HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VUSION Ointment safely and effectively. See full prescribing information for VUSION Ointment.

VUSION® (miconazole nitrate, zinc oxide, and white petrolatum) Ointment, for topical use only

Initial U.S. Approval: 2006

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

- VUSION Ointment is indicated for adjunctive treatment of diaper dermatitis when complicated by documented candidiasis (microscopic evidence of pseudohyphae and /or budding yeast) in immunocompetent pediatric patients 4 weeks and older. (1)
- VUSION Ointment should not be used as a substitute for frequent diaper changes. (1)
- VUSION Ointment should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance. (1)

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

- VUSION Ointment is for topical use only. VUSION Ointment is not for oral, ophthalmic, or intravaginal use. (2)
- VUSION Ointment should be applied as a thin layer to the affected area at each diaper change for 7 days. (2)
- VUSION Ointment should be used as part of a treatment regimen that includes gentle cleansing of the diaper area and frequent diaper changes. (2)

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

- Ointment with 0.25% miconazole nitrate, 15% zinc oxide, and 81.35% white petrolatum. (3)

---------- CONTRAINDICATIONS ----------

- None

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

- If irritation occurs or if the disease worsens, discontinue use of the medication, and contact the health care provider. (5)

----------ADVERSE REACTIONS----------

To report SUSPECTED ADVERSE REACTIONS, contact Stiefel Laboratories, Inc. at 1-866-440-5508 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

*SECTIONS OR SUBSECTIONS OMITTED FROM THE FULL PRESCRIBING INFORMATION ARE NOT LISTED.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

VUSION Ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *Candida albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

VUSION should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.

VUSION should not be used as a substitute for frequent diaper changes. VUSION should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

1.2 Limitations of Use

The safety and efficacy of VUSION have not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of VUSION have not been evaluated in incontinent adult patients. **VUSION should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.**

2 DOSAGE AND ADMINISTRATION

VUSION is not for oral, ophthalmic, or intravaginal use.

Before applying VUSION, gently cleanse the skin with lukewarm water and pat dry with a soft towel. Avoid using any scented soaps, shampoos, or lotions on the diaper area.

Apply VUSION to the affected area at each diaper change for 7 days. Continue treatment for the full 7 days, even if there is improvement. The safety of VUSION when used for longer than 7 days is not known. Do not use VUSION for longer than 7 days. If symptoms have not improved by day 7, see your health care provider.

Gently apply a thin layer of VUSION to the diaper area with the fingertips. Do not rub VUSION into the skin as this may cause additional irritation. Thoroughly wash hands after applying VUSION.

3 DOSAGE FORMS AND STRENGTHS

White ointment containing 0.25% miconazole nitrate, 15% zinc oxide, and 81.35% white petrolatum.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

If irritation occurs or if the disease worsens, discontinue use of the medication, and contact the health care provider.

The safety and efficacy of VUSION have not been evaluated in incontinent adult patients. **VUSION should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.**

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rate observed in the 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 clinical practice.

A total of 835 infants and young children were evaluated in the clinical development program. Of 418 subjects in the VUSION group, 58 (14%) reported one or more adverse events. Of 417 subjects in the zinc oxide/white petrolatum control group, 85 (20%) reported one or more adverse events. Adverse events that occurred at a rate of ≥ 1% for subjects who were treated with VUSION were approximately the same in type and frequency as for subjects who were treated with zinc oxide/white petrolatum ointment.

6.2 Post-marketing Experience

The following adverse reactions have been identified during post approval use of VUSION.

GASTROINTESTINAL DISORDERS: vomiting
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: burning sensation, condition aggravated, inflammation, pain
INJURY, POISONING AND PROCEDURAL COMPLICATIONS: accidental exposure
SKIN AND SUBCUTANEOUS TISSUE DISORDERS: blister, dermatitis contact, diaper dermatitis, dry skin, erythema, pruritus, rash, skin exfoliation

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

7 DRUG INTERACTIONS

Drug-drug interaction studies were not conducted. Women who take a warfarin anticoagulant and use a miconazole intravaginal cream or suppository may be at risk for developing an increased prothrombin time, international normalized ratio (INR), and bleeding. The potential for this interaction between warfarin and VUSION is unknown.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: There are no adequate and well-controlled studies of VUSION in pregnant women. Therefore, VUSION should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Miconazole nitrate administration has been shown to result in prolonged gestation and decreased numbers of live young in rats and in increased number of resorptions and decreased number of live young in rabbits at oral doses of 100 mg/kg/day and 80 mg/kg/day, which are 28 and 45 times the maximum possible topical exposure of caregivers, respectively, assuming 100% absorption.

8.3 Nursing Mothers

Safety and efficacy of VUSION have not been established in nursing mothers. It is not known if the active components of VUSION may be present in milk.

8.4 Pediatric Use

Efficacy was not demonstrated in infants less than 4 weeks of age. Safety and efficacy have not been established in very-low-birth-weight infants.

VUSION should not be used to prevent diaper dermatitis.

The safety of VUSION when used for longer than 7 days is not known. Do not use more than 7 days.

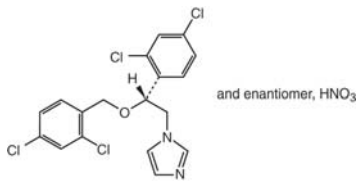
8.5 Geriatric Use

Safety and efficacy in a geriatric population have not been evaluated.

11 DESCRIPTION

VUSION contains the synthetic antifungal agent, miconazole nitrate (0.25%) USP, zinc oxide (15%) USP, and white petrolatum (81.35%) USP.

The chemical name of miconazole nitrate is 1-[2, 4-dichloro-ß-{(2,4-dichlorobenzyl)oxy} phenethyl] imidazole mononitrate with empirical formula $C_{18}H_{14}Cl_4N_2O \cdot HNO_3$ and molecular weight of 479.15. The structural formula of miconazole nitrate is as follows:



The zinc oxide has an empirical formula of ZnO and a molecular weight of 81.39.

The white petrolatum, which is obtained from petroleum and is wholly or nearly decolorized, is a purified mixture of semisolid saturated hydrocarbons having the general chemical formula C_nH_{2n+2}. The hydrocarbons consist mainly of branched and unbranched chains. White petrolatum contains butylated hydroxytoluene (BHT) as stabilizer.

Each gram of VUSION contains 2.5 mg of miconazole nitrate USP, 150 mg of zinc oxide USP, and 813.5 mg of white petrolatum USP containing butylated hydroxytoluene, trihydroxystearin, and Chemoderm® 1001/B fragrance. [1]

VUSION is a smooth, uniform, white ointment.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The miconazole component of VUSION is an antifungal agent [see Clinical Pharmacology (12.4)]. The mechanism of action of white petrolatum and zinc oxide for the adjunctive treatment of diaper dermatitis is unknown.

12.2 Pharmacodynamics

[1] Chemoderm® is a registered trademark of Firmenich Inc.

The human pharmacodynamics of Vusion is unknown [see Clinical Pharmacology (12.4) for fungal pharmacodynamics].

12.3 Pharmacokinetics

The topical absorption of miconazole from VUSION was studied in immunocompetent male and female infants and children (n=17) with diaper dermatitis complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast) ranging in age from 1 month to 21 months. After multiple daily applications to the affected area at every diaper change (approximately 5-12 times per day) for 7 days, the plasma concentrations of miconazole were below the lower limit of quantitation (LOQ) of 0.5 ng/mL in 15 out of 17 (88%) subjects. In the other 2 remaining subjects, the plasma concentrations of miconazole were 0.57 and 0.58 ng/mL, respectively at a single timepoint (4 hours after the last application) on Day 7.

12.4 Microbiology

The miconazole nitrate component in this product has been shown to have *in vitro* activity against *Candida albicans*, an organism that is associated with diaper dermatitis. The activity of miconazole nitrate against *C. albicans* is based on the inhibition of the ergosterol biosynthesis in the cell membrane. The accumulation of ergosterol precursors and toxic peroxides results in cytolysis of the cell. *In vitro* minimal inhibitory concentration (MIC) test results for *C. albicans* isolates obtained from treatment failures in Clinical Study 1 (*see Clinical Studies (14)*) does not appear to indicate that resistance to miconazole nitrate was the reason for treatment failure. The clinical significance of the *in vitro* activity of miconazole nitrate against *C. albicans* in the setting of diaper dermatitis is unclear.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of VUSION in animals has not been evaluated.

Miconazole nitrate was negative in a bacterial reverse mutation test, a chromosome aberration test in mice, and micronucleus assays in mice and rats.

Miconazole nitrate had no adverse effect on fertility in a study in rats at oral doses of up to 320 mg/kg/day, which is 89 times the maximum possible topical exposure of caregivers, assuming 100% absorption.

14 CLINICAL STUDIES

Study 1 was a double-blind, multicenter study in which VUSION was compared to the zinc oxide and white petrolatum combination treatment and included 236 infants and toddlers with diaper dermatitis, complicated by candidiasis as documented by KOH tests that demonstrated psuedohyphae and/or budding yeasts. Study medication was applied at every diaper change for 7 days.

The primary endpoint was “Overall Cure” and required that subjects be both clinically cured (total resolution of all signs and symptoms of infection) and microbiologically cured (eradication of candidiasis). Primary efficacy was assessed 1 week following the end of treatment, at Day 14.

Study results are shown in the following table.

Overall Cure at Day 14		
	VUSION n=112	Zinc Oxide/White Petrolatum n=124
	26 (23%)	12 (10%)

Two additional studies provided supportive evidence of the clinical efficacy of VUSION in infants and toddlers with diaper dermatitis, some of whom cultured positive for *C. albicans*. However, candidal infection was not documented in the culture-positive subjects, as microscopic testing (e.g. KOH) was not done. Therefore, the positive culture results may have reflected colonization rather than infection.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

VUSION is a smooth, uniform, white ointment supplied in an aluminum tube, as follows:
50g (NDC 0145-0002-04)

16.2 Storage Conditions

Store at controlled room temperature between 20°C and 25°C (68°F and 77°F); with excursions permitted between 15°C and 30°C (59°F and 86°F).

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling

Patients using VUSION should be informed about the following information:

- VUSION is to be used only for diaper dermatitis that is complicated by documented candidiasis (i.e. documented by microscopic testing).
- VUSION should not be used as a substitute for frequent diaper changes.
- VUSION should not be used to prevent diaper dermatitis.
- VUSION should not be used long term.
- VUSION should be used only as directed by the health care provider.
- VUSION is for external use only. It is not for oral, ophthalmic, or intravaginal use.
- Gently cleanse the diaper area with lukewarm water or a very mild soap and pat the area dry with a soft towel before applying VUSION.
- Gently apply VUSION to the diaper area with the fingertips after each diaper change. Do not rub VUSION into the skin as this may cause additional irritation.
- Thoroughly wash hands after applying VUSION.
- Treatment should be continued for 7 days, even if there is improvement. Do not use VUSION for longer than 7 days. If symptoms have not improved by day 7, see your health care provider.
- VUSION should not be used on children for whom it is not prescribed.

FDA-Approved Patient Labeling

VUSION® (Vu-sion) Ointment

(0.25% miconazole nitrate, 15% zinc oxide and 81.35% white petrolatum)

IMPORTANT: For Skin Use Only. Do not use in the mouth, eyes, or vagina.
Read the Patient Information that comes with VUSION before you use it on your child. This leaflet does not take the place of talking to your health care provider about your child's medical condition or treatment. If you have any questions or if you are not sure about any of the information on VUSION, ask your health care provider, or pharmacist.

What is VUSION?
VUSION is a prescription skin medicine used to treat diaper rash that also has a yeast infection in children who are at least 4 weeks old and who have a normal immune system. VUSION contains medicines that will help treat the yeast infection and the diaper rash, *but you must also change your child's diapers very often so that your child is not wearing a wet or soiled diaper.* Even if you use VUSION, *diaper rash will not go away if you do not keep your child's diaper area clean and dry.* You should use water or a very mild cleanser to clean your child's diaper area. VUSION is not to be used to prevent diaper rash or to be used for more than 7 days.

Your health care provider will need to do a special test to tell if your child's diaper rash also has a yeast infection. Do not use VUSION on your child's diaper rash unless your health care provider tells you that there is also a yeast infection.

Who should not use VUSION?
VUSION is not for treatment of all cases of diaper rash. VUSION is only for diaper rash that also has a yeast infection. Most cases of diaper rash do not need the yeast medicine that is in VUSION because most cases of diaper rash do not also have a yeast infection.

Do not use VUSION on any other children or other family member.

Do not use VUSION on your child's diaper rash if they are allergic to anything in it. See the end of this leaflet for a list of ingredients in VUSION.

Do not use on infants less than 4 weeks of age.

Do not use in infants or children who do not have a normal immune system.

How should I use VUSION on my child?
VUSION is applied to the skin on your child's diaper area at each diaper change for 7 days.

Apply VUSION for the full 7 days even if the diaper rash starts to go away. Call your child's health care provider if the diaper rash gets worse or does not go away with 7 days of treatment with VUSION. *VUSION should not be used for more than 7 days.*

To apply VUSION:
- Gently, clean the skin on your child's diaper area with warm (*not hot*) water. You may also use a very mild soap. Pat the area dry with a soft towel.
- Use your fingertips and gently apply a thin layer of VUSION to your child's diaper area at each diaper change. Do not rub VUSION into your child's skin. Rubbing the skin can cause more irritation.
- Wash your hands after applying VUSION on your child.

VUSION is for skin use only.

Call your child's health care provider or poison control center right away if any VUSION is swallowed. Call your child's health care provider if VUSION gets in the eye.
Keep out of reach of children.

What other steps will help diaper rash go away?

- Check your child's diaper often. Change the diaper at the first sign of wetness.
- Clean your child's diaper area after each diaper change. Gently wipe the diaper area from the front to back using warm **(***not hot***)** water. You may also use a mild soap. Rinse the diaper area well. Pat dry with a soft towel.
- Keep the diaper area open to air when possible.
- Even if you use VUSION, *diaper rash will not go away if you do not keep your child's diaper area clean and dry.*

What are the possible side effects of VUSION?
VUSION may cause irritation. You should call your child's health care provider if irritation appears or if the diaper rash gets worse.

How should I store VUSION?

- *Keep VUSION out of the reach of children to avoid the risk of accidental ingestion.*
- Store VUSION at room temperature between 68°F to 77°F (20°C to 25°C).

General information about VUSION
Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets.

Do not use VUSION for a condition for which it was not prescribed. Do not give VUSION to other children or family members, even if they have the same symptoms your child has. It may harm them.

This leaflet summarizes the most important information about VUSION. If you would like more information, talk to your child's health care provider. You can ask your child's health care provider or pharmacist for information about VUSION that is written for healthcare professionals.

Side effects may be reported to Stiefel Laboratories, Inc. at 1-866-440-5508 or the FDA at 1-800-FDA-1088.

What are the ingredients in VUSION?
Active Ingredients: miconazole nitrate, zinc oxide, and white petrolatum
Inactive Ingredients: trihydroxystearin, butylated hydroxyltoluene (BHT), and Chemoderm® 1001/B fragrance

This Patient Information leaflet has been approved by the U.S. Food and Drug Administration.
The Patient Information leaflet was last revised: January 2010

Manufactured for:
Stiefel Laboratories, Inc.
Coral Gables, FL 33134 USA

Manufactured by:
DSM Pharmaceuticals, Inc.
Greenville, NC 27834

Chemoderm® is a registered trademark of Firmenich Inc.

Revised March 2010

SAP#
P/N #