HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use terconazole vaginal cream, 0.8% safely and effectively. See full prescribing information for terconazole vaginal cream, 0.8%.

Terconazole vaginal cream, 0.8%.

For vaginal use only.

Initial U.S. Approval: December 1987

----------**INDICATIONS AND USAGE**----------

Terconazole is a triazole antifungal indicated for the treatment of vulvovaginal candidiasis. (1)

--------**DOSAGE AND ADMINISTRATION**--------

Apply one full applicator (5g) of terconazole vaginal cream 0.8% intravaginally once daily at bedtime for three (3) consecutive days. (2)

----------**DOSAGE FORMS AND STRENGTHS**----

Vaginal cream containing terconazole 0.8%: supplied in a 20 gram tube with a measured dose applicator. Each applicator delivers 40 mg of terconazole. (3)

----------**CONTRAINDICATIONS**----------

Known hypersensitivity to terconazole or any other component of the cream (4)

----------**WARNINGS AND PRECAUTIONS**--------

Discontinue use and do not retreat with terconazole if, irritation, fever, chills or flu-like symptoms are reported during use. (5)

----------**ADVERSE REACTIONS** ----------

Most common adverse reactions (incidence ≥ 2%) were headache, and dysmenorrhea, genital burning and itching. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Fougera at 1-800-645-9833 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------**USE IN SPECIAL POPULATIONS**--------

- Pregnancy: Based on animal data, may cause fetal harm (8.1).
- Nursing Mothers: Caution should be exercised when administered to a nursing woman (8.3).

See 17 for PATIENT COUNSELING INFORMATION AND FDA-approved labeling.

FULL PRESCRIBING INFORMATION: CONTENTS*

***** Sections or subsections omitted from the full prescribing information are not listed here

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
Terconazole vaginal cream, 0.8% is indicated for the treatment of vulvovaginal candidiasis .

2 DOSAGE AND ADMINISTRATION
The recommended dose is one applicator full of terconazole vaginal cream 0.8% (5 grams of cream containing 40 mg terconazole) administered intravaginally once daily at bedtime for three consecutive days. [*See Patient Counseling Information (17.1)]*
Terconazole vaginal cream, 0.8% is not for oral or ophthalmic use.

3 DOSAGE FORMS AND STRENGTHS
Terconazole vaginal cream, 0.8% contains 8mg terconazole per gram of cream. Each measured dose applicator delivers 5 grams of cream containing 40 mg of terconazole.

4 CONTRAINDICATIONS
Terconazole vaginal cream, 0.8% is contraindicated in patients with known hypersensitivity to terconazole or to any of the components of the cream.
There is no information regarding cross-hypersensitivity between terconazole and other azole antifungal agents. Monitor patients with a history of hypersensitivity to azoles.

5 WARNINGS AND PRECAUTIONS
Discontinue use and do not retreat with terconazole if irritation, fever, chills or flulike symptoms are reported during use.

6 ADVERSE REACTIONS
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse reactions that appear to be related to drug use and estimating their relative rates.

6.1 Clinical Trial Experience
During controlled clinical studies conducted in the United States, patients with vulvovaginal candidiasis were treated with terconazole vaginal cream, 0.8% for 3 days. Based on comparative analyses with placebo (Table 1), the adverse experiences considered most likely related to terconazole vaginal cream, 0.8% were headache (21% vs. 16% with placebo) and dysmenorrhea (6% vs. 2% with placebo). Other adverse experiences reported with terconazole vaginal cream 0.8% were abdominal pain (3.4% vs. 1% with placebo), fever (1% vs. 0.3% with placebo), and genital burning and itching (5% vs. 6%-9% with placebo). The therapy-related dropout rate was 2.0% for terconazole vaginal cream 0.8%. The adverse drug experience most frequently causing

discontinuation of terconazole vaginal cream, 0.8% therapy was vulvovaginal itching (0.7% vs. 0.3% placebo).

Table 1		
Adverse Reactions Most Likely Related to Terconazole Vaginal Cream, 0.8%		
	Terconazole Vaginal Cream, 0.8% n=231 (%)	**Terazol®3 (Placebo) n=229 (%)**
Headache	49 (21)	37(16)
Dysmenorrhea	14 (6)	5 (2)
Other Adverse Events Reported with Terconazole Vaginal Cream 0.8%		
	Terconazole Vaginal Cream 0.8% n=231 (%)	**Terazol®3 n=229 (%)**
Abdominal Pain	8 (3.4)	2 (1)
Fever	2 (1)	1 (0.3)
Genital Burning and Itching	12 (5)	15-21 (6-9)
Adverse Events Most Frequently Causing Discontinuation		
	Terconazole Vaginal Cream 0.8% n=231 (%)	**Terazol®3 n=229 (%)**
Vulvovaginal Itching	2 (0.7)	1 (0.3)

Photosensitivity reactions were observed in some normal volunteers following repeated dermal application of terconazole 2.0% and 0.8% creams under conditions of filtered artificial ultraviolet light. Photosensitivity reactions were not observed in U.S. and foreign clinical trials in patients who were treated with terconazole suppositories or vaginal cream, 0.8%.

7 DRUG INTERACTIONS

Oral Contraceptives: There is no known interaction with the concomitant use of this product and oral contraceptives.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C:
Terconazole vaginal cream, 0.8% should not be used during pregnancy unless the potential benefit to the mother outweighs the potential risk to the fetus. There are no adequate and well-controlled clinical trials of terconazole vaginal cream, 0.8% in pregnant women.

Animal data
There was no evidence of teratogenicity when terconazole was administered orally up to (10 times the recommended intravaginal human dose based on body surface area comparisons) in rats, or rabbits.

There was a delay in fetal ossification at 10 mg/kg/day in rats (about 2 times the recommended intravaginal human dose based on body surface area comparisons). Higher doses, up to 10 times the recommended intravaginal human dose based on body surface area comparisons, resulted in decreased litter size, decreased number of viable young and reduced fetal weight in rats. There was also delay in ossification and an increase incidence of skeletal variants.

The dose of 10 mg/kg/day resulted in a mean peak plasma level of terconazole in pregnant rats of 0.176 mcg/mL which exceeds by 30 times the mean peak plasma level (0.006 mcg/mL) seen in normal subjects after intravaginal administration of terconazole vaginal cream 0.8%. This safety assessment does not account for possible exposure of the fetus through direct transfer to terconazole from the irritated vagina by diffusion across amniotic membranes. Since terconazole is absorbed from the human vagina, it should not be used in the first trimester of pregnancy unless the potential benefit to the mother outweighs the potential risk to the fetus.

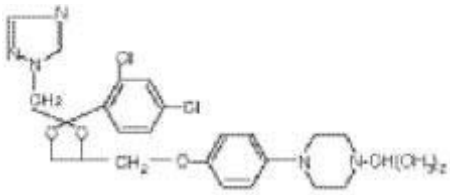
8.2 Nursing Mothers
It is not known whether terconazole is excreted in human milk. Caution should be exercised when terconazole is administered to a nursing woman.

8.3 Pediatric Use
The safety and effectiveness of terconazole vaginal cream, 0.8% have not been established in pre-menarchal females.

8.4 Geriatric Use
Clinical studies of terconazole vaginal cream, 0.8% did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

10 OVERDOSAGE
Overdosage of terconazole in humans has not been reported to date.

11 DESCRIPTION
Terconazole vaginal cream 0.8% is a white to off-white, water washable cream for intravaginal administration containing 0.8% of the antifungal agent terconazole, *cis*-1-[*p*-[[2-(2,4-Dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-4-isopropylpiperazine, compounded in a cream base consisting of butylated hydroxyanisole, cetyl alcohol, isopropyl myristate, polysorbate 60, polysorbate 80, propylene glycol, stearyl alcohol, and purified water. The structural formula of terconazole is as follows:



Terconazole, a triazole derivative, is a white to almost white powder with a molecular weight of 532.47. It is insoluble in water; sparingly soluble in ethanol; and soluble in butanol.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Terconazole is an antifungal agent [*see Clinical Pharmacology, Microbiology (12.4)*].

12.3 Pharmacokinetics

Following intravaginal administration of terconazole vaginal cream, 0.8% in females, absorption ranged from 5-8% in three hysterectomized subjects and 12-16% in two non-hysterectomized subjects with tubal ligations.

Following daily intravaginal administration of 0.8% terconazole 40 mg (0.8% cream x 5 g) for seven days to healthy female subjects, plasma concentrations were low and gradually rose to a daily peak (mean of 5.9 ng/mL or 0.006 mcg/mL) at 6.6 hours. Results from similar studies in female patients with vulvovaginal candidiasis indicate that the slow rate of absorption, the lack of accumulation, and the mean peak plasma concentration of terconazole was not different from that observed in healthy females. The absorption characteristics of terconazole vaginal cream, 0.8% in pregnant or non-pregnant patients with vulvovaginal candidiasis were also similar to those found in healthy subjects.

Following oral (30 mg) administration of ^{14}C-labelled terconazole, the mean half-life of elimination from the blood for the parent terconazole was 6.9 hours (range 4.0-11.3). Terconazole is extensively metabolized; the plasma AUC for terconazole compared to the AUC for total radioactivity was 0.6%. Total radioactivity was eliminated from the blood with a mean elimination half-life of 52.2 hours (range 44-60). Excretion of radioactivity was both by renal (32-56%) and fecal (47- 52%) routes.
In vitro, terconazole is highly protein bound (94.9%) and the degree of binding is independent of drug concentration.

12.4 Microbiology

Mechanism of Action
Terconazole inhibits the enzyme cytochrome P450 14α-demethylase which leads to inhibition of ergosterol synthesis, an essential component of the fungal cell membrane

Activity *in vitro*
Terconazole exhibits fungicidal activity *in vitro* against *Candida albicans*.

Drug Resistance
Studies showed no development of resistance to terconazole during successive passages of *C. albicans*. However, the clinical significance of such an effect is not known.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, mutagenesis, impairment of fertility. Studies to determine the carcinogenic potential of terconazole have not been performed. Terconazole was not mutagenic when tested *in vitro* for induction of microbial point mutations (Ames test), or for inducing cellular transformation, or in vivo for chromosome breaks (micronucleus test) or dominant lethal mutations in mouse germ cells. No impairment of fertility occurred when female rats were administered terconazole orally up to 40 mg/kg/day (about 10 times the recommended intravaginal human dose based on body surface area comparisons) for a three month period.

14 CLINICAL STUDIES

The efficacy of terconazole vaginal cream, 0.8% in the treatment of vulvovaginal candidiasis in adult women was evaluated in a multicenter, randomized, double-blind, controlled non-inferiority trial comparing terconazole vaginal cream, 0.8% for 3 days (n =231) to another preparation of terconazole vaginal cream 0.8% active comparator for 3 days (n=229). The modified intent-to-treat population (randomized patients who received treatment and had a positive baseline culture for *Candida*) consisted of 140 terconazole vaginal cream, 0.8% patients and 153 active comparator patients. Therapeutic cure defined as clinical and mycological cure was assessed at Visit 3 (Day 21-30). Table 2 shows the therapeutic, clinical and mycological cure rates in this trial. The therapeutic cure rate at Visit 3 was 67.1% for the terconazole group and 52.3% for the active comparator group (95% confidence interval about the 14.8% difference in therapeutic cure rate: 3.0% to 26.6%).

Table 2 Efficacy of Terconazole Vaginal Cream 0.8% for the Treatment of Vulvovaginal Candidiasis in a Randomized, Double-Blind Active Controlled Study*

Outcome	Terconazole Vaginal Cream 0.8% n=140 (%)	Active Control n=153	Treatment Difference (%) [95% Confidence Interval]
	% Cure	% Cure	
Therapeutic Cure	67.1	52.3	14.8 [3.0, 26.6]
Clinical Cure	79.3	66.0	13.3 [2.5, 24.0]
Mycological Cure	70.7	56.9	13.8 [2.2, 25.4]

* Modified intent-to-treat population

16 HOW SUPPLIED/STORAGE AND HANDLING

Terconazole Vaginal Cream 0.8% is supplied in 20 gram tubes with a measured dose applicator.
NDC 0168-0347-20
Store at 20°-25°C (68°-77°F)[see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

17.1 Instructions for Use

Patients using terconazole vaginal cream, 0.8% should receive the following information and instructions:

- Terconazole vaginal cream, 0.8% is for intravaginal use only. Avoid contact with eyes and inside the nose and mouth.
- This medication should be used for three days as directed, even if you feel better quickly.
- Do not use this medication for any disorder other than the one for which it was prescribed.
- Terconazole vaginal cream, 0.8% should be used once a day as directed.
- If your sexual partner has itching, redness or discomfort in the genital area, tell your partner to consult a physician and that you are being treated for a yeast infection.
- Terconazole vaginal cream, 0.8% can be used during a menstrual period but external pads should be used until the medication treatment has been completed. Tampons may absorb the medication and should not be used. You may wish to wear an absorbent panty liner while using terconazole vaginal cream, 0.8%.
- Don't scratch the vaginal area. Scratching can cause more irritation and spread the infection.
- Wash hands before and after applying terconazole vaginal cream, 0.8%.

Patients prone to vaginal yeast infections should receive the following instructions:

- Dry the genital area thoroughly after showering, bathing, or swimming. Change out of a wet bathing suit or damp exercise clothes as soon as possible. A dry environment is less likely to encourage the growth of yeast.
- Wipe from front to rear (away from the vagina) after a bowel movement.
- Don't douche unless the healthcare provider specifically tells you to do so. Douching may disturb the balance of normal bacterial flora and the pH of secretions.
- See FDA-Approved Patient Labeling (17.2)

17.2 FDA-Approved Patient Labeling

PATIENT INFORMATION

TERCONAZOLE
(ter kon ah zol)
VAGINAL CREAM, 0.8%

Important: For use in the vagina only. Terconazole vaginal cream, 0.8% is not for use in the mouth, eyes or inside the nose.

Read the Patient Information that comes with terconazole vaginal cream, 0.8% before you start using it and each time you get a refill. There may be new information. This

leaflet does not take the place of talking with your doctor about your medical condition or treatment.

What is terconazole vaginal cream, 0.8%?
Terconazole vaginal cream, 0.8% is prescription medicine used to treat vaginal yeast infections caused by a fungus called *Candida (KAN di duh)*.
It is not known if terconazole vaginal cream, 0.8% is safe or effective in females who have not reached puberty.

Who should not use terconazole vaginal cream, 0.8%?
Do not use terconazole vaginal cream, 0.8% if you are allergic to terconazole or any of the other ingredients of the cream. See the end of this leaflet for a complete list of ingredients in terconazole vaginal cream, 0.8%.

What should I tell my doctor before using terconazole vaginal cream, 0.8%?

Before using terconazole vaginal cream, 0.8%, tell your doctor if you:

- Have had an allergic reaction to another antifungal medicine.
- If you are pregnant or plan to become pregnant. Terconazole vaginal cream, 0.8% is absorbed from the vagina. You should not use terconazole during pregnancy without first talking to your doctor.
- If you are breastfeeding or plan to breastfeed. It is not known if terconazole vaginal cream, 0.8% passes into your breast milk.

Tell your doctor about all the medicines that you take including prescription and non-prescription medicines, vitamins and herbal supplements. Certain types of medicines can increase the chance of getting vaginal infections.

How should I use terconazole vaginal cream, 0.8%?

- Use terconazole vaginal cream, 0.8% exactly as prescribed.
- Apply one full applicator of terconazole vaginal cream, 0.8% each night at bedtime for as many days as your doctor tells you (usually 3 days in a row).
- Do not stop using terconazole vaginal cream, 0.8% before your doctor tells you to, even if you feel better very quickly. Your infection may not clear up completely.
- Terconazole vaginal cream, 0.8% is not for use in the mouth, eyes, or inside the nose.
- See the end of this leaflet for detailed Instructions for Use about how to use Terconazole vaginal cream correctly.
- Avoid scratching the affected area. Scratching may cause more irritation and spread the infection.
- If your sexual partner has itching, redness, or discomfort in the genital area, tell your partner to see their doctor and tell their doctor that you being treated for a yeast infection.
- Terconazole vaginal cream, 0.8%can be used during a menstrual period. You should not use tampons because they absorb the medicine. Use external pads until treatment with terconazole vaginal cream, 0.8% has been completed.

- Follow your doctor's instructions about how to reduce your chances of getting vaginal yeast infections.

What are possible side effects with terconazole vaginal cream, 0.8%?
Tell your doctor if you get any of the following symptoms during treatment with terconazole vaginal cream, 0.8%:

- Skin irritation.
- Fever, chills, or flu-like symptoms

If you have any of the symptoms listed above, your doctor may tell you to stop using terconazole vaginal cream, 0.8% and prescribe a different medicine to treat your fungal infection.
Common side effects of terconazole vaginal cream, 0.8% include

- Headaches
- Painful menstrual periods

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of terconazole vaginal cream, 0.8%. Ask your doctor or pharmacist for more information.

Call your doctor for advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088

How should I store terconazole vaginal cream, 0.8%?
• Store terconazole vaginal cream, 0.8% at room temperature, 68° to 77°F (20° - 25°C)
• Keep terconazole vaginal cream, 0.8% and all medicines out of the reach of children

General information about terconazole vaginal cream, 0.8%
Medicines are sometimes prescribed for purposes other than those listed in patient information leaflet. Do not use terconazole vaginal cream, 0.8% for a condition for which it was not prescribed. Do not give terconazole vaginal cream, 0.8% to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about terconazole vaginal cream, 0.8%. If you would like more information, talk with your doctor. You can also ask your pharmacist or doctor for information about terconazole vaginal cream, 0.8% that is written for healthcare professionals. If you have questions about terconazole vaginal cream, 0.8% you can also call: 1-800-645-9833 or go to www.nycomedus.com

What are the ingredients in terconazole vaginal cream, 0.8%?

- **Active Ingredients:** terconazole 0.8**%**

- **Inactive Ingredients:** butylated hydroxyanisole, cetyl alcohol, isopropyl myristate, polysorbate 60, polysorbate 80, propylene glycol, stearyl alcohol, and purified water.

Terconazole vaginal cream, 0.8%
Instructions for Use
Be sure to read, understand, and follow the instructions below for how to use terconazole vaginal cream, 0.8% correctly.

1. **Wash your hands.**
2. **Fill the Applicator:**
   • Remove the cap from the tube.

   • Use the pointed tip on the top of the cap to puncture the seal on the tube.
   • Screw the applicator onto the tube.
   • Squeeze the tube from the bottom and fill the applicator until the plunger stops.

   • Unscrew the applicator from the tube.
3. **Insert the Cream:**
   • Lie on your back with knees drawn up toward your chest.
   • Holding the applicator by the ribbed end of the barrel, insert the filled applicator into the vagina as far as it will comfortably go.

   • Slowly press the plunger of the applicator to release the cream into the vagina.
   • Remove the applicator from the vagina. Wash the applicator.
4. **Wash the Applicator after Use**
   • Wash the applicator after each use.
   • Pull the plunger out of the barrel.
   • Wash the applicator pieces with lukewarm, soapy water and then dry them thoroughly.
   • Put the dry applicator pieces back together by gently pushing the plunger into the barrel as far as it will go.

5. **Wash you hands well after you finish washing and drying the applicator.**

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