

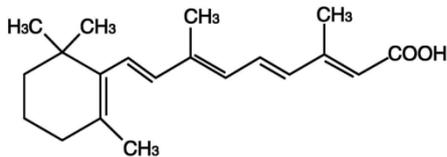
Product Information

ReTrieve® Cream

(Tretinoin 0.05 % w/w)

Name of the medicine

Tretinoin



CAS No: 302-79-4

Description

Tretinoin is a yellow to light orange crystalline powder. It is practically insoluble in water, sparingly soluble in methylene chloride and slightly soluble in ethanol (96 per cent).

ReTrieve Cream contains tretinoin 0.05% w/w (0.5mg/g) in a smooth, off-white to pale yellow hydrophilic cream base of cetyl alcohol, diazolidinylurea, disodium edetate, dl-alpha tocopheryl acetate, glyceryl monostearate, isopropyl palmitate, methyl hydroxybenzoate, polysorbate 60, propylene glycol, propyl hydroxybenzoate, retinyl palmitate, sorbitan monostearate and purified water.

Pharmacology

Tretinoin, an all-*trans* retinoic acid, occurs in the body as a tissue metabolite of vitamin A. Unlike retinol and its esters, it does not accumulate in the body but metabolises rapidly and excretes in the form of inactive glucuronides or oxidation products.

These metabolites are mainly excreted in the faeces and some oxidised metabolites are found in the urine.

Topically applied tretinoin appears to be slightly absorbed from the skin. *In vitro* studies in human skin showed that only a small percentage of the applied dose could be detected in urine.

The precise mechanism of action of topical tretinoin has not been fully elucidated.

Tretinoin, being a metabolite of retinol, is both pharmacologically and structurally related to vitamin A which regulates cell growth and differentiation. It has been postulated that it acts by enhancing epithelial proliferation and accelerating epithelial differentiation.

Indications

Adjunctive treatment of dry photoaged skin and related conditions.

Contraindications

Hypersensitivity to tretinoin or any of the ingredients in the formulation.

Precautions

Concomitant application of other topical preparations including cosmetics should be avoided because of possible incompatibility and interaction with tretinoin.

Particular caution should be exercised in the use of keratolytic agents such as sulphur, salicylic acid, benzoyl peroxide or resorcinol and chemical abrasives. If the patient has been treated with such preparations, the effect of the peeling agents must subside before any commencement of topical ReTrieve therapy.

Some medicated cleansers and scrubbing solutions have a strong drying effect. They should not be used in patients receiving tretinoin topical therapy.

Exposure of the treated areas to sunlight including sunlamps should be minimised during the course of topical treatment with ReTrieve.

Patients receiving tretinoin treatment are more susceptible to the effect of UV irradiation especially at the start of the therapy. Animal studies suggest that tretinoin may accelerate the tumorigenic potential of ultraviolet radiation in hairless albino mice, especially at high concentrations of the drug. Although the significance to human is unknown, patients undergoing tretinoin treatment should exercise utmost caution.

Patients with sunburn should be advised to use ReTrieve only after the skin is fully recovered.

Exposure to ultraviolet irradiation increases the intensity of inflammatory reaction. Patients receiving ReTrieve therapy should avoid exposure to artificial sunlamps or solarium.

Patients should be counselled to routinely use high SPF sunscreens as well as protective clothing while undergoing ReTrieve topical treatment, especially those individuals at risk of chronic sun exposure or having a family history of light sensitivity.

Extreme weather conditions, such as strong wind or cold dry air may cause skin irritation to patients receiving tretinoin treatment.

Do not swallow and avoid contact with mucous membranes or open wounds.

ReTrieve should not be applied to the eyes, mouth, lips, mucosa, or angles of the nose.

Should any of these occur, rinse the affected areas thoroughly with water to avoid local irritation. Particular caution is indicated for patients with eczema, since tretinoin has been reported to cause severe irritation on eczematous skin. The hands should be washed thoroughly with water after each application.

Over enthusiastic use or too frequent application may cause redness, stinging and discomfort. If severe irritation occurs, especially in the early stage of therapy, patient should be advised to discontinue temporarily or reduce the frequency of application.

Use in pregnancy (Category D)

There have been isolated reports of birth defects in babies born to women using topical tretinoin in pregnancy. To date, there have been no adequate and well controlled prospective studies in women using topical tretinoin in pregnancy. A retrospective cohort study of babies born to 215 women exposed to topical tretinoin during the first trimester of pregnancy found no more birth defects among these babies than those born to 430 women in the same cohort who were not similarly exposed.

Oral tretinoin has been shown to be teratogenic in rats when given at doses of 5 mg/kg/day and fetotoxic in rats when given at doses of 2.5 mg/kg/day. Oral doses of tretinoin have caused limb defects in mice.

However, topical tretinoin has not been shown to be teratogenic in rats and rabbits when given at doses of 0.5 mg/kg/day and 1.6 mg/kg/day, respectively.

These latter changes may be considered variants of normal development and are usually corrected after weaning.

In view of the possible association of tretinoin with fetal disorders, ReTrieve therapy is not recommended during pregnancy or in women of childbearing potential.

Use during lactation

Safe use during lactation has not been established. It is not known whether this drug is excreted in human milk. Therefore, use during lactation is not recommended.

Interactions with other medicines

Concomitant use of other topical medications (especially those containing keratolytic agents such as resorcinol, sulphur, salicylic acid, benzoyl peroxide and abrasive chemicals etc.) should be avoided in patients undergoing treatment with ReTrieve because of possible interactions with tretinoin. The application of ReTrieve should only commence after the effect of the peeling agents has completely subsided (see Precautions). Tretinoin is an unstable compound that is often incompatible with substances found in topical preparations.

Some topical products and certain cosmetics contain high concentrations of alcohol, spices, lime, or menthol. They should be used with caution especially in the early phase of treatment due to stinging action of these chemicals.

ReTrieve Cream should not be administered if the patient is also taking medicines known to be photosensitisers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulphonamides) because of the possibility of augmented phototoxicity,

Adverse effects

ReTrieve is generally well tolerated after nightly application. Side effects have been limited to mild irritation, evidenced by peeling and erythema, especially in the early stage of treatment. Some patients may experience a transitory sensation of warmth or slight stinging after application of the drug.

If excessive reactions occur, the frequency of application may be reduced or treatment discontinued temporarily till the reactions subside. The dose and frequency may then be adjusted to a level which the patient can tolerate.

Temporary hyperpigmentation or hypopigmentation has occurred with repeated topical application of the drug.

Contact allergy has been reported in isolated instances.

Increased sensitivity to UV light may be experienced in patients undergoing treatment and appropriate measures should be taken (see Precautions).

Reversible changes in liver function tests have been reported after administration of tretinoin topical therapy but do not appear to be of clinical significance. Elevated serum level of bilirubin, alkaline phosphatase, glutamic-pyruvic transaminase, glutamic oxaloacetic transaminase and increase in thymol turbidity and flocculation were observed but in all cases reported, the results reverted to normal on discontinuing treatment.

Dosage and administration

ReTrieve should be applied sparingly to the affected areas once daily at bedtime. Treatment with tretinoin should be individualised according to tolerance and response. No other topical preparations should be applied over the nightly inunction, but suitable moisturisers may be used during the day.

Begin the treatment program slowly, as follows:

1. Wash the affected areas prior to any application with mild soap free cleansers and pat dry.
2. First night: apply, leave for five minutes, then wash off.
3. Second night: apply, leave for ten minutes, then wash off.
4. Third, fourth, fifth and sixth nights: increase the treatment time each night by 30 minutes until the application is left on for two hours.
5. If, after a two hour application, no redness or irritation has developed on the skin the following day, then the application may be left on overnight and washed off next morning.
6. If excessive skin reactions occur, adjust the schedule to alternate nights until the skin accommodates.

Certain types of skin could be too sensitive to use ReTrieve Cream. Patients with very sensitive skin should consult a dermatologist before commencing treatment.

Overdosage

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

No data are available on the consequences of overdosage from accidental ingestion of ReTrieve. Tretinoin is a normal metabolite of vitamin A and has similar toxicity profile. The LD₅₀ of tretinoin in mice and rats has been found to be 4g/kg and 2g/kg respectively.

The concentration of tretinoin present in ReTrieve at 0.5mg/g is unlikely to cause any symptomatic effects. Any acute toxicity arising from accidental ingestion of the preparation will be more related to the toxicity of the vehicle components.

Symptoms of acute toxicity would be of gastrointestinal disturbance. In such event, treatment such as gastric lavage, inducing emesis and/or forced fluids should be performed as soon as possible.

Overdosage from excessive dermal application may produce marked erythema and skin inflammatory reactions. Should this occur, discontinue use and if necessary, apply cold compresses and/or mild emollient.

Presentation and storage conditions

ReTrieve Cream is a smooth off-white to pale yellow cream contained in a metal tube with an outer carton and is available in the following pack sizes:

- 5g tube
- 10g tube*
- 50g tube (with patient instruction leaflet)

Store below 25°C.

Name and address of the Sponsor

iNova Pharmaceuticals Australia Pty Ltd
Level 10, 12 Help St,
Chatswood, NSW 2067

Poison Schedule of the medicine

S4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG)

20 September 1991

Date of most recent amendment

09 Jan 2014

* - not currently distributed in Australia