Retin-A®

For the topical treatment of acne.

Therapeutic Class
Treatment of acne

Composition
Retin-A contains as active ingredient tretinoin (retinoic acid) and is presented in three different forms.
Gel 0.01% or 0.025% tretinoin
Cream 0.025%, 0.05% or 0.1% tretinoin
Solution 0.1% tretinoin
Conserv: butylhydroxytoluol – Cream: plus acid. sorbinic and excip.

Pharmacodynamic Properties
Although the exact mode of action of tretinoin is unknown, current evidence suggests the effectiveness of tretinoin in acne is primarily due to its ability to modify abnormal follicular keratinization. Acne comedones form in follicles with excessively keratinized epithelial cells. The accumulation of keratinized material in the follicle initiates comedone formation. Tretinoin promotes detachment of cornified cells and enhanced shedding of corneocytes from the follicle. By increasing the mitotic activity of follicular epithelia, tretinoin also increases the turnover rate of thin, loosely adherent corneocytes. Through these actions, tretinoin prevents formation of the microcomedo, the precursor lesion of acne vulgaris.
Additionally, tretinoin acts by modulating the proliferation and differentiation of skin cells. These effects are mediated by tretinoin's interaction with a family of nuclear proteins, retinoic acid receptors. Activation of these nuclear receptors causes changes in gene expression, which in turn, modify abnormal cellular processes. The exact mechanisms whereby tretinoin-induced changes in gene expression regulate skin function are not understood.

Indication
Retin-A is indicated as topical therapy for the treatment of acne vulgaris.

Recommended Dosage
Adults
Retin-A should be applied once daily before retiring to the area of skin where acne lesions occur. Only a sufficient quantity of medication should be applied to cover the affected areas lightly, using a gauze swab, cotton wool or the tips of clean fingers. Over-saturation should be avoided since excess medication could run into the eyes, angles of the nose or other areas where treatment is not intended. Application of Retin-A may cause a transitory feeling of warmth or slight stinging. When administered according to recommended guidelines, Retin-A may produce a slight erythema similar to that of mild sunburn. In cases where it is necessary to temporarily discontinue therapy or reduce the frequency of application, therapy should be resumed or the frequency of the application increased when the patient becomes able to tolerate the treatment.
Excess application of Retin-A does not provide more rapid or better results. In fact, marked redness, peeling or discomfort can occur. If excess application occurs accidentally or through over-enthusiastic use, Retin-A should be discontinued for several days before resuming therapy.
Therapeutic effects may be noticed after two to three weeks of use but more than six weeks of therapy may be required before definite beneficial effects are seen. During the early weeks of treatment, 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. Once a satisfactory response has been obtained, it may be possible to maintain this improvement with less frequent applications.
Prior to treatment with Retin-A, areas being treated should be thoroughly cleansed with water and a mild, non-medicated soap. The treated area should be washed no more than twice a day. After washing the skin should be dried gently and completely without rubbing it. Areas of the skin being treated should be allowed to dry for at least 20 to 30 minutes before application of Retin-A.
Cosmetics and moisturizers may be used during therapy with Retin-A, but the areas of the skin to be treated should be washed thoroughly before Retin-A is applied. Astringent toiletries should be avoided.

Contraindications
Hypersensitivity to any component of this product.

Warnings
General Precautions
In order to minimize the potential for additional skin irritation, care should be taken to avoid contact with the eyes, eyelids, angles of the nose, mouth, mucous membranes or other areas where treatment is not intended.
Patients will be able to remove hair as usual (e.g. plucking, electrolysis, depilatories) but should avoid these procedures at night before applying Retin-A as they might result in skin irritation.
Permanent wave solutions, waxing preparations,

medicated soaps and shampoos can sometimes irritate even normal skin. Caution should be used so that these products do not come into contact with skin treated with Retin-A.

Local Irritation
It is not recommended to initiate treatment with Retin-A or continue its use in the presence of skin irritation (e.g. erythema, peeling, pruritus, sunburn, etc.) until these symptoms subside.
In certain sensitive individuals, Retin-A may induce severe local erythema, swelling, pruritus, warmth, burning or stinging, blistering, crusting and /or peeling at the site of application. If the degree of local irritation warrants, the patient should be instructed to either apply the medication less frequently or discontinue its use temporarily.
Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition. If a patient experiences severe or persistent irritation, the patient should be advised to discontinue application of Retin-A completely, and if necessary, consult a physician.
Weather extremes, such as wind, cold and low humidity may be irritating to skin treated with Retin-A and may increase its dryness.

Exposure to Sunlight
Exposure to sunlight, including ultraviolet sunlamps, may provoke additional irritation. Therefore, exposure should be avoided or minimized during the use of tretinoin. A patient experiencing considerable sun exposure due to occupational duties, and /or any patient inherently sensitive to the sun, should exercise particular caution. When exposure to sunlight cannot be avoided, use of sunscreen products and protective clothing over treated areas is recommended.

Children
Safety and effectiveness have not been established in children.

Pregnancy and Lactation
Topical tretinoin has not been shown to be teratogenic in Wistar rats and rabbits when given in doses 1000 and 320 times the topical human dose, respectively, assuming that a 50 kg adult applies 250 mg of 0.1% Retin-A cream topically. At these topical doses, however, a delayed ossification of several bones occurred in rabbits. In rats, a dose dependent increase of supernumerary ribs was observed. These changes are considered variants of normal development. The ossification changes are usually spontaneously corrected after weaning.
There have been isolated reports of birth defects among babies born to women exposed to topical tretinoin during pregnancy. To date, there have been no adequate and well- controlled prospective studies performed in pregnant women and the teratogenic blood level of tretinoin is not known. However, a well-conducted retrospective cohort study of babies born to women exposed to topical tretinoin during the first trimester of pregnancy found no excess birth defects among these babies when compared with babies born to women in the same cohort who were not similarly exposed. Topical tretinoin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether tretinoin is excreted in human milk. Since many drugs are excreted in human milk, caution should be exercised when Retin-A is administered to a nursing mother.

Undesirable Effects
Some degree of local irritation is expected. The most commonly reported undesirable effects are dry skin, burning, stinging, warmth, erythema, pruritus, rash, peeling and temporarily hypo and hyperpigmentation. Rarely reported undesirable effects are blistering and crusting of the skin, eye irritation and edema. True contact allergy to topical tretinoin is rarely encountered.

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 is also advisable to "rest" a patient's skin until the effects of such preparations subside before use of Retin-A is begun.

Overdosage
Topical application of Retin-A is characterized by little systemic absorption, hence overdosage is unlikely. Retin-A is intended for topical use only. In the event of accidental ingestion, if the ingestion is recent, the stomach should be emptied immediately by gastric lavage or by induction of emesis. All other treatment should be appropriately supportive. Oral ingestion of Retin-A may lead to the same adverse events as those associated with excessive oral intake of Vitamin A.

Storage Conditions
Cream: Store at or below 25°C
Gel: Store at or below 25°C
Solution: Store at or below 25°C, protect from light

Supplied
0.01%: 15 g gel
0.025%: 15 g, 30 g gel / 20 g, 30 g cream
0.05%: 20 g, 30 g cream
0.1%: 20 g cream / 15 ml solution
Dispensed in pharmacies on physician's prescription.

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