAK™ includes a single-dose vaginal insert, most women do not get complete relief of their symptoms in just 1 day. The majority of women experience complete relief of symptoms within 7 days. While you are waiting for the infection to clear, the external vulvar cream can be used to soothe and relieve the itching and irritation outside the vagina. If your symptoms do not improve in 3 days, or if you still have symptoms after 7 days, call your health professional.

**Can I use the MONISTAT® DUAL-PAK™ during my menstrual period?**

Yes, the MONISTAT® DUAL- PAK™ can be used during your menstrual period. In fact, many women get vaginal yeast infections just before their period because of hormonal changes. Using the MONISTAT® DUAL- PAK™ during your period will not affect how well this medicine works. Do not use tampons while using this medicine, because tampons may remove some of the medicine from the vagina. Use deodorant-free sanitary napkins or pads instead and change them often.

**Can I use other vaginal products with the MONISTAT® DUAL-PAK™?**

The MONISTAT® DUAL- PAK™ should not be used with other vaginal products.

- Douches and tampons may remove some of the medicine from the vagina. Do not use douches and tampons for 7 days after using the MONISTAT® DUAL- PAK™ medicines.
- Spermicides may interfere with the medicines. Do not use spermicides for 7 days after using the MONISTAT® DUAL- PAK™ medicines.
- Condoms and diaphragms may be damaged by the medicines and may not prevent pregnancy and sexually transmitted diseases (STDs). Do not rely on condoms or diaphragms to prevent STDs or pregnancy for 3 days after you have finished using the MONISTAT® DUAL- PAK™ medicines.

**How can I get the best results when treating my infection?**

- Use the MONISTAT® DUAL- PAK™ medicines as directed by your health professional.
- Dry the genital area thoroughly after a shower, bath, or swim. Change out of a wet bathing suit or damp clothes as soon as possible. A dry area is less likely to lead to the overgrowth of yeast.
- Wear cotton underwear and loose-fitting clothes.
- Wipe from front to back after a bowel movement or after urination.
- Do not douche unless your health professional tells you to do so, because douching may wash the medicine out of the vagina.
- Do not use tampons, because they may remove some of the medicine from the vagina.
- Use deodorant-free sanitary napkins or pads as needed.
- Do not use spermicides, as they may interfere with the MONISTAT® DUAL- PAK™ medicines.
- Do not have vaginal intercourse (sex) while using the MONISTAT® DUAL- PAK™ medicines.
- Do not scratch the skin outside the vagina. Scratching can cause more irritation and can spread the infection.
- If you have any other medical questions or concerns about vaginal yeast infections, call your health professional.

**What warnings should I know about when using the MONISTAT® DUAL-PAK™?**

**Do not use the MONISTAT® DUAL-PAK™ if you are allergic to the active ingredient miconazole nitrate or any of the inactive ingredients in the medicine. (see ACTIVE INGREDIENT and INACTIVE INGREDIENTS)**

**For vaginal use only. Do not take by mouth or use in eyes.**

**If you develop hives or a skin rash while using this medicine, discontinue use and call your health professional.**

**When using this product**

- Do not rely upon condoms or diaphragms to prevent sexually transmitted diseases (STDs) or pregnancy for 3 days after you have finished using the medicines. The MONISTAT® DUAL- PAK™ medicines may damage diaphragms or condoms.
- Do not use tampons, douches, or spermicides or other vaginal products for 7 days after you have finished using the medicines.
- Do not have vaginal intercourse (sex).

**Call your health professional if**

- Symptoms do not get better after 3 days.
- Symptoms last more than 7 days.
- You get rash, abdominal pain, fever, chills, nausea, vomiting, or foul-smelling discharge.

These may be signs that this medicine is not working, or you may have a more serious condition or an allergic reaction.

**If you are pregnant or breast-feeding, ask a health professional before use.**

**Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.**

**What side effects may occur with the MONISTAT® DUAL-PAK™?**

A mild increase in vaginal burning, itching, or irritation may occur when the MONISTAT® DUAL- PAK™ medicines are used.

Call your health professional if you have abdominal pain, hives, skin rash, or if you have severe vaginal burning, itching, irritation or swelling.

**What should I do if I have a question about the MONISTAT® DUAL-PAK™?**

If you have any medical questions, call your health professional. If you have any other questions or need more information on this product, call our TOLL-FREE NUMBER, 1-877-MONISTAT. The answer line is staffed by registered nurses between 8:00 a.m. and 5:00 p.m. Eastern Time, Monday through Friday. After business hours, our automated response system can provide helpful information and answer many of your questions.

**ACTIVE INGREDIENT**

MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert – miconazole nitrate, 1200 mg

MONISTAT® (miconazole nitrate cream) External Vulvar Cream – miconazole nitrate, 2%

**INACTIVE INGREDIENTS**

MONISTAT® (miconazole nitrate vaginal insert) Soft Gel Vaginal Insert – gelatin, glycerin, lecithin, mineral oil, titanium dioxide, white petrolatum

MONISTAT® (miconazole nitrate cream) External Vulvar Cream – purified water, propylene glycol, stearyl alcohol, polysorbate 60, isopropyl myristate, benzoic acid, and potassium hydroxide.

**STORAGE**

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Avoid heat over 30°C (86°F). Avoid high humidity.

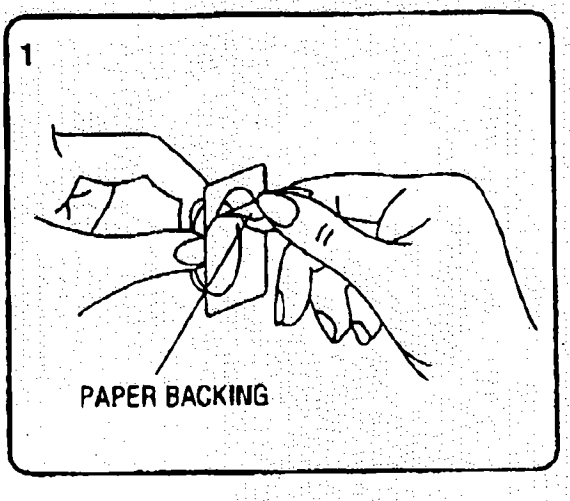
See end of carton for the lot number and expiration date.

**How should I use the MONISTAT® DUAL-PAK™?**

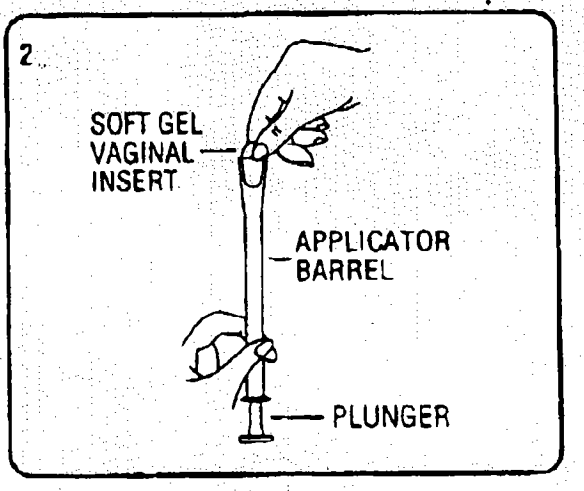
**To use the MONISTAT® Soft Gel Vaginal Insert**

**Begin treatment before going to bed:**

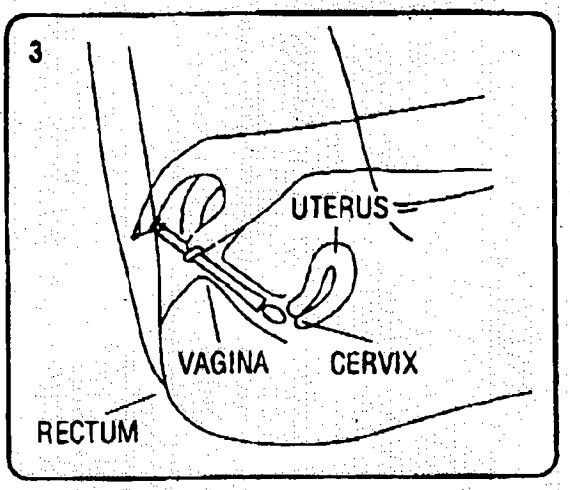
1. Separate the paper backing from the blister pack by peeling back the cover from the corner (FIG. 1).




2. Place the Soft Gel Vaginal Insert firmly into the top of the applicator so it will not fall out (FIG. 2).



3. Hold the applicator containing the Soft Gel Vaginal Insert by the barrel.
4. Gently insert the applicator into the vagina as far back as it will go comfortably. This can be done while lying on your back with your knees bent (FIG. 3). You can also do this while standing with your feet spread a few inches apart and your knees bent.
5. Push in the plunger to place the Soft Gel Vaginal Insert as far back in the vagina as possible.
6. Remove the applicator from the vagina.
7. Lie down as soon as possible after inserting the Soft Gel Vaginal Insert. This will reduce leakage.

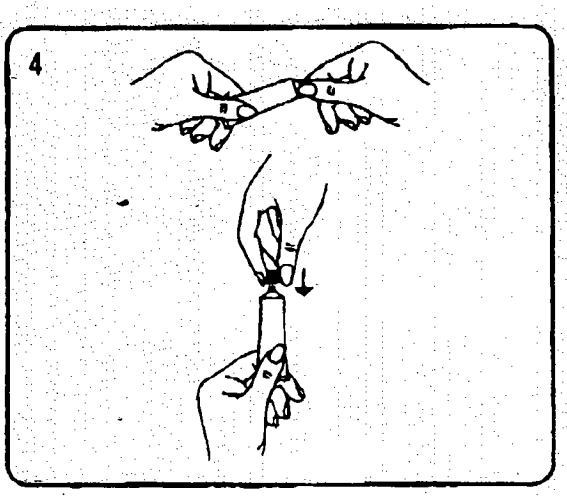



To protect your clothing, you may want to use deodorant-free minipads or panty shields while you are using the MONISTAT® Soft Gel Vaginal Insert. This is because the Soft Gel Vaginal Insert can leak and/or you may see some discharge. **Do not use tampons.**

Throw away the applicator after use. **Do not flush it down the toilet.**

**To use the MONISTAT® External Vulvar Cream**

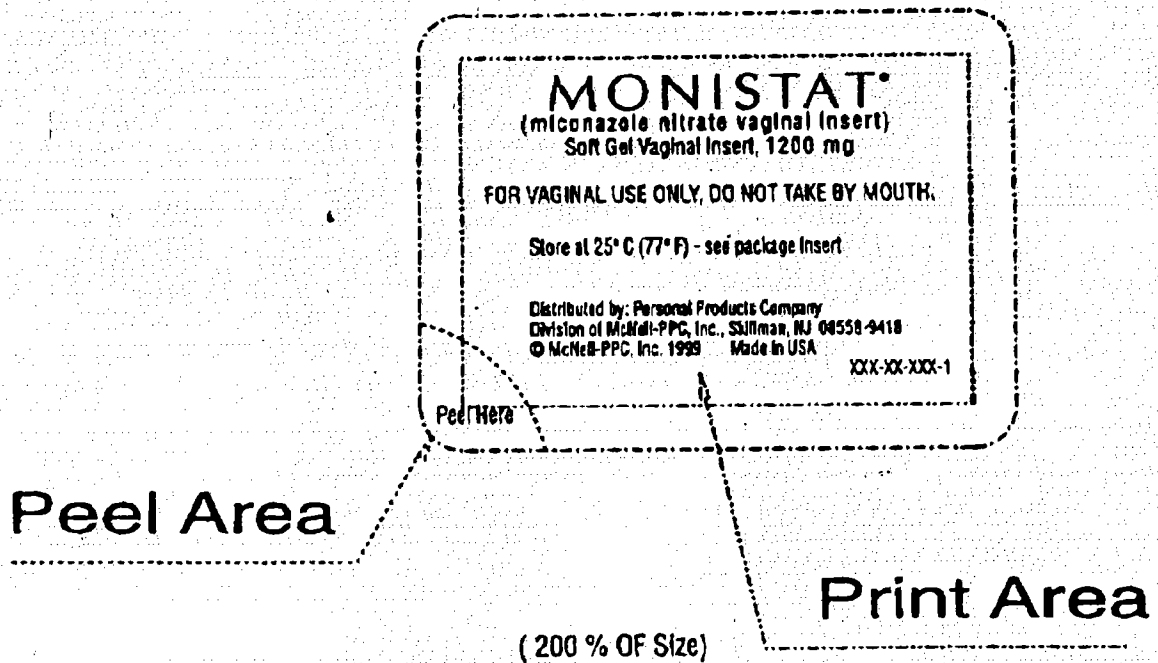
Use the cream twice daily, for up to 7 days as needed or as directed by your health professional.




1. Open the tube by unscrewing the cap. The first time the tube is opened, press the sharp point of the cap into the sealed end of the tube. Push down firmly until the seal is open (FIG. 4).
2. Squeeze a small amount of cream onto your fingertip.
3. Gently apply the cream onto the skin outside the vagina (vulva) that itches and is irritated.
4. Screw the cap back on the tube.
5. Repeat steps 1-4 each morning and at bedtime for up to 7 days as needed, or as directed by your physician.

Distributed by: Personal Products Company
Division of McNeil-PPC, Inc., Skillman, NJ 08558-9148

Covered under patent number 5,514,698
XXX-XX-XXX-X

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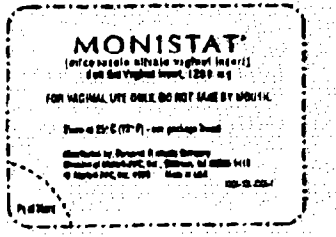


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# MONISTAT®
## EXTERNAL VULVAR CREAM

MICONAZOLE NITRATE EXTERNAL VULVAR CREAM 2%

ORTHO

RELIEVES EXTERNAL VULVAR ITCHING & IRRITATION ASSOCIATED WITH A YEAST INFECTION

Net Wt. 0.32 oz. (9 grams)

106-80-369-1

FOR EXTERNAL VULVAR USE ONLY. DO NOT TAKE BY MOUTH OR USE IN EYES. KEEP OUT OF REACH OF CHILDREN. Before using, read the enclosed brochure for DIRECTIONS and WARNINGS.

TAMPER RESISTANT FEATURE: SEAL OVER TUBE OPENING. DO NOT USE IF SEAL HAS BEEN PUNCTURED OR EMBOSSED DESIGN ▽ IS NOT VISIBLE. TO OPEN: USE CAP TO PUNCTURE SEAL.

ACTIVE INGREDIENT: miconazole nitrate 2%

See end of tube for lot number and expiration date.

Store at room temperature 15° to 30°C (59° to 86°F). Avoid heat (over 30°C or 86°F).

[redacted]

*Advanced Care Products*

Ortho Pharmaceutical Corp. Raritan, NJ 08869

 Made in U.S.A.

ARTWORK IS 200%