For Philippines

Artwork of insert "**ACNETREX 10 & 20**" MTD (PCL) code ***I-I022-M25-00-06***

Size: 132 x 186 mm *(F-I022-M25-D7, F-I023-M25-D7)*

(Front)

ISOTRETINOIN
ACNETREX 10
10 mg softgel capsule
Anti - acne

ISOTRETINOIN
ACNETREX 20
20 mg softgel capsule
Anti - acne

Rx

FORMULATION

Each softgel capsule contains :	Each softgel capsule contains :
Isotretinoin (13-cis retinoic acid), USP 10 mg	Isotretinoin (13-cis retinoic acid), USP 20 mg

PROPERTIES AND EFFECTS

Isotretinoin is a synthetic stereoisomer of all-trans retinoic acid (tretinoin). Improvement observed in the clinical picture of severe acne is associated with dose and time related time suppression of the sebaceous gland activity and reduction in the size of sebaceous glands.

INDICATIONS

Isotretinoin is a retinoid for systemic treatment of acne. It is indicated for severe forms of cystic acne and acne conglobata, especially when the lesions involve the trunk.

Isotretinoin is also effective in correcting severe keratinization disorders. However, longer periods of isotretinoin therapy may be required, thus increasing the risks of side effects, including skeletal changes and cardiovascular complications.

CLINICAL PHARMACOKINETICS

The exact mechanism of action of isotretinoin is not known, However, isotretinoin reduces sebaceous gland size and inhibits sebaceous gland activity, thereby decreasing sebum secretion, In addition, isotretinoin has been shown to have anti-keratinizing and anti-inflammatory actions. The exact role of these actions in clinical improvement of cystic acne is not known, especially with respect to prolonged remissions.

Rapidly absorbed from the gastrointestinal tract, taking isotretinoin with food increases bioavailability relative to fasting conditions. This is probably as a result of easier absorption of this highly lipophilic medication.

Isotretinoin is metabolized in liver and possibly in the gut wall. The major identified metabolite in the blood and urine is 4-oxo-isotretinoin, other identified metabolites are tretinoin and 4-oxo-tretinoin.

Isotretinoin appears to be eliminated almost exclusively by hepatic metabolism and biliary excretion.

CONTRAINDICATIONS

1. Hepatic and renal insufficiency; hypervitaminosis A; patients with excessively elevated blood lipid values; hypersensitivity to isotretinoin.

2. Blood donation by patients during and within one (1) month of isotretinoin treatment to women of childbearing potential should be avoided.

3. Pregnancy, Nursing Mother

Isotretinoin is highly teratogenic, it is therefore contraindicated in women who are pregnant or who may become pregnant while undergoing treatment. There is an extremely high risk that a deformed infant will result if pregnancy occurs while taking isotretinoin in any amount even for short periods. Potentially all exposed fetuses can be affected, Major human fetal abnormalities related to isotretinoin administration have documented, including hydrocephalus, microdephalus, abnormalities of the external ear (micropinna, small or absent external auditory canals), microphthalmia, cardiovascular abnormalities and cerebellar malformation.

As isotretinoin is highly lipophilic, the passage of the drug in human milk is very likely. Because of the potenital for adverse effects, the use of isotretinoin should be avoided by in nursing mothers.

It is recommended that the patient use two forms of effective contraception to prevent pregnancy, during treatment and for one (1) month after discontinuation of treatment, Testing serve to remind the patient of the importance of avoiding pregnancy. If pregnancy occurs, patient should be counseled on whether to continue the pregnancy. Isotretinoin therapy starts only on the second or third day of the next normal period.

PRECAUTIONS

1. Isotretinoin should only be prescribed by physicians who are experienced in the use of systemic retinoids, preferably dermatologists who understand the risk of teratogenicity if isotretinoin is used during pregnancy.

2. Liver function should be checked before and one (1) month after the start of treatment, and subsequently at three (3) monthly intervals.
Serum lipids (fasting value) should also be checked (before and one month after the start of therapy, and also at the end of the 3-4 months treatment period).

3. Depression, psychotic symptoms and rarely, suicide and suicide attempts have been reported in patients treated with isotretinoin. Although a casual relationship has not been established, particular care needs to be taken in patients with a history of depression and refered for appropriate treatment if necessary.

4. Checking with physician anytime vision problems occur; wearing contact lenses may be uncomfortable, vision impairment can occur including photophobia, blurred vision or dryness of eyes. Vision problems can make driving a car or operating machinery dangerous.

5. A careful evaluation of the risk/benefit ratio should be carried out in every patient and isotretinoin administration should be restricted to severe cases.

6. Since acne is an androgen-dependent disease, contraceptives containing an androgen progestational substance, such as one derived from 19-nortestosterone (norsteroid), particularly in the presence of gyne-endocrinological problems should be avoided.

7. Dermabrasion should be avoided in patients on isotretinoin and for a period of 5-6 months after treatment because of the risk of hypertrophic scarring in atypical areas.

8. Wax epilation should be avoided in patients on isotretinoin and for a period of 5-6 months after treatment because of the risk of dermatitis.

9. Special Patient Groups : In high-risk patients (with diabetes, obesity, alcoholism or disorders of lipid metabolism) undergoing treatment with isotretinoin, more frequent checks of the relevant laboratory parameters will be necessary.

In known or suspected diabetics, frequent determination of blood glucose levels is recommended. Although no casual relationship has been established, elevated fasting blood sugars have diagnosed during isotretinoin therapy.

Dental problems can occur resulting from dryness of mouth and may increase dental disease, including tooth decay, gum disease and fungus infections; regular dental appointments are needed and use of sugarless candy or saliva substitute or melting ice in mouth may be necessary to lessen dental problems.

10. Female patients should have a negative pregnancy test two (2) weeks prior to the start of therapy. She should use contraception without interruption for one (1) month before beginning therapy, during therapy and for one (1) month following discontinuation of therapy.

ADVERSE REACTIONS

Most of the adverse reactions of isotretinoin are dose-related. With recommended dosage, the risk/benefit ratio is generally acceptable considering the severity of the disease.

Incidence more frequent: chelitis (scaling, redness, burning, pain and other signs of inflammation of lips), epistaxis (nosebleeds) and skin infection.

Symptoms associated with Hypervitaminosis A: The following symptoms are the most frequently reported: Dryness of the skin, dryness of the mucosae, e.g. of the lips, the nasal mucosa (epistaxis), the eyes (conjunctivitis, reversible corneal opacities and intolerance to contact lenses).

(Back)

Skin and Appendages Disorders: Exanthema, pruritis, dermatitis facialis, sweating,pyogenic granuloma, paronychia, nail dystrophy, increased formation of granulation tissue, persistent hair thinning, reversible alopecia, acne fulminans, hirsutism, hyperpigmentation, photosensitivity.

Musculoskeletal System Disorder: Muscle pain, joint pain, hyperostosis and other bone changes, tendonitis.

Psychiatric and Central Nervous System Disorders: Behavioral disorders, depression, headache, increased intracranial pressure, seizures.

Sensory Disorders: Isolated cases of visual disturbances, impaired hearing at certain frequencies, photophobia, dark adaptation disturbances (decreased night vision), lenticular cataract, keratitis.

Gastrointestinal System Disorders: Nausea, inflammatory bowel disease, e.g. colitis, ileitis and hemorrhage have been reported to occur.

Liver and Biliary System Disorders: Transitory and reversible increase in transaminases, some cases of hepatitis. In many such cases, the changes have been within the normal range and values have returned to baseline levels during treatment. In other cases however, it has been necessary to reduce the dose or discontinue treatment with isotretinoin.

Respiratory System Disorders: Bronchospasm.

Disorders of the Blood: Decrease in white cell count, red blood cell parameters, increase or decrease in platelet count, elevated sedimentation rate.

Laboratory Findings: Increase in serum triglyceride and cholesterol levels, hyperuricemia. Decreases in HDL have also been observed, particularly at high dosages and in predisposed patients (with a family history of lipid-metabolism disorders, diabetes, obesity or alcoholism). These changes too, are dose-related, and values return to normal on reduction of the dosage or withdrawal of the drug. Every patient should be warned about the possible occurrence of adverse effects.

Resistance Mechanism Disorders: Local or systemic infections due to Gram-positive microorganisms (Staphylococcus aureus).

Miscellaneous Reactions:

- Lymphadenopathy, hematuria, and proteinuria, pancreatitis (especially patients with high serum trigylceride levels (>800 mg) treated with isotretinoin are at risk developing pancreatitis), vasculitis (eg. Wegener's granulomatosis).
- Bleeding or inflammation of gums; cataracts or corneal opacities.

INTERACTIONS

Concurrent therapy with isotretinoin and vitamin A must be avoided as symptoms of hypervitaminosis A may be intensified.

Rare cases of benign intracranial hypertension 'pseudotumor cerebri' have been reported after isotretinoin and after tetracyclines, Supplementary treatment with tetracyclines should therefore be avoided.

The effect of microdosed progesterone preparations may be diminished by interaction with isotretinoin. Therefore microdosed progesterone preparations should not be used.

DOSAGE & ADMINISTRATION

The usual adult and adolescent dose is 0.5 to 1 mg/kg of body weight per day (in two divided doses) for 15 to 20 weeks; the maximum recommended dose is 2 mg/kg of body weight per day and may be required in patients whose disease is very severe or is primarily located on the chest or back instead of on the face. During the initial period of isotretinoin therapy, transient exacerbation of acne may occur; concomitant adrenocorticoid therapy may be required.

Efficacy and side effects vary according to the individual patient; after about 4 weeks, therefore, dosage for the maintenance treatment should be adjusted within the range of 0.1-1 mg/kg daily to meet individual needs. Treatment usually lasts a total of 16 weeks. When assessing the results of the therapy, it should be borne in mind that there is often a further improvement after discontinuation of treatment. There should be an interval of at least eight (8) weeks before restarting treatment, which should be resumed in accordance with the previously mentioned dosage guidelines.

The capsules are taken with meals, low doses once daily, and higher amounts as a single dose or in several doses spread over the day.

Concurrent Topical Therapy: Concurrent administration of other keratolytic or exfoliative anti-acne agents is not indicated, nor is concurrent radiation therapy with ultraviolet light indicated, Patients should avoid exposure to the sun. Adjuvant therapy with mild topical anti-acne drugs may be given, as required.

OVERDOSAGE

Signs of hypervitaminosis A could appear in cases of accidental overdose. Evacuation of the stomach may be indicated in the first few hours after overdosage. The symptoms have been abdominal pain, dizziness, intracranial pressure, headache, severe nausea, vomiting, irritability, itchy skin.

Treatment of overdose:

To decrease absorption - Evacuation of stomach should be considered within 2 hours of ingestion of acute overdose. Medication should be discontinued in patients with symptoms of overdose who were given therapeutic doses.

Monitoring:

Monitor for increased intracranial pressure.

- Female patients with childbearing potential should have a pregnancy test at time of overdose and 1 month later; if positive, teratogenic risk and continuance of pregnancy should be discussed.
- Blood samples should be collected and isotretinoin and metabolite concentrations determined.

STORAGE

Store at temperatures not exceeding 25°C.
Protect from heat and light.

AVAILABILITY

Alu/Alu Blister Pack x 10's (Box of 30's)

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Manufactured by:
MEGA LIFESCIENCES Public Company Limited
384 Moo 4, Soi 6, Bangpoo Industrial Estate,
Pattana 3 Road, Phraeksa, Mueang,
Samutprakarn 10280, Thailand

Manufactured under license from:
MEGA LIFESCIENCES (AUSTRALIA) PTY. LTD.
60, National Avenue, Pakenham, Victoria 3810, Australia

Imported by: **MEGA LIFESCIENCES LIMITED INC.**
Unit 5B 5/F BA Lepanto Bldg., 8747 Paseo de Roxas,
Bel-Air, Makati City, Philippines

Distributed by: **METRO DRUG, INC**
Sta. Rosa Estate, Barangay Macabling,
Santa Rosa, Laguna Philippines

For suspected adverse drug reaction, report to the FDA:
www.fda.gov.ph

Isotretinoin (Acnetrex 10)
DR-XY28739
Date of First Authorization: 04 July 2003
Isotretinoin (Acnetrex 20)
DR-XY31203
Date of First Authorization: 26 October 2005

Date of Renewal of the Authorization : 07 September 2022
Date of Revision of Package Insert : January 2024

I-I022-M25-00-06

Artwork Check / Layout Check

PC TEAM		PRODUCTION		RA
Provide by : *Supawan* Date : *08-May-24* - Change to new Importer's address as change control no.CC-ML-RA-24-0083, CC-ML-RA-24-0084.	PC Check ☐ Pass : …… …… …… ☐ Not Pass : …… …… ……	Production Check 1 :	☐ Pass : …… ☐ Not pass : ……	Need to send for customer approval ☐ Yes, please send …… …… ☐ Not require …… ……
Department head approved : ……		Production Check 2 :	☐ Pass : …… ☐ Not pass : ……	
Date : ……		Production Department Head :	☐ Pass : …… ☐ Not pass : ……	
Final artwork from RA/Customer approved : …… Date : ……				

Specification
Offset Printing Paper 060 gsm
Verified by : ……