ISOTRETINOIN

Understanding the Treatment, Understanding the Risks, and Overcoming Common Misconceptions

A Brief Guide for Patients and Physicians



Prof. Francesco Bruno
Dermatologist in Milan
Clinical experience with isotretinoin since 1982

NOTE TO THE READER: This guide is intended for informational and educational purposes. It does not replace a dermatological consultation, the official package leaflet, the Summary of Product Characteristics, or current regulatory requirements. Treatment decisions are the responsibility of the physician, based on the individual patient's circumstances.

🇬🇧 ENGLISH EDITION
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PREFACE

Why This Guide?
For more than forty years, isotretinoin has been an important part of my clinical experience in the treatment of acne. Over the years, I have observed both the results of treatment and the concerns of patients and their families. I have seen how profoundly acne can affect quality of life, self-esteem, and personal relationships, particularly when it is persistent, severe, or leaves scars.
Accurate information, legitimate concerns, and common misconceptions about isotretinoin circulate side by side, sometimes fuelling unjustified fears. At the same time, genuine risks exist and must be understood, prevented, and carefully managed. The aim of this guide is to distinguish scientific evidence from unsubstantiated interpretations, explain what we know in clear and accessible language, and clarify where caution is still necessary. This is not about advocating a medication at all costs, but about supporting an informed decision: understanding the indications, appreciating the expected benefits, observing the necessary precautions, and maintaining an appropriate relationship with the dermatologist. Knowledge does not eliminate the need for caution; it enables us to exercise it more effectively.
Prof. Francesco Bruno
Milan

FOREWORD by Prof Gerd Plewig Dermatology Clinic Munich

ABOUT THE AUTHOR

Prof. Francesco Bruno, Dermatologo

Who is this man, living and working in Milan?
Our paths have crossed repeatedly over the decades, through visits and professional encounters in Italy and Munich. His dedication to dermatology is impressive. His particular areas of expertise include acne vulgaris, acne conglobata, hidradenitis suppurativa (also known as acne inversa), Gram-negative folliculitis, rosacea, and Demodex folliculorum. It is a pleasure to talk with him and exchange views on the latest advances from around the world. He is a blessing to his patients and an asset to the reputation of Italian dermatology.

Gerd Plewig

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1. WHAT IS ISOTRETINOIN?

Isotretinoin is a retinoid derived from vitamin A, administered orally to treat selected forms of acne, particularly severe cases, acne resistant to conventional therapies, or acne associated with a significant risk of permanent scarring, in accordance with its authorised indications.
It acts on several fundamental mechanisms involved in acne: it reduces sebaceous gland activity and sebum production, modifies the follicular keratinisation process, and helps reduce inflammation. Its overall effect makes it a particularly important treatment for cases in which other therapies have not achieved adequate results. However, isotretinoin is not a medication to be taken without medical supervision. Prescribing it requires a medical assessment, individualised dose selection, and an appropriate monitoring programme.

2. WHY IS IT IMPORTANT TO TREAT ACNE PROMPTLY?

Acne is not merely a cosmetic problem. It is an inflammatory disease that, in some people, can cause permanent scarring and have a significant psychological impact.
Not every form of acne requires isotretinoin. Topical and systemic treatments are effective for many mild or moderate presentations. When acne is severe, resistant to appropriate therapies, or associated with a high risk of scarring, the dermatologist may consider isotretinoin. The decision should take into account severity, duration, previous treatments, the risk of permanent sequelae, clinical circumstances, and the patient's informed preferences. The key point: do not wait for acne to leave scars before seeking specialist assessment.

3. COMMON MISCONCEPTIONS ABOUT ISOTRETINOIN

- **Misconception 1 — "Isotretinoin remains in the body for years"**
  What do we know? No. Isotretinoin is progressively eliminated from the body. The drug's mean plasma half-life is approximately 19–21 hours, while that of its main metabolite is longer. Half-life indicates the time required for the concentration to decrease by half; it does not, by itself, represent the exact time required for complete elimination. For women who could become pregnant, official precautions require pregnancy to be avoided during treatment and for at least one month after discontinuation. The pregnancy prevention programme also includes pregnancy testing and contraceptive measures in accordance with the applicable requirements. In practice: it is incorrect to claim that the drug remains in the body for years. However, it is essential to observe the pregnancy prevention period specified by official guidance.
- **Misconception 2 — "It is too dangerous a medication to use"**
  What do we know? Isotretinoin can be highly effective, but it carries important risks and requires appropriate prescribing and adequate monitoring. The most serious risk is the possibility of fetal harm if exposure occurs during pregnancy. Dry lips and skin are also common; blood test abnormalities and other adverse effects may occur. The appropriate approach is neither to describe the medication as harmless nor to label it dangerous in absolute terms, but to weigh the expected benefits against the risks for each individual.
- **Misconception 3 — "It always causes depression"**
  What do we know? The available evidence does not support the claim that isotretinoin inevitably causes depression. Nevertheless, regulatory authorities maintain warnings concerning possible mood disorders and other neuropsychiatric symptoms. Acne itself can have significant psychological consequences. For this reason, emotional well-being should be assessed before and during treatment, and the physician should be informed of any significant changes in mood or behaviour. Significant symptoms or psychological deterioration require prompt medical assessment.
- **Misconception 4 — "If my blood tests are normal, I no longer need monitoring"**
  What do we know? Laboratory tests are one part of monitoring, not the whole process. The physician determines which checks are necessary and how often they should be performed, taking into account baseline findings, dosage, risk factors, and the course of treatment. The occurrence of adverse effects, treatment tolerability, and the progress of the acne must also be assessed during follow-up visits.
- **Misconception 5 — "Everyone must take the same dose"**
  What do we know? The dosage is not the same for everyone. It is selected by the dermatologist according to the clinical presentation, body weight, response, tolerability, and any conditions requiring particular caution. Patients should not change their dose independently or compare their treatment with that of other people.
- **Misconception 6 — "Once my skin improves, I can stop treatment on my own"**
  What do we know? Improvement is good news, but it is not sufficient reason to decide independently when to discontinue treatment. The duration of therapy and the total cumulative dose are assessed by the dermatologist according to the

clinical response, the appearance of new lesions, and tolerability. Discontinuation and the possible management of a recurrence of acne should be discussed with the physician.

- **Misconception 7 — "Acne always comes back after treatment"**
  What do we know? It is not true that acne must inevitably return. After a course of isotretinoin, some people maintain long-lasting improvement, while others may experience a recurrence of varying severity. The outcome depends on several clinical factors. A relapse does not automatically mean that treatment was ineffective or that another course is necessary: a new assessment is required.

4. WHAT ADVERSE EFFECTS MAY OCCUR?

"...Remember, there are no medications without side effects!"
The most common adverse effects are associated with reduced sebum production and include:

- Dry, chapped lips and cheilitis.
- Dry skin and increased skin sensitivity.
- Dry or irritated eyes.
- Dryness of the nasal mucosa, sometimes with minor nosebleeds (frequent in men and rare in women).
- Muscle or joint pain in some patients.

Changes in triglyceride levels, cholesterol, or liver enzymes may also occur. The physician evaluates the test results and determines whether additional monitoring or treatment adjustments are necessary. Not all patients develop the same adverse effects, and their severity may vary. Contact your physician if you experience new, significant, or persistent symptoms, changes in mood, visual disturbances, or other unusual signs.

The Initial Flare-Up: A Phase to Face with Serenity
At the beginning of isotretinoin therapy, acne may go through a phase of apparent worsening, called *flare-up*
New pustules may appear, which can cause concern. It is important, however, not to panic: this is a transient phase of the therapeutic journey.
The *flare-up* can last for about two months.
It is a period to face with patience and serenity, knowing that an initial worsening does not necessarily mean that the cure is not working.
The response to therapy must be evaluated over time, without being discouraged by initial manifestations.
When indicated by the dermatologist, new pustules can be treated with a local antibiotic therapy. The goal is to guide the skin through this initial phase, controlling inflammatory manifestations and continuing the treatment under specialist supervision.
Do not lose heart: evaluating results requires considering the overall evolution of acne during the course of therapy.

5. ESSENTIAL PRECAUTIONS

Isotretinoin requires several important safety measures.

- **Pregnancy:** The medication is contraindicated during pregnancy because it can cause severe fetal malformations. Patients who could become pregnant must strictly follow the official pregnancy prevention programme, including contraception and pregnancy testing at the required times. If pregnancy occurs during treatment or during the subsequent period specified by the programme, the medication must be stopped and the physician contacted urgently.
- **Other medicines and supplements:** It is important to inform the physician about all medicines and supplements being taken. Concomitant use of tetracyclines must be avoided; vitamin A supplements should not be taken without medical advice.
- **Tests and monitoring:** Patients must follow the schedule agreed upon with their dermatologist and report any medical conditions or changes in their health.
- **Blood donation:** Blood must not be donated during treatment or for the period specified after treatment has ended, in order to prevent the risk of exposing a pregnant woman to blood containing the medication.
- **Skin protection:** Gentle cleansing, use of a moisturiser, and sun protection in accordance with medical advice are generally helpful.

6. HOW TO MANAGE TREATMENT IN EVERYDAY LIFE

During treatment, it is often helpful to simplify the skincare routine. A lip emollient can be applied regularly; for the face, a gentle cleanser and a moisturiser suitable for the individual's skin can be used. If dry eyes occur, contact lenses become difficult to tolerate, or persistent irritation develops, the physician should be consulted.
It is preferable to avoid independently adding irritating products or intensive exfoliating treatments. Advice regarding physical activity, sun exposure, cosmetic procedures, and other lifestyle considerations should be individualised. There is no single skincare routine suitable for everyone: the best approach is one that is effective, well tolerated, and agreed upon with the healthcare professional.

7. DIET AND ISOTRETINOIN

There is no universal diet that can replace medical treatment for acne. A balanced diet is reasonable, without demonising individual foods or resorting to drastic restrictions without a medical indication.
Administration requirements may depend on the formulation of the medication. Patients should follow the instructions for the prescribed product and the advice provided by their physician or pharmacist. Alcohol warrants caution because it may contribute to liver problems or elevated triglyceride levels. Patients should discuss alcohol consumption with their physician, who may recommend avoiding it during treatment.

8. FREQUENTLY ASKED QUESTIONS (FAQ)

- **Is isotretinoin suitable for every type of acne?**
  No. The decision depends on severity, response to previous therapies, and the risk of scarring. The dermatologist assesses whether treatment is indicated.

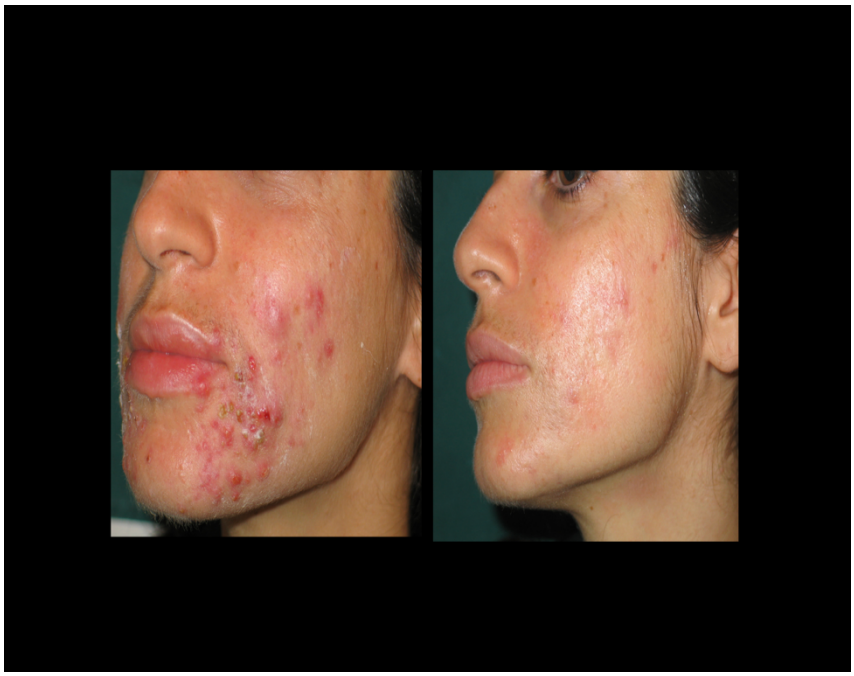
- **How long does treatment last?**
  Duration varies from person to person. It depends on the clinical response, dosage, and tolerability; it should not be determined independently.
- **Are blood tests necessary?**
  Monitoring is planned by the physician according to the treatment and individual risk factors. The tests required and their frequency may vary.
- **Can I become pregnant immediately after stopping treatment?**
  Patients who could become pregnant must wait at least one month after the last dose and comply with all other measures in the official programme, including the final pregnancy test at the required time.
- **If my acne returns, does that mean the treatment has failed?**
  No. A recurrence is possible and should be assessed. It does not automatically mean that another course is necessary. If isotretinoin is prescribed at the correct dosage, from 0.5 to 1 mg/kg of body weight, for a period of at least six months, acne can heal permanently in 95% of cases and relapse (return) in only 5% of treated cases.
- **Can I stop taking the medication if I experience adverse effects?**
  Do not change the treatment independently. Contact your physician to assess the symptoms and decide how to proceed. Seek urgent medical attention if symptoms are severe.

9. CLINICAL PHOTOGRAPHS: RESULTS IN CLINICAL PRACTICE

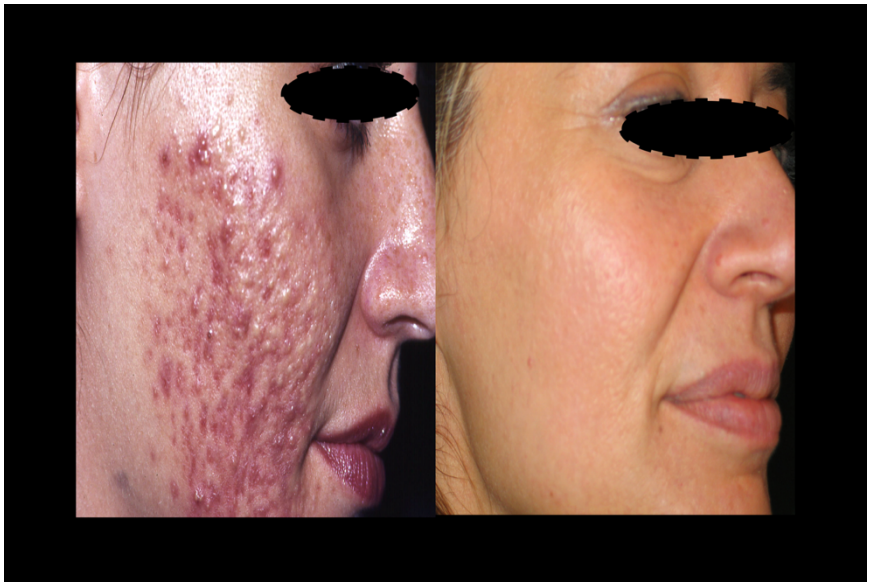
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(The three pairs of original clinical before-and-after photographs clearly illustrate the acute flare-up phase/deep nodulocystic state on the left, and the complete clinical clearance and skin recovery after six months of systemic treatment on the right).



Left: Initial "flare-up" phenomenon. Right: Resolution after six months of isotretinoin therapy.



Left: Initial “flare-up” phenomenon. Right: Resolution after six months of isotretinoin therapy.



Clearance after six months of isotretinoin therapy

10. CONCLUSIONS

Isotretinoin is an important treatment for certain forms of acne, but it must be prescribed and monitored carefully. Accurate information requires two complementary approaches: avoiding fears based on unsubstantiated claims and not underestimating documented risks. Patients should be able to understand the reasons for prescribing the medication, the expected benefits, the possible adverse effects, and the necessary precautions. Physicians should individualise treatment and maintain clear, ongoing communication. Informed treatment begins with accurate information.

SELECTED REFERENCES

1. **Italian Medicines Agency (AIFA).** *Oral isotretinoin for acne: the AIFA–ADOI ten-point guide*. Informational material concerning indications, prescribing, and precautions.
2. **European Medicines Agency (EMA).** *Retinoid-containing medicinal products: referral*. Official information on pregnancy prevention and safety warnings.
3. **Italian Medicines Agency (AIFA).** *Oral retinoids: reminder on measures to prevent exposure during pregnancy*, 2024.
4. **National Institute for Health and Care Excellence (NICE).** *Acne vulgaris: management*. Clinical recommendations for the management of acne.