VUSION- miconazole nitrate, zinc oxide, white petrolatum ointment
Mylan Pharmaceuticals Inc.

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
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. (1.1)
- VUSION Ointment should not be used as a substitute for frequent diaper changes. (1.1)
- VUSION Ointment should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance. (1.2)

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. (5.1)

ADVERSE REACTIONS

To report SUSPECTED ADVERSE REACTIONS, contact Mylan at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 8/2018

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.

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.

Gently apply a thin layer of VUSION to the diaper area with each diaper change for 7 days. Do not rub VUSION into the skin as this may cause additional irritation. Thoroughly wash hands after applying VUSION. Continue treatment for the full 7 days, even if there is improvement.

Do not use VUSION for longer than 7 days. The safety of VUSION when used for longer than 7 days is not known. If symptoms have not improved by day 7, see your health care provider.

3 DOSAGE FORMS AND STRENGTHS

VUSION (miconazole nitrate, zinc oxide and white petrolatum) contains 2.5 mg of miconazole nitrate USP, 150 mg of zinc oxide USP and 813.5 mg of white petrolatum USP per gram.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Skin Irritation

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

care provider.

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. 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.

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

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

Risk Summary

There are no available data on VUSION Ointment use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. In animal reproduction studies, prolonged gestation, increased number of resorptions, and decreased numbers of live young were observed after oral administration of miconazole nitrate during organogenesis to pregnant rats and rabbits. No comparisons of animal exposure with human exposure may be calculated due to minimal systemic exposure in humans after topical administration of VUSION *[see Clinical Pharmacology (12.3)]*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

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.

8.2 Lactation

Risk Summary

There is no available information on the presence of miconazole in human milk, or the effects on the breastfed child, or the effects on milk production following use of VUSION.

The developmental and health benefits of breastfeeding should be considered along with the mother’s

clinical need for VUSION and any potential adverse effects on the breastfed infant from VUSION or from the underlying maternal condition.

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 (less than 1500 g).

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.

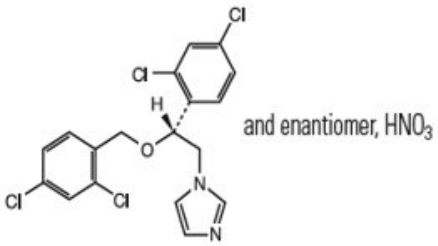
8.5 Geriatric Use

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.

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

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.

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 pseudohyphae 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 (miconazole nitrate, zinc oxide and white petrolatum) contains 2.5 mg of miconazole nitrate USP, 150 mg of zinc oxide USP and 813.5 mg of white petrolatum USP per gram. The smooth, uniform, white ointment supplied in an aluminum tube is available as follows:

NDC 0378-9730-50
carton containing one 50 gram tube

16.2 Storage Conditions

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

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 should be used only as directed by the health care provider.
- VUSION should not be used as a substitute for frequent diaper changes.
- VUSION should not be used to prevent diaper dermatitis.
- 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.

Patient Information

VUSION® (Vu-sion)
(miconazole nitrate, zinc oxide, and white petrolatum) Ointment

Important Information:VUSION is for use on the skin only. Do not use VUSION in the eyes, mouth, or vagina.

What is VUSION?
VUSION Ointment is a prescription medicine used on the skin (topical) to treat children 4 weeks of age and older with a normal immune system who have diaper rash (dermatitis) **and** who also have a yeast infection (candidiasis).

- Your child's healthcare provider should do a test to check to make sure that your child also has a yeast infection before starting treatment with VUSION.
- VUSION should be used along with gentle cleaning of the diaper area and changing your child's diaper often. See, **"How should I use VUSION?"** for detailed instructions on how to use VUSION the right way.
- VUSION should not be used to prevent diaper rash from developing (preventative treatment). Using VUSION as preventative treatment may cause VUSION to no longer work (resistance).

It is not known if VUSION is safe and effective for use in incontinent adults.
It is not known if VUSION is safe and effective for use in children less than 4 weeks of age or very low birth weight (less than 1500 grams).

Before using VUSION, tell your child's healthcare provider about all their medical conditions..

How should I use VUSION?

- Use VUSION exactly as your child's healthcare provider tells you to use it.
- Gently clean the skin on your child's diaper area with warm (not hot) water and pat the area dry with a soft towel.
- Using your fingertips, apply a thin layer of VUSION to the affected area at each diaper change for 7 days. **Do not** rub VUSION into your child's skin. Rubbing the skin can cause more irritation.
- Wash your hands after applying VUSION.
- VUSION should be used for the full 7 days of treatment. **Do not** stop treatment before the full 7 days, even if the symptoms improve.
- VUSION should not be used for longer than 7 days. Call your child's healthcare provider if the diaper rash gets worse or does not go away with 7 days of treatment with VUSION.
- Call your child's healthcare provider or poison control center right away if VUSION is swallowed or gets in the eyes.

What should I avoid while using VUSION?

- Avoid using scented soaps, shampoos or lotions in the diaper area during treatment with VUSION.

What are the possible side effects of VUSION?
VUSION may cause serious side effects, including:

- **Skin irritation.** Stop using VUSION and call your child's healthcare provider if your child's diaper rash gets worse or if your child develops skin irritation at the application site during treatment with VUSION.

These are not all the possible side effects of VUSION. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store VUSION?

- Store VUSION at room temperature between 68° to 77°F (20° to 25°C).

- **Keep VUSION and all medicines out of the reach of children.**

General information about the safe and effective use of VUSION.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use VUSION for a condition for which it was not prescribed. Do not give VUSION to other people, even if they have the same symptoms your child has. It may harm them. You can ask your child's healthcare provider or pharmacist for information about VUSION that is written for healthcare professionals.

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

Manufactured for: Mylan Pharmaceuticals Inc., Morgantown, WV 26505 U.S.A.

This Patient Information leaflet has been approved by the U.S. Food and Drug Administration. Revised: 8/2018

VUSION is a registered trademark of Stiefel Laboratories, Inc., a GSK Company, exclusively licensed to the Mylan Companies.

Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Manufactured by:
Confab Laboratories, Inc.
Saint-Hubert, QC, Canada

Revised: 8/2018
CON:MZPOIN:R1

PRINCIPAL DISPLAY PANEL – 50 grams

NDC 0378-9730-50 Rx only

Vusion®
(miconazole nitrate USP, 0.25%; zinc oxide USP, 15%; white petrolatum USP, 81.35%)
Ointment

For Topical Use Only

50 grams

Usual Dosage: See package insert.

Caution: Not for oral, ophthalmic, or intravaginal use. Keep out of reach of children. If seal is damaged or punctured, do not use, and return product to place of purchase.

Description: Each gram of VUSION® Ointment contains 2.5 mg miconazole nitrate USP, 150 mg zinc oxide USP, and 813.5 mg white petrolatum USP containing butylated hydroxytoluene, trihyforxystearin, and Chemoderm 1001/B fragrance.

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

See flap for lot number and expiration date.

For additional information, call Mylan at 1-877-446-3679 (1-877-4-INFO-RX).

Serious side effects associated with the use of this product may be reported to this

number.

VUSION is a registered trademark of
Stiefel Laboratories, Inc., a GSK Company,
exclusively licensed to the Mylan Companies.

Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Made in Canada

Mylan.com

CON:9730:50:1C:R2

VUSION

miconazole nitrate, zinc oxide, white petrolatum ointment

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0378-9730
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MICONAZOLE NITRATE (UNII: VW4H1CYW1K) (MICONAZOLE - UNII:7NNO0D7S5M)	MICONAZOLE NITRATE	2.5 mg in 1 g
ZINC OXIDE (UNII: SOI2LOH54Z) (ZINC OXIDE - UNII:SOI2LOH54Z)	ZINC OXIDE	150 mg in 1 g
PETROLATUM (UNII: 4T6H12BN9U) (PETROLATUM - UNII:4T6H12BN9U)	PETROLATUM	813.5 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
BUTYLATED HYDROXYTOLUENE (UNII: 1P9D0Z171K)	
TRIHYDROXYSTEARIN (UNII: 06YD7896S3)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0378-9730-50	1 in 1 CARTON	02/06/2020	
1		50 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021026	02/06/2020	

Labeler - Mylan Pharmaceuticals Inc. (059295980)

Revised: 8/2018 Mylan Pharmaceuticals Inc.