

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SOLAGÉ Topical Solution safely and effectively. See full prescribing information for SOLAGÉ Topical Solution.

SOLAGÉ[®] (mequinol, tretinoin) Topical Solution

For Topical use only. Initial U.S. Approval: 1999

INDICATIONS AND USAGE

- Solagé Topical Solution is indicated for the treatment of solar lentigines. (1)

DOSAGE AND ADMINISTRATION

- Solagé Topical Solution should be applied twice daily to the affected area for 24 weeks. (2)
- Not for oral, ophthalmic or intravaginal use.

DOSAGE FORMS AND STRENGTHS

- Mequinol 2% and tretinoin 0.01%, by weight, in a solution. (3)

CONTRAINDICATIONS

- Should not be used in women of childbearing potential. (4, 8.1)
- Should not be used in pregnant women. (4, 8.1)

WARNINGS AND PRECAUTIONS

- Solagé Topical Solution should not be used if the patient is also taking drugs known to be photosensitizers. (5.1, 7)
- Solagé Topical Solution is a dermal irritant and the results of continued irritation of the skin for greater than 52 weeks in chronic, long-term use are not known. (5.2)

- Solagé Topical Solution should be used with utmost caution in irritated or eczematous skin. (5.2)
- Solagé Topical Solution should only be used as an adjunct to a comprehensive skin care and sun avoidance program. (1, 5.3)
- Solagé Topical Solution should be used with caution by patients with a history or family history of vitiligo. (5.3)
- Solagé Topical Solution is flammable. (5.4)

ADVERSE REACTIONS

- The most common adverse reactions ($\geq 5\%$) in patients in the pivotal clinical trials treated with Solagé Topical Solution were erythema, burning, stinging or tingling, desquamation, pruritus, skin irritation, halo hypopigmentation, and hypopigmentation. (6.1)
- In post-marketing reports, the most common adverse reactions were skin discoloration, erythema, skin exfoliation, skin irritation, and skin burning sensation.

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.

DRUG INTERACTIONS

- Concomitant topical products with a strong skin drying effect should be used with caution in patients being treated with Solagé Topical Solution. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Should not be used in women of childbearing potential. (4, 8.1)
- Pediatrics: Should not be used in children. (4, 8.4)

See 17 for FDA-approved patient labeling.

Revised: 12/2009

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

(To understand fully the indication for this product, please read the entire *Indications and Usage* section of the labeling).

Solag  (mequinol 2%, tretinoin 0.01%) Topical Solution is indicated for the treatment of solar lentigines.

Solag  should only be used under medical supervision as an adjunct to a comprehensive skin care and sun avoidance program where the patient should primarily either avoid the sun or use protective clothing.

Neither the safety nor effectiveness of Solag  for the prevention or treatment of melasma or postinflammatory hyperpigmentation has been established.

The efficacy of using Solag  daily for greater than 24 weeks has not been established.

2 DOSAGE AND ADMINISTRATION

Patients require detailed instruction to obtain maximal benefits and to understand all the precautions necessary to use this product with greatest safety. The physician should review the Patient Information. Apply Solag  to the solar lentigines using the applicator tip while avoiding application to the surrounding skin. Use twice daily, morning and evening at least 8 hours apart, or as directed by a physician. Patients should not shower or bathe the treatment areas for at least 6 hours after application of Solag . Special caution should be taken when applying Solag  to avoid the eyes, mouth, paranasal creases, and mucous membranes.

Application of Solag  may cause transitory stinging, burning or irritation.

Improvement continues gradually through the course of therapy and should be apparent by 24 weeks. Patients should avoid exposure to sunlight (including sunlamps) or wear protective clothing while using Solag . Data are not available to establish how or whether Solag  is degraded (either by sunlight or by normal interior lighting) following application to the skin.

With discontinuation of Solag  therapy, a majority of patients will experience some repigmentation over time of their lesions.

Applications of larger amounts of medication or more frequently than recommended will not lead to more rapid or better results, and marked redness, peeling, irritation, or hypopigmentation (abnormal lightening) of the skin may occur.

Patients treated with Solag  may use cosmetics but should wait 30 minutes before applying.

Not for oral, ophthalmic or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Mequinol 2% and tretinoin 0.01%, by weight, in a solution base of ethyl alcohol (77.8% v/v)

4 CONTRAINDICATIONS

No adequate or well-controlled trials have been conducted with Solag  in pregnant women. The combination of mequinol and tretinoin may cause fetal harm when administered to a pregnant woman. Due to the known effects of these active ingredients, Solag  should not be used in women of childbearing potential.

In a dermal teratology study in New Zealand White rabbits, there were no statistically significant differences among treatment groups in fetal malformation data; however, marked hydrocephaly with visible doming of the head was observed in one mid-dose litter (12 and 0.06 mg/kg or 132 and 0.66 mg/m² of mequinol and tretinoin, respectively) and two fetuses in one high dose litter (40 and 0.2 mg/kg or 440 and 2.2 mg/m² of mequinol and tretinoin, respectively) of Solag , and two high-dose tretinoin (0.2 mg/kg, 2.2 mg/m²) treated litters. These malformations were considered to be treatment related and due to the known effects of tretinoin. This was further supported by coincident appearance of other malformations associated with tretinoin, such as cleft palate and appendicular skeletal defects. No effects attributed to treatment were observed in rabbits in that study treated topically with mequinol alone (dose 40 mg/kg, 440 mg/m²). A no-observed-effect level (NOEL) for teratogenicity in rabbits was established at 4 and 0.02 mg/kg (44 and 0.22 mg/m² mequinol and tretinoin, respectively) for Solag  which is approximately the maximum possible human daily dose, based on clinical application to 5% of total body surface area. Plasma tretinoin concentrations were not raised above endogenous levels, even at teratogenic doses. Plasma mequinol concentrations in rabbits at the NOEL at one hour after application were 124 ng/mL or approximately twelve times the mean peak plasma concentrations of that substance seen in human subjects in a clinical pharmacokinetic study.

In a repeated study in pregnant rabbits administered the same dose levels as the study described above, additional precautionary measures were taken to prevent ingestion, although there is no evidence to confirm that ingestion occurred in the initial study. Precautionary measures additionally limited transdermal absorption to a six hour exposure period, or approximately one-fourth of the human clinical daily continuous exposure time. This study did not show any significant teratogenic effects at doses up to approximately 13 times the human dose on a mg/m² basis. However, a concurrent tretinoin dose group (0.2 mg/kg/day) did include two litters with limb malformations.

In a published study in albino rats (*J. Am. Coll. Toxicology* 4(5):31-63, 1985), topical application of 5% of mequinol in a cream vehicle during gestation was embryotoxic and embryolethal. Embryonic loss prior to implantation was noted in that study where animals were treated throughout gestation. Coincidentally, mean preimplantation embryonic loss was increased in the first rabbit study in all mequinol treated groups, relative to control, and in the high dose mequinol/tretinoin and tretinoin only treated groups in the second study. In those studies, dosing began at

gestation day 6, when implantation is purported to occur. Increased preimplantation loss was also noted at the high combination dose in a study of early embryonic effects in rats, as was decreased body weight in male pups; these findings are consistent with the published study.

Solagé was not teratogenic in Sprague-Dawley rats when given in topical doses of 80 and 0.4 mg/kg mequinol and tretinoin, respectively (480 and 2.4 mg/m² or 11 times the maximum human daily dose). The maximum human dose is defined as the amount of solution applied daily to 5% of the total body surface area.

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 casual association has been established from these cases, 6 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 the fetus is not known.

5 WARNINGS AND PRECAUTIONS

5.1 Augmented Phototoxicity

Solagé should not be administered if the patient is also taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the possibility of augmented phototoxicity. Because of heightened burning susceptibility, exposure to sunlight (including sunlamps) to treated areas should be avoided or minimized during the use of Solagé. Patients must be advised to use protective clothing and comply with a comprehensive sun avoidance program when using Solagé. Data are not available to establish how or whether Solagé is degraded (either by sunlight or by normal interior lighting) following application to the skin. Patients with sunburn should be advised not to use Solagé until fully recovered. Patients who may have considerable sun exposure due to their occupation and those patients with inherent sensitivity to sunlight should exercise particular caution when using Solagé and ensure that the precautions outlined in the Patient Information are observed.

Solagé should be kept out of the eyes, mouth, paranasal creases, and mucous membranes.

5.2 Local Events

Solagé is a dermal irritant and the results of continued irritation of the skin for greater than 52 weeks in chronic, long-term use are not known. Tretinoin has been reported to cause severe irritation on eczematous skin and should be used only with utmost caution in patients with this condition.

Solagé may cause skin irritation, erythema, burning, stinging or tingling, peeling, and pruritis. If the degree of such local irritation warrants, patients should be directed to use less medication, decrease the frequency of application, discontinue use temporarily, or discontinue use altogether. The efficacy at reduced frequencies of application has not been established.

5.3 Precautions: General

Solagé should only be used as an adjunct to a comprehensive skin care and sun avoidance program. (*see Indications and Usage [1]*).

If a drug sensitivity, chemical irritation, or a systemic adverse reaction develops, use of Solagé should be discontinued.

Weather extremes, such as wind or cold, may be more irritating to patients using Solagé.

Solagé should be used with caution by patients with a history, or family history, of vitiligo. One patient in the trials, whose brother had vitiligo, experienced hypopigmentation in areas that had not been treated with study medication. Some of these areas continued to worsen for at least one month post treatment with Solagé. Six weeks later the severity of the hypopigmentation had decreased from moderate to mild and 106 days post treatment, the patient had resolution of some but not all lesions.

Application of larger amounts of medication than recommended will not lead to more rapid or better results, and marked redness, peeling, discomfort, or hypopigmentation of the skin may occur.

5.4 Flammable Contents

Keep away from heat and open flame.

6 ADVERSE REACTIONS

6.1 Adverse Reactions in Clinical Trials

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.

In the pivotal clinical trials, adverse reactions were primarily mild to moderate in intensity, occurring in 66% and 30% of patients, respectively. The majority of these events were limited to the skin and 64% had an onset of a skin related adverse reaction early in treatment (by week 8). The most frequent adverse reactions in patients treated with Solagé were erythema (49% of patients), burning, stinging, or tingling (26%), desquamation (14%), pruritis (12%), and skin irritation (5%). Some patients experienced temporary hypopigmentation of treated lesions (5%) or of the skin surrounding treated lesions (7%). Ninety-four of 106 patients (89%) had resolution of hypopigmentation upon discontinuation of treatment to the lesion, and/or re-instruction on proper application to the lesion only. Another 8% (9/106) of patients with hypopigmentation events had resolution within 120 days after the end of treatment. Three of the 106 patients (2.8%) had persistence of hypopigmentation beyond 120 days. Approximately 6% of patients discontinued study participation with Solagé due to adverse reactions. These discontinuations were due primarily to skin redness (erythema) or related cutaneous adverse reactions. Rare cases of depigmentation at sites distant from the application have been reported in Post Marketing Surveillance.

Adverse Events Occurring in >1% of the Population – All Studies								
Body System	Solagé (mequinol 2% tretinoin 0.01%)		Tretinoin, 0.01%		Mequinol, 2%,		Vehicle	
	N	%	N	%	N	%	N	%
Skin and Appendages								
Erythema	613	41.1	261	55.3	13	5.1	8	4.6
Burning/Stinging/ Tingling	270	18.1	173	36.7	26	10.2	20	11.4
Desquamation	171	11.5	93	19.7	7	2.8	2	1.1
Pruritus	148	9.9	66	14.0	12	4.7	3	1.7
Irritation Skin*	90	6.0	25	5.3	1	0.4	1	0.6
Halo Hypopigmentation	96	6.4	16	3.4	2	0.8	2	1.1
Hypopigmentation	62	4.2	8	1.7	2	0.8	0	0.0
Skin Dry	46	3.1	18	3.8	3	1.2	1	0.6
Rash	31	2.0	21	4.4	0	0.0	1	0.6
Crusting	30	2.0	18	3.8	0	0.0	1	0.6
Rash Vesicular Bullae	18	1.2	8	1.7	0	0.0	0	0.0
Dermatitis	29	1.9	0	0.0	0	0.0	0	0.0
Discomfort Skin	52	3.5	0	0.0	0	0.0	0	0.0
Irritant Dermatitis	17	1.1	0	0.0	0	0.0	0	0.0

*In study RD.06.SRE.18091 irritant dermatitis included signs & symptoms of scaling, dryness, stinging/burning, and erythema.

6.2 Post-marketing Experience

The following adverse reactions have been reported during post-approval use of Solagé: skin discoloration, erythema, skin exfoliation, skin irritation, and skin burning sensation. 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

Concomitant topical products with a strong skin drying effect, products with high concentrations of alcohol, astringents, spices or lime, medicated soaps or shampoos, permanent wave solutions, electrolysis, hair depilatories or waxes, or other preparations that might dry or irritate the skin should be used with caution in patients being treated with Solagé because they may increase irritation when used with Solagé.

Solagé should not be administered if the patient is also taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the possibility of augmented phototoxicity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

TERATOGENIC EFFECTS: PREGNANCY CATEGORY X.

Although the magnitude of the potential for teratogenicity may not be well-defined, Solagé is labeled as a pregnancy category “X” because the potential risk of the use of this drug to treat this particular indication (solar lentiginosities) in a pregnant woman clearly outweighs any possible benefit (see *Contraindications [4]*). Solagé should not be used in women of childbearing potential.

8.3 Nursing Mothers

It is not known to what extent mequinol and/or tretinoin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Solagé is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of this product have not been established in pediatric patients. Solagé should not be used on children.

8.5 Geriatric Use

Of the total number of patients in clinical studies of Solagé, approximately 43% were 65 and older, while approximately 8% were 75 and over. No overall differences in effectiveness or safety were observed between these patients and younger patients.

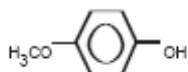
10 OVERDOSAGE

If Solagé is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, discomfort, or discoloration, including hypopigmentation, may occur. Oral ingestion of the drug may lead to the same adverse effects as those associated with excessive oral intake of vitamin A (hypervitaminosis A). If oral ingestion occurs, the patient should be monitored, and appropriate supportive measures should be administered as necessary. The maximal no-effect level for oral administration of Solagé in rats was 5.0 mL/kg (30 mg/m²). Clinical signs observed were attributed to the high alcohol content (77%) of the drug formulation.

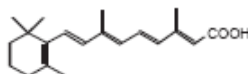
11 DESCRIPTION

Solagé contains mequinol 2% and tretinoin 0.01%, by weight, in a solution base of ethyl alcohol (77.8% v/v), polyethylene glycol 400, butylated hydroxytoluene, ascorbic acid, citric acid, ascorbyl palmitate, edetate disodium, and purified water.

Mequinol is 4-hydroxyanisole, the monomethyl ether of hydroquinone or 1-hydroxy-4-methoxybenzene. It has the chemical formula, C₇H₈O₂, a molecular weight of 124.14, and the structural formula:



The chemical name for tretinoin, a retinoid, is (all-*E*)-3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid, also referred to as all-*trans*-retinoic acid. It has the chemical formula, C₂₀H₂₈O₂, a molecular weight of 300.44, and the structural formula:



12 CLINICAL PHARMACOLOGY

Solar lentigines are localized, pigmented, macular lesions of the skin on the areas of the body which have been chronically exposed to sunlight. Biopsy specimens of solar lentigines were collected in a clinical study with Solagé at baseline, at the end of a 24 week treatment period, and at the end of a subsequent 24 week, no treatment, follow-up period. The end of treatment specimens showed a decrease in melanin pigmentation in both melanocytes and keratinocytes, and an increased lymphocytic infiltration, which may have been the result of irritation or an immunologic reaction. The end of follow-up period specimens showed repigmentation of the melanocytes and keratinocytes to a state similar to the baseline specimens. These results indicate that there is no assurance that any improvement obtained would persist upon discontinuation of drug therapy.

12.1 Mechanism of Action

The mechanism of action of mequinol is unknown. Although mequinol is a substrate for the enzyme tyrosinase and acts as a competitive inhibitor of the formation of melanin precursors, the clinical significance of these findings is unknown. The mechanism of action of tretinoin as a depigmenting agent also is unknown.

12.3 Pharmacokinetics

The percutaneous absorption of tretinoin and the systemic exposure to tretinoin and mequinol were assessed in healthy subjects (n=8) following two weeks of twice daily topical treatment of Solagé. Approximately 0.8 mL of Solagé was applied to a 400 cm² area of the back, corresponding to a dose of 37.3 µg/cm² for mequinol and 0.23 µg/cm² for tretinoin. The percutaneous absorption of tretinoin was approximately 4.4%, and systemic concentrations did not increase over endogenous levels. The mean C_{max} for mequinol was 9.92 ng/mL (range 4.22 to 23.62 ng/mL) and the T_{max} was 2 hours (range 1 to 2 hours).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Although a dermal carcinogenicity study in CD-1 mice indicated that Solagé applied topically at daily doses up to 80 and 0.4 mg/kg (240 and 1.2 mg/m²) of mequinol and tretinoin, respectively, representing approximately 5 times the maximum possible systemic human exposure was not carcinogenic, in a photocarcinogenicity study utilizing CrI:Skh-1(hr/hr BR) hairless albino mice, median time to onset of tumors decreased. Also, the number of tumors increased in all dose groups administered 1.4, 4.3, or 14 µl of Solagé /cm² of skin (24 and 0.12, 72 and 0.36, or 240 and 1.2 mg/m² of mequinol and tretinoin, respectively; 0.6, 1.9, or 6.5 times the daily human dose on a mg/m² basis) following chronic topical dosing with intermittent exposure to ultraviolet radiation for up to 40 weeks. Similar animal studies have shown an increased tumorigenic risk with the use of retinoids when followed by ultraviolet radiation. Although the significance of these studies to human use is not clear, patients using this product should be advised to avoid or minimize exposure to either sunlight or artificial ultraviolet irradiation sources.

Mequinol was non-mutagenic in the Ames/Salmonella assay using strains TA98, TA100, TA1535, and TA1537, all of which are insensitive to mutagenic effects of structurally-related quinones. Solagé was non-genotoxic in an *in vivo* dermal micronucleus assay in rats, but exposure of bone marrow to drug was not demonstrated.

A dermal reproduction study with Solagé in Sprague-Dawley rats at a daily dose of 80 and 0.4 mg/kg (480 and 2.4 mg/m²) of mequinol and tretinoin, respectively, approximately 11 times the corresponding maximum possible human exposure, assuming 100% bioavailability following topical application to 5% of the total body surface area, showed no impairment of fertility.

14 CLINICAL STUDIES

Two adequate and well-controlled trials evaluated changes in treated hyperpigmented lesions on the face, forearms/back of hands in 421 patients treated with Solagé, 422 patients treated with tretinoin topical solution, 209 patients treated with mequinol topical solution and 107 patients treated with vehicle for up to 24 weeks. In these studies, patients were to avoid sun exposure and use protective clothing, and use of sunscreens was prohibited. Patients were allowed to apply Moisturel® Lotion 30 minutes after application of Solagé. Physicians assessed the extent of improvement or worsening of all the treated lesions from the baseline condition on a 7 point scale. The results of these evaluations are shown below.

	Face		Forearms/Back of Hands	
	Solagé Solution	Vehicle	Solagé Solution	Vehicle
Moderate Improvement or greater ¹	57%	15%	54%	14%
Slight Improvement	28%	36%	26%	33%
No Change ²		49%	20%	53%

	15%			
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¹ Includes the following grades: Moderate Improvement, Marked Improvement, Almost Clear, Completely Clear. Moderate Improvement or greater was considered clinically meaningful.

² Includes the following grades: No Change, Worse (less than 1% of patients treated with Solagé were rated as worse).

Improvement (lightening) of the solar lentigines occurred gradually over time during the 24 week treatment period. At 24 weeks of treatment, 57% and 54% of patients experienced moderate improvement or greater, and 3% and 1% of patients were completely clear of all treated lesions for the face and forearms/back of hands, respectively. It should be noted that approximately 9% of patients, from both treatment areas in these studies, with moderate improvement or greater also experienced hypopigmentation of the skin surrounding at least one treated lesion. There are no vehicle-controlled effectiveness data on the course of lesions treated beyond 24 weeks.

After 24 weeks of treatment, for the forearm/back of hands treatment site, the percentage of patients treated with tretinoin topical solution with moderate improvement or greater, slight improvement, or no change, were 38%, 37%, and 26%, respectively, and for mequinol topical solution were 24%, 40%, and 36%, respectively. For the face treatment site, the percentage of patients treated with tretinoin topical solution with moderate improvement or greater, slight improvement, or no change, were 46%, 33%, and 21%, respectively, and for mequinol topical solution were 33%, 30%, and 37% respectively.

The duration of effect was investigated during a period of up to 24 weeks following the discontinuation of treatment. Results from these studies showed that patients may maintain the level of clinical improvement of their treated lesions from the end of treatment through the 24 week follow-up period. However, some degree of repigmentation of treated lesions was observed over time, demonstrating reversibility of the depigmenting action of Solagé.

In the pivotal clinical trials of 24 weeks duration, some patients experienced temporary hypopigmentation of treated lesions (5%) or of the skin surrounding treated lesions (7%). Hypopigmentation of the skin surrounding treated lesions occurs even in the setting of proper application of the drug within the lesion border. The majority (94/106 - 89%) resolved upon discontinuation of treatment to the lesion, and/or re-instruction on proper application to the lesion only. Another 8% (9/106) of patients with hypopigmentation events had resolution within 120 days after the end of treatment.

Three of the 106 patients (2.8%) had persistence of hypopigmentation beyond 120 days. This further demonstrates the reversibility of the depigmenting action of Solagé.

Over 150 patients used Solagé twice daily for 52 weeks in an open label clinical study. The safety profile for Solagé in this long-term study was similar to that seen in the 24 week studies although burning/stinging/tingling, desquamation, pruritis, and irritation of the skin occurred at lower rates and halo hypopigmentation and hypopigmentation occurred at a slightly greater rate.

Over 90 patients used Solagé twice daily and a concomitant sunscreen (PreSun® 29) daily for up to 24 weeks in an open label clinical study. The safety profile for Solagé in this study was similar to that seen in studies which prohibited sunscreen use although desquamation, pruritis, and halo hypopigmentation occurred at slightly lower rates.

The initial clinical trials for Solagé included 1794 individuals of Skin Type I-V, 94.5% of whom were Caucasian. The trials also included 5% of individuals who were Asian/Pacific Islander (1.2%), African-American (0.8%), and Hispanic/Latino (3.5%). An additional open label study was conducted in 259 patients in the Asian (24.3%), Hispanic/Latino (62.2%), and African American (13.5%) ethnic groups with skin types II to V. This number reflects approximately three times as many subjects in this population as were represented in the initial clinical trials. In this study, as in the earlier studies, Solagé was used twice daily for a period of 24 weeks. The overall safety profile in this study was generally consistent with the initial clinical trials although erythema, desquamation, and pruritis occurred at lower rates and halo hypopigmentation occurred at a higher rate (7.7% versus 6.2%). The safety of Solagé in women of childbearing potential has not been established (*see Contraindications [4]*).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Solagé (mequinol 2%, tretinoin 0.01%) Topical Solution is available in 30mL plastic bottles with an applicator.
NDC 13478-001-01

16.2 Storage Conditions

The bottle should be protected from light by continuing to store in the carton after opening. Store at 25°C (77°F); excursions permitted to 15° - 30°C (59° - 86°F).

FLAMMABLE. Keep away from heat and open flame.
Keep out of reach of children.

17. PATIENT COUNSELING INFORMATION

17.1 FDA APPROVED PATIENT LABELING

-SEE BELOW-

PATIENT INFORMATION

SOLAGÉ® (so-la-jay) Topical Solution

(mequinol 2%, tretinoin 0.01%)

Important: For skin use only

Read the Patient Information that comes with Solagé 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 to your doctor about your medical condition or treatment.

What is Solagé?

Solagé is a prescription medicine used on the skin to treat solar lentigines. Solar lentigines are also called “brown spots”, “age spots”, or “liver spots”. Solar lentigines can happen on areas of skin that have been exposed to too much sunlight over time.

Do not use for greater than 24 weeks unless you are directed to do so by your doctor.

Solagé should only be used under medical care along with a skin care and sun avoidance program. The patient should avoid the sun or use protective clothing.

Who should not use Solagé?

Do not use Solagé if you are:

- *a woman who is pregnant, planning to become pregnant, or is able to become pregnant.* Solagé may harm a fetus (unborn baby).
- *allergic to anything in Solagé.* See the end of this leaflet for a list of ingredients in Solagé.

Solagé has not been studied in children and should not be used on children.

Solagé may not be right for you. Before starting Solagé, tell your doctor about all of your health conditions, including, if you:

- have eczema
- have skin irritation
- have vitiligo or a family history of vitiligo. Vitiligo is a condition where color is lost on areas of the skin and white patches appear.
- have a sunburn
- have skin that is sensitive to sunlight
- are exposed to sunlight often because of your job
- are breastfeeding. It is not known if Solagé passes into breast milk and to your baby.

Tell your doctor about all of the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Solagé should not be used with other medicines that can make your skin sensitive to sunlight including:

- blood pressure medicines called “thiazides”
- some antibiotic medicines (tetracyclines, fluoroquinolones, or sulfonamides)
- antipsychotic medicines called “phenothiazines”

Know the medicines you take. Keep a list of your medicines with you to show your doctor. Your doctor will decide if you can use Solagé with your other medicines.

Tell your doctor about all of the skin products you use. Your doctor will tell you which skin products you can use with Solagé. *You must be careful about using skin products that can dry or irritate your skin because dryness and irritation are increased with Solagé.* Skin products that can dry and irritate your skin include:

- products that contain alcohol, astringents, spices, or limes
- medicated soaps or shampoos
- hair “perms” hair removal products such as electrolysis, depilatories, or waxes

How should I use Solagé?

- ***Solagé is for skin use only.***
- Apply Solagé exactly as prescribed and instructed by your doctor. Solagé is usually applied twice a day, at least 8 hours apart. Do not use more Solagé or use it more often than prescribed.
- Apply Solagé to the “spots” to be treated using the applicator tip of the Solagé bottle. Be careful and do not apply Solagé to “normal” skin.
- ***Do not use Solagé around your eyes, mouth, crease of your nose, or on mucous membranes.*** Solagé can cause severe redness, itching, burning, stinging, and peeling if applied to these areas. If Solagé gets in your eyes, rinse them well with water and call your doctor right away. If you get Solagé in your mouth or swallow any, get medical treatment right away.
- Do not bathe or shower for at least 6 hours after applying Solagé.
- Cosmetics may be applied 30 minutes after using Solagé. Talk to your doctor about cosmetics and other skin care products that are okay to use with Solagé.
- You must avoid sun exposure (including the use of sunlamps.). Always wear protective clothing when you go outside. If your skin gets sunburned, stop Solagé until the sunburn has healed.
- Wind or cold weather may cause more irritation when using Solagé.

What are the possible side effects of Solagé?

Common side effects of *Solagé* include changes in skin color, redness, stinging, burning, tingling, peeling, itching, or irritation on areas of the skin where it is applied. If any of these occur, discontinue use and contact your doctor.

Solagé may cause the treated age spots or surrounding skin to become lighter than your normally colored skin, especially if too much *Solagé* is used or it is used for too long. Hyperpigmentation (darkening of skin) has also been reported as a possible side effect. Call your doctor if changes in your skin color occur. Skin color may return when *Solagé* is stopped.

These are not all of the side effects of *Solagé*. Ask your doctor or pharmacist for more information.

How should I store Solagé?

- Store *Solagé* at 59°F to 86°F (15° to 30°C). Protect *Solagé* from light by returning the bottle to the carton after each use.
- *Solagé* is flammable. Keep away from heat and flames.
- Keep *Solagé* and all medicines out of the reach of children.

General information about Solagé.

Medicines can be prescribed for conditions that are not in patient information leaflets. Use *Solagé* only for what your doctor prescribed. Do not give it to other people, even if they have the same symptoms that you have. It may harm them.

This leaflet gives the most important information about *Solagé*. For more information about *Solagé*, talk with your doctor or pharmacist. For more information call 1-866-440-5508 or visit www.solage.com.

What are the ingredients in Solagé?

Active ingredients: mequinol and tretinoin

Inactive ingredients: ethyl alcohol (77.8% v/v), polyethylene glycol 400, butylated hydroxytoluene, ascorbic acid, citric acid, ascorbyl palmitate, edetate disodium, and purified water.

This Patient Information leaflet has been approved by the U.S. Food and Drug Administration.

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Rx Only

Marketed by:
Stiefel Laboratories, Inc.
255 Alhambra Circle
Coral Gables, FL 33134

Manufactured by:
Contract Pharmaceutical Laboratories, Buffalo, NY 14213 USA

Questions? Call 1-866-440-5508. Serious side effects associated with use of this product may be reported to this number.

Revised December 2009

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P/N

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