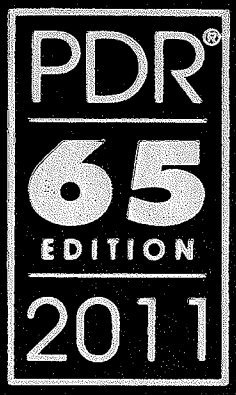

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Once you stop taking Soriatane, your psoriasis may return. Do not treat this new psoriasis with leftover Soriatane. It is important to see your prescriber again for treatment recommendations because your situation may have changed.

What should I avoid while taking Soriatane?

- **Avoid pregnancy.** See "What is the most important information I should know about Soriatane?", and "What are the important warnings and instructions for females taking Soriatane?".
- **Avoid breast feeding.** See "What are the important warnings and instructions for females taking Soriatane?"
- **Avoid alcohol.** Females must avoid drinks, foods, medicines, and over-the-counter products that contain alcohol. The risk of birth defects may continue for longer than 3 years if you swallow any form of alcohol during Soriatane treatment and for 2 months after stopping Soriatane (see "What are the important warnings and instructions for females taking Soriatane?").
- **Avoid giving blood. Do not donate blood** while you are taking Soriatane and **for at least 3 years after stopping** Soriatane treatment. Soriatane in your blood can harm an unborn baby if your blood is given to a pregnant woman. Soriatane does not affect your ability to receive a blood transfusion.
- **Avoid progestin-only birth control pills ("minipills").** This type of birth control pill may not work while you take Soriatane. Ask your prescriber if you are not sure what type of pills you are using.
- **Avoid night driving if you develop any sudden vision problems.** Stop taking Soriatane and call your prescriber if this occurs (see "Serious side effects").
- **Avoid non-medical ultraviolet (UV) light.** Soriatane can make your skin more sensitive to UV light. Do not use sunlamps, and avoid sunlight as much as possible. If you are taking light treatment (phototherapy), your prescriber may need to change your light dosages to avoid burns.
- **Avoid dietary supplements containing vitamin A.** Soriatane is related to vitamin A. Therefore, do not take supplements containing vitamin A, because they may add to the unwanted effects of Soriatane. Check with your prescriber or pharmacist if you have any questions about vitamin supplements.
- **DO NOT SHARE Soriatane with anyone else, even if they have the same symptoms.** Your medicine may harm them or their unborn child.

What are the possible side effects of Soriatane?

- **Soriatane can cause birth defects.** See "What is the most important information I should know about Soriatane?" and "What are the important warnings and instructions for females taking Soriatane?"
- Psoriasis gets worse for some patients when they first start Soriatane treatment. Some patients have more redness or itching. If this happens, tell your prescriber. These symptoms usually get better as treatment continues, but your prescriber may need to change the amount of your medicine.

Serious side effects.

These do not happen often, but they can lead to permanent harm, or rarely, to death. Stop taking Soriatane and call your prescriber right away if you get the following signs or symptoms:

- **Bad headaches, nausea, vomiting, blurred vision.** These symptoms can be signs of increased brain pressure that can lead to blindness or even death.
- **Decreased vision in the dark** (night blindness). Since this can start suddenly, you should be very careful when driving at night. This problem usually goes away when Soriatane treatment stops. If you develop any vision problems or eye pain stop taking Soriatane and call your prescriber.
- **Depression.** There have been some reports of patients developing mental problems including a depressed mood, aggressive feelings, or thoughts of ending their own life (suicide). These events, including suicidal behavior, have been reported in patients taking other drugs similar to Soriatane as well as patients taking Soriatane. Since other things may have contributed to these problems, it is not known if they are related to Soriatane. It is very important to stop taking Soriatane and call your prescriber right away if you develop such problems.
- **Yellowing of your skin or the whites of your eyes, nausea and vomiting, loss of appetite, or dark urine.** These can be signs of serious liver damage.
- **Aches or pains in your bones, joints, muscles, or back; trouble moving; loss of feeling in your hands or feet.** These can be signs of abnormal changes to your bones or muscles.
- **Frequent urination, great thirst or hunger.** Soriatane can affect blood sugar control, even if you do not already have diabetes. These are some of the signs of high blood sugar.
- **Shortness of breath, dizziness, nausea, chest pain, weakness, trouble speaking, or swelling of a leg. These may be** Soriatane can cause serious changes in blood fats (lipids). It is possible for these changes to cause blood vessel blockages that lead to heart attacks, strokes, or blood clots.

Common side effects.

If you develop any of these side effects or any unusual reaction, check with your prescriber to find out if you need to change the amount of Soriatane you take. These side effects usually get better if the Soriatane dose is reduced or Soriatane is stopped.

- **Chapped lips; peeling fingertips, palms, and soles; itching; scaly skin all over; weak nails; sticky or fragile (weak) skin; runny or dry nose, or nosebleeds.** Your prescriber or pharmacist can recommend a lotion or cream to help treat drying or chapping.
- **Dry mouth**
- **Joint pain**
- **Tight muscles**
- **Hair loss.** Most patients have some hair loss, but this condition varies among patients. No one can tell if you will lose hair, how much hair you may lose or if and when it may grow back.
- **Dry eyes.** Soriatane may dry your eyes. Wearing **contact lenses** may be uncomfortable during and after treatment with Soriatane because of the dry feeling in your eyes. If this happens, remove your contact lenses and call your prescriber. Also read the section about vision under "Serious side effects".
- **Rise in blood fats (lipids).** Soriatane can cause your blood fats (lipids) to rise. Most of the time this is not serious. But sometimes the increase can become a serious problem (see information under "Serious side effects"). You should have blood tests as directed by your prescriber.

These are not all the possible side effects of Soriatane. For more information, ask your prescriber or pharmacist.

How should I store Soriatane?

Keep Soriatane away from sunlight, high temperature, and humidity. **Keep Soriatane away from children.**

What are the ingredients in Soriatane?

Active ingredient: acitretin

Inactive ingredients: microcrystalline cellulose, sodium ascorbate, gelatin, black monogramming ink and maltodextrin (a mixture of polysaccharides). Gelatin capsule shells contain gelatin, iron oxide (yellow, black, and red), and titanium dioxide. They may also contain benzyl alcohol, carboxymethylcellulose sodium, edetate calcium disodium.

General information about the safe and effective use of Soriatane

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Soriatane for a condition for which it was not prescribed. Do not give Soriatane to other people, even if they have the same symptoms that you have.

This Medication Guide summarizes the most important information about Soriatane. If you would like more information, talk with your prescriber. You can ask your pharmacist or prescriber for information about Soriatane that is written for health professionals.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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STIEFEL®

Manufactured for
Stiefel Laboratories, Inc.
Coral Gables, FL 33134 USA
July 2009
303795

Shown in Product Identification Guide, page 319

VELTIN™ ℞

[*vel-tin*]

(clindamycin phosphate and tretinoin)
Gel 1.2%/0.025%
For topical use only

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

VELTIN™ (clindamycin phosphate and tretinoin) Gel 1.2%/0.025%

For topical use only

Initial U.S. Approval: 2006

INDICATIONS AND USAGE

- VELTIN Gel is a lincosamide antibiotic and retinoid combination product indicated for the topical treatment of

DOSAGE AND ADMINISTRATION

- Apply a pea size amount once daily in the evening lightly covering the entire affected area. Avoid the eyes, lips, and mucous membranes. (2)
- Not for oral, ophthalmic, or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS

- Topical gel: clindamycin phosphate 1.2% and tretinoin 0.025% in 30 gram and 60 gram tubes. (3)

CONTRAINDICATIONS

- VELTIN Gel is contraindicated in patients with regional enteritis, ulcerative colitis, or history of antibiotic-associated colitis. (4)

WARNINGS AND PRECAUTIONS

- Colitis: Clindamycin can cause severe colitis, which may result in death. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of clindamycin. VELTIN Gel should be discontinued if significant diarrhea occurs. (5.1)
- Ultraviolet Light and Environmental Exposure: Avoid exposure to sunlight, sunlamps, and weather extremes. Wear sunscreen daily. (5.2)

ADVERSE REACTIONS

- Observed local treatment-related adverse reactions (≥ 1%) in clinical studies with VELTIN Gel were application site reactions, including dryness, irritation, exfoliation, erythema, pruritus, and dermatitis. Sunburn was also reported. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Stiefel Laboratories, Inc. at 1-888-784-3335 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- VELTIN Gel should not be used in combination with erythromycin-containing products because of its clindamycin component. (7.1)

USE IN SPECIFIC POPULATIONS

- Pediatric Use: The efficacy and safety have not been established in pediatric patients below the age of 12 years. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 07/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VELTIN™ (clindamycin phosphate and tretinoin) Gel, 1.2%/0.025% is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

2 DOSAGE AND ADMINISTRATION

VELTIN Gel should be applied once daily in the evening, gently rubbing the medication to lightly cover the entire affected area. Approximately a pea sized amount will be needed for each application. Avoid the eyes, lips, and mucous membranes.

VELTIN Gel is not for oral, ophthalmic, or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

VELTIN Gel, containing clindamycin phosphate 1.2%

Table 1: Treatment-Related Adverse Reactions Reported by ≥1% of Subjects

	VELTIN Gel N=1104 n (%)	Clindamycin Gel N=1091 n (%)	Tretinoin Gel N=1084 n (%)	Vehicle Gel N=552 n (%)
Patients with at least one adverse reaction	140 (13)	38 (3)	141 (13)	17 (3)
Application site dryness	64 (6)	12 (1)	62 (6)	3 (1)
Application site irritation	50 (5)	4 (<1)	57 (5)	5 (1)
Application site exfoliation	50 (5)	2 (<1)	56 (5)	2 (<1)
Application site erythema	40 (4)	6 (1)	39 (4)	3 (1)
Application site pruritus	26 (2)	7 (1)	23 (2)	6 (1)
Sunburn	11 (1)	6 (1)	7 (1)	3 (1)
Application site dermatitis	6 (1)	0 (0)	8 (1)	1 (<1)

Table 2: VELTIN GEL-Treated Patients with Local Skin Reactions

	VELTIN GEL		VEHICLE GEL	
Local Reaction	Baseline N= 476 N (%)	End of Treatment N= 409 N (%)	Baseline N= 219 N (%)	End of Treatment N= 209 N (%)
Erythema	24%	21%	31%	35%
Scaling	8%	19%	14%	12%
Dryness	11%	22%	18%	13%
Burning	8%	13%	8%	4%
Itching	17%	15%	22%	14%

of VELTIN Gel contains, as dispensed, 10 mg (1%) clindamycin as clindamycin phosphate, and 0.25 mg (0.025%) tretinoin solubilized in an aqueous based gel.

4 CONTRAINDICATIONS

VELTIN Gel is contraindicated in patients with regional enteritis, ulcerative colitis, or history of antibiotic-associated colitis.

5 WARNINGS AND PRECAUTIONS

5.1 Colitis

Systemic absorption of clindamycin has been demonstrated following topical use. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical clindamycin. If significant diarrhea occurs, VELTIN Gel should be discontinued.

Severe colitis has occurred following oral or parenteral administration of clindamycin with an onset of up to several weeks following cessation of therapy. Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen severe colitis. Severe colitis may result in death.

Studies indicate a toxin(s) produced by clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Stool cultures for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

5.2 Ultraviolet Light and Environmental Exposure

Exposure to sunlight, including sunlamps, should be avoided during the use of VELTIN Gel, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. Patients who may be required to have considerable sun exposure due to occupation and those with inherent sensitivity to the sun should exercise particular caution. Daily use of sunscreen products and protective apparel (e.g., a hat) are recommended. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with VELTIN Gel.

6 ADVERSE REACTIONS

6.1 Adverse Reactions in Clinical Studies

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

and were treated once daily in the evening for 12 weeks. Adverse reactions that were reported in ≥1% of patients treated with VELTIN Gel are presented in Table 1.

[See table 1 above]

Local skin reactions actively assessed at baseline and end of treatment with a score > 0 are presented in Table 2.

[See table 2 above]

During the twelve weeks of treatment, each local skin reaction peaked at week 2 and gradually reduced thereafter.

7 DRUG INTERACTIONS

7.1 Erythromycin

VELTIN Gel should not be used in combination with erythromycin-containing products due to possible antagonism to the clindamycin component. *In vitro* studies have shown antagonism between these 2 antimicrobials. The clinical significance of this *in vitro* antagonism is not known.

7.2 Neuromuscular Blocking Agents

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, VELTIN Gel should be used with caution in patients receiving such agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. There are no well-controlled studies in pregnant women treated with VELTIN Gel. VELTIN Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A limit teratology study performed in Sprague Dawley rats treated topically with VELTIN Gel or 0.025% tretinoin gel at a dose of 2 mL/kg during gestation days 6 to 15 did not result in teratogenic effects. Although no systemic levels of tretinoin were detected, craniofacial and heart abnormalities were described in drug-treated groups. These abnormalities are consistent with retinoid effects and occurred at 16 times the recommended clinical dose assuming 100% absorption and based on body surface area comparison. For purposes of comparison of the animal exposure to human exposure, the recommended clinical dose is defined as 1 g of VELTIN Gel applied daily to a 50 kg person.

Clindamycin

Reproductive developmental toxicity studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (480 and 240 times the recommended clinical dose based on body surface area comparison, respectively) or subcutaneous doses of clindamycin up to 180 mg/kg/day (140 and 70 times the recommended clinical

Tretinoin

Oral tretinoin has been shown to be teratogenic in mice, rats, hamsters, rabbits, and primates. It was teratogenic and fetotoxic in Wistar rats when given orally at doses greater than 1 mg/kg/day (32 times the recommended clinical dose based on body surface area comparison). However, variations in teratogenic doses among various strains of rats have been reported. In the cynomologous monkey, a species in which tretinoin metabolism is closer to humans than in other species examined, fetal malformations were reported at oral doses of 10 mg/kg/day or greater, but none were observed at 5 mg/kg/day (324 times the recommended clinical dose based on body surface area comparison), although increased skeletal variations were observed at all doses. Dose-related teratogenic effects and increased abortion rates were reported in pigtail macaques.

With widespread use of any drug, a small number of birth defect reports associated temporally with the administration of the drug would be expected by chance alone. Thirty cases of temporally associated congenital malformations have been reported during two decades of clinical use of another formulation of topical tretinoin. Although no definite pattern of teratogenicity and no causal association have been established from these cases, 5 of the reports describe the rare birth defect category, holoprosencephaly (defects associated with incomplete midline development of the forebrain). The significance of these spontaneous reports in terms of risk to fetus is not known.

8.3 Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of VELTIN Gel. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. It is not known whether tretinoin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VELTIN Gel is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of VELTIN Gel in pediatric patients below the age of 12 years have not been established. Clinical trials of VELTIN Gel included 2,086 patients 12-17 years of age with acne vulgaris. *[See Clinical Studies (14).]*

8.5 Geriatric Use

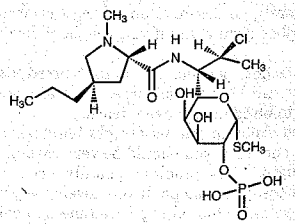
Clinical studies of VELTIN Gel did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

VELTIN (clindamycin phosphate and tretinoin) Gel, 1.2%/0.025%, is a fixed combination of two solubilized active ingredients in an aqueous based gel. Clindamycin phosphate is a water soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic lincomycin.

The chemical name for clindamycin phosphate is methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate). The structural formula for clindamycin phosphate is represented below:

Clindamycin phosphate:



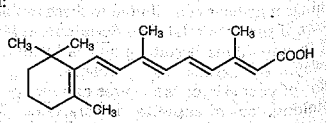
Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$

Molecular Weight: 504.97

The chemical name for tretinoin is all-*trans* 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid. It is a member of the retinoid family of compounds.

The structural formula for tretinoin is represented below:

Tretinoin:



Molecular Formula: $C_{20}H_{28}O_2$

Molecular Weight: 300.44

VELTIN Gel contains the following inactive ingredients: butylated hydroxytoluene, carbomer 940, anhydrous citric acid, edetate disodium, methylparaben, laureth 4, propylene glycol, tromethamine, and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tretinoin

Although the exact mode of action of tretinoin is unknown, current evidence suggests that topical tretinoin decreases cohesiveness of follicular epithelial cells with decreased microcomedone formation. Additionally, tretinoin stimulates mitotic activity and increased turnover of follicular epithelial cells causing extrusion of the comedones.

12.3 Pharmacokinetics

In an open-label study of 17 patients with moderate-to-severe acne vulgaris, topical administration of approximately 3 grams of VELTIN Gel once daily for 5 days, clindamycin concentrations were quantifiable in all 17 patients starting from 1 hour post dose. All plasma clindamycin concentrations were ≤5.56 ng/mL on day 5, with the exception of one subject who had a maximum clindamycin concentration of 8.73 ng/mL at 4 hours post-dose. There was no appreciable increase in systemic exposure to tretinoin, as compared to the baseline value. The average tretinoin concentration across all sampling times on day 5 ranged from 1.19 to 1.23 ng/mL compared with the corresponding baseline mean tretinoin concentration range of 1.16 to 1.30 ng/mL.

12.4 Microbiology

No microbiology studies were conducted in the clinical trials with this product.

Mechanism of Action

Clindamycin binds to the 50S ribosomal subunit of susceptible bacteria and prevents elongation of peptide chains by interfering with peptidyl transfer, thereby suppressing protein synthesis. Clindamycin has been shown to have *in vitro* activity against *Propionibacterium acnes (P. acnes)*, an organism that has been associated with acne vulgaris; however, the clinical significance of this activity against *P. acnes* was not examined in clinical studies with VELTIN Gel. *P. acnes* resistance to clindamycin has been documented.

Inducible Clindamycin Resistance

The treatment of acne with antimicrobials is associated with the development of antimicrobial resistance in *P. acnes* as well as other bacteria (e.g. *Staphylococcus aureus, Streptococcus pyogenes*). The use of clindamycin may result in developing inducible resistance in these organisms. This resistance is not detected by routine susceptibility testing.

Cross Resistance

Resistance to clindamycin is often associated with resistance to erythromycin.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of VELTIN Gel or the effect of VELTIN Gel on fertility. VELTIN Gel was negative for mutagenic potential when evaluated in an *in vitro* Ames *Salmonella* reversion assay. VELTIN Gel was equivocal for clastogenic potential in the absence of metabolic activation when tested in an *in vitro* chromosomal aberration assay.

Clindamycin

Once daily dermal administration of 1% clindamycin as clindamycin phosphate in the VELTIN Gel vehicle (32 mg/kg/day, 13 times the recommended clinical dose based on body surface area comparison) to mice for up to 2 years did not produce evidence of tumorigenicity.

Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (240 times the recommended clinical dose based on body surface area comparison) revealed no effects on fertility or mating ability.

Tretinoin

In two independent mouse studies where tretinoin was administered topically (0.025% or 0.1%) three times per week for up to two years no carcinogenicity was observed, with maximum effects of dermal amyloidosis. However, in a dermal carcinogenicity study in mice, tretinoin applied at a dose of 5.1 µg (1.4 times the recommended clinical dose based on body surface area comparison) three times per week for 20 weeks acted as a weak promoter of skin tumor formation following a single application of dimethylbenz[α]anthracene (DMBA).

In a study in female SENCAR mice, papillomas were induced by topical exposure to DMBA followed by promotion with 12-O-tetradecanoyl-phorbol 13-acetate or mezerein for up to 20 weeks. Topical application of tretinoin prior to each application of promoting agent resulted in a reduction in the number of papillomas per mouse. However, papillomas resistant to topical tretinoin suppression were at higher risk for pre-malignant progression.

Tretinoin has been shown to enhance photocarcinogenicity in properly performed specific studies, employing concurrent or intercurrent exposure to tretinoin and UV radiation. The photocarcinogenic potential of the clindamycin tretinoin combination is unknown. Although the significance of these studies to humans is not clear, patients should avoid exposure to sun.

The genotoxic potential of tretinoin was evaluated in an *in vitro* Ames *Salmonella* reversion test and an *in vitro* chromosomal aberration assay in Chinese hamster ovary cells. Both tests were negative.

In oral fertility studies in rats treated with tretinoin, the no-observed-effect-level was 2 mg/kg/day (64 times the recommended clinical dose based on body surface area comparison).

0	Clear	Normal, clear skin with no evidence of acne vulgaris.
1	Almost Clear	Skin almost clear; rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red) requiring no further treatment in the Investigator's opinion.
2	Mild	Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only, no nodulo-cystic lesions).
3	Moderate	Non-inflammatory lesions predominate, with multiple inflammatory lesions evident; several to many comedones and papules/pustules, and there may or may not be 1 small nodulo-cystic lesion.
4	Severe	Inflammatory lesions are more apparent; many comedones and papules/pustules, there may or may not be a few nodulo-cystic lesions.
5	Very Severe	Highly inflammatory lesions predominate; variable numbers of comedones, many papules/pustules and nodulo-cystic lesions.

Table 3: Efficacy Results at Week 12

Study 1	VELTIN Gel N=476	Clindamycin Gel N=467	Tretinoin Gel N=464	Vehicle Gel N=242
Investigator's Global Assessment				
Percentage of subjects achieving Two Grade Improvement	36.3%	26.6%	26.1%	20.2%
Percentage of subjects achieving an IGA of 0 or 1 with a Two Grade Improvement	33.2%	24.0%	22.6%	17.8%
Inflammatory Lesions:				
Mean absolute reduction	15.5	14.5	13.9	11.1
Mean percentage (%) reduction	60.4%	56.5%	54.5%	43.3%
Non-inflammatory Lesions:				
Mean absolute reduction	23.2	19.5	22.1	17.0
Mean percentage (%) reduction	51.0%	42.9%	47.3%	36.0%
Total Lesions:				
Mean absolute reduction	38.7	34.0	36.0	28.1
Mean percentage (%) reduction	55.0%	49.0%	50.5%	39.1%

14 CLINICAL STUDIES

The safety and efficacy of VELTIN Gel, applied once daily for the treatment of acne vulgaris, was evaluated in 12-week multicenter, randomized, blinded studies in subjects 12 years and older.

Treatment response was defined as the percent of subjects who had a two grade improvement from baseline to Week 12 based on the Investigator's Global Assessment (IGA) and a mean absolute change from baseline to Week 12 in two out of three (total, inflammatory and non-inflammatory) lesion counts. The IGA scoring scale used in all the clinical trials for VELTIN Gel is as follows:

[See first table above]

In Study 1, 1649 subjects were randomized to VELTIN Gel, Clindamycin gel, Tretinoin gel, and vehicle gel. The median age of subjects was 17 years old and 58% were females. At baseline, subjects had an average of 71 total lesions of which the mean number of inflammatory lesions was 25.5 lesions and the mean number of non-inflammatory lesions was 45.1 lesions. The majority of subjects enrolled with a baseline IGA score of 3. The efficacy results at week 12 are presented in Table 3.

[See table 3 above]

The safety and efficacy of clindamycin-tretinoin gel was also evaluated in two additional 12-week, multi-centered, randomized, blinded, studies in patients 12 years and older. A total of 2219 subjects with mild-to-moderate acne vulgaris were treated once daily for 12 weeks. Of the 2219 subjects, 634 subjects were treated with clindamycin-tretinoin gel.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

VELTIN Gel is supplied as follows:
30 g aluminum tubes NDC 0145-0071-30
60 g aluminum tubes NDC 0145-0071-60

Storage and Handling

- Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F).
- Protect from heat.
- Protect from light.
- Protect from freezing.
- Keep out of reach of children.
- Keep tube tightly closed.

17 PATIENT COUNSELING INFORMATION

[See FDA-approved Patient Labeling].

17.1 Instructions for Use

- At bedtime, the face should be gently washed with a mild soap and water. After patting the skin dry, apply VELTIN Gel as a thin layer over the entire affected area (excluding the eyes and lips).
- Patients should be advised not to use more than a pea sized amount to cover the face and not to apply more often than once daily (at bedtime) as this will not make for faster results and may increase irritation.
- A sunscreen should be applied every morning and reapplied over the course of the day as needed. Patients should be advised to avoid exposure to sunlight, sunlamp, ultraviolet light, and other medicines that may increase sensitivity to sunlight.
- Other topical products with a strong drying effect, such as abrasive soaps or cleansers, may cause an increase in skin irritation with VELTIN Gel.

17.2 Skin Irritation

VELTIN Gel may cause irritation such as erythema, scaling, itching, burning, or stinging.

17.3 Colitis

In the event a patient treated with VELTIN Gel experiences severe diarrhea or gastrointestinal discomfort, VELTIN Gel should be discontinued and a physician should be contacted.

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