PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

RETIN-A® 0.05 % cream

RETIN-A® 0.025 % gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each one gram of cream contains 0.5 mg of the active ingredient, tretinoin and sorbic acid 0.2 % m/m as preservative.

Each one gram of gel contains 0.25 mg of the active ingredient, tretinoin.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

RETIN-A 0,05 % cream: Yellow, oil-in water cream having a faint waxy odour.

RETIN-A 0,025 % gel: Smooth, clear viscous yellow gel, having an odour of alcohol.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RETIN-A is indicated for topical application in the treatment of hyperkeratotic follicular and related conditions such as *acne vulgaris,* primarily grades I-II in which comedones, papules and pustules predominate. It is not effective in most cases of severe pustular and deep cystic nodular varieties (*acne conglobate*).

RETIN-A is used as adjunctive therapy for the topical treatment of mottled hyperpigmentation, roughness, and fine wrinkling of photodamaged skin due to chronic sun exposure in patients who do not respond to comprehensive skin care programs and sun avoidance measures.

There is no convincing evidence that RETIN-A permanently removes wrinkles, repairs sun damaged skin, reverses photo-aging, or restores a more youthful dermatological pattern.

4.2 Posology and method of administration

Posology

For topical administration only.

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 not 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.

Patients treated with RETIN-A may use cosmetics, but the areas to be treated should be cleansed thoroughly before the medication is applied.

Astringent toiletries should be avoided.

RETIN-A should be applied once daily, before retiring to the area of the 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 may cause a transitory feeling of warmth or slight stinging. When administered as directed, RETIN-A may produce a slight erythema like that of mild sunburn.

In cases where it has been necessary to discontinue therapy temporarily, or reduce the frequency of application, therapy may be resumed or the frequency of application increased when the patients become able to tolerate the treatment.

Frequency of application 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. Results may not be optimal until after six weeks of therapy. Once the acne lesions have responded satisfactorily, it may be possible to maintain the improvement with less frequent applications.

Duration of treatment:

Improvements in signs of photodamage with RETIN-A do not appear immediately but develop progressively throughout the course of treatment. The time at which visible changes become

noticeable varies among individuals; however, improvements typically begin to appear within 3 to 4 months after starting therapy. In some cases, up to six months of consistent use may be needed to observe clear beneficial effects. After reaching the maximum level of improvement, results can be maintained by applying RETIN-A one to three times per week. Without ongoing maintenance therapy, the achieved benefits will gradually diminish over time.

Paediatric population

Safety and efficacy have not been established in children.

Method of administration

Applied topically.

4.3 Contraindications

- Use of RETIN-A should be discontinued if hypersensitivity to any of the ingredients listed in section 6.1 are noted.
- Pregnancy and lactation (see section 4.6).
- Eczematous skin conditions.

4.4 Special warnings and precautions for use

For external use only.

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, persistent dry skin, swelling, rash, 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 medical practitioner. In order to minimize the potential for additional skin irritation, RETIN-A should be kept away from the eyes, the mouth, paranasal creases of the nose, and mucous membranes or other areas where treatment is not intended.

Weather extremes, such as wind, cold and low humidity may be irritating to skin treated with RETIN-A and may increase its dryness.

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.

Gels are flammable. Avoid fire, flame or smoking during use.

Exposure to Sunlight

Exposure to sunlight, including ultraviolet sunlamps, may provoke additional irritation. Therefore, exposure should be avoided or minimized during the use of RETIN-A . Patients with sunburn should

be advised not to use the product until fully recovered because of potential severe irritation to sensitive skin.

Patients who may be required to have considerable sun exposure due to their occupation and those with inherent sensitivity 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.

RETIN-A contains:

- Stearyl alcohol and Sorbic Acid (E200) which may cause local skin reactions (e.g. contact dermatitis).
- Butylated hydroxytoluene which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

4.5 Interaction with other medicines and other forms of interaction

The following products or medications should be used with caution because of possible interaction with tretinoin. It is advised to allow the effects of such preparations to subside before use of RETIN-A is begun:

- concomitant topical medication;
- preparations containing benzoyl peroxide, sulphur, resorcinol, or salicylic acid;
- toiletry preparations having an abrasive, drying, or desquamative effect, including soaps, shampoos, cosmetics, and products with high concentrations of alcohol, astringents, spices or lime.

Paediatric population

Interaction with other medicines and other forms of interaction have not yet been established in

children.

4.6 Fertility, pregnancy and lactation

Women of child-bearing potential / Contraception in males and females

No information available.

Pregnancy

Safety and /or efficacy has not yet been established.

Oral tretinoin has been shown to be teratogenic in a wide variety of animals. Limited animal data urge caution in the use of preparations containing tretinoin during the first trimester of pregnancy.

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.

If an eventual pregnancy occurs, the patient should discontinue treatment and inform her doctor (see section 4.3).

Breastfeeding

It is not known whether tretinoin is excreted in human milk. Since many medicines are excreted in human milk, RETIN- A should not be administered to a nursing mother (see section 4.3).

Fertility

No fertility data available.

4.7 Effects on ability to drive and use machines

Use of RETIN-A is not known to affect the ability to drive a motor vehicle or operate machinery.

4.8 Undesirable effects

Summary of the safety profile

Adverse drug reactions first identified during post-marketing experience with RETIN-A are hypersensitivity, eye irritation, photosensitivity reaction, urticaria, scab. Adverse drug reactions reported during clinical trials are listed below.

Tabulated list of adverse reactions

Clinical Trial Data

The safety of tretinoin topical formulations including RETIN-A was evaluated in 4160 patients (of whom 3035 were treated with topical tretinoin and 1125 received placebo) who participated in 23 clinical trials, including 4 open-label and 19 double-blind, placebo-controlled clinical trials. The 23 clinical trials evaluated the safety of tretinoin in male and female patients, 10 to 79 years of age with photodamaged skin or acne vulgaris. Adverse drug reactions (ADRs) reported for ≥ 1 % of RETIN-A treated patients in 19 double blind, placebo- controlled clinical trials are shown in Table 1.

Table 1. Adverse Drug Reactions Reported by ≥ 1 % of RETIN-A Treated Patients in 19 Double Blind, Placebo-Controlled Clinical Trials of RETIN-A		
System Organ Class **Adverse Reaction**	**RETIN-A %** **(N = 1701)**	**Placebo %** **(N = 1125)**
Skin and Subcutaneous Tissue Disorders		

Hyperkeratosis	12,2	4,5
Skin irritation	10,7	8,5
Pain of skin	10,1	3,4
Erythema	8,0	3,6
Pruritus	5,9	3,0
Rash papular	5,7	4,5
Rash	3,8	2,4
Dermatitis	2,7	1,7
Dry skin	2,7	0,7
Skin exfoliation	2,4	2,6
Nervous System Disorders		
Headache	3,5	4,7

Adverse drug reactions reported by < 1 % of RETIN-A treated patients (N = 3035) in 23 clinical trials are shown in Table 2

Table 2. Adverse Drug Reactions Reported by < 1 % of RETIN-A Treated Patients in 23 Clinical Trials of RETIN-A
System/Organ Class Adverse Reaction
Skin and Subcutaneous Tissue Disorders Swelling face Blister Skin discolouration Skin hyperpigmentation Skin hypopigmentation Skin burning sensation

General Disorders and Administration Site Conditions
Feeling hot

Post-marketing Experience

Adverse drug reactions first identified during post-marketing experience with RETIN-A are included in Table 3.

Table 3. Adverse Drug Reactions Identified During Post-marketing Experience with RETIN-A	
Immune System Disorders Hypersensitivity	Frequency unknown
Eye Disorders Eye irritation	Frequency unknown
Skin and Subcutaneous Tissue Disorders Photosensitivity reaction, urticaria, scab	Frequency unknown

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 providers are asked to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Reporting can also be done directly to MC Pharma (Pty) Ltd. at:

MC Pharma (Pty) Ltd:

E-mail: Pharmacovigilance@mcpharma.co.za

Tel: 012 668 3019

4.9 Overdose

Topical application of RETIN-A is characterised by little systemic absorption, hence overdosage from topical application is unlikely. Excessive use does not increase therapeutic effects and may produce marked inflammatory reactions (e.g. erythema, peeling, pruritus, sunburn, etc).

Accidental oral ingestion of RETIN-A may lead to the same adverse events associated with excessive oral intake of Vitamin A. Appropriate symptomatic management should be applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 13.12 Acne preparations

ATC code: D10AD

Mechanism of action

Tretinoin has an inflammatory action which is reported to be related to its vessels the surface prevents the impaction of horny material into comedones therapeutic activity.

This inflammation appears to consist of an enlargement of in the papillary body and a slight perivascular cellular infiltration.

The inflammatory action may result from labialisation of lysosomes and the release of hydralases and proteases which are capable of inciting inflammatory reactions. It has been suggested that the

therapeutic activity of tretinoin in the treatment of acne results from it increasing the rate of production of loose horny material.

This increased production and resulting flow of dehiscing material to the surface prevents the impaction of horny material into comedones.

5.2 Pharmacokinetic properties

Minimal systemic absorption through topical application.

5.3 Preclinical safety data

No preclinical data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyoxy 40 stearate, stearyl alcohol, stearic acid, Isopropyl myristate, butylated hydroxytoluene, sorbic acid, xanthan gum, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

32 months

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

RETIN-A 0,05 % cream and 0,025 % gel are packed in screw-capped aluminium tubes containing 20 g.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

MC Pharma (Pty) Ltd

62 Constantia Avenue

Mnandi, Centurion

0157, South Africa

Telephone: 0126683019

Email: pharmacist@mcpharma.co.za

8. REGISTRATION NUMBER(S)

RETIN-A 0,05 % cream: F/13.12/106

RETIN-A 0,025 % gel: J/13.12/350

9. DATE OF FIRST AUTHORISATION

RETIN-A 0,025 % gel: 30 June 1977

RETIN-A 0,05 % cream: 09 October 1973

10. DATE OF REVISION OF THE TEXT

10 February 2026

Nam Reg. No's.:

RETIN-A 0,05 % cream: 90/13.12/00648

RETIN-A 0,025 % gel: 90/13.12/00647

NS 2

Botswana Reg. No's.:

RETIN-A 0,05 % cream: B9315455

RETIN-A 0,025 % gel: B9315460

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