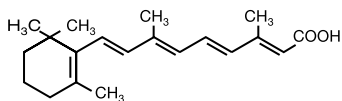


# Retin-A<sup>®</sup> (tretinoin)A

## Cream · Gel · Liquid For Topical Use Only

### Prescribing Information

**Description:** RETIN-A Gel, Cream and Liquid, containing tretinoin are used for the topical treatment of acne vulgaris. RETIN-A Gel contains tretinoin (retinoic acid, vitamin A acid) in either of two strengths, 0.025% or 0.01% by weight, in a gel vehicle of butylated hydroxytoluene, hydroxypropyl cellulose and alcohol (denatured with *tert*-butyl alcohol and brucine sulfate) 90% w/w. RETIN-A (tretinoin) Cream contains tretinoin in either of three strengths, 0.1%, 0.05%, or 0.025% by weight, in a hydrophilic cream vehicle of stearic acid, isopropyl myristate, polyoxyl 40 stearate, stearyl alcohol, xanthan gum, sorbic acid, butylated hydroxytoluene, and purified water. RETIN-A Liquid contains tretinoin 0.05% by weight, polyethylene glycol 400, butylated hydroxytoluene and alcohol (denatured with *tert*-butyl alcohol and brucine sulfate) 55%. Chemically, tretinoin is *all-trans*-retinoic acid and has the following structure:



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

**Indications and Usage:** RETIN-A is indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of the long-term use of this product in the treatment of other disorders have not been established.

**Contraindications:** Use of the product should be discontinued if hypersensitivity to any of the ingredients is noted.

**Precautions:** *General:* If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during the use of RETIN-A, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. Patients who may be required to have considerable sun exposure due to occupation and those with inherent sensitivity to the sun should exercise particular caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with tretinoin.

RETIN-A (tretinoin) acne treatment should be kept away from the eyes, the mouth, angles of the nose, and mucous membranes. Topical use may induce severe local erythema and peeling at the site of application. If the degree of local irritation warrants, patients should be directed to use the medication less frequently, discontinue use temporarily, or discontinue use altogether. Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition.

**Drug Interactions:** Concomitant topical medication, medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime should be used with caution because of possible interaction with tretinoin. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid with RETIN-A. It also is advisable to "rest" a patient's skin until the effects of such preparations subside before use of RETIN-A is begun.

**Carcinogenesis:** Long-term animal studies to determine the carcinogenic potential of tretinoin have not been performed. Studies in hairless albino mice suggest that tretinoin may accelerate the tumorigenic potential of weakly carcinogenic light from a solar simulator. In other studies, when lightly pigmented hairless mice treated with tretinoin were exposed to carcinogenic doses of UVB light, the incidence and rate of development of skin tumors was reduced. Due to significantly different experimental conditions, no strict comparison of these disparate data is possible. Although the significance of these studies to man is not clear, patients should avoid or minimize exposure to sun.

**Pregnancy:** Teratogenic effects. Pregnancy Category C. Oral tretinoin has been shown to be teratogenic in rats when given in doses 1000 times the topical human dose. Oral tretinoin has been shown to be fetotoxic in rats when given in doses 500 times the topical human dose. Topical tretinoin has not been shown to be teratogenic in rats and rabbits when given in doses of 100 and 320 times the topical human dose, respectively (assuming a 50 kg adult applies 250 mg of 0.1% cream topically). However, at these topical doses, delayed ossification of a number of bones occurred in both species. These changes may be considered variants of normal development and are usually corrected after weaning. There are no adequate and well-controlled studies in pregnant women. Tretinoin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RETIN-A is administered to a nursing woman.

**GELS ARE FLAMMABLE.** Note: Keep away from heat and flame. Keep tube tightly closed.

**Adverse Reactions:** The skin of certain sensitive individuals may become excessively red, edematous, blistered, or crusted. If these effects occur, the medication should either be discontinued until the integrity of the skin is restored, or the medication should be adjusted to a level the patient can tolerate. True contact allergy to topical tretinoin is rarely encountered. Temporary hyper- or hypopigmentation has been reported with repeated application of RETIN-A. Some individuals have been reported to have heightened susceptibility to sunlight while under treatment with RETIN-A. To date, all adverse effects of RETIN-A have been reversible upon discontinuance of therapy (see Dosage and Administration Section).

**Overdosage:** If medication is applied excessively, no more rapid or better results will be obtained 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:** RETIN-A Gel, Cream or Liquid should be applied once a day, before retiring, to the skin where acne lesions appear, using enough to cover the entire affected area lightly. Liquid: The liquid may be applied using a fingertip, gauze pad, or cotton swab. If gauze or cotton is employed, care should be taken not to oversaturate it to the extent that the liquid would run into areas where treatment is not intended. Gel: Excessive application results in "pilling" of the gel, which minimizes the likelihood of over application by the patient.

Application may cause a transitory feeling of warmth or slight stinging. In cases where it has been necessary to temporarily discontinue therapy or to reduce the frequency of application, therapy may be resumed or frequency of application increased when the patients become able to tolerate the treatment.

Alterations of vehicle, drug concentration, or dose frequency should be closely monitored by careful observation of the clinical therapeutic response and skin tolerance.

During the early weeks of therapy, an *apparent* exacerbation of inflammatory lesions may occur. This is due to the action of the medication on deep, previously unseen lesions and should not be considered a reason to discontinue therapy.

Therapeutic results should be noticed after two to three weeks but more than six weeks of therapy may be required before definite beneficial effects are seen.

Once the acne lesions have responded satisfactorily, it may be possible to maintain the improvement with less frequent applications, or other dosage forms.

Patients treated with RETIN-A (tretinoin) acne treatment may use cosmetics, but the area to be treated should be cleansed thoroughly before the medication is applied. (See Precautions.)

#### How Supplied:

RETIN-A (tretinoin) is supplied as:

RETIN-A Cream		
NDC Code	RETIN-A Strength/Form	RETIN-A Qty.
0062-0165-01	0.025% Cream	20g
0062-0165-02	0.025% Cream	45g
0062-0175-12	0.05% Cream	20g
0062-0175-13	0.05% Cream	45g
0062-0275-23	0.1% Cream	20g
0062-0275-01	0.1% Cream	45g

RETIN-A Gel		
NDC Code	RETIN-A Strength/Form	RETIN-A Qty.
0062-0575-44	0.01% Gel	15g
0062-0575-46	0.01% Gel	45g
0062-0475-42	0.025% Gel	15g
0062-0475-45	0.025% Gel	45g

RETIN-A Liquid		
NDC Code	RETIN-A Strength/Form	RETIN-A Qty.
0062-0075-07	0.05% Liquid	28mL

**Storage Conditions:** RETIN-A Liquid, 0.05%, and RETIN-A Gel, 0.025% and 0.01%: store below 86°F. RETIN-A Cream, 0.1%, 0.05%, and 0.025%: store below 80°F.

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