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ORIGINAL ARTICLE

A consensus-based practical and daily guide for the treatment of acne patients

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Abstract

Background Many current guidelines provide detailed evidence-based recommendations for acne treatment.

Objective To create consensus-based, simple, easy-to-use algorithms for clinical acne treatment in daily office-based practice and to provide checklists to assist in determining why a patient may not have responded to treatment and what action to take.

Methods Existing treatment guidelines and consensus papers were reviewed. The information in them was extracted and simplified according to daily clinical practice needs using a consensus-based approach and based on the authors' clinical expertise.

Results As outcomes, separate simple algorithms are presented for the treatment of predominant comedonal, predominant papulopustular and nodular/conglobate acne. Patients with predominant comedonal acne should initially be treated with a topical retinoid, azelaic acid or salicylic acid. Fixed combination topicals are recommended for patients with predominant papulopustular acne with treatment tailored according to the severity of disease. Treatment recommendations for nodular/conglobate acne include oral isotretinoin or fixed combinations plus oral antibiotics in men, and these options may be supplemented with oral anti-androgenic hormonal therapy in women. Further decisions regarding treatment responses should be evaluated 8 weeks after treatment initiation in patients with predominant comedonal or papulopustular acne and 12 weeks after in those with nodular/conglobate acne. Maintenance therapy with a topical retinoid or azelaic acid should be commenced once a patient is clear or almost clear of their acne to prevent the disease from recurring. The principal explanations for lack of treatment response fall into 5 main categories: disease progression, non-drug-related reasons, drug-related reasons, poor adherence, and adverse events.

Conclusion This practical guide provides dermatologists with treatment algorithms adapted to different clinical features of acne which are simple and easy to use in daily clinical practice. The checklists to establish the causes for a lack of treatment response and subsequent action to take will facilitate successful acne management.

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Conflicts of Interest

The Expert Board was organized by Meda. HG: study investigator for or speaker at several symposia sponsored by Meda, Galderma, IMTM, Roche-Posay, Intendis, GSK, Hermal-Almirall, Vichy and Bayer Healthcare; advisory board for Galderma, Meda, Novartis, Intendis, Merz, Pierre Fabre, Hermal-Almirall and Bayer Healthcare. BD: consultant for Meda, Galderma and Pierre Fabre. VB: Biogena, Difa Cooper, Galderma, GSK, Meda, Pharcos, Pierre Fabre and Visupharma. JL: Meda, Galderma and Pierre Fabre. EA: speaker for L'Oreal, La Roche-Posay, Vichy, Bioderma, Pierre Fabre, Uriage, Galderma, Glenmark, Bayer Health Care, Merz and Stiefel/GSK; advisory board for Galderma. IB: none. CD: honorarium as a speaker for GSK; advisory board for Galderma. IG: none. RG: speaker at several symposia sponsored by Meda and GSK. Nİ: GSK and Bioderma. MK: consultant for Galderma, Meda, Novartis, L'Oreal, Pfizer and Filabe. LK: study investigator and speaker sponsored by Galderma and La Roche-Posay. JLLE: speaker at several symposia sponsored by Meda, Galderma, Intendis, GSK, Leo and Novartis. AM: none. CO: lectures sponsored by Galderma. WS: advisory board for Galderma and Novartis. Numerous talks sponsored by Galderma, Astellas and 3M; attended several meetings in Europe as part of the Global Alliance for Improvement of Outcomes in Acne, sponsored by Galderma. No financial or personal conflict of interest exists with regards to this publication. JS: advisory board/consultant for Pierre Fabre; speaker for Actavis, Meda and Polfa Tarchomin.

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Introduction

Acne is a chronic, inflammatory disease of the pilosebaceous unit, which is common during adolescence, and imposes a considerable burden on those affected by the disease.[1–3] The primary pathogenic factors of acne are increased sebum production by the sebaceous gland, alterations in the keratinisation process, follicular colonization by *Propionibacterium acnes* and activation of innate immunity followed by increased inflammation.[1] This multifactorial pathophysiology means that acne treatments need to target the full spectrum of pathogenic factors to be effective, which is optimally addressed using combination therapy.[4,5]

The clinical presentation of acne varies greatly. In this article, three main types of acne are considered: predominant comedonal facial acne, predominant papulopustular facial acne and nodular and/or conglobate acne affecting the face, trunk and upper limbs (Fig. 1).

Currently, there are many national and international guidelines which provide detailed, evidence-based recommendations for acne treatment.[4,6–9] However, there remains a need to provide dermatologists with simple, easy-to-use practical guidance on acne treatment. We therefore decided to create simple treatment algorithms for predominant comedonal, predominant papulopustular and nodular/conglobate acne based on expert consensus of how to integrate existing guidelines and consensus recommendations into daily clinical practice. We also developed checklists to help dermatologists quickly determine why a patient may not have responded to a treatment and offer guidance on subsequent action to take. This article will not address special clinical situations such as infant acne, adult female acne or acne associated with syndromes.

[a]Equal contribution.
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Methods

The treatment algorithms were developed by 17 acne experts and were based on a review of current, frequently cited, international, evidence-based acne treatment guidelines, i.e. those of the Global Alliance to Improve Outcomes in Acne Group,[4,6] the European Dermatology Forum,[7] the American Academy of Dermatology[9] and groups from Asia.[8,10,11] The information in these guidelines was simplified and modulated based on consensus and the clinical experience of the authors, and are supported by recently published literature.

Results

For easy to use in daily practice, we present separate, simple algorithms for the treatment of predominant comedonal, predominant papulopustular and nodular/conglobate acne (Figs 2–4). Treatment responses should be evaluated using the Global Evaluation Acne scale (Table 1).[12] A patient is considered to have clinical improvement when there is a reduction of at least one or two grades in the Global Evaluation Acne scale.[12] On the basis of our experience, we propose that patients with predominant comedonal or papulopustular acne should be evaluated 6–8 weeks after treatment initiation to determine whether they have responded or whether further therapeutic decisions should be considered. For more severe cases, e.g. nodular and/or conglobate acne, clinical outcomes should be evaluated twice within the first 12 weeks of treatment initiation, although regulations

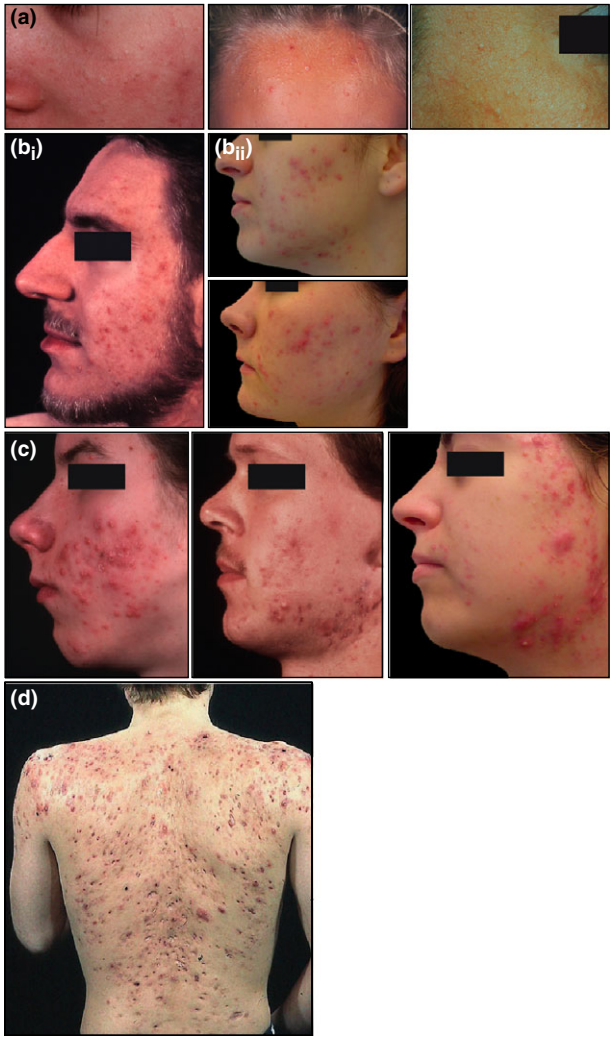

Figure 1 Examples of different types of acne. (a) Predominant comedonal acne: some macrocomedones and inflammatory lesions are present. (bi) Long-persisting papulopustular acne with scarring. (bii) Acute papulopustular acne with small nodules (<0.5–1.0 cm). (c) Severe papulopustular acne and transition to conglobate acne with sinus development and deep scarring. (d) Conglobate acne of the trunk.

for individual acne treatments should be followed. This follow-up is necessary to evaluate the efficacy of the therapy against the grade of inflammation and tendency for scarring. It may take more time for a treatment response to be observed in these special cases. Patients may present at the clinic earlier if they are experiencing tolerability issues.

If a patient has not responded to treatment, the dermatologist should establish the reasons for this. The current practical guide includes simple checklists of the most common causes for a lack of treatment response and advice on subsequent action to take (Tables 2–4).

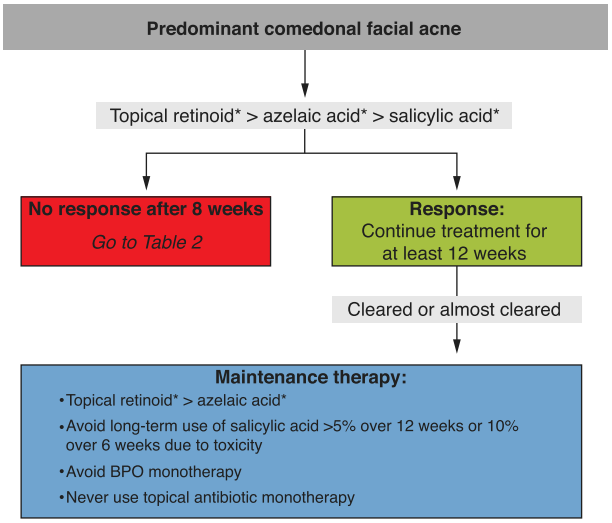

Figure 2 Treatment algorithm for predominant comedonal facial acne. *Dose of treatments adjusted according to adverse events (e.g. irritation). Please refer to text for further information.

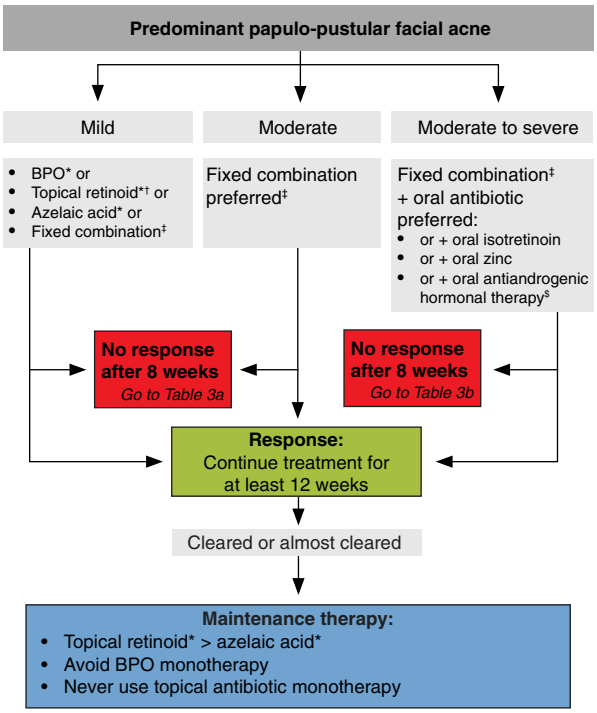

Figure 3 Treatment algorithm for predominant papulopustular facial acne. *Dose of treatments adjusted according to adverse events (e.g. irritation). †Second generation. ‡Clindamycin 1%/tretinoin 0.025% (not with oral antibiotic), adapalene 0.1%/BPO 2.5%, clindamycin 1%/BPO 5% (not with oral antibiotic).§Female patients only; contraceptive pill containing a progestin with anti-androgenic activity preferred. Please refer to text for further information.

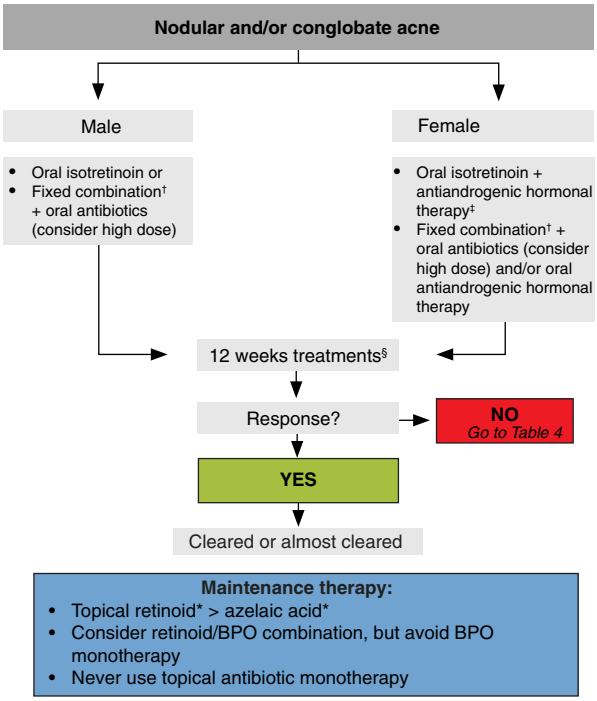

Figure 4 Treatment algorithm for nodular and/or conglobate acne. *Dose of treatments adjusted according to adverse events (e.g. irritation). †Clindamycin 1%/tretinoin 0.025% (not with oral antibiotic), adapalene 0.1%/BPO 2.5%, clindamycin 1%/BPO 5% (not with oral antibiotic).‡Contraceptive pill containing a progestin with anti-androgenic activity preferred. §16–24 weeks for oral isotretinoin. Please refer to text for further information.

Table 1 Global Evaluation Acne scale for facial acne[12]

Grade	Severity	Description
0	Clear, no lesions	Residual pigmentation and erythema may be seen
1	Almost clear, almost no lesions	A few scattered open or closed comedones and very few papules
2	Mild	*Easily recognizable*: less than half of the face is involved. A few open or closed comedones and a few papules and pustules
3	Moderate	*More than half of the face* is involved. *Many* papules and pustules, many open or closed comedones. One nodule may be present
4	Severe	*Entire face* is involved, *covered* with many papules and pustules, open or closed comedones and rare nodules
5	Very severe	*Highly inflammatory acne* covering the face with presence of *nodules*

General skin care measures such as the use of anti-UVA and -UVB sunscreen, appropriate cleansers with a pH close to the skin and non-comedogenic moisturizers are recommended for all acne patients as part of their overall management plans.[13]

Predominant comedonal acne

Topical treatment with either a retinoid,[14,15] azelaic acid[16] or salicylic acid[9] is recommended as a first-line approach for patients with predominant comedonal facial acne without significant inflammatory lesions (Fig. 2). Topical retinoids are considered to be more effective at treating comedonal acne than azelaic acid, which in turn is thought to be more effective than salicylic acid.[9,17] Topical retinoids and azelaic acid inhibit the formation of microcomedones, the precursor to all other types of acne lesions, and are both comedolytic and anti-comedogenic, as well as having anti-inflammatory properties.[18–21] Retinoid-based therapy is recommended as a first-line approach for almost all acne patients by the Global Alliance.[4] The dose of first-line treatment approaches may need to be lowered (reduced concentration or application frequency) if the patient complains of adverse events such as skin irritation.[22,23]

Maintenance therapy with a topical retinoid[24–26] or azelaic acid[21,27] is recommended when a patient has responded to treatment and is clear or almost clear of acne. The aim is to prevent the disease from recurring by suppressing the development of clinically invisible microcomedones, which can be present in normal-appearing skin.[18,28,29] Retinoids are preferred to azelaic acid, given the stronger evidence base for the former.[4] However, a recent study showed that azelaic acid and adapalene had similar efficacy as maintenance treatment in adult female acne.[21] The dose of maintenance treatment needs to be lowered if the patient reports adverse events such as irritation.[22,23] Salicylic acid >5% for over 12 weeks or 10% for over 6 weeks is not recommended as maintenance therapy due to potential toxicity.[30] Benzoyl peroxide (BPO) monotherapy should not be used as maintenance treatment due to its lack of effect on microcomedones and comedones.[31] Topical antibiotic monotherapy is also not recommended, as long-term therapy may lead to an increase in antibiotic-resistant *P. acnes*.[32,33]

Predominant papulopustular acne

For patients with predominant papulopustular acne, the first step is to categorize the disease severity as mild (grades 1 and 2), moderate (grade 3) or severe (grades 4 and 5) (Table 1).[12]

Topical treatment of mild papulopustular acne (grades 1 to 2) with either BPO,[34] a second generation retinoid,[14,35] or azelaic acid[16,36] is proposed. A fixed combination of two active agents (e.g. clindamycin 1%/tretinoin 0.025%,[37] adapalene 0.1%/BPO 2.5%,[34,38,39] clindamycin 1%/BPO 3%/5%[40–42]) can be considered as an alternative (Fig. 3). The final choice of treatment is left to the physician's discretion taking individual patient characteristics and preferences into account.

Topical fixed combinations are recommended as the preferred approach for patients with moderate papulopustular acne (>grade 3 to 4). Retinoid/antimicrobial combinations enable more of the pathogenic factors of acne to be targeted resulting in faster and more complete clearance of acne lesions than their

Table 2 Summary of reasons for lack of response in predominant comedonal facial acne

Reasons for no response	Actions
Progression to papulopustular acne	• Go to Figure 3
Non-drug-related reasons	• Severe seborrhoea* • Check exposure of patient to acne-provoking agents • Check stress and diet • Check comedogenicity of facial make-up and moisturizing cream
Drug-related reasons	• Adapt vehicle (cream or gel) to skin type and environmental conditions • Change retinoid vehicle from cream to gel • If a retinoid, change to alternative retinoid or higher concentration of retinoid • If azelaic or salicylic acid, change to retinoid • Mechanically remove comedones • Check if treatment was only applied to spots • Females: Check type of contraception
Poor adherence	• Check frequency of treatment application • Check if patient understands how the drug works • Check adverse event profile
Adverse events	• Change treatment class or decrease treatment concentration • Change to better tolerated retinoid and/or formulation (e.g., crystalline formulation) • Reduce frequency of application • Check skin care and cosmetic products, overuse of oily skin care products, inadequate skin hydration • Avoid overuse of cleansers (use cleanser with pH around 5 and without α- or β-hydroxyl acids) • Consider possible contact dermatitis and photosensitivity

*Consider oral isotretinoin or oral anti-androgenic hormonal therapy in females. Please refer to text for further information.

individual monotherapies.[4,5] Retinoid/antimicrobial combinations, similar to antibiotic/BPO combinations, may also limit development of antibiotic resistance in *P. acnes* over 16 weeks.[4,43,44] Fixed combinations are also more convenient for patients than applying two medications separately, which may result in improved adherence.[45]

The preferred approach for patients with moderate to severe papulopustular acne is a topical fixed combination plus an oral antibiotic.[46–48] Other recommended oral treatments are isotreti-

Table 3 Summary of reasons for lack of response in (a) predominant mild and moderate papulopustular facial acne and (b) predominant moderate to severe papulopustular facial acne

(a) Reasons for no response	Actions
Progression to more severe acne	Go to respective severity grade in Figure 3
Non-drug-related reasons	• Severe seborrhoea* • Check exposure of patient to acne-provoking agents Check stress and diet • Check for *Malassezia furfur* or Gram-negative bacteria • Check comedogenicity of facial make-up and moisturizing cream • Check endocrine profile
Drug-related reasons	• Adapt vehicle (cream or gel) to skin type and environmental conditions • **Change from monotherapy or separate monotherapies to fixed combination** • **Change to a higher concentration of topical agent** • Check if treatment was only applied to spots • Check if patient develops early acne scarring during treatment • Females: Check type of contraception
Poor adherence	• Check frequency of treatment application • Check if patient understands how the drug works • Check adverse event profile
Adverse events	• Change treatment class or decrease treatment concentration • Change to better tolerated retinoid and/or formulation (e.g. crystalline formulation) • Reduce frequency of application • Check skin care and cosmetic products, overuse of oily skin care products, inadequate skin hydration • Avoid overuse of cleansers (use cleanser with pH around 5 and without α- or β-hydroxyl acids) • Consider possible contact dermatitis and photosensitivity

Table 3 *Continued*

(b) Reasons for no response	Actions
Non-drug-related reasons	• Severe seborrhoea* • Check exposure of patient to acne-provoking agents • Check stress and diet • Check for *M. furfur* or Gram-negative bacteria • Check comedogenicity of facial make-up and moisturizing cream • Check endocrine profile
Drug-related reasons	• Adapt vehicle (cream or gel) to skin type and environmental conditions • **Check type and dose of oral antibiotic** • **Check *Propionibacterium acnes* resistance** • **Change to another oral treatment** • Check if patient develops early acne scarring during treatment • Check if topical treatment was only applied to spots • Females: Check type of contraception
Poor adherence	• Check frequency of applying topical treatment • **Check frequency of taking oral treatment** • Check if patient understands how the drugs work • Check adverse event profile
Adverse events	• Change treatment class or decrease treatment concentration • Change to better tolerated retinoid and/or formulation (e.g. crystalline formulation) • **Consider changing oral agent** • Check skin care and cosmetic products, overuse of oily skin care products, inadequate skin hydration • Avoid overuse of cleansers (use cleanser with pH around 5 and without α- or β-hydroxyl acids) • Consider possible contact dermatitis and photosensitivity

*Consider oral isotretinoin or oral anti-androgenic hormonal therapy in females. (a) Text in bold font represents differences to Table 3b; (b) text in bold font represents differences to Table 3a. Please refer to text for further information.

noin[49] or, in certain situations, zinc.[50] Oral hormonal therapies, which may be used in females, include oral contraceptives containing progestins with anti-androgenic properties, e.g. cyproterone acetate, drospirenone and chlormadinone acetate. Androgen receptor antagonists, such as cyproterone acetate and spironolactone can also be used alone, without oestrogen, in patients who cannot take oral contraceptives.[51–56] Hormonal therapies predominantly target excess sebum production (but also follicular keratinocyte proliferation), and so need to be used together with topical fixed combination therapy to enable all four acne pathogenic factors to be targeted.[53,55]

Maintenance therapy recommendations are the same as for predominant comedonal acne.

Nodular and/or conglobate acne

Separate suggestions are provided for the treatment of nodular and/or conglobate acne according to gender (Fig. 4). In men, oral isotretinoin[57] or a topical fixed combination plus an oral antibiotic[58,59] is advised as first-line therapy. In women, either of these treatment options can be supplemented with oral anti-androgenic hormonal therapy.[55,60] Females of childbearing age taking oral isotretinoin must use effective contraception due to the potential for teratogenicity.[61] An initial high antibiotic dose should be considered in all patients.[62] Usually a minimum of 12–16 weeks of treatment is essential to significantly improve this type of acne. The dose and duration of treatment has to be individually adapted. Maintenance therapy with topical retinoid/BPO can be considered when a good response is achieved.[63]

Principal reasons for lack of treatment response

The main causes for a lack of treatment response and subsequent action to take are summarized in Tables 2–4.

Disease progression

A patient with predominant comedonal or mild or moderate papulopustular acne may not have responded to initial treatment because their acne has increased in severity and so requires a different therapeutic approach (Tables 2, 3a).

Non-drug-related reasons

Non-drug-related reasons for treatment failure include severe seborrhoea, exposure to acne-provoking agents and the use of inappropriate moisturizers and make-up products (Tables 2–4). Severe seborrhoea may lead to treatment failure by limiting the amount of time that topical medication stays on the skin. It may be treated using oral isotretinoin in males or females, or oral anti-androgenic hormonal therapy in females.[61,64] The application of greasy products to the skin, exposure to dioxins and certain medications (e.g. anti-epileptics, anabolic steroids) may provoke or worsen acne and, where possible, should be avoided.[1] Other factors such as stress, smoking, a high glycaemic index diet and dairy products have been implicated in worsening, provoking or maintaining acne.[1,2,65] Dermatologists should ensure their patients are using non-comedogenic moisturizers and make-up products which do not worsen the disease.[53] Acne cosmetica should be considered in patients with predominant comedonal acne.

Table 4 Summary of reasons for lack of response in nodular and/or conglobate acne

Reasons for no response	Actions
Non-drug-related reasons	• Severe seborrhoea* • Check exposure of patient to acne-provoking agents • Check stress and diet • Check for *Malassezia furfur* or Gram-negative bacteria • Check comedogenicity of facial make-up and moisturizing cream • Exclude hidradenitis suppurativa/acne inversa and sebocystomatosis • Check endocrine profile
Drug-related reasons	• Check type and dose of oral antibiotic • Check *Propionibacterium acnes* resistance • Check if topical treatment was only applied to spots • Mechanically remove macrocomedones • Consider intralesional injection with corticosteroid • Check type and dose of oral isotretinoin; consider adding prednisone • Check oral isotretinoin is taken with fat-containing meal • Check if patient develops early acne scarring during treatment • Females: Check type of contraception and anti-androgenic agent†
Poor adherence	• Check frequency of applying topical treatment • Check frequency of taking oral treatment • Check if patient understands how the drug works • Check adverse event profile • Check adherence to isotretinoin • Check if patient is using a moisturizer and sun protection
Adverse events	• Avoid using topical treatment together with isotretinoin • Consider changing oral agent‡ • Avoid overuse of cleansers (use cleanser with pH around 5 and without α- or β-hydroxyl acids) • Consider possible contact dermatitis and photosensitivity • Check skin hydration and sun protection, and prevent xerosis of the skin, in particular with high isotretinoin doses

*Consider oral isotretinoin, or oral anti-androgenic hormonal therapy in females.
†Consider contraceptive pill containing a progestin with anti-androgenic activity or additional cyproterone acetate dose.
‡Consider oral isotretinoin. Please refer to text for further information.

For patients with papulopustular and conglobate acne who do not respond to treatment, folliculitis caused by *Malassezia furfur* or Gram-negative bacteria should be excluded (Tables 3–4).[66–68] Patients with papulopustular or conglobate acne which is unresponsive to treatment may have an endocrine abnormality such as polycystic ovary disease, Cushing syndrome, congenital adrenal hyperplasia, hyper/hypothyroidism or acromegaly.[55,69,70] An endocrine profile evaluation is essential to diagnose these conditions.[55] A diagnosis of hidradenitis suppurativa/acne inversa[71] or sebocystomatosis has to be excluded in patients with treatment-refractory conglobate acne.

Drug-related reasons

The main drug-related reasons for a lack of treatment response are a suboptimal vehicle, an insufficient active agent and an insufficient drug concentration.

Vehicles are crucial components of acne treatments. If a patient with predominant comedonal or papulopustular acne does not respond to topical treatment, another treatment should be considered with the vehicle adapted to the patient's skin type and environmental conditions (Tables 2–3).[72] Optimal vehicles may improve the tolerability of acne treatments and those which are associated with less skin irritation may help to improve treatment adherence.[72–75] Vehicles also contribute towards the therapeutic efficacy of topical acne treatments and can improve the active agent's bioavailability.[76–78]

A lack of improvement in a patient's acne may be due to the active agent being insufficiently effective or too low in concentration. An alternative retinoid or a higher concentration of retinoid could be evaluated in patients with predominant comedonal acne and an unsuccessful course of azelaic or salicylic acid could be followed with a retinoid. Based on practical experience, a higher concentration of a topical retinoid used once-daily in the evening is recommended, together with a moisturizer in the morning, rather than changing to twice-daily application of a lower concentration of retinoid. If used twice daily, the morning application of retinoid may be inactivated by UV light, and may cause additional photosensitivity and skin irritation.[22,79]

Patients with mild or moderate papulopustular acne who have not responded to a topical monotherapy or two separate monotherapies could change to a higher concentration of topical

agent(s) or to topical fixed combination (Table 3a). These latter treatments have greater efficacy than their monotherapies and are associated with better adherence as they are more convenient to use.[5,45]

Patients with moderate to severe papulopustular acne or nodular/conglobate acne who are unresponsive to an oral antibiotic could have the dose of antibiotic increased or try an alternative antibiotic (Tables 3b, 4).[9] The efficacy of different oral antibiotics can be affected by factors such as bacterial resistance and bioavailability.[32,48,80,81]

An alternative more effective oral treatment could be evaluated in patients with moderate to severe papulopustular acne who have not responded to initial treatment (Table 3b). Oral isotretinoin is considered the most effective acne therapy.[61] If a patient with nodular/conglobate acne is unresponsive to oral isotretinoin, a higher isotretinoin dose should be considered (Table 4).[61,82,83] Prednisone may be added for 2 weeks and then gradually tapered. The dermatologist should advise the patient to take isotretinoin with a fat-containing meal as this optimizes its bioavailability.[84] In addition, the type of oral isotretinoin being taken should be checked as the pharmaceutical quality of generic versions can be questionable resulting in variable activity.[71,85]

Early acne scarring in patients with papulopustular or conglobate acne indicates that the therapeutic regimen is ineffective and needs to be rapidly changed (Tables 3–4). For example, patients being treated with topical therapy/therapies should be moved to systemic therapies. Patients being treated with systemic therapies should change to oral isotretinoin as this will more rapidly reduce inflammation and prevent scarring.[7,9,86]

Another drug-related reason for treatment failure is the type of contraception being used by female patients. Acne may be exacerbated if females are taking oral contraceptives or have progestin implants with androgenic activity.[52,55] Third- or fourth-generation pills with anti-androgenic activity are preferred.[52,55]

The dermatologist should determine whether patients regularly applied topical treatment to the entire area or only to visible spots (Tables 2–4). The latter could be a reason for therapy failure since microcomedones in the surrounding skin are not treated.[1]

Mechanical removal of comedones may be required in patients with predominant comedonal acne. Macrocomedones or micro/macrocysts may need mechanical removal particularly in conglobate acne or late-onset adult acne. Extractors, light cautery or laser puncture may be used.[6,87]

Poor adherence

Fifty per cent of acne patients have poor adherence,[88] so this is a common reason for treatment failure. The dermatologist must establish if the patient has adhered to their treatment regimen by checking the frequency the patient has applied their topical treatment or taken their oral medication (Tables 2–4). If the patient has not adhered to their regimen, the dermatologist must try to establish the reasons for non-adherence. Side-effects and lack of knowledge about acne treatments are two principal causes of non-adherence.[88,89] The method of treatment application and dosing, the slow onset of action of acne treatments and possible adverse events should be discussed with the patients and their questions should be clearly answered. Clinical improvement typically requires 6–8 weeks of therapy.[90,91] Patient preferences should also be taken into account to improve adherence. Acne medication attributes which patients prefer include gel formulations, once-daily application and room-temperature storage.[92] For patients with nodular/conglobate acne who are being treated with oral isotretinoin, the dermatologist should check whether the patient is using a moisturizer (Table 4), as skin irritation is a common side effect of this therapy and using a moisturizer can increase treatment adherence.[13,88]

Adverse events

Adverse events, in particular skin irritation, are a common cause of therapy failure as they can lead to premature treatment discontinuation.[88,89] If a patient is dissatisfied with their acne treatment due to adverse effects, an alternative treatment and/or formulation with a more favourable side effect profile or a reduced concentration of the same treatment should be evaluated.[22,23,93]

For patients using topical retinoids, short contact application, no longer than 30 minutes, followed by rinsing, or application every other day may improve tolerability.[94,95] In addition, a better tolerated retinoid should be considered (Tables 2–3).[96,97] The tolerability of retinoids has evolved from initial alcohol-based formulations to gels without alcohol and creams containing lower retinoid concentrations, and subsequently to new classes of retinoids and new formulations such as crystalline suspensions and microsphere technology to slowly release the retinoid.[23,96–98] Of these newer formulations, a fixed combination containing clindamycin and tretinoin in a crystalline suspension was shown to be significantly better tolerated than tretinoin in microsphere technology.[98] This fixed combination was also associated with significantly less skin irritation than a fixed combination of adapalene and BPO.[99] Consequently, crystalline formulations can be considered as better tolerated than microsphere formulations, which in turn are better tolerated than ordinary retinoid formulations.

Topical BPO is another agent associated with cutaneous irritation, which can be reduced using a lower concentration of the active agent[100] or less frequent application such as every other day.

Topical treatments should be avoided in patients with nodular/conglobate acne taking oral isotretinoin given its propensity to cause additional skin irritation (Table 4).[13] In addition, xerosis is a side effect of high-dose oral isotretinoin,[82] and so patients

on this treatment should be prescribed a moisturizer and advised to avoid wax epilation, peelings and sun exposure. Oral comedication with an antihistamine may increase the efficacy and lower adverse events of isotretinoin.[101]

Another strategy to mitigate the impact of side-effects for patients with predominant comedonal or mild or moderate papulopustular acne is to reduce the frequency of topical treatment application (Table 2, 3a). For example, the frequency of topical retinoid monotherapy application may be reduced to every other night for a few weeks to enable the skin to develop tolerance to the treatment.[95]

The dermatologist should check the patient's daily skin care regimen since this may be a cause of skin irritation. All acne patients should be advised not to overuse cleansers and to only use cleansers with a pH of around five which do not contain α- or β-hydroxyl acids.[102–104]

Topical acne treatments such as BPO may rarely cause allergic contact dermatitis,[100] and treatments such as retinoids and certain oral antibiotics may cause photosensitivity.[79,105] If these adverse events are identified, patients should be offered an alternative treatment, and to prevent the latter, appropriate UV protection should be used and sun exposure should be avoided.

Conclusions

Successful acne management requires a close partnership between physicians and patients, and treatments which are both effective and well tolerated. The algorithms presented here provide physicians with simple, easy-to-use practical guides on how to treat predominant comedonal, papulopustular and nodular/conglobate acne in everyday clinical practice. These algorithms highlight the central role of fixed combinations in the treatment of acne, the importance of maintenance treatment and the avoidance of antibiotic monotherapy and the need to provide patients with better tolerated therapies. The checklists to establish the causes for a lack of treatment response and subsequent action to take will facilitate optimal acne management. Treatment decisions must take into consideration local prescribing regulations, the clinical presentation of individual patients, environmental factors, quality of life, reimbursement systems and insurance practices, individual patient preferences and their understanding about acne and the therapy selected.

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