RENOVA®

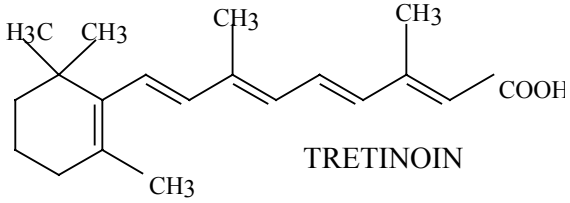
(tretinoin cream)
0.02%

FOR TOPICAL USE ON THE FACE. NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

DESCRIPTION:

RENOVA (tretinoin cream) 0.02% contains the active ingredient tretinoin in a cream base. Tretinoin is a yellow-to-light orange crystalline powder having a characteristic floral odor. Tretinoin is soluble in dimethylsulfoxide, slightly soluble in polyethylene glycol 400, octanol, and 100% ethanol. It is practically insoluble in water and mineral oil, and it is insoluble in glycerin. The chemical name for tretinoin is (all-*E*)-3,7-dimethyl-9- (2,6,6-trimethyl-1-cyclonexen-1-yl)-2,4,6,8-nonatetraenoic acid. Tretinoin is also referred to as all-*trans*-retinoic acid and has a molecular weight of 300.44. The structural formula is represented below.

Tretinoin is available as RENOVA at a concentration of 0.02% w/w% in an oil-in-water emulsion formulation consisting of benzyl alcohol, butylated hydroxytoluene, caprylic/capric triglyceride, cetyl alcohol, edetate disodium, fragrance, methylparaben, propylparaben, purified



TRETINOIN

water, stearic acid, stearyl alcohol, steareth 2, steareth 20, and xanthan gum.

CLINICAL PHARMACOLOGY:

Tretinoin is an endogenous retinoid metabolite of Vitamin A that binds to intracellular receptors in the cytosol and nucleus, but cutaneous levels of tretinoin in excess of physiologic concentrations occur following application of a tretinoin-containing topical drug product. Although tretinoin activates three members of the retinoic acid (RAR) nuclear receptors (RARα, RARβ, and RARγ) which may act to modify gene expression, subsequent protein synthesis, and epithelial cell growth and differentiation, it has not been established whether the clinical effects of tretinoin are mediated through activation of retinoic acid receptors, other mechanisms such as irritation, or both.

The effect of tretinoin on skin with chronic photodamage has not been evaluated in animal studies. When hairless albino mice were treated topically with tretinoin shortly after a period of UVB irradiation, new collagen formation was demonstrated only in photodamaged skin. However, in human skin treated topically, adequate data have not been provided to demonstrate any increase in desmosine, hydroxyproline, or elastin mRNA. Application of 0.1% tretinoin cream to photodamaged human forearm skin was associated with an increase in antibody staining for procollagen I

propeptide. No correlation was made between procollagen I propeptide staining with collagen I levels or with observed clinical effects. Thus, the relationships between the increased collagen in rodents, increased procollagen I propeptide in humans, and the clinical effects of tretinoin have not yet been clearly defined.

Tretinoin was shown to enhance UV-stimulated melanogenesis in pigmented mice. Generalized amyloid deposition in the basal layer of tretinoin-treated skin was noted in a two-year mouse study. In a different study, hyalinization at tretinoin-treated skin sites was noted at doses beginning at 0.25 mg/kg in CD-1 mice.

The transdermal absorption of tretinoin from various topical formulations ranged from 1% to 31% of applied dose, depending on whether it was applied to healthy skin or dermatitic skin. No percutaneous absorption study was conducted with RENOVA 0.02% in human volunteers. When percutaneous absorption of the oil-in-water emulsion formulation at 0.05% concentration was assessed in healthy male subjects with radiolabeled cream after a single application (n=7), as well as after repeated daily applications (n=7) for 28 days, the absorption of tretinoin was less than 2% and the extent of bioavailability was less after repeated application. No significant difference in endogenous concentrations of tretinoin was observed between single and repeated daily applications.

INDICATIONS AND USAGE:

(To understand fully the indication for this product, please read the entire INDICATIONS AND USAGE section of the labeling.)

RENOVA (tretinoin cream) 0.02% is indicated as an adjunctive agent (see second bullet point below) for use in the mitigation (palliation) of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs. **RENOVA DOES NOT ELIMINATE WRINKLES, REPAIR SUN-DAMAGED SKIN, REVERSE PHOTOAGING, or RESTORE MORE YOUTHFUL or YOUNGER SKIN.** In double-blinded, vehicle-controlled clinical studies, many patients in the vehicle group achieved desired palliative effects on fine wrinkling of facial skin with the use of comprehensive skin care and sunlight avoidance programs including sunscreens, protective clothing, and non-prescription emollient creams.

- RENOVA 0.02% has NOT DEMONSTRATED A MITIGATING EFFECT on significant signs of chronic sunlight exposure such as coarse or deep wrinkling, tactile roughness, mottled hyperpigmentation, lentigines, telangiectasia, skin laxity, keratinocytic atypia, melanocytic atypia, or dermal elastosis

- RENOVA should be used under medical supervision as an adjunct to a comprehensive skin care and sunlight avoidance program that includes the use of effective sunscreens (minimum SPF of 15) and protective clothing.

- Patients with visible actinic keratoses and patients with a history of skin cancer were excluded from clinical trials of RENOVA 0.02%. Thus the effectiveness and safety of RENOVA 0.02% in these populations are not known at this time.

- Neither the safety nor the effectiveness of RENOVA for the prevention or treatment of actinic keratoses or skin neoplasms has been established.

- Neither the safety nor the efficacy of using RENOVA 0.02% daily for greater than 52 weeks has been established, and daily use beyond 52 weeks has not been systematically and histologically investigated in adequate and well-controlled trials. (See **WARNINGS** section.)

Clinical Trials:

Four adequate and well-controlled multi-center trials and one single-center randomized, controlled trial were conducted involving a total of 324 evaluable patients treated with RENOVA 0.02% and 332 evaluable patients treated with the vehicle cream on the face for 24 weeks with a comprehensive skin care and sun avoidance program, to assess the effects on fine and coarse wrinkling, mottled hyperpigmentation, tactile skin roughness, and laxity. Patients were evaluated at baseline on a 10 unit scale and changes from that baseline rating were categorized as follows:

Worsening:	Increase of 1 unit or more.
No improvement:	No change.
Minimal improvement:	Reduction of 1 unit.
Mild improvement:	Reduction of 2 units.
Moderate improvement:	Reduction of 3 units or more.

In these trials, the fine and coarse wrinkling, mottled hyperpigmentation, tactile roughness, and laxity of the facial skin were thought to be caused by multiple factors which included intrinsic aging or environmental factors, such as chronic sunlight exposure.

Two of the five trials provided adequate demonstration of efficacy for mitigation of fine facial wrinkling. No two of the five trials adequately demonstrated efficacy for mitigation of coarse wrinkling, mottled hyperpigmentation, tactile skin roughness, and laxity. Data for fine wrinkling (the indication for which RENOVA 0.02% demonstrated efficacy) from all five trials (four studies in lightly pigmented subjects with Fitzpatrick Skin Types I-III and one study in darkly pigmented subjects with Fitzpatrick Skin Types IV-VI) is provided below:

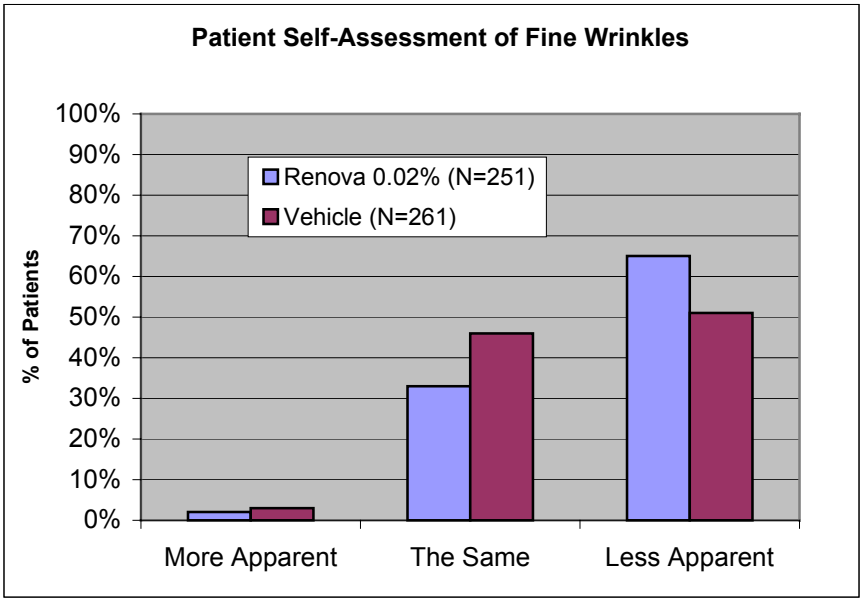
FINE WRINKLING IN LIGHTLY PIGMENTED SUBJECTS		
	Subjects using RENOVA 0.02% + CSP* (N = 279)	Vehicle + CSP* (N = 280)
Worsened	1%	3%
No Change	40%	58%
Minimal Improvement	35%	27%
Mild Improvement	15%	9%
Moderate Improvement	10%	3%

A single-center study (N = 107) in darkly pigmented, mostly African-American, subjects with Fitzpatrick Skin Types IV-VI demonstrated minimal or mild improvement in fine

facial wrinkling in 43% of patients using Vehicle + CSP* compared to 29% of subjects using RENOVA 0.02% + CSP*. Although fewer darkly pigmented subjects improved with RENOVA 0.02% than with vehicle, these findings may reflect the small size of this study.

* CSP = Comprehensive skin protection and sunlight avoidance programs including use of sunscreens, protective clothing, and non-prescription emollient creams.

Self-assessment of fine wrinkles after 24 weeks of treatment with either RENOVA 0.02% or Vehicle from the four studies in lightly pigmented patients showed the following:



No studies have been conducted comparing the facial irritation or efficacy of RENOVA 0.02% to RENOVA 0.05% (older marketed formulation).

Patients may lose some of the mitigating effects of RENOVA 0.02% after 12 weeks of discontinuation of RENOVA 0.02% from their comprehensive skin care and sunlight avoidance program.

CONTRAINDICATIONS:

This drug is contraindicated in individuals with a history of sensitivity reactions to any of its components. It should be discontinued if hypersensitivity to any of its ingredients is noted.

WARNINGS:

- RENOVA 0.02% is a dermal irritant, and the results of continued irritation of the skin for greater than 52 weeks in chronic use with RENOVA are not known. There is evidence of atypical changes in melanocytes and keratinocytes and of increased dermal elastosis in some patients treated with RENOVA 0.05% for longer than 48 weeks. The significance of these findings and their relevance for RENOVA 0.02% are unknown.

- RENOVA 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.

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of RENOVA because of heightened sunburn susceptibility. Patients should be warned to use sunscreens (minimum SPF of 15) and protective clothing when using RENOVA. Patients with sunburn should be advised not to use RENOVA until fully recovered. Patients who may have considerable sun exposure, e.g., due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using RENOVA and follow the precautions outlined in the Patient Package Insert.

RENOVA should be kept out of the eyes, mouth, angles of the nose, and mucous membranes. Topical use may cause severe local erythema, pruritus, burning, stinging, and peeling at the site of application. If the degree of local irritation warrants, patients should be directed to use less medication, decrease the frequency of application, discontinue use temporarily, or discontinue use altogether and consider additional appropriate therapy.

Tretinoin has been reported to cause severe irritation on eczematous skin and should be used only with caution in patients with this condition.

Application of larger amounts of medication than recommended has not been shown to lead to more rapid or better results, and marked redness, peeling, or discomfort may occur.

PRECAUTIONS:

General: RENOVA should be used only as an adjunct to a comprehensive skin care and sunlight avoidance program. (See **INDICATIONS AND USAGE** section.)

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

Weather extremes, such as wind or cold, may be more irritating to patients using tretinoin-containing products.

Information for Patients: RENOVA 0.02% is to be used as described below unless otherwise directed by your physician:

1. It is for use on the face.
2. Avoid contact with the eyes, ears, nostrils, angles of the nose, and mouth. RENOVA may cause severe redness, itching, burning, stinging, and peeling if used on these areas.
3. In the evening, gently wash your face with a mild soap. Pat skin dry and wait 20-30 minutes before applying RENOVA. Apply only a small pearl-sized (about 1/4 inch or 5 millimeter diameter) amount of RENOVA to your face at one time. This should be enough to cover the entire affected area lightly.

4. Do not wash your face for at least one hour after applying RENOVA.
5. For best results, you are advised not to apply another skin care product or cosmetic for at least one hour after applying RENOVA.
6. In the morning, apply a moisturizing sunscreen, SPF 15 or greater.
7. RENOVA is a serious medication. Do not use RENOVA if you are pregnant or attempting to become pregnant. If you become pregnant while using RENOVA, please contact your physician immediately.
8. Avoid sunlight and other medicines that may increase your sensitivity to sunlight.
9. RENOVA does not remove wrinkles or repair sun-damaged skin.

Please refer to the Patient Package Insert for additional patient information.

Drug Interactions: Concomitant topical medications, medicated or abrasive soaps, shampoos, cleansers, cosmetics with a strong drying effect, products with high concentrations of alcohol, astringents, spices or lime, permanent wave solutions, electrolysis, hair depilatories or waxes, and products that may irritate the skin should be used with caution in patients being treated with RENOVA because they may increase irritation with RENOVA.

RENOVA 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.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 91-week dermal study in which CD-1 mice were administered 0.017% and 0.035% formulations of tretinoin, cutaneous squamous cell carcinomas and papillomas in the treatment area were observed in some female mice. These concentrations are near the tretinoin concentration of this clinical formulation (0.02%). A dose-related incidence of liver tumors in male mice was observed at those same doses. The maximum systemic doses associated with the 0.017% and 0.035% formulations are 0.5 and 1.0 mg/kg/day. These doses are 10 and 20 times the maximum human systemic dose, when adjusted for total body surface area. The biological significance of these findings is not clear because they occurred at doses that exceeded the dermal maximally tolerated dose (MTD) of tretinoin and because they were within the background natural occurrence rate for these tumors in this strain of mice. There was no evidence of carcinogenic potential when 0.025 mg/kg/day of tretinoin was administered topically to mice (0.5 times the maximum human systemic dose, adjusted for total body surface area). For purposes of comparisons of the animal exposure to systemic human exposure, the maximum human systemic dose is defined as 1 gram of 0.02% RENOVA applied daily to a 50 kg person (0.004 mg tretinoin/kg body weight).

Studies in hairless albino mice suggest that concurrent exposure to tretinoin may enhance the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar simulator. This effect has been confirmed in a later study in pigmented mice, and dark pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05% tretinoin. Although the significance of these studies to humans is not clear, patients should minimize exposure to sunlight or artificial ultraviolet irradiation sources.

The mutagenic potential of tretinoin was evaluated in the Ames assay and in the *in vivo* mouse micronucleus assay, both of which were negative.

In dermal Segment I fertility studies in rats, slight (not statistically significant) decreases in sperm count and motility were seen at 0. 5 mg/kg/day (20 times the maximum human systemic dose adjusted for total body surface area), and slight (not statistically significant) increases in the number and percent of nonviable embryos in females treated with 0.25 mg/kg/day (10 times the maximum human systemic dose adjusted for total body surface area) and above were observed. A dermal Segment III study with RENOVA has not been performed in any species. In oral Segment I and Segment III

studies in rats with tretinoin, decreased survival of neonates and growth retardation were observed at doses in excess of 2 mg/kg/day (83 times the human topical dose adjusted for total body surface area).

Pregnancy:

Teratogenic effects: Pregnancy Category C.

ORAL tretinoin has been shown to be teratogenic in rats, mice, rabbits, hamsters, and subhuman primates. It was teratogenic and fetotoxic in Wistar rats when given orally or topically in doses greater than 1 mg/kg/day (42 times the maximum human systemic dose normalized for total body surface area). However, variations in teratogenic doses among various strains of rats have been reported. In the cynomolgus monkey, which, metabolically, is closer to humans for tretinoin than the other species examined, fetal malformations were reported at doses of 10 mg/kg/day or greater, but none were observed at 5 mg/kg/day (417 times the maximum human systemic dose adjusted for total body surface area), although increased skeletal variations were observed at all doses. A dose-related increase in embryolethality and abortion was reported. Similar results have also been reported in pigtail macaques.

TOPICAL tretinoin in animal teratogenicity tests has generated equivocal results. There is evidence for teratogenicity (shortened or kinked tail) of topical tretinoin in Wistar rats at doses greater than 1 mg/kg/day (42 times the maximum human systemic dose adjusted for total body surface area). Anomalies (humerus: short 13%, bent 6%, os parietal incompletely ossified 14%) have also been reported when 10 mg/kg/day was dermally applied.

There are other reports in New Zealand White rabbits administered doses of greater than 0.2 mg/kg/day (17 times the maximum human systemic dose adjusted for total body surface area) of an increased incidence of domed head and hydrocephaly, typical of retinoid-induced fetal malformations in this species.

In contrast, several well-controlled animal studies have shown that dermally applied tretinoin may be fetotoxic, but not overtly teratogenic, in rats and rabbits at doses of 1.0 and 0.5 mg/kg/day, respectively (42 times the maximum human systemic dose adjusted for total body surface area in both species).

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 human cases of temporally-associated congenital malformations have been reported during two decades of clinical use of another formulation of topical tretinoin (Retin-A). Although no definite pattern of teratogenicity and no causal association has 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 the fetus is not known.

Non-teratogenic effects:

Dermal tretinoin has been shown to be fetotoxic in rabbits when administered 0.5 mg/kg/day (42 times the maximum human systemic dose normalized for total body surface area). Oral tretinoin has been shown to be fetotoxic, resulting in skeletal variations and increased intrauterine death, in rats when administered 2.5 mg/kg/day (104 times the maximum human systemic dose adjusted for total body surface area).

There are, however, no adequate and well-controlled studies in pregnant women. RENOVA should not be used during pregnancy.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Since many drugs are excreted in human milk, mitigation of fine facial wrinkles with RENOVA 0.02% may be postponed in nursing mothers until after completion of the nursing period.

Pediatric Use: Safety and effectiveness in patients less than 18 years of age have not been established.

Geriatric Use: In clinical studies with RENOVA 0.02%, patients aged 65 to 71 did not demonstrate a significant difference for improvement in fine wrinkling when compared to patients under the age of 65. Patients aged 65 and over may demonstrate slightly more irritation, although the differences were not statistically significant in the clinical studies for RENOVA 0.02%. Safety and effectiveness of RENOVA 0.02% in individuals older than 71 years of age have not been established.

ADVERSE REACTIONS:

(See **WARNINGS** and **PRECAUTIONS** sections.)

In double-blind, vehicle-controlled studies involving 339 patients who applied RENOVA 0.02% to their faces, adverse reactions associated with the use of RENOVA were limited primarily to the skin. Almost all patients reported one or more local reactions such as peeling, dry skin, burning, stinging, erythema, and pruritus. In 24% of all study patients, skin irritation was reported that was either severe (about 7%), led to temporary discontinuation of RENOVA 0.02% (about 20%), or led to use of a mild topical corticosteroid. About 5% of patients using RENOVA 0.02%, compared to less than 1% of the control patients, had sufficiently severe local irritation to warrant short-term use of mild topical corticosteroids to alleviate local irritation. About 4% of patients had to discontinue use of RENOVA because of adverse reactions.

Approximately 2% of spontaneous post-marketing adverse event reporting for RENOVA 0.05% were for skin hypo- or hyperpigmentation. Other spontaneously reported adverse events for RENOVA 0.05% predominantly appear to be local reactions similar to those seen in clinical trials.

OVERDOSAGE:

Application of larger amounts of medication than recommended has not been shown to lead to more rapid or better results, and marked redness, peeling, or discomfort may occur. Oral ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

DOSAGE AND ADMINISTRATION:

- Do NOT use RENOVA if the patient is pregnant or is attempting to become pregnant or is at high risk of pregnancy,
- Do NOT use RENOVA if the patient is sunburned or if the patient has eczema or other chronic skin conditions of the face,
- Do NOT use RENOVA if the patient is inherently sensitive to sunlight,
- Do NOT use RENOVA if the patient is also taking drug(s) known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the possibility of augmented phototoxicity.

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 Package Insert.

RENOVA should be applied to the face once a day in the evening, using only enough to cover the entire affected area lightly. Patients should gently wash their faces with a mild soap, pat the skin dry, and wait 20 to 30 minutes before applying RENOVA. The patient should apply a small pearl-sized (about ¼ inch or 5 millimeter diameter) amount of cream to cover the entire affected area lightly. Caution should be taken when applying the cream to avoid the eyes, ears, nostrils, and mouth.

Application of RENOVA may cause a transitory feeling of warmth or slight stinging.

Mitigation (palliation) of fine facial wrinkling may occur gradually over the course of therapy. Up to six months of therapy may be required before the effects are seen.

With discontinuation of RENOVA therapy, some patients may lose the mitigating effects of RENOVA on fine facial wrinkles. **The safety and effectiveness of using RENOVA 0.02% daily for greater than 52 weeks have not been established.**

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

Patients treated with RENOVA may use cosmetics but the areas to be treated should be cleansed before the medication is applied. (See **PRECAUTIONS** section.)

HOW SUPPLIED:

RENOVA® (tretinoin cream), 0.02% is available in tubes containing 40 grams (NDC 0062-0187-02).

Storage: Store at 25° (77°F), excursions permitted to 15-30°C (59°–86°F).

QUESTIONS: Physicians and Pharmacists can call 1-800-426-7762, from 8:30 a.m. to 4:30 p.m. Eastern Time, Monday through Friday.

Rx only.

Ortho Dermatological
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RENOVA® (reh-NO-vah)
Generic Name: Tretinoin Cream (0.02%)
Use only on the Face

Read this leaflet carefully before you start to use your medicine. Read the information you get every time you get more medicine. There may be new information about the drug. This leaflet does not take the place of talks with your doctor. It is important for you to talk with your doctor about how to use RENOVA for the best results and how to reduce side effects.

What is the Most Important Information about RENOVA?

RENOVA is a serious medicine. **Do not use RENOVA if you are pregnant or attempting to become pregnant.** If you become pregnant while using RENOVA, please contact your doctor immediately.

Avoid sunlight and other medicines that may increase your sensitivity to sunlight (See "Who should not use RENOVA?").

RENOVA 0.02% does **not** remove wrinkles or repair sun-damaged skin. (See "What is RENOVA?" for more details.)

What is RENOVA?

RENOVA 0.02% is a prescription medicine that may reduce fine facial wrinkles. It is for patients who are using a total skin care and sunlight avoidance program. RENOVA does not remove wrinkles or repair sun-damaged skin. RENOVA does not work for everyone who uses it. It may work better for some patients than for others.

RENOVA should be used only under the guidance of your doctor as part of a sunlight avoidance and total skin care program. This program should include avoiding sunlight as much as possible, using clothing to protect you from sunlight, using sunscreens with a minimum SPF of 15, and using face creams that add moisture to the skin.

When you use RENOVA, you will not see improvement right away. Generally, you may notice some effects in 3 to 4 months. If RENOVA treatment is stopped, the improvement may gradually disappear.

The use of RENOVA 0.02% in patients for more than 52 weeks has not been studied. Therefore, it is not known if RENOVA 0.02% is safe or works if used longer than 52 weeks. In a study in people with medium to dark skin color, RENOVA 0.02% has not demonstrated a benefit over a sunlight avoidance program and total skin care. RENOVA 0.02% has not been studied in people with visible actinic keratoses or in people with a history of skin cancer.

Who should not use RENOVA?

Do not use RENOVA if:

- you are pregnant or plan to become pregnant. If you become pregnant while using RENOVA, please contact your doctor immediately.
- you are sunburned or your skin is irritated
- you are highly sensitive to sunlight
- you are allergic to any of the ingredients in RENOVA. The active ingredient is tretinoin. Ask your doctor or pharmacist about the inactive ingredients.

RENOVA can cause increased skin irritation and increased chance of sunburn.

Tell your doctor if you have any skin condition. RENOVA may not be right for you.

Because RENOVA may make your skin more likely to burn from sunlight, tell your doctor if you are using other medicines that increase sensitivity to sunlight. You should not use RENOVA with such medicines. These include, but are not limited to:

- thiazides (to treat high blood pressure)
- tetracyclines, fluoroquinolones, sulfonamides (to treat infection)
- phenothiazines (to treat serious emotional problems)

If you are taking any prescription or non-prescription medicines, check with your doctor to make sure you can use RENOVA with them.

We do not know if RENOVA is passed to infants through breast milk. Therefore, tell your doctor if you are breast feeding.

How should I use RENOVA?

Use RENOVA as part of a total skin care and sun avoidance program. Follow your doctor's instructions on how to use RENOVA. RENOVA is usually applied to the face once a day in the evening, following the 3 steps listed below:

1. Gently wash your face with a mild soap.
2. Pat the skin dry and wait 20-30 minutes before applying RENOVA.
3. Apply only a small pearl-sized amount (about ¼ inch or 5 mm diameter) of RENOVA to the face at one time. It should be enough to cover your affected area lightly.

Be especially careful when applying RENOVA to avoid your eyes, ears, nostrils, angles of the nose, and mouth. RENOVA may cause severe redness, itching, burning, stinging, and peeling if used on these areas.

Using too much RENOVA may increase discomfort and skin redness and peeling.

You may use cosmetics one hour after applying RENOVA. If you do, be sure to clean your face before applying RENOVA again. Skin moisturizers should be used at least every morning to protect the treated areas from dryness.

Use sunscreen and wear protective clothing to protect the treated areas from sunlight. If you sunburn easily, or if you spend a lot of time exposed to sunlight, be especially careful to protect your skin.

What should I avoid while using RENOVA?

RENOVA can make your treated skin more sensitive to sunlight. Therefore, keep out of the sunlight as much as possible and do not use sunlamps. Avoid as much as possible products that can increase skin irritation, such as:

- other skin medicines
- medicated or abrasive (rough) soaps
- permanent wave solutions
- chemical hair removers or waxes
- electrolysis
- products with alcohol, spices, astringents, or lime
- cleansers, shampoos, or cosmetics with a strong drying effect
- other products that may irritate your skin

What are the possible side effects of RENOVA?

You may feel brief warmth or stinging on your skin after you use RENOVA. Most patients report peeling, dry skin, burning, stinging, itching, and redness,. These are usually mild to moderate and occur early in treatment. Contact your doctor if the side effects are a problem.

General advice about prescription medicines

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Only use RENOVA to treat the condition that your doctor has prescribed it for. Do not give RENOVA to other people. It may harm them.

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

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/s/

Jonathan Wilkin
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