

NEW ZEALAND DATA SHEET

RETRIEVE® Cream

1 PRODUCT NAME

ReTrieve Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 0.5 mg (0.05% w/w) tretinoin

Excipients with known effect:

Methyl hydroxybenzoate

Propyl hydroxybenzoate

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Topical cream

ReTrieve is a smooth, pale yellow cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ReTrieve Cream is indicated for topical application in the treatment of acne vulgaris, primary grades I-III in which comedones, papules and pustules predominate. It is not recommended as monotherapy in cases of severe pustular and deep cystic nodular varieties (acne conglobata).

Adjunctive treatment of dry skin due to chronic exposure to sunlight and related conditions

4.2 Dose and method of administration

Dosage

ReTrieve should be applied sparingly to the affected areas once daily at bedtime.

Procedural steps critical to the safe administration of the medicine

Begin the treatment program slowly.

- (a) Wash the affected areas with mild soap-free cleansers prior to any application. Pat dry.
- (b) First night apply, leave for five minutes; then wash off.
- (c) Second night apply, leave for ten minutes; then wash off.
- (d) Third, fourth, fifth and sixth nights, increase the treatment time each night by 30 minutes until the application is left on for two hours.
- (e) 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.
- (f) If excessive skin reactions occur, adjust the schedule to alternate nights until the skin accommodates.

Advice for monitoring

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.

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

4.3 Contraindications

Hypersensitivity to tretinoin or any of the ingredients in the formulation (see section 6.1).

4.4 Special warnings and precautions for use

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.

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

Eczema

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.

Concomitant application of topical preparations

Concomitant application of other topical preparations including cosmetics should be avoided if possible during the nightly inunction, 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 to Sunlight

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 humans 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 sunscreen 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.

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4.5 Interaction with other medicines and other forms of interaction

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 inter-actions with tretinoin. The application of ReTrieve should only commence after the effect of the peeling agents has completely subsided (see section 4.4).

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, menthol. They should be used with caution especially in the early phase of treatment due to stinging action of these chemicals.

Laboratory Tests

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, or increase in thymol turbidity and flocculation were observed but in all cases reported, the results reverted to normal on discontinuing treatment.

4.6 Fertility, pregnancy and lactation

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 foetal disorders, ReTrieve therapy is not recommended during pregnancy or in women of childbearing potential.

Lactation

There is insufficient information on the excretion of topical tretinoin into human milk during breast feeding. The use of ReTrieve during lactation is not recommended.

4.7 Effects on ability to drive and use machines

It is unlikely that ReTrieve will have any effects on the ability to drive and use machines.

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4.8 Undesirable 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 section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

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 and 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Retinoids for topical use in acne. ATC Code: D10AD01

Skin Protectant

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

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cell growth and differentiation. It has been postulated that it acts by enhancing epithelial proliferation and accelerating epithelial differentiation.

5.2 Pharmacokinetic properties

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. Studies in human skin showed that only a small percentage of the applied dose could be detected in urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetyl alcohol
Diazolidinyl urea
Disodium edetate
DL-alpha tocopheryl acetate
Glyceryl monostearate
Isopropyl palmitate
Methyl hydroxybenzoate
Polysorbate 60
Propyl hydroxybenzoate
Propylene glycol
Purified water
Retinol palmitate
Sorbitan stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Tube, aluminium, polypropylene cap: 5g, 50g

6.6 Special precautions for disposal <and other handling>

No special requirements

7 MEDICINE SCHEDULE

Prescription

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RETRIEVE® Cream

8 SPONSOR

iNova Pharmaceuticals (New Zealand) Limited
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88 Shortland Street,
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Toll-free number: 0508 375 394

9 DATE OF FIRST APPROVAL

26 November 2009

10 DATE OF REVISION OF THE TEXT

7 March 2018

SUMMARY TABLE OF CHANGES

Date	Change
7 March 2018	Data sheet reformatted Section 4.7: Added statement on driving and using machinery. Section 5.1: added Pharmacotherapeutic group and ATC code Section 6.5 added container details Section 8: Sponsor name and address changed to iNova Pharmaceuticals (New Zealand) Limited