



EUROPEAN ACADEMY OF
DERMATOLOGY AND VENEREOLOGY

Information Leaflet for Patients

ACNE: HOW TO TREAT IT

The aim of this leaflet

This leaflet is designed to help you understand more about acne vulgaris and in particular it tells you about different types of treatments for acne.

ACNE: HOW TO TREAT IT

How can your acne be treated?

Type of acne	Mild acne	Moderate acne	Severe acne
1 st choice	Topical retinoid	Fixed combination of Topical retinoid, Benzoyl peroxide, topical antibiotic variably combined	Oral isotretinoin
2 nd choice	Topical retinoid and/or Benzoyl peroxide and/or Azelaic acid / and Topical antibiotic	Systemic antibiotic + Fixed combination of Topical retinoid + Benzoyl peroxide	Systemic antibiotic + Fixed combination of Topical retinoid + Benzoyl peroxide
Possible addition in female patients		Combined oral contraceptives or antiandrogens	Combined oral contraceptives or antiandrogens

TOPICAL PRODUCTS

Topical drugs are of major importance and widely prescribed in acne therapy. The most effective topical treatments in acne are retinoids, benzoyl peroxide, antibiotics and azelaic acid. They are indicated in mild to moderate acne, and also in moderate to severe acne in association with systemic treatments.

What are the main topical retinoids, their efficacy, and side effects?

Topical retinoids, such as tretinoin, adapalene, isotretinoin, and tazarotene, are unanimously considered to be the core of topical acne therapy thanks to their effects on: 1) reducing *comedones* (non-inflammatory lesions, also called “blackheads” and “whiteheads”) that are already present, 2) preventing the development of new *comedones*, and 3) reducing skin inflammation.

They have an effect on both inflammatory and non-inflammatory acne lesions, and no direct effects on *sebum* production (by *sebaceous glands*) and *C. acnes* have been

found. Topical retinoids are used alone in cases of acne where non-inflammatory lesions (*comedones*) largely prevail over inflammatory lesions (*papules* and *pustules*; see leaflet 1 for complete definitions), or when the aim is to prevent recurrences after “clearing” or disappearance of acne lesions (maintenance therapy). They are frequently used in combination with other topical products like benzoyl peroxide and antibiotics, with improvement in terms of efficacy. They should be used preferentially at night.

About one-third to over half (30-60%) of acne lesions decrease after 3 months of topical use alone.

Allergic contact dermatitis: negligible/very rare occurrence.

Irritative contact dermatitis: quite frequent during the first weeks of application. It appears with redness, burning sensation, and skin peeling. It is usually mild and subsides within 2-4 weeks. The most tolerable *formulations* are creams and aqueous gels that contain no drug/active substance.

What strategies can be used during the first weeks of topical retinoid application to avoid or minimize irritation?

- before application, use a non-aggressive cleanser and avoid over-cleansing
- dab instead of rubbing to dry the skin
- wait a few minutes after cleansing before applying the product
- the most tolerable version of the retinoid (i.e. lowest concentration is usually better) should be selected according to skin type and environmental factors (temperature, humidity, etc.)
- apply the product in a thin layer
- if irritation is most likely to occur, begin to apply the retinoid every other day or two non-consecutive days per week, or for a short time (30-60 min per day), then wash off
- after absorption of the active agent, apply a moisturizing product
- use an appropriate sunscreen during summertime.

Systemic absorption: negligible, but use during pregnancy is not allowed.

Use in summer: allowed with caution. It must be used in the evening. It makes the skin more sensitive to sunrays so adequate sun protection is necessary.

What is benzoyl peroxide, its efficacy, and side effects?

Benzoyl peroxide is an antimicrobial agent, and it reduces *C. acnes* in number without creating resistant strains since it is not an antibiotic, but it has no effect on production of *sebum*.

Its main clinical effect is on inflammatory lesions (*papules* and *pustules*). It can be used alone, but it works better in a *fixed combination* (in the same product) with topical retinoids or antibiotics.

About one-third to over half (30-60%) of acne lesions decrease after 3 months of being used alone.

Allergic contact dermatitis: rare occurrence.

Irritative contact dermatitis: quite frequent during the first weeks of application. Using a moisturizer is advisable.

Systemic absorption: none. The use during pregnancy is allowed.

Use in summer: allowed with caution. It must be used in the evening. It makes the skin more sensitive to sunrays so adequate sun protection is necessary.

Other precautions: Benzoyl peroxide may bleach clothes and hair.

What are the main topical antibiotics, their efficacy, and side effects?

The most effective topical antibiotics are clindamycin 1% and erythromycin 2-4%. Their effect is both antibacterial, reducing *C. acnes*, and anti-inflammatory. Its use alone is not advisable for the risk of inducing antibiotic resistance. *Fixed combinations*, with retinoids or benzoyl peroxide, are more effective, better tolerated and provide higher adherence to the treatment than separated products.

About one-third to two-thirds (30-70%) of acne lesions decrease after 3 months of being used in combination with other products.

Allergic contact dermatitis: negligible/very rare occurrence.

Irritative contact dermatitis: negligible/rare occurrence.

Systemic absorption: minimal. The use of clindamycin and erythromycin during pregnancy is allowed.

Use in summer: allowed. Evening use is preferable in case of sun exposure.

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What is azelaic acid, its efficacy, and side effects?

It reduces inflammation, levels of *C. acnes*, and *comedones*. No direct effect on *sebum* production has been shown. The more relevant clinical effect is on inflammatory acne lesions, *papules* and *pustules*.

About one-fourth to half (25-50%) of acne lesions decrease after 3 months of being used alone.

Allergic contact dermatitis: negligible/rare occurrence.

Irritative contact dermatitis: rare.

Systemic absorption: negligible. Use during pregnancy is allowed.

Use in summer: allowed with caution and at night. It makes the skin slightly more sensitive to sunrays so adequate sun protection is necessary.

SYSTEMIC THERAPY

What are the main oral antibiotics, their efficacy, and side effects?

Oral antibiotics act by reducing *C. acnes* and directly decreasing inflammation. They are used for moderate and severe acne, and also acne extending over the chest and/or back.

Tetracyclines (like doxycycline, lymecycline and minocycline) are the first choice before macrolides (like erythromycin and azithromycin) due to fewer side effects, including in particular antibiotic resistance. Their efficacy is increased when associated with topical treatments, such as retinoids, benzoyl peroxide, azelaic acid, and specific anti-acne oral contraceptives. The advisable duration of the treatment is 6 to 12 weeks, and a longer period of treatment is rarely more beneficial. The use of oral antibiotics alone is not advisable.

About one-third to three-fourths (35-75%) of inflammatory acne lesions decrease after 3 months of being used in combination with other topical products.

During pregnancy: erythromycin and clindamycin are allowed, but tetracyclines are contraindicated.

Sun exposure: it may lead to mild *erythematous* (reddening of the skin) reactions in some patients using doxycycline, which increases with higher doses. *Photosensitivity* (increased skin sensitivity to the sun) has not been shown with lymecycline, minocycline and macrolides.

What are the main hormones, their role in female acne therapy, their efficacy, and side effects?

Male hormones (androgens) are strongly involved in acne development. Hormonal therapy which counteract is indicated in females with moderate-to-severe inflammatory acne: *papular-pustular* (inflammatory lesions), *nodular* or *cystic* acne (with nodules or cysts). It is more effective in combination with topical treatments or oral antibiotics rather than as a stand-alone therapy, and it works whether or not the blood levels of androgens are increased. The most effective hormonal treatments for acne are combined oral contraceptives and spironolactone. Among the available combined oral contraceptives, the ones containing progestins with an anti-androgenic effect (like cyproterone acetate, drospirenone and chlormadinone acetate) are preferred among patients with acne.

Duration of treatment: on average, it takes 3-4 months before you may see a clinical improvement of your acne. The full effect is expected to be seen at 6-9 months, with a reduction of acne lesions by 30-70%.

Side effects: mood changes, breast tenderness, decreased libido, irregular menstrual bleeding, weight gain, and headache may occur. A slightly increased risk for blood clots should be considered.

Contraindications for combined oral contraceptives: risk for *deep vein thrombosis* (blood clots), blood coagulation disorders, ischemic heart disease at a young age, estrogen-dependent cancer (breast), strong smoking in over 35 years of age.

Use in summer: combined oral contraceptives may be used during summertime.

Concurrent use with antibiotics:

Rifamycin is the only antibiotic recognized to potentially reduce hormone levels of the blood, with a reduced contraceptive efficacy.

What is oral isotretinoin (a vitamin A derivative), its efficacy, and unique side effects?

Oral isotretinoin is a naturally occurring molecule, and part of the metabolic chain that ends up in vitamin A products. It is physiologically present within all human beings and no individual is allergic to it. At therapeutic doses, it is the most effective anti-acne therapy, considering both short and long-term effects. It is indicated in severe acne or acne that doesn't respond adequately to an appropriate course of therapy with systemic antibiotics and topical treatments.

What are the contraindications for this drug?

- 1) Pregnancy: It must be absolutely avoided, during treatment and one month after stopping. The risk of major fetal malformations is high. Female patients must use two forms of contraception (hormonal and barrier). A specific Pregnancy Prevention Program (PPP), providing information about prescription, follow-up, and informed consent, has been prepared by health authorities.
- 2) Cardiac and liver insufficiency.
- 3) Allergy to soy.

It is important to note that tetracyclines and vitamin A cannot be taken at the same time. Isotretinoin should be taken on a full stomach to improve absorption. The correct dose starts low and progressively increases until the highest dose tolerated by the patient. This way incidence and the severity of side effects are reduced and

their management facilitated. Laboratory tests, including a pregnancy test, must be done before, during, and one month after stopping the drug.

Clinical effects: In the vast majority of cases (95%), acne lesions may completely clear/disappear. For severe cases, oral isotretinoin is definitely the most effective antiacne treatment. In the right patient, taken the correct way and at the right dose, and when managed by an experienced dermatologist, it can provide clinical improvement and prevent/minimize possible side effects.

Side effects: Dry lips/*cheilitis* is always present, which is dose-related and indirectly represents the absorption of the drug. It may be easily managed by reducing the dose of the drug and applying a moisturizing agent. *Skin xerosis* (dryness) and *facial erythema* (redness) may occur. Dry eyes are less frequent and are dose-related. Weakness, headache and muscle pain after strong physical exercise may rarely occur. Increased blood cholesterol levels may also occur, in particular in predisposed patients. Blood levels of *liver enzymes* may rarely increase when high dosages of the drug are used. Mood changes may also be seen but it must be kept in mind that, in female patients, oral contraceptives are frequently responsible for that. Psychiatric side effects have been described in patients taking oral isotretinoin, but it has not been proven to be caused by the drug. The association with an increased risk of depression is controversial. In addition, an improvement of acne-related depressive symptoms has been shown.

Use in summer: Oral isotretinoin may reduce the thickness of the skin so that it may become more sensitive to the effects of sunrays. The use of oral isotretinoin in the summer is not contraindicated, but reduction of the dosage, extent of sun exposure and application of efficient sunscreens must be taken into account.

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OTHER ACNE THERAPIES

Are light therapies effective in active acne?

A recently published study shows that red light, blue light, yellow light, infrared light, and pulsed dye laser can't be considered as a first-line therapy in acne. These procedures can be used in association with standard therapies in selected cases.

What about superficial chemical peelings in active acne?

It is difficult to understand the real effects of superficial chemical peelings in active acne. Experts suppose that their use could be appropriate in association with other established treatments, or as the sole treatment in rare instances when the patient can't tolerate other treatment modalities.

What is the maintenance therapy?

This is a very important point. Once acne has been cleared, in order to avoid recurrences, maintenance therapy should be initiated. A topical retinoid alone or in combination with benzoyl peroxide is the treatment of choice.

May cosmetics (cleansers, moisturizing agents, sunscreens) help in managing acne?

Cosmetic products provide an unavoidable support to standard treatments. Their correct use may counteract the irritation induced by some standard therapies and

help maintain the skin in a physiologically balanced situation. There is no evidence to say that acne is caused, exaggerated, or cured by washing. The advisable number of daily washing in acne is two times, with no worsening of the condition if the number is higher.

Do dermocosmetics have a role in acne therapy?

Although a widely accepted definition of dermocosmetics has not been established yet, they are usually considered to be products that may be effective in counteracting acne lesions with a non-pharmacologic mechanism of action. Their effect is less evident in comparison with what is provided by drugs.

Extrusion of open comedones (blackheads)

It is advisable! This way the content of the follicle can be released outside, avoiding rupture of the wall and preventing the formation of papules and pustules. It is well known that inflammatory acne lesions tend to grow up over a pre-existing non-inflammatory lesion.

Before manual squeezing, the skin must be disinfected, and after the extrusion a topical antiseptic (to avoid bacterial infections), must be applied. Of note that open comedones may come back. In the early phases, the procedure of extrusion must be repeated every 3-4 weeks, and then less frequently. ■

