Severe acne (such as nodular acne, acne conglobata or acne likely to result in permanent scarring) unresponsive to appropriate conventional treatment with systemic antibiotics and topical therapy.

CURACNÉ® Gé* 5, 10, 20 mg
CURACNÉ® 40 mg
Isotretinoin

We remind you that any side effects should be reported to:

National Pharmacovigilance and Drug Safety Center (NPC)
Email: **npc.drug@sfda.gov.sa**
Toll Free Number: 19999
Fax: +966 11 2057662
Website: https://ade.sfda.gov.sa/

Or

Pierre Fabre Middle East
Dubai, UAE
Email: **PV_MiddleEast@pierre-fabre.com**
Mobile in KSA: 00966 505 404 345
Mobile in UAE: 00971 525 878 223

*Belongs to the class of generic medicinal products.
Excipient with a known effect: soya oil.

This medicine is teratogenic. As part of the pregnancy prevention programme, effective contraception is compulsory.

Pierre Fabre
DERMATOLOGIE

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DOCTOR'S Guide
to prescribing oral Isotretinoin soft capsules

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DOCTOR'S Guide
to prescribing oral Isotretinoin soft capsules

This document is part of the risk minimisation plan implemented for oral Isotretinoin.

Important Notes:

- **This guide summarizes the most important safety information about the risks of teratogenicity, occurrence of psychiatric disorders, lipid disorders, transaminases increased and hepatitis.**
- **The information in this brochure has been reviewed and approved by the Saudi Food and Drug Authority.**

Isotretinoin should only be prescribed by or under the supervision of physicians with expertise in the use of systemic retinoid for the treatment of severe acne and a full understanding of the risks of isotretinoin therapy and monitoring requirements.

Oral Isotretinoin should only be prescribed in severe forms of acne (i.e nodular and conglobata or acne at risk of permanent scarring), resistant to adequate courses of standard therapy with systemic antibacterial and topical therapy.

Drug requiring a specific monitoring during treatment

The Risk Management Plan aims to minimize the following important identified risks identified for isotretinoin:

Teratogenicity and drug exposure during pregnancy: oral isotretinoin is subject to a Pregnancy Prevention Program to make all persons involved (doctors, pharmacists and patients) aware of the teratogenic nature of isotretinoin, to improve compliance with contraception in women of child-bearing potential and thus to minimize the risk of pregnancy in women of child-bearing age.

- Psychiatric disorders: To improve awareness of prescribers and patients regarding the risk of occurrence of psychiatric disorders during the treatment.
- Lipid disorders, transaminases increased and hepatitis: To remind the prescriber about the mandatory biologic monitoring.
- Teratogenicity and drug exposure during pregnancy

Isotretinoin is a teratogenic drug. Exposure to Isotretinoin during pregnancy is associated with a **high risk of major fetal malformations**. Isotretinoin can only be prescribed to women of childbearing potential under strict pregnancy prevention measures supported by Marketing Authorization Holder (MAH's) Pregnancy Prevention Programme (PPP).

FOR WOMEN OF CHILDBEARING AGE

Before prescription of oral Isotretinoin

Give to your female patient:

- the care and contraception consent form,
- a women brochure and the letters to be given to the health care professional in charge of ensuring contraception (general practitioner or gynecologist),

First prescription of oral isotretinoin

- The prescriber should evaluate the patient's level of understanding.
- The prescriber must ensure that the patient is using two methods of effective contraception (a barrier device is relevant as second method of contraception) for at least 4 weeks prior to the start of treatment and is able to continue the use of an effective contraception method throughout the treatment period and for at least 4 weeks after cessation of treatment.
- Signature of the care and contraception consent form.
- Prescription is limited to 4 weeks of treatment, which continuation requires a new prescription subordinated by a negative pregnancy test. The pregnancy test has to be done within the 3 days preceding the new prescription. It is recommended to perform the tests in the first 3 days of the menstrual cycle.
- The Doctor's guide includes also liaison letters between the physician who initiates the treatment and other phycisians involved in the follow-up of the patient (Id. General practitioner and Gynecologist).

DOCTOR'S Guide
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Specific Information to female patients:

- Make sure that contraception is initiated, at least, 4 weeks before the initiation of the treatment with Isotretinoin.
- Check the negative result of the pregnancy test.
- Inform your patient that the dispensing must be done at the latest 7 days after the prescription of Isotretinoin.
- Verify that your patient understands the risks in case of pregnancy and the absolute requirement of an efficient contraception and ensure the patient signs the consent form.
- Prescribe plasmatic hCG levels for the following month (Must be done at least 3 days before the renewal of Isotretinoin prescription).
- Give to your female patient a women brochure and the letters to be given to her health care professional in charge of ensuring contraception and renewal of the treatment (general practitioner or gynecologist).

Monthly renewal:

- Make sure that the continuation of an effective contraception is continued.
- Evaluate the patient's level of understanding of the teratogenic risk.
- Dates of the monthly pregnancy test (plasmatic hCG).
- Verify the negative result of the pregnancy test.
- Inform your patient that the new dispensing must be done at the latest 7 days after the prescription of oral Isotretinoin.
- Every 4 weeks with each oral Isotretinoin prescription, you have to prescribe plasmatic hCG levels for the following month (Must be done at least 3 days before the renewal of oral Isotretinoin prescription)

If a pregnancy occurs in a woman treated with oral Isotretinoin, the treatment must be stopped immediately and the patient should be referred to a physician specialized or experienced in teratology for evaluation and advice.

At the end of the treatment

- Remind your female patient that she must continue to use two methods of effective contraception (a barrier device is relevant as second method of contraception) for at least 4 weeks after stopping treatment with oral Isotretinoin.
- Prescribe a final pregnancy test to be done 5 weeks after stopping treatment. Verify the negative result of this test.

Specific Information for male patients:

- Inform male patient that the available data suggests that the level of maternal exposure from the semen of male patients receiving oral Isotretinoin is not of a sufficient magnitude to be associated with the teratogenic effects of oral Isotretinoin. However, male patients should be reminded that they must not share their medication with anyone, particularly not females and not give their blood during the treatment.
- Give to your male patient a men brochure.

Pharmacovigilance and Medical Information departments are at your disposal to answer to your questions regarding oral Isotretinoin and their Risk Minimisation Tools. Email Addresses are available on the folder containing all the Risk Minimisation Tools.

- **Psychiatric disorders including depression, suicide, suicide attempt, suicide ideation**
  Your patient is suffering from severe acne, which is known to be possibly a disfiguring disease and that may alter the self esteem; consequently you must be vigilant towards mood disorders.

  Moreover depression, depression aggravated, anxiety, aggressive tendencies, mood alteration, psychotic symptoms and very rarely, suicidal ideations, suicide attempts and suicide were reported in patients treated with oral Isotretinoin. Even though the link between isotretinoin intake and the occurrence of these troubles is not established, special care should be taken in case of mood changes.

Do not forget before initiating oral Isotretinoin, and all along the treatment duration:

- To question your patient about his/her psychiatric history (before the start of treatment).
- To discuss with your patient (and with the parents if accompanying their son/daughter) about mood changes or other troubles she/he could have observed during oral Isotretinoin treatment, or troubles that could have been notified by her/his entourage.
- To help you discussing with your patient about his/her psychological status, you can use a tool (based on the Adolescent Depression Rating Scale) provided in this document.
- To reinforce your surveillance or to refer the patient to a specialist, in case of history of mood disorders or psychiatric disease.

Discontinuation of oral Isotretinoin may be insufficient to alleviate symptoms and therefore further psychiatric or psychological evaluation may be necessary.

Do not hesitate to refer your patient to a psychiatric consultation in case of suspicion of psychiatric disorders e.g.:

- Verbalization of suicidal ideas
- Appearances of aggressiveness to the circle of acquaintances disrupting the family or social life or the significant disorders (confusions) of the behaviour.
- Persistance and/or aggravation of depressive symptoms and also in case of spontaneous request of the patient and more generally as soon as you have a doubt on psychiatric status. Particular care needs to be taken in patients with history of depression and all patients should be monitored for signs of depression and referred for appropriate treatment if necessary.
- Lipid metabolism disorders possibly leading to acute pancreatitis, transaminases increased and hepatitis.
  Oral Isotretinoin treatment alters the plasma lipid levels but the mechanisms and the effects on the metabolism of triglyceride-rich lipoproteins such as chylomicrons and very-low-density lipoproteins remain unclear. The treatment can also alter the transaminases levels, and may cause hepatitis.

Do not forget:

- To prescribe Serum lipids and transaminases (fasting values) before treatment, 1 month after the start of treatment, and subsequently at 3 monthly intervals unless more frequent monitoring is clinically indicated.
- Discontinue oral Isotretinoin if hypertriglyceridaemia cannot be controlled at an acceptable level or if symptoms of pancreatitis occur. The levels in excess of 800 mg/dL or 9mmol/L are sometimes associated with acute pancreatitis, which may be fatal.

- Decrease the dose or discontinue oral Isotretinoin if transaminases cannot be controlled.

CHECK-POINT LIST

FOR PRESCRIPTION.FOLLOW-UP PATIENT TABLE

☑ In women patient :

AT EACH MONTHLY CONSULTATION

Prescription requirement	Before prescription	1st prescription	1st month	2nd month	3rd month	Nth month	Last consultation	5 weeks after ceasing treatment
Give to your patient: - the women brochure - the contraception brochure - the consent form - the letters to be given to the health care professional in charge of ensuring contraception or following/renewing treatment with oral Isotretinoin	✕ ✕ ✕ ✕							
Discuss with your patient about her psychological status. You can use a tool (based on the Adolescent Depression Rating Scale) provided in this document.	✕	✕	✕	✕	✕	✕	✕	
Signature of the consent form by the patient		✕						
Evaluation of the patient's level of understanding of the risks		✕	✕	✕	✕	✕	✕	
Effective Contraception [1]	✕	✕	✕	✕	✕	✕	✕	
Pregnancy test [2,3] - Prescribe pregnancy test - Check the negative result to the last pregnancy test prescribed	✕	✕ ✕	✕ ✕	✕ ✕	✕ ✕	✕ ✕	✕ ✕	✕
Dosage of transaminases, cholestérol, triglycerides [4] - Prescription of the dosage - Verify the results	✕	✕ ✕	✕			(every 3 months) ✕		
Clinical examination	✕		✕	✕	✕	✕	✕	

☑ In male patients:

Prescription requirement	Before prescription	1st prescription	After 1 month	At every consultation
Give to your patient: - the men brochure - the letter to be given to the health care professional in charge of following/renewing treatment with oral Isotretinoin	✕ ✕			
Discuss with your patient about his psychological status. You can use a tool (based on the Adolescent Depression Rating Scale) provided in this document.	✕	✕	✕	✕
Dosage of transaminases, cholestérol, triglycerides [4] - Prescription of the dosage - Verify the results	✕	✕ ✕	✕	✕
Clinical examination	✕		✕	✕

1. Two methods of effective contraception for at least 4 weeks prior starting treatment and is continuing to use effective contraception throughout the treatment period and for at least 4 weeks after cessation of treatment
2. First test: pregnancy test (plasmatic hCG) to be performed the 2nd or 3rd days of menstrual cycle.
3. Following test : monthly pregnancy tests (plasmatic hCG) to be performed within 3 days preceding the prescription
4. Dosage to be performed before treatment, 1 month after the start of treatment, and subsequently at 3 monthly intervals, except if particular medical circumstances justify more frequent control.