METAPHARMACEUTICAL IND SL
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TECHNICAL DATA SHEET

000223-TDS-ENG-2024

ACIDO TRANS RETINOICO (EUR. PH.) WHO-GMP		
DESCRIPTION DCI: TRETINOIN	DESCRIPTION DOE: TRETINOINA	
CAS Nº: 302-79-4	EC Nº: 206-129-0	AEMPS CODE: 155A
MOL. WEIGHT: 300,41	MOL. FORMULA: C20H28O2	ARTICLE CODE: 000223

ATTRIBUTES	SHOULD BE
Appearance	Yellow or light-orange, crystalline powder
Solubility	Practically insoluble in water, sparingly soluble in methylene chloride, slightly soluble in ethanol (96 %)
Melting point	about 182 ºC, with decomposition
Identification A	Complies
Related substances	
Impurity A	=< 0.5 %
Unspecified impurities	=< 0.2 %
Total impurities	=< 1.0 %
Loss on drying	=< 0.5 %
Sulfated ash	=< 0.1 %
Assay	98.0 - 102.0 %

COMPLIES WITH

European Pharmacopoeia 11.0

STORAGE

Store the containers in a dry and well-ventilated place, away from sources of heat and direct sunlight.

REMARKS

Tretinoin is subjected to the requirements of the ICH Q3D "Elemental Impurities" and the requirements of guides EMA/CHMP/ICH/82260/2006.

Absence of N-nitrosamines impurities has been ensured after a risk evaluation according to ICH Q9, ICH M7 and in accordance with guidelines EMA/428592/2019 Rev 2 and EMA/189634/2019.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE, among others, are available upon request.

All methods of analysis are validated by official pharmacopoeias or are validated by internal methods of the manufacturer, which can be obtained at specific request. The above information does not exempt from the obligation to identify the product before use.

Properties and uses

Trans-retinoic acid (or TRETINOIN) seems to stimulate mitosis and metabolism of follicular epithelial cells, reducing cohesion and facilitating the extrusion of existing comedones and preventing the formation of new ones by keratolytic effect. It also seems that the thickness of the stratum corneum decreases. It is used mainly in the topical treatment of acne vulgaris, especially in which comedones, papules, and pustules predominate, in the form of creams, gels, and hydroalcoholic solutions. The therapeutic response against acne is not evident until after 6 or 8 weeks of treatment, and even in the first phases of treatment hidden comedones may appear. Once acne has resolved, applications should be less frequent. It is also used in cases of ichthyosis, psoriasis, lichen planus, palmoplantar keratoderma, warts, papillomas, and actinic keratosis. Finally, it has a preventive effect on the appearance of wrinkles.

Dosage

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Topical route, 0.01 - 0.1%, normally 1-2 times a day (although this may vary depending on the patient, the response, irritation ...). In keratosis plantar and disorders of keratinization genetic or resistant to other treatments has been used up to 0.3%. As an anti-wrinkle agent, usually at 0.025 - 0.01% (sometimes more). For oral lichen planus, 0.1% in oral adhesive excipient.

Side effects
Retinoic acid is an irritant to the skin. During the first minutes of its application it can produce burning sensation and burning sensation. With the use it produces erythema and "peeling" (similar to that which occurs with minor sunburn). Depending on the individual sensitivity, the effects vary, from edemas to blisters or scabs. Other side effects are photosensitivity, and hyper and hypopigmentation. They are usually reversible symptoms, which subside when treatment is interrupted, but changes in pigmentation may persist for months.

Contraindications
Hypersensitivity to TRETINOIN. Pregnant patients and nursing mothers.

Precautions
Retinoic acid should not be applied to the eyes, mouth and nose, and other mucous surfaces, nor on damaged, eczematous skin, with open wounds, with abrasions, or burned by the sun. Do not use in conjunction with other topical therapies, especially with keratolytic agents, as well as excessive use of soap, but it can be used with benzoyl peroxide, with an interval of 12 to 24 hours between each application. You must avoid or minimize sun exposure or solar lamps, or protect yourself with creams and appropriate clothing.

Incompatibilities
Strong oxidizing agents.

Other observations
The product is served packed under a nitrogen atmosphere. All operations with the product must be carried out as quickly as possible, since it is very sensitive to air, heat and light. It is advisable not to give more than 1 month of expiration to the formulations. Add an antioxidant to the formulations (eg BHT 0.03%, or BHT 0.05% / BHA 0.05%).

Formulation examples

Cream with retinoic acid
TRETINOIN - 0.1%
Triamcinolone acetonide - 0.1%
Urea - 10%
Antioxidants q.s.
Emulsion O / W c.s.p. - 250 g

Modus operandi: Prepare the O / W emulsion by dissolving the urea in the water. Mix the retinoic acid, the triamcinolone acetonide, and the antioxidants in mortar, and moisten them with a little propylene glycol. Add the cream little by little and mix well with the pistil.

Anti-wrinkle cream
TRETINOIN - **0.025 %**
Antioxidants q.s.
Emulsion O / W c.s.p. - **100 g**

Gel with retinoic acid
TRETINOIN - **0.05 %**

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Erythromycin - **4 %**
Zinc sulfate -**1.2 %**
Antioxidants q.s.
Hydroalcoholic gel c.s.p. - **25 g**

Modus operandi: The gel can be prepared, for example, with 2% Hydroxypropyl guar gum and 75% purified water. Predispose zinc sulfate in the purified water part Predispose erythromycin, retinoic acid, and antioxidants in a little ethyl alcohol. Incorporate the gel to the previous mixture and homogenize well.

Ointment with retinoic acid
TRETINOIN - **0.1%**
Antioxidants q.s.
Vaselina filante c.s.p. - **60 g**

Modus operandi: Moisten the retinoic acid in mortar with a little liquid petrolatum. Incorporate the excipient and homogenize well.

Oral ointment of retinoic acid
TRETINOIN - **0.1%**
Antioxidants q.s.
Excipient Acrylic oral adhesive - **30 g**

Modus operandi: Moisten the retinoic acid in mortar with a little liquid petrolatum. Incorporate the excipient and homogenize well.

Retinoic acid solution
TRETINOIN - **0.05 %**
Antioxidants q.s.
Propylene glycol - **30 mL**
Ethyl alcohol 96% - **30 mL**

Modus operandi: Dissolve retinoic acid and antioxidants in alcohol, and then add propylene glycol.

Keratolytic collodion
TRETINOIN - **200 mg**
Salicylic acid - **5 g**
Lactic acid - **5 g**
Antioxidants q.s.
Elastic collodion - **30 g**

Retinoic acid capsules
TRETINOIN - **16 mg** for a 30 capsule