

RENOVA[®]

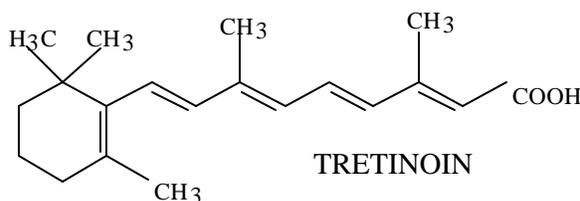
(tretinoin cream)

0.05%

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

DESCRIPTION:

RENOVA (tretinoin cream) 0.05% 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-cyclohexen-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 0.05% w/w in a water-in-oil emulsion formulation consisting of butylated hydroxytoluene, citric acid monohydrate, dimethicone 50 cs, edetate disodium, fragrance, hydroxyoctacosanyl hydroxystearate, light mineral oil, methoxy PEG-22/dodecyl glycol copolymer, methylparaben, PEG-45/dodecyl glycol copolymer, purified water, quaternium-15, stearyoxytrimethylsilane and stearyl alcohol, and sorbitol solution.

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 (RAR α , RAR β , and RAR γ) 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.

1 The effect of tretinoin on skin with chronic photodamage has not been evaluated in animal
2 studies. When hairless albino mice were treated topically with tretinoin shortly after a
3 period of UVB irradiation, new collagen formation was demonstrated only in
4 photodamaged skin. However, in human skin treated topically, adequate data have not
5 been provided to demonstrate any increase in desmosine, hydroxyproline, or elastin
6 mRNA. Application of 0.1% tretinoin cream to photodamaged human forearm skin was
7 associated with an increase in antibody-staining for procollagen I propeptide. No
8 correlation was made between procollagen I propeptide staining with collagen I levels or
9 with observed clinical effects. Thus, the relationships between the increased collagen in
10 rodents, increased procollagen I propeptide in humans, and the clinical effects of tretinoin
11 have not yet been clearly defined.

12
13 Tretinoin was shown to enhance UV stimulated melanogenesis in pigmented mice.
14 Generalized amyloid deposition in the basal layer of tretinoin treated skin was noted in a
15 two year mouse study. In a different study, hyalinization at tretinoin treated skin sites was
16 noted at doses beginning at 0.25 mg/kg in CD-1 mice.

17
18 The transdermal absorption of tretinoin from various topical formulations ranged from 1%
19 to 31% of applied dose, depending on whether it was applied to healthy skin or dermatitic
20 skin. When percutaneous absorption of RENOVA 0.05% was assessed in healthy male
21 subjects (n=14) after a single application, as well as after repeated daily applications for
22 28 days, the absorption of tretinoin was less than 2% and endogenous concentrations of
23 tretinoin and its major metabolites were unaltered.

24
25

26 **INDICATIONS AND USAGE:**

27

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

30

31 RENOVA (tretinoin cream) 0.05% is indicated as an adjunctive agent (see second bullet
32 point below) for use in the mitigation (palliation) of fine wrinkles, mottled
33 hyperpigmentation, and tactile roughness of facial skin in patients who use comprehensive
34 skin care and sunlight avoidance programs (see bullet point 3 for populations in which
35 effectiveness has not been established). **RENOVA DOES NOT ELIMINATE**
36 **WRINKLES, REPAIR SUN DAMAGED SKIN, REVERSE PHOTOAGING, or**
37 **RESTORE MORE YOUTHFUL or YOUNGER SKIN.** In double-blinded, vehicle-
38 controlled clinical studies, many patients in the vehicle group achieved desired palliative
39 effects on fine wrinkling, mottled hyperpigmentation, and tactile roughness of facial skin
40 with the use of comprehensive skin care and sunlight avoidance programs including
41 sunscreens, protective clothing, and non-prescription emollient creams.

42

- 1 • RENOVA 0.05% has NOT DEMONSTRATED A MITIGATING EFFECT on significant
2 signs of chronic sun exposure such as coarse or deep wrinkling, skin yellowing,
3 lentigines, telangiectasia, skin laxity, keratinocytic atypia, melanocytic atypia, or
4 dermal elastosis.
5
- 6 • RENOVA should be used under medical supervision as an adjunct to a
7 comprehensive skin care and sunlight avoidance program that includes the use of
8 effective sunscreens (minimum SPF of 15) and protective clothing when desired
9 results on fine wrinkles, mottled hyperpigmentation, and roughness of facial skin have
10 not been achieved with a comprehensive skin care and sunlight avoidance program
11 alone.
12
- 13 • The effectiveness of RENOVA 0.05% in the mitigation of fine wrinkles, mottled
14 hyperpigmentation, and tactile roughness of facial skin has not been established in
15 people greater than 50 years of age OR in people with moderately to heavily
16 pigmented skin. In addition, patients with visible actinic keratoses and patients with a
17 history of skin cancer were excluded from clinical trials of RENOVA 0.05%. Thus the
18 effectiveness and safety of RENOVA 0.05% in these populations are not known at this
19 time.
20
- 21 • Neither the safety nor the effectiveness of RENOVA for the prevention or treatment of
22 actinic keratoses or skin neoplasms has been established.
23
- 24 • Neither the safety nor the efficacy of using RENOVA 0.05% daily for greater than 48
25 weeks has been established, and daily use beyond 48 weeks has not been
26 systematically and histologically investigated in adequate and well-controlled trials.
27 (See **WARNINGS** section.)
28
29

30 **CLINICAL TRIALS:**

31
32 Two adequate and well-controlled trials were conducted involving a total of 161 evaluable
33 patients (under 50 years of age) treated with RENOVA 0.05% and 154 evaluable patients
34 treated with the vehicle cream on the face for 24 weeks as an adjunct to a comprehensive
35 skin care and sun avoidance program, to assess the effects on fine wrinkling, mottled
36 hyperpigmentation, and tactile skin roughness. Patients were evaluated at baseline on a
37 10 point scale and changes from that baseline rating were categorized as follows:
38

39 No Improvement: No change or an increase of 1 unit or more.
40 Minimal Improvement: Reduction of 1 unit.
41 Moderate Improvement: Reduction of 2 units or more.
42

- 1 In these trials, the fine wrinkles, mottled hyperpigmentation, and tactile roughness of the
- 2 facial skin were thought to be caused by multiple factors which included intrinsic aging or
- 3 environmental factors, such as chronic sunlight exposure.
- 4
- 5 The results of these assessments are as follows:

1

FINE WRINKLING			
	NO IMPROVEMENT	MINIMAL IMPROVEMENT	MODERATE IMPROVEMENT
RENOVA 0.05% + CSP*	36%	40%	24%
Vehicle + CSP	62%	30%	8%

2

MOTTLED HYPERPIGMENTATION			
	NO IMPROVEMENT	MINIMAL IMPROVEMENT	MODERATE IMPROVEMENT
RENOVA 0.05% + CSP	35%	27%	38%
Vehicle + CSP	53%	21%	27%

3

TACTILE SKIN ROUGHNESS			
	NO IMPROVEMENT	MINIMAL IMPROVEMENT	MODERATE IMPROVEMENT
RENOVA 0.05% + CSP	49%	35%	16%
Vehicle + CSP	67%	23%	10%

4 * CSP = Comprehensive skin protection and sun avoidance programs included
5 use of sunscreens, protective clothing, and non-prescription emollient creams.

6

7 Most of the improvement in these signs was noted during the first 24 weeks of therapy.
8 Thereafter, therapy primarily maintained the improvement realized during the first 24
9 weeks.

10

11 A majority of patients will lose most mitigating effects of RENOVA 0.05% on fine wrinkles,
12 mottled hyperpigmentation, and tactile roughness of facial skin with discontinuation of a
13 comprehensive skin care and sun avoidance program including RENOVA 0.05%;
14 however, the safety and effectiveness of using RENOVA 0.05% daily for greater than 48
15 weeks have not been established.

16

17

18 **CONTRAINDICATIONS:**

1
2 This drug is contraindicated in individuals with a history of sensitivity reactions to any of its
3 components. It should be discontinued if hypersensitivity to any of its ingredients is noted.
4

5
6 **WARNINGS:**
7

- 8 • RENOVA is a dermal irritant, and the results of continued irritation of the skin for
9 greater than 48 weeks in chronic use with RENOVA are not known. There is evidence
10 of atypical changes in melanocytes and keratinocytes, and of increased dermal
11 elastosis in some patients treated with RENOVA for longer than 48 weeks. The
12 significance of these findings is unknown.
13
14 • Safety and effectiveness of RENOVA 0.05% in individuals with moderately or heavily
15 pigmented skin have not been established.
16
17 • RENOVA should not be administered if the patient is also taking drugs known to be
18 photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines,
19 sulfonamides) because of the possibility of augmented phototoxicity.
20

21 Exposure to sunlight (including sunlamps) should be avoided or minimized during use of
22 RENOVA because of heightened sunburn susceptibility. Patients should be warned to use
23 sunscreens (minimum SPF of 15) and protective clothing when using RENOVA. Patients
24 with sunburn should be advised not to use RENOVA until fully recovered. Patients who
25 may have considerable sun exposure, e.g., due to their occupation, and those patients with
26 inherent sensitivity to sunlight should exercise caution when using RENOVA and follow the
27 precautions outlined in the Patient Package Insert.
28

29 RENOVA should be kept out of the eyes, mouth, angles of the nose, and mucous
30 membranes. Topical use may cause severe local erythema, pruritus, burning, stinging, and
31 peeling at the site of application. If the degree of local irritation warrants, patients should
32 be directed to use less medication, decrease the frequency of application, discontinue use
33 temporarily, or discontinue use altogether, and consider additional appropriate therapy.
34

35 Tretinoin has been reported to cause severe irritation on eczematous skin and should be
36 used only with caution in patients with this condition.
37

38 Application of larger amounts of medication than recommended has not been shown to
39 lead to more rapid or better results, and marked redness, peeling, or discomfort may
40 occur.
41

42
43 **PRECAUTIONS:**

1
2 **General:** RENOVA should be used only as an adjunct to a comprehensive skin care and
3 sunlight avoidance program. (See **INDICATIONS AND USAGE** section.)
4

5 If a drug sensitivity, chemical irritation, or a systemic adverse reaction develops, use of
6 RENOVA should be discontinued.
7

8 Weather extremes, such as wind or cold, may be more irritating to patients using tretinoin
9 containing products.
10

11 **Information for Patients:** RENOVA 0.05% is to be used as described below unless
12 otherwise directed by your physician:
13

- 14 1. It is for use on the face only.
- 15 2. Avoid contact with the eyes, ears, nostrils, angles of the nose, and mouth. RENOVA
16 may cause severe redness, itching, burning, stinging, and peeling if used on these
17 areas.
- 18 3. In the evening, gently wash your face with a mild soap. Pat skin dry and wait 20-30
19 minutes before applying RENOVA. Apply only a pea-sized amount of RENOVA to your
20 face at one time. This should be enough to cover the entire affected area lightly.
- 21 4. Do not wash your face for at least one hour after applying RENOVA.
- 22 5. For best results, you are advised not to apply another skin care product or cosmetic for
23 at least one hour after applying RENOVA.
- 24 6. In the morning, apply a moisturizing sunscreen, SPF 15 or greater.
- 25 7. RENOVA is a serious medication. Do not use RENOVA if you are pregnant or
26 attempting to become pregnant. If you become pregnant while taking RENOVA, please
27 contact your physician immediately.
- 28 8. Avoid sunlight and other medicines that may increase your sensitivity to sunlight.
- 29 9. RENOVA does not remove wrinkles or repair sun-damaged skin.
30

31 Please refer to the Patient Package Insert for additional patient information.
32

33 **Drug Interactions:** Concomitant topical medications, medicated or abrasive soaps,
34 shampoos, cleansers, cosmetics with a strong drying effect, products with high
35 concentrations of alcohol, astringents, spices or lime, permanent wave solutions,
36 electrolysis, hair depilatories or waxes, and products that may irritate the skin should be
37 used with caution in patients being treated with RENOVA because they may increase
38 irritation with RENOVA.
39

40 RENOVA should not be administered if the patient is also taking drugs known to be
41 photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines,
42 sulfonamides) because of the possibility of augmented phototoxicity.
43

1 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 91-week dermal study in
2 which CD-1 mice were administered 0.017% and 0.035% formulations of tretinoin,
3 cutaneous squamous cell carcinomas and papillomas were observed in some female
4 mice. These concentrations are lower than the concentration of tretinoin in the clinical
5 formulation (0.05%). A dose related incidence of liver tumors in male mice was observed
6 at those same doses. The maximum systemic doses associated with 0.017% and 0.035%
7 formulations are 0.5 and 1.0 mg/kg/day. These doses are 4 and 8 times the maximum
8 human systemic dose, when adjusted for total body surface area. The biological
9 significance of the neoplastic findings is not clear because they occurred at doses that
10 exceeded the maximally tolerated dermal dose of tretinoin and because they were within
11 the background natural occurrence rate for these tumors in this strain of mice. There was
12 no evidence of carcinogenic potential when 0.025 mg/kg/day of tretinoin was administered
13 topically to mice (1/5th of the maximum human systemic dose, adjusted for total body
14 surface area). For purposes of comparisons of the systemic animal exposure to the
15 systemic human exposure, the maximum human systemic dose is 1 gram of 0.05%
16 RENOVA applied daily to a 50 kg person (0.01 mg tretinoin/kg body weight, or 0.37 mg/m²
17 total body surface area).

18
19 Studies in hairless albino mice suggest that concurrent exposure to tretinoin may enhance
20 the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar
21 simulator. This effect has been confirmed in a later study in pigmented mice, and dark
22 pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05%
23 tretinoin. Although the significance of these studies in humans is not clear, patients should
24 minimize exposure to sunlight or artificial ultraviolet irradiation sources.

25
26 The mutagenic potential of tretinoin was evaluated in the Ames assay and in the *in vivo*
27 mouse micronucleus assay, both of which were negative.

28
29 In dermal Segment I fertility studies in rats, slight (not statistically significant) decreases in
30 sperm count and motility were seen at 0.5 mg/kg/day (8 times the maximum human
31 systemic dose adjusted for total body surface area), and slight (not statistically significant)
32 increases in the number and percent of nonviable embryos in females treated with 0.25
33 mg/kg/day (4 times the maximum human systemic dose adjusted for total body surface
34 area) and above were observed. A dermal Segment III study with RENOVA has not been
35 performed in any species. In oral Segment I and Segment III studies in rats with tretinoin,
36 decreased survival of neonates and growth retardation were observed at doses in excess
37 of 2 mg/kg/day (>33 times the maximum human systemic dose adjusted for total body
38 surface area).

39
40 **Pregnancy:**

41
42 **Teratogenic effects: Pregnancy Category C.**

43

1 ORAL tretinoin has been shown to be teratogenic in rats, mice, rabbits, hamsters, and
2 subhuman primates. It was teratogenic and fetotoxic in Wistar rats when given orally or
3 topically in doses greater than 1 mg/kg/day (17 times the maximum human systemic dose
4 normalized for total body surface area). However, variations in teratogenic doses among
5 various strains of rats have been reported. In the cynomolgus monkey, which,
6 metabolically, is closer to humans for tretinoin than the other species examined, fetal
7 malformations were reported at doses of 10 mg/kg/day or greater, but none were observed
8 at 5 mg/kg/day (167 times the maximum human systemic dose adjusted for total body
9 surface area), although increased skeletal variations were observed at all doses. A dose-
10 related increase in embryoletality and abortion was reported. Similar results have also
11 been reported in pigtail macaques.

12
13 TOPICAL tretinoin in animal teratogenicity tests has generated equivocal results. There is
14 evidence for teratogenicity (shortened or kinked tail) of topical tretinoin in Wistar rats at
15 doses greater than 1 mg/kg/day (17 times the maximum human systemic dose adjusted for
16 total body surface area). Anomalies (humerus: short 13%, bent 6%, os parietal
17 incompletely ossified 14%) have also been reported when 10 mg/kg/day was dermally
18 applied.

19
20 There are other reports in New Zealand White rabbits administered doses of greater than
21 0.2 mg/kg/day (7 times the maximum human systemic dose adjusted for total body surface
22 area) of an increased incidence of domed head and hydrocephaly, typical of retinoid-
23 induced fetal malformations in this species.

24
25 In contrast, several well-controlled animal studies have shown that dermally applied
26 tretinoin may be fetotoxic, but not overtly teratogenic, in rats and rabbits at doses of 1.0
27 and 0.5 mg/kg/day, respectively (17 times the maximum human systemic dose adjusted for
28 total body surface area in both species).

29
30 With widespread use of any drug, a small number of birth defect reports associated
31 temporally with the administration of the drug would be expected by chance alone. Thirty
32 human cases of temporally-associated congenital malformations have been reported
33 during twenty-five years of clinical use of another formulation of topical tretinoin (Retin-A).
34 Although no definite pattern of teratogenicity and no causal association has been
35 established from these cases, 5 of the reports describe the rare birth defect category
36 holoprosencephaly (defects associated with incomplete midline development of the
37 forebrain). The significance of these spontaneous reports in terms of risk to the fetus is not
38 known.

39 40 **Non-teratogenic effects:**

41
42 Dermal tretinoin has been shown to be fetotoxic in rabbits when administered 0.5
43 mg/kg/day (17 times the human topical dose normalized for total body surface area). Oral

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

4
5 There are, however, no adequate and well-controlled studies in pregnant women.
6 RENOVA should not be used during pregnancy.

7
8 Nursing Mothers: It is not known whether this drug is excreted in human milk. Since many
9 drugs are excreted in human milk, mitigation of fine wrinkles, mottled hyperpigmentation,
10 and tactile roughness on the face with RENOVA may be postponed in nursing mothers until
11 after completion of the nursing period.

12
13 Pediatric Use: Safety and effectiveness in patients less than 18 years of age have not
14 been established.

15
16 Geriatric Use: Clinical studies of RENOVA 0.05% did not include sufficient number of
17 subjects aged 65 and over to determine whether they respond differently from younger
18 subjects. Other reported clinical experience has not identified differences in responses
19 between elderly and younger patients.

20 21 **ADVERSE REACTIONS:**

22
23 (See **WARNINGS** and **PRECAUTIONS** sections.)

24
25 In double-blind, vehicle-controlled studies involving 179 patients who applied RENOVA
26 0.05% to their face, adverse reactions associated with the use of RENOVA 0.05% were
27 limited primarily to the skin. During these trials, 4% of patients had to discontinue use of
28 RENOVA 0.05% because of adverse reactions. These discontinuations were due to skin
29 irritation or related cutaneous adverse reactions.

30
31 Local reactions such as peeling, dry skin, burning, stinging, erythema, and pruritus were
32 reported by almost all subjects during therapy with RENOVA 0.05%. These signs and
33 symptoms were usually of mild to moderate severity and generally occurred early in
34 therapy. In most patients the dryness, peeling, and redness recurred after an initial (24
35 week) decline.

36
37 In spontaneous post-marketing adverse event reporting for RENOVA 0.05%,
38 approximately 2% of those were for skin hypo- or hyperpigmentation. Other spontaneously
39 reported adverse events predominantly appear to be local reactions similar to those seen
40 in clinical trials.

41 42 43 **OVERDOSAGE:**

1
2 Application of larger amounts of medication than recommended has not been shown to
3 lead to more rapid or better results, and marked redness, peeling, or discomfort may
4 occur. Oral ingestion of the drug may lead to the same side effects as those associated
5 with excessive oral intake of Vitamin A.
6

7 8 **DOSAGE AND ADMINISTRATION:**

- 9
- 10 • Do NOT use RENOVA if the patient is pregnant or is attempting to become pregnant or
 - 11 is at high risk of pregnancy,
 - 12 • Do NOT use RENOVA if the patient is sunburned or if the patient has eczema or other
 - 13 chronic skin conditions of the face,
 - 14 • Do NOT use RENOVA if the patient is inherently sensitive to sunlight,
 - 15 • Do NOT use RENOVA if the patient is also taking drug(s) known to be photosensitizers
 - 16 (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because
 - 17 of the possibility of augmented phototoxicity.
- 18

19 Patients require detailed instruction to obtain maximal benefits and to understand all the
20 precautions necessary to use this product with greatest safety. The physician should
21 review the Patient Package Insert.
22

23 RENOVA should be applied to the face once a day in the evening, using only enough to
24 cover the entire affected area lightly. Patients should gently wash their face with a mild
25 soap, pat the skin dry, and wait 20 to 30 minutes before applying RENOVA. The patient
26 should apply a pea-sized amount of cream to cover the entire affected face lightly. Caution
27 should be taken when applying the cream to avoid the eyes, ears, nostrils, and mouth.
28

29 Application of RENOVA may cause a transitory feeling of warmth or slight stinging.
30

31 Mitigation (palliation) of facial fine wrinkling, mottled hyperpigmentation and tactile
32 roughness may occur gradually over the course of therapy. Up to six months of therapy
33 may be required before the effects are seen. Most of the improvement noted with
34 RENOVA 0.05% is seen during the first 24 weeks of therapy. Thereafter, therapy primarily
35 maintains the improvement realized during the first 24 weeks.
36

37 With discontinuation of RENOVA 0.05% therapy, a majority of patients will lose most
38 mitigating effects of RENOVA 0.05% on fine wrinkles, mottled hyperpigmentation, and
39 tactile roughness of facial skin; **however, the safety and effectiveness of using**
40 **RENOVA 0.05% daily for greater than 48 weeks have not been established.**
41

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

1
2 Patients treated with RENOVA may use cosmetics but the areas to be treated should be
3 cleansed before the medication is applied. (See **PRECAUTIONS** section.)
4

5
6 **HOW SUPPLIED:**

7
8 RENOVA is available in these sizes:

9 NDC 0062-0185-00 20 gram tube

10 NDC 0062-0185-05 40 gram tube

11 NDA 0062-0185-03 60 gram tube

12
13 **Storage:** Store at 25°C (77°F), excursions permitted to 15-30°C (59°F-86°F). DO NOT
14 FREEZE.
15

16 **QUESTIONS:** Physicians and Pharmacists can call 1-800-462-7762, from 8:30 a.m. to
17 4:30 p.m. Eastern Time, Monday through Friday.
18

19 **Rx only.**

20
21 ORTHO DERMATOLOGICAL DIVISION

22 A division of ORTHO-McNEIL PHARMACEUTICAL CORPORATION

23 Raritan, New Jersey 08869
24

25 © OPC 1991

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28 U.S. Patents 4,603,146 and 4,423,041

RENOVA® (reh-NO-vah)

Generic Name: Tretinoin Cream (0.05%)

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 taking 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 does **not** remove wrinkles or repair sun-damaged skin. (See “What is RENOVA?” for more details.) RENOVA 0.05% has not been tested in people over age 50 or in people with medium or dark skin color. (See “Who should not use RENOVA?”)

What is RENOVA 0.05%?

RENOVA 0.05% is a prescription medicine that may reduce fine facial wrinkles, facial mottled hyperpigmentation, and facial skin roughness. It is for patients who are also using a 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 skin care and sunlight avoidance 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 0.05% in patients for more than 48 weeks has not been studied. Therefore, it is not known if RENOVA 0.05% is safe or works if used longer than 48 weeks. RENOVA 0.05% has not been shown to work or to be safe

1 in people over age 50, in people with medium to dark skin color, in people with
2 visible actinic keratosis, or in people with a history of skin cancer.

4 **Who should not use RENOVA?**

5 Do not use RENOVA if:

- 6 • you are pregnant or plan to become pregnant. If you become pregnant while
7 taking RENOVA, please contact your doctor immediately.
- 8 • you are sunburned or your skin is irritated
- 9 • you are highly sensitive to sunlight
- 10 • you are allergic to any of RENOVA's ingredients. The active ingredient is
11 tretinoin. Ask your doctor or pharmacist about the inactive ingredients.

12
13 RENOVA can cause increased skin irritation and increased chance of sunburn.

14
15 Tell your doctor if you have any skin condition. RENOVA may not be right for you.

16
17 Because RENOVA may make your skin more likely to burn from sunlight, tell your
18 doctor if you are using other medicines that increase sensitivity to sunlight. You
19 should not use RENOVA with such medicines. These include, but are not limited to:

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

23
24 If you are taking any prescription or non-prescription medicines, check with your
25 doctor to make sure you can use RENOVA with them.

26
27 We do not know if RENOVA is passed to infants through breast milk. Therefore, tell
28 your doctor if you are breast feeding.

30 **How should I use RENOVA?**

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

- 34
35 1. Gently wash your face with a mild soap.
- 36 2. Pat the skin dry and wait 20-30 minutes before applying RENOVA.
- 37 3. Apply only a pea-sized amount of RENOVA to the face at one time. It should be
38 enough to cover the entire affected area lightly.

39
40 Be especially careful when applying RENOVA to avoid your eyes, ears, nostrils,
41 angles of the nose, and mouth. RENOVA may cause severe redness, itching,
42 burning, stinging, and peeling if used on these areas.

43
44 Using too much RENOVA may increase discomfort and skin redness and peeling.

45

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

4
5 Use sunscreen and wear protective clothing to protect the treated areas from
6 sunlight. If you sunburn easily, or if you spend a lot of time exposed to sunlight, be
7 especially careful to protect your skin.

8 9 **What should I avoid while using RENOVA?**

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

- 13
- 14 • other skin medicines
 - 15 ! medicated or abrasive (rough) soaps
 - 16 • permanent wave solutions
 - 17 ! chemical hair removers or waxes
 - 18 ! electrolysis
 - 19 ! products with alcohol, spices, astringents, or lime
 - 20 • cleansers, shampoos, or cosmetics with a strong drying effect
 - 21 • other products that may irritate your skin
- 22

23 **What are the possible side effects of RENOVA?**

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

28 29 **General advice about prescription medicines**

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

34
35 This leaflet summarizes the most important information about RENOVA. If you
36 would like more information, talk with your doctor. You can ask your pharmacist or
37 doctor for information about RENOVA that is written for health professionals.

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