Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Acretin 0.05% Cream

2. Qualitative and quantitative composition

Tretinoin 0.05% w/w Cream

For excipients, see section 6.1

3. Pharmaceutical form

Topical Cream

Off-white to cream colored homogeneous smooth cream, free from grit or lumps, filled in Aluminum collapsible tubes.

4. Clinical particulars

4.1 Therapeutic indications

Acretin is indicated for the topical application in treatment of acne vulgaris.

4.2 Posology and method of administration

Route of Administration: Topical
Adults
Acretin 0.05% w/w Cream should be applied once or twice daily to the area of skin where acne lesions occur. Only apply sufficient to cover the affected areas lightly, using a gauze swab, cotton wool or the tips of clean fingers. Avoid over-saturation to the extent that excess medication could run into the eyes, angles of the nose or other areas where treatment is not intended. Initial application may cause transitory stinging and a feeling of warmth. The correct frequency of administration should produce a slight erythema similar to that of mild sunburn. If Acretin 0.05% w/w Cream is applied excessively, no more rapid or better results will be obtained and marked redness, peeling or discomfort may occur. Should this occur accidentally or through over enthusiastic use, application should be discontinued for a few days. Patience is needed in this treatment, since the therapeutic effects will not usually be observed until after 6-8 weeks of treatment. 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 come dones and papules. Once the acne lesions have responded satisfactorily, it should be possible to maintain the improvement with less frequent applications. Moisturisers and cosmetics may be used during treatment with Acretin 0.05% w/w Cream but should not be applied to the skin at the same time. The skin should be thoroughly washed before application of Acretin. Astringent toiletries should be avoided.

Children
The safety and efficacy of tretinoin in children aged less than 10 years has not been established.

4.3 Contraindications

Acretin 0.05% w/w Cream is contraindicated in patients with:

- A history of sensitivity/hypersensitivity reactions to any of the components
- Pregnancy
- Personal or familial history of cutaneous epithelioma
- Acute eczemas (as tretinoin has been reported to cause severe irritation on eczematous skin)
- Rosacea and perioral dermatitis.

4.4 Special warnings and precautions for use

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 ACRETIN. Some individuals have, been reported to have heightened susceptibility to sunlight while under, treatment with ACRETIN. To date, all adverse effects of ACRETIN have been reversible upon discontinuance of therapy.

4.5 Interaction with other medicinal products 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 Acretin 0.05% w/w Cream is begun:
− concomitant topical medications
− preparations containing benzoyl peroxide
− toiletry preparations having a strong drying, abrasive or desquamative effect including soaps, shampoos, cosmetics, and products with high concentrations of alcohol, astringents, spices or lime.

4.6 Fertility, pregnancy and lactation

The topical human dose used in a 50 kg adult applying a maximum volume of 500 mg of 0.05% Acretin 0.05% w/w Cream is 0.005 mg/kg. In animal reproductive studies, oral tretinoin is known to be teratogenic and has been shown to be foetotoxic in rats when given in doses 500 times the topical human dose. In reproduction studies in rats and rabbits, topical tretinoin, when used at doses 500 and 320 times the topical human dose, respectively, induced minor skeletal abnormalities, eg irregularly contoured or partially ossified skull bones. These changes may be considered variants of normal development and are usually corrected after weaning. Acretin 0.05% w/w Cream should not be used during pregnancy. It is not known whether tretinoin is excreted in

human milk, therefore caution should be exercised when Acretin 0.05% w/w Cream is administered to a nursing mother.

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable effects

Like all medicines, Acretin can cause side effects, although not everybody gets them.
Stop using Acretin and tell your doctor straight away if you notice any of the following serious side effects.
You may need medical treatment.
• Severe irritation or reddening of your skin, hives or nettle rash (urticaria) or other signs of allergy during the first few days of treatment. This only happens in a small number of people
• Blistering or scabby skin
• A burning feeling on the skin or swollen face
• Your eye or eyes become irritated.
If you get any of the above, stop using this medicine and tell your doctor straight away.
Other possible side effects include:
Very common (affects more than 1 in 10 people)
• Scaly hard skin
• Painful skin such as a stinging feeling
Common (affects fewer than 1 in 10 people)
• Headache
• Itchy, irritated or red skin
• Rash (sometimes with pimples), dermatitis
• Dry or peeling skin Uncommon (affects fewer than 1 in 100 people)
• Changes in skin colour
• Sensitivity to light
• Feeling hot
Rare (affects fewer than 1 in 1000 people)
• Light or dark patches on your skin

Reporting of suspected adverse reactions:

Drug Control Department
Directorate General of Pharmaceutical Affairs & Drug Control
Ministry of Health
P.O. Box: 393, Muscat, Postal Code:100,
Sultanate of Oman
Ph: +968-2-4692115/4744 Fax: +968-2-4602287
E-mail: mohphar@omantel.net.om

4.9 Overdose

Excessive application of Acretin 0.05% w/w Cream does not improve the results of treatment and may induce marked irritation, eg erythema, peeling, pruritus, etc. Oral ingestion of Acretin 0.025% w/w Cream may lead to the same effects associated with excessive oral intake of vitamin A (eg pruritus, dry skin, arthralgias, anorexia, vomiting). In the event of accidental ingestion, if the ingestion is recent an appropriate method of gastric emptying should be used as soon as possible.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacodynamic properties
Pharmacotherapeutic group: Retinoid for topical use in acne ATC code: D10AD01
Tretinoin (β-*all trans* retinoic acid, vitamin A acid) produces profound metabolic changes in keratinizing epithelia. Tretinoin increases the proliferative activity of epidermal cells in *in vivo* and *in vitro* studies, and cellular differentiation (keratinization and cornification) is also altered.

5.2 Pharmacokinetic properties

Absorption
Tretinoin is an endogenous metabolite of Vitamin A metabolism in man. Upon topical application, tretinoin is minimally absorbed, penetrating both the epidermis and dermis. Percutaneous absorption of tretinoin, as determined by the cumulative excretion of radiolabeled drug into urine and feces, was assessed in healthy men and women after single and/or repeated daily applications of a 0.025%, 0.1% or 0.5% tretinoin cream formulation or a 0.025%tretinoin Cream formulation, at doses of 100, 150 or 500 mg. The mean percutaneous absorption ranged from 1.0 to 4.3%. Endogenous plasma concentrations of tretinoin and its metabolites, 13-cis-retinoic acid, alltrans- 4-oxo-retinoic acid and 13-cis-4-oxo-retinoic acid were essentially unaltered after either single or multiple daily applications relative to baseline levels.

Distribution
Approximately 80% of tretinoin applied remains on the skin surface, whereas its penetration through the stratum corneum and the hair follicle is vehicle-dependent. After the initial diffusion into the stratum corneum that occurs within a few minutes, further diffusion into epidermis and dermis proceeds more slowly.

Metabolism
Topically-applied tretinoin is metabolized by CYP2S1 and CYP26. Metabolites are 13-cisetinoic acid, all-trans-4-oxo-retinoic acid and 13-cis-4-oxo-retinoic acid.

Elimination
After application of radiolabelled tretinoin emollient cream or cream, urinary excretion occurred mainly in the first 48 hours, whereas radioactivity was eliminated in the faeces throughout the 7 days after dose application. On average 1 – 1.5% of the radioactivity was recovered in urine and less than 1 % was recovered in feces.

Paediatric Population
Although there is limited data available, it is considered likely that the pharmacokinetic behaviour of tretinoin topical formulations and drug-drug interactions with tretinoin topical formulations will be similar to those in adults. In a study in 20 adolescent patients with moderate to severe acne treated for 12 weeks with tretinoin Cream, none of the plasma samples obtained at Week 12 of the treatment period contained quantifiable tretinoin levels.

5.3 Preclinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Polyoxyl-40 Stearate
Stearyl Alcohol
Isopropyl Myristate
Stearic Acid
Butylated Hydroxy Toulene
Sorbic Acid
Xanthan Gum
Purified Water

6.2 Incompatibilities

Not Known

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Do not store above 30°C
Discard the tube after 3 months from opening.

6.5 Nature and contents of container

30 gm printed collapsible aluminium tubes, internally lacquered, latex end seal, membrane nozzle, white full dia HDPE cap with spike for piercing.

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder

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8. Marketing authorisation number(s)

B4-7658

9. Date of first authorisation/renewal of the authorisation

31-Oct-2017

10. Date of revision of the text
