TREAT THE FIELD

SEQUENTIAL TREATMENT

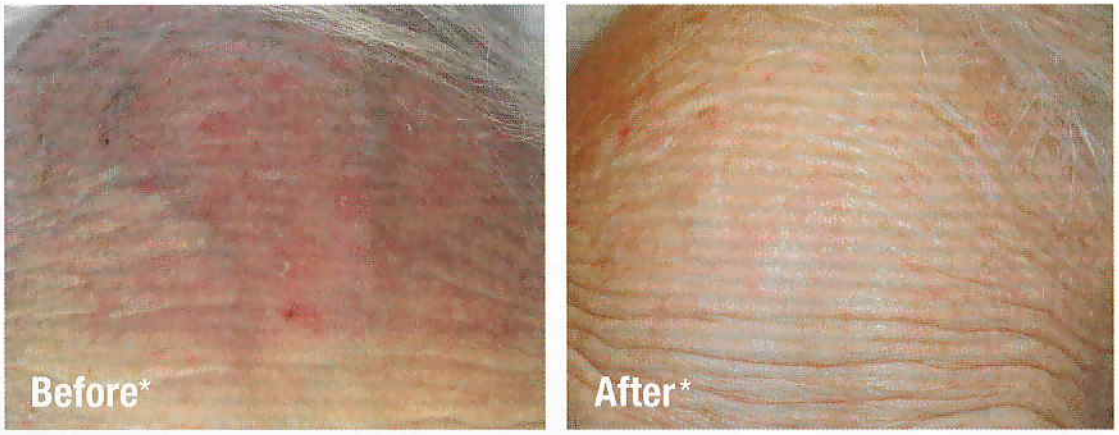
CRYOTHERAPY

FOLLOWED BY

R_x Only

SOLARAZE® GEL

Diclofenac Sodium-3%



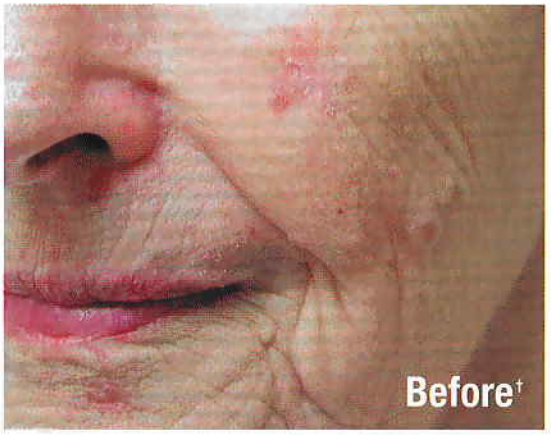
TREAT THE FIELD

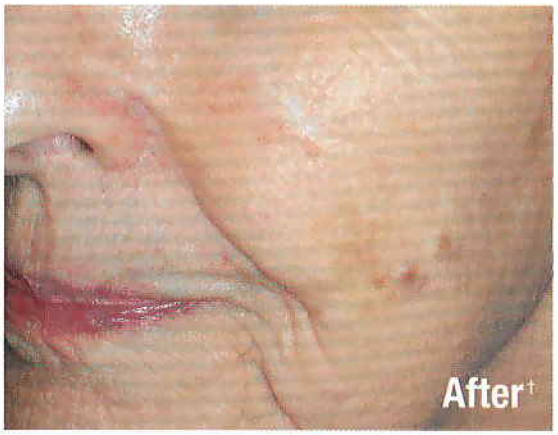
CRYOTHERAPY to treat defined AK lesions and

Rx Only SOLARAZE® GEL to treat the field of lesions you can't see or feel

Diclofenac Sodium-3%

- Field damage is defined by the presence of one or more areas consisting of epithelial cells that have genetic alterations.
- These areas, likely prone to sun damage, provide a fertile environment for the development of genetically altered cells.
- "Treat the Field" is the successful operative removal of obvious actinic keratoses, enhanced by treating the source of the lesions after cryotherapy with Solaraze® Gel to eliminate the potential for additional AK development or recurrence.





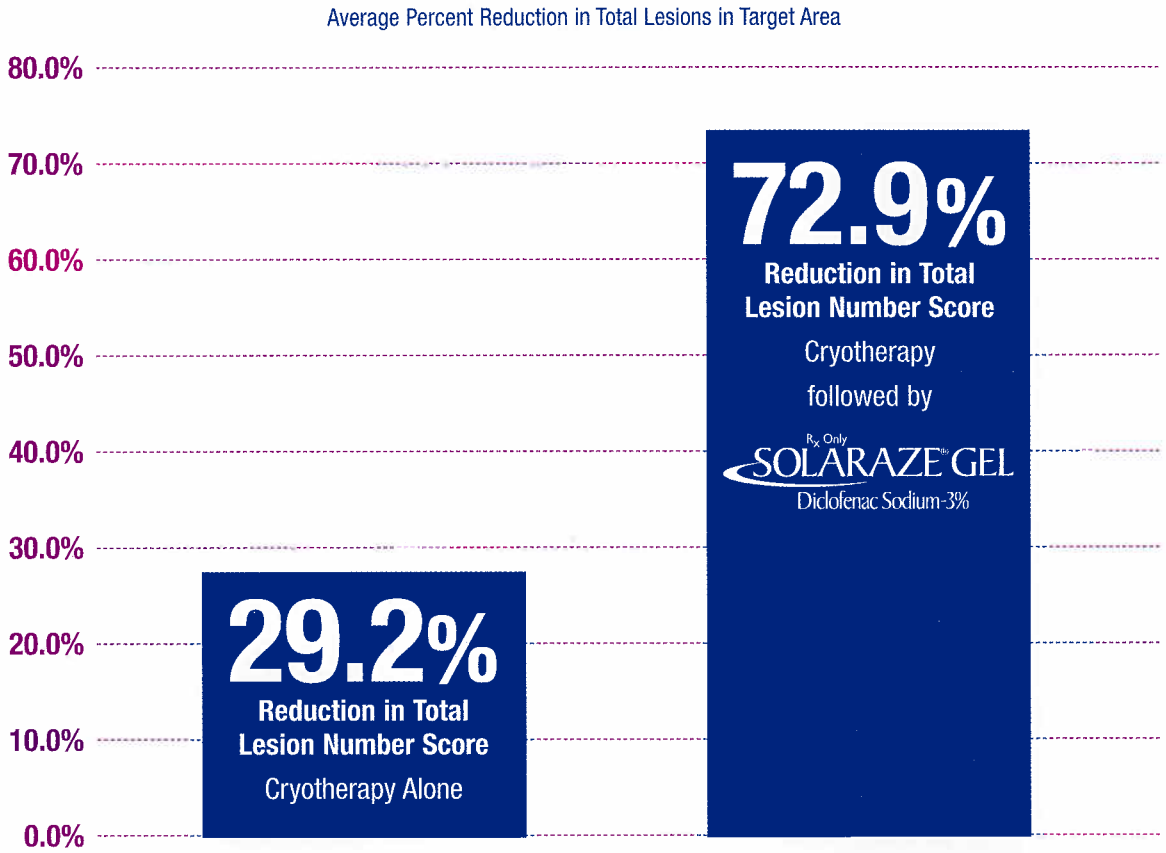
* Cover photographs are unretouched images of the same patient depicting results achieved after cryotherapy with two weeks healing, followed by 90 day treatment with Solaraze® Gel. Individual results may vary.

† Above photographs are unretouched images of the same patient depicting results achieved after cryotherapy with two weeks healing, followed by 90 day treatment with Solaraze® Gel. Individual results may vary.

Solaraze® Gel is indicated for the topical treatment of actinic keratosis (AK).

An investigation conducted by Mark Lebwohl, MD and Joshua Zeichner, MD, Department of Dermatology, Mount Sinai School of Medicine, New York to evaluate a sequential approach to AK therapy by "treating the field"

- An assessment of the efficacy of cryotherapy alone compared to sequential treatment with Solaraze® Gel (diclofenac sodium-3%) after cryotherapy for the treatment of actinic keratosis.



This study shows:

- **"Treating the Field" utilizing a sequential treatment of Solaraze® Gel subsequent to cryotherapy is likely more effective than cryotherapy alone.**
- **Potential additional effect that Solaraze® Gel may alleviate sub-clinical or mild lesions that may not be treated by cryotherapy alone.**

SUN AVOIDANCE IS INDICATED DURING SOLARAZE® GEL THERAPY. As with other NSAIDs, anaphylactoid reactions may occur in patients without prior exposure to diclofenac. Diclofenac sodium should be given with caution to patients with the aspirin triad. In clinical trials, the most common adverse reactions involved the skin, and included contact dermatitis, rash, dry skin and exfoliation. The majority of these reactions were mild to moderate, and resolved upon discontinuation of therapy. SOLARAZE® GEL should not be applied to open skin wounds, infections, or exfoliative dermatitis.

Please see package insert attached for full Prescribing Information.

TREAT THE FIELD

SEQUENTIAL TREATMENT

"Treating the field" utilizing a sequential treatment of Solaraze® Gel subsequent to cryotherapy is likely more effective than cryotherapy alone.[1]

Mark Lebwohl, MD and Joshua Zeichner, MD, Department of Dermatology, Mount Sinai Medical Center, New York.

[1] Lebwohl M, Zeichner J. Ten patients treated with cryotherapy with two week healing followed by Solaraze® Gel for three months, or cryotherapy alone. Study data compiled December 2005 from: An Assessment of the Safety and Efficacy of Cryotherapy Alone Compared to Sequential Treatment with Solaraze® Gel (diclofenac sodium-3%) After Cryotherapy for the Treatment of Actinic Keratoses. Study conducted at Mount Sinai Medical Center, Department of Dermatology; New York, NY.

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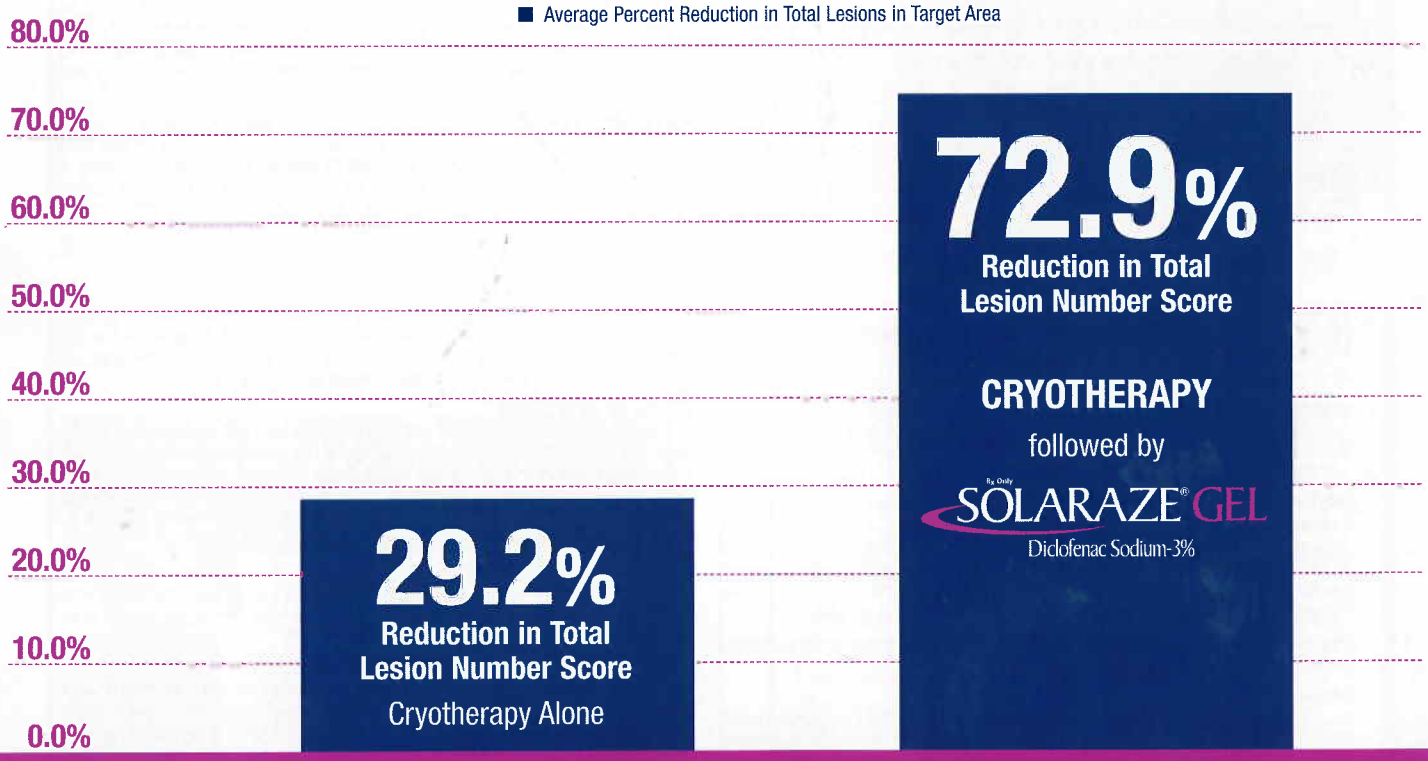
TREAT THE FIELD

CRYOTHERAPY followed by Rx Only SOLARAZE® GEL

Diclofenac Sodium-3%

A recent study showed that for patients with multiple actinic keratosis (AK) lesions, **"Treating the Field"*** utilizing a sequential treatment of ***SOLARAZE® Gel*** subsequent to cryotherapy is likely more effective than cryotherapy alone.[1]



*Field damage is defined by the presence of one or more areas consisting of epithelial cells that have genetic alterations.

Solaraze® Gel is indicated for the topical treatment of actinic keratosis.

SUN AVOIDANCE IS INDICATED DURING SOLARAZE® GEL THERAPY. As with other NSAIDs, anaphylactoid reactions may occur in patients without prior exposure to diclofenac. Diclofenac sodium should be given with caution to patients with the aspirin triad. In clinical trials, the most common adverse reactions involved the skin, and included contact dermatitis, rash, dry skin and exfoliation. The majority of these reactions were mild to moderate, and resolved upon discontinuation of therapy. SOLARAZE® GEL should not be applied to open skin wounds, infections, or exfoliative dermatitis.

Please see package insert on adjacent page for full Prescribing Information.

[1]Lebwohl M, Zeichner J. Ten patients treated with cryotherapy with two week healing followed by Solaraze® Gel for three months, or cryotherapy alone. Study data compiled December 2005 from: An Assessment of the Safety and Efficacy of Cryotherapy Alone Compared to Sequential Treatment with Solaraze® Gel (diclofenac sodium 3%) After Cryotherapy for the Treatment of Actinic Keratoses. Study conducted at Mount Sinai School of Medicine, Department of Dermatology; New York, NY.

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BRIEF SUMMARY

SOLARAZE® GEL

Rx Only

Diclofenac Sodium-3%

FOR DERMATOLOGIC USE ONLY. NOT FOR OPHTHALMIC USE.

INDICATIONS AND USAGE

Solaraze® (diclofenac sodium) Gel is indicated for the topical treatment of actinic keratoses (AK). Sun avoidance is indicated during therapy.

CLINICAL STUDIES

Clinical trials were conducted involving a total of 427 patients (213 treated with Solaraze® and 214 with a gel vehicle). Each patient had no fewer than five AK lesions in a major body area, which was defined as one of five 5 cm x 5 cm regions: scalp, forehead, face, forearm and hand. Up to three major body areas were studied in any patient. All patients were 18 years of age or older (male and female) with no clinically significant medical problems outside of the AK lesions and had undergone a 60-day washout period from disallowed medications (masoprocol, 5-fluorouracil, cyclosporine, retinoids, trichloroacetic acid/lactic acid/peel, 50% glycolic acid peel) and hyaluronan-containing cosmetics. Patients were excluded from participation for reasons of known or suspected hypersensitivity to any Solaraze® ingredient, pregnancy, allergies to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs), or other dermatological conditions which might affect the absorption of the study medication. Application of dermatologic products such as sunscreens, cosmetics, and other drug products was not permitted. Patients were instructed to apply a small amount of Solaraze® Gel (approximately 0.5 g) onto the affected skin, using their fingers, and gently smoothing the gel over the lesion. In addition, all patients were instructed to avoid sun exposure. Complete clearing of the AK lesions 30 days after completion of treatment was the primary efficacy variable. No long-term patient follow-ups, after the 30-day assessments, were performed for the detection of recurrence.

Complete Clearance of Actinic Keratosis Lesions 30 Days Post-Treatment (all locations)

	Solaraze® Gel	Vehicle	p-value
Study 1 90 days treatment	27/58 (47%)	11/59 (19%)	<0.001
Study 2 90 days treatment	18/53 (34%)	10/55 (18%)	0.061
Study 3 60 days treatment	15/48 (31%)	5/49 (10%)	0.021
Study 3 30 days treatment	7/49 (14%)	2/49 (4%)	0.221

CONTRAINDICATIONS

Solaraze® (diclofenac sodium) Gel is contraindicated in patients with a known hypersensitivity to diclofenac, benzyl alcohol, polyethylene glycol monomethyl ether 350 and/or hyaluronate sodium.

WARNINGS

As with other NSAIDs, anaphylactoid reactions may occur in patients without prior exposure to diclofenac. Diclofenac sodium should be given with caution to patients with the aspirin triad.

PRECAUTIONS

General

Solaraze® (diclofenac sodium) Gel should be used with caution in patients with active gastrointestinal ulceration or bleeding and severe renal or hepatic impairments. Solaraze® should not be applied to open skin wounds, infections, or exfoliative dermatitis. It should not be allowed to come in contact with the eyes.

The safety of the concomitant use of sunscreens, cosmetics or other topical medications and Solaraze® is unknown.

Information for Patients

In clinical studies, localized dermal side effects such as contact dermatitis, exfoliation, dry skin and rash were found in patients treated with Solaraze® at a higher incidence than in those with placebo.

If severe dermal reactions occur, treatment with Solaraze® may be interrupted until the condition subsides. Exposure to sunlight and the use of sunlamps should be avoided.

Drug Interactions

Although the systemic absorption of Solaraze® is low, concomitant oral administration of other NSAIDs such as aspirin at anti-inflammatory/analgesic doses should be minimized.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There did not appear to be any increase in drug-related neoplasms following daily topical applications of diclofenac sodium gel for 2 years at concentrations up to 0.035% diclofenac sodium and 2.5% hyaluronate sodium in albino mice.

A photococarcinogenicity study with up to 0.035% diclofenac in the Solaraze® vehicle gel was conducted in hairless mice at topical doses up to 2.8 mg/kg/day. Median tumor onset was earlier in the 0.035% group (Solaraze® contains 3% diclofenac sodium).

Diclofenac was not genotoxic in *in vitro* point mutation assays in mammalian mouse lymphoma cells and Ames microbial test systems, or when tested in mammalian *in vivo* assays including dominant lethal and male germinal epithelial chromosomal studies in mice, and nucleus anomaly and chromosomal aberration studies in Chinese hamsters. It was also negative in the transformation assay utilizing BALB/3T3 mouse embryo cells.

Fertility studies have not been conducted with Solaraze® Gel. Diclofenac sodium showed no evidence of impairment of fertility after oral treatment with 4 mg/kg/day (7 times the estimated systemic human exposure) in male or female rats.

* Based on body surface area and assuming 10% bioavailability following topical application of 2 g Solaraze® Gel per day (1 mg/kg diclofenac sodium).

Pregnancy:

Teratogenic Effects: Pregnancy Category B

The safety of Solaraze® (diclofenac sodium) Gel has not been established during pregnancy. However, reproductive studies performed with diclofenac sodium alone at oral doses up to 20 mg/kg/day (15 times the estimated systemic human exposure*) in mice, 10 mg/kg/day (15 times the estimated systemic human exposure) in rats, and 10 mg/kg/day (30 times the estimated systemic human exposure) in rabbits have revealed no evidence of teratogenicity despite the induction of maternal toxicity. In rats, maternally toxic doses were associated with dystocia, prolonged gestation, reduced fetal weights and growth, and reduced fetal survival.

* Based on body surface area and assuming 10% bioavailability following topical application of 2 g Solaraze® Gel per day (1 mg/kg diclofenac sodium).

Because animal reproduction studies are not always predictive of human response, this drug should not be used during pregnancy unless the benefits to the mother justify the potential risk to the fetus. Because of the risk to the fetus resulting in premature closure of the ductus arteriosus, diclofenac should be avoided in late pregnancy.

Labor and Delivery

The effects of diclofenac on labor and delivery in pregnant women are unknown. Because of the known effects of prostaglandin-inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), use of diclofenac during late pregnancy should be avoided and, as with other nonsteroidal anti-inflammatory drugs, it is possible that diclofenac may inhibit uterine contractions and delay parturition.

Nursing Mothers

Because of the potential for serious adverse reactions in nursing infants from diclofenac sodium, 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.

Pediatric Use

Actinic keratosis is not a condition seen within the pediatric population. Solaraze® should not be used by children.

Geriatric Use

No overall differences in safety or effectiveness were observed between geriatric subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Of the 423 patients evaluable for safety in adequate and well-controlled trials, 211 were treated with Solaraze® drug product and 212 were treated with a vehicle gel. Eighty-seven percent (87%) of the Solaraze®-treated patients (183 patients) and 84% of the vehicle-treated patients (178 patients) experienced one or more adverse events (AEs) during the studies. The majority of these reactions were mild to moderate in severity and resolved upon discontinuation of therapy.

Eighteen percent of Solaraze®-treated patients and 4% of vehicle-treated patients discontinued from the clinical trials due to adverse events (whether considered related to treatment or not). These discontinuations were mainly due to skin irritation or related cutaneous adverse reactions.

OVERDOSAGE

Due to the low systemic absorption of topically-applied Solaraze® Gel, overdosage is unlikely. There have been no reports of ingestion of Solaraze®. In the event of oral ingestion, resulting in significant systemic side effects, it is recommended that the stomach be emptied by vomiting or lavage. Forced diuresis may theoretically be beneficial because the drug is excreted in the urine.

DOSAGE AND ADMINISTRATION

Solaraze® Gel is applied to lesion areas twice daily. It is to be smoothed onto the affected skin gently. The amount needed depends upon the size of the lesion site. Assure that enough Solaraze® Gel is applied to adequately cover each lesion. Normally 0.5 g of gel is used on each 5 cm x 5 cm lesion site. The recommended duration of therapy is from 60 days to 90 days. Complete healing of the lesion(s) or optimal therapeutic effect may not be evident for up to 30 days following cessation of therapy. Lesions that do not respond to therapy should be carefully re-evaluated and management reconsidered.

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