The treatment of acne is often hampered by misunderstandings about the condition and unrealistic expectations of treatment. Patients often abandon treatment early because of slowness of response, skin irritation caused by treatment or inconvenient regimens. It is important to recognise that patients want treatment that produces rapid results with minimum inconvenience. Successful treatment depends not merely on the provision of efficacious products but also on support and encouragement to carry on with treatment for months rather than just days or weeks.

Treatment options
The aims of acne treatment are to:

- Clear acne lesions
- Prevent long-term scarring
- Relieve psychosocial stress and improve self-esteem

The available therapeutic agents are active against one or more of the causes and symptoms of acne. These treatments can:

- Reduce sebum secretion
- Clear existing microcomedones and prevent further microcomedo formation
- Reduce *Propionibacterium acnes* colonisation and inflammation

Selection of the most appropriate treatment depends on assessment of the acne and the impact that it is having on the sufferer. This involves consideration of possible contributing factors, assessment of the objective severity of acne and assessment of its psychosocial impact. An acne treatment algorithm from the US Institute for Clinical Systems Improvement is reproduced in Figure 1 (p170).

Topical retinoids
Topical retinoids (e.g., tretinoin gel 0.01% and 0.025%, isotretinoin gel 0.035%, adapalene 0.1%) inhibit the formation and reduce the number of microcomedones. Because these are the precursors for almost all other acne lesions, topical retinoids effectively tackle the condition at an early stage. They are the treatment of choice for comedonal (non-inflammatory) acne. Treatment should start with the lowest strength, which can be built up gradually as required.

The use of topical retinoids can be limited by dose-related side effects, such as erythema, burning, skin peeling and dryness. Retinoids increase the risk of sunburn and use of a sunscreen is recommended for treated, exposed areas. Although systemic absorption of adapalene and tretinoin is low, in view of the known teratogenicity of systemic retinoids neither product should be used during pregnancy. Adapalene should only be used by young women who use adequate contraception. It can take up to three or four months for the maximum clinical benefit of topical retinoid treatment to be seen. Adapalene is generally better tolerated than other topical retinoids.

When a topical retinoid is combined with another topical treatment (e.g., benzoyl peroxide, topical antibiotics), the retinoid should be applied in the evening and the other treatment in the morning (to minimise the risk of photosensitivity). Topical retinoids should be applied to the whole of the acne-prone area, not just to visible lesions.
IT CAN TAKE UP TO THREE OR FOUR MONTHS FOR THE MAXIMUM CLINICAL BENEFIT OF TOPICAL RETINOID TREATMENT TO BE SEEN

Benzoyl peroxide

Benzoyl peroxide is an oxidising agent that has bactericidal action against *P. acnes* and also has some anticomedonal activity. It is effective for treating both inflammatory and non-inflammatory acne. A range of preparations is available, including gels, lotions, creams, soaps and washes, in concentrations ranging from 2.5% to 10%.

Dose-related irritation (redness, dryness, stinging and scaling) is the most common side effect and treatment should therefore start with the lowest strength and be stepped up if necessary.

In practice, benzoyl peroxide is often the first-line treatment for acne because people tend to seek treatment once signs of inflammation appear. Moreover, benzoyl peroxide preparations are available over the counter. Six to eight weeks of treatment is usually necessary before a clear improvement is noticeable.

**Practice points** The following points are applicable to the use of benzoyl peroxide:

- The product should be applied to the whole of the affected area, not just the spots (eg, for spots on the face, the entire face should be treated)
- For patients with sensitive skin, it is best to start by applying it once a day or every other day and build up gradually to a more liberal application twice a day. Application of a light (oil-free) moisturiser 30–60 minutes after the benzoyl peroxide will help to minimise irritation.
- Benzoyl peroxide will bleach clothes, towels and bedlinen, and hair. Hands should be washed thoroughly after each application

Azelaic acid

Azelaic acid is a naturally occurring decarboxylic acid that has been shown to be effective in reducing both inflammatory and non-inflammatory acne lesions. It is said to be less irritant than the other topical treatments and can therefore be a useful alternative if benzoyl peroxide and topical retinoids are not tolerated.

Antibiotic treatment

Erythromycin, tetracyclines and clindamycin are used topically and erythromycin, tetracyclines and trimethoprim are used orally to treat acne. Increasing concerns about bacterial resistance have prompted some experts to question this use of antibiotics. Systematic reviews have shown that there is no difference in efficacy between tetracyclines, and researchers have concluded that there is little justification for combining prescription minocycline (on cost grounds) — oxytetracycline (500mg twice daily) or lymecycline (408mg daily) can be used instead. Oral erythromycin is now used infrequently for acne because of the emergence of resistant strains of *P. acnes* and the high incidence of gastrointestinal side effects.

Antibiotic treatment should be continued for three to six months and then tapered off gradually. Antibiotics should be combined with topical retinoids to enhance efficacy against comedones and inflammatory lesions.

Systemic retinoids

Retinoids exert their action on acne through several mechanisms that are not fully understood. Among these mechanisms is induction of sebaceous gland atrophy, which, in turn, reduces sebum secretion and is believed to contribute to ongoing benefit after finishing treatment.

Oral isotretinoin is indicated for the treatment of severe nodular acne and for moderate or severe acne that is unresponsive to other treatments. Treatment with oral isotretinoin is associated with extensive clearing of acne lesions. Many patients require only a single course of treatment (0.5–1.0mg/kg/day) — usually lasting four to six months. The effects of treatment appear to persist for one or two months after discontinuation.

Isotretinoin is teratogenic and so it can only be supplied to women who are able and prepared to sign up to a pregnancy prevention programme. This includes making a commitment to attend follow-up clinics regularly for monitoring that may include pregnancy testing. The Medicines and Healthcare products Regulatory Agency has published detailed guidance for prescribers, pharmacists and patients about isotretinoin and pregnancy prevention.

The basic components of the scheme are:

- Provision of educational material to patients
- Medically supervised pregnancy testing before, during and five weeks after the end of treatment
Use of at least one method of contraception or, preferably, two complementary forms of contraception, including a barrier method, for at least one month before initiating therapy, continuing throughout the treatment period and for at least one month after stopping therapy.

A checklist for pharmacists who dispense isotretinoin is presented in the Box below.

**Isotretinoin and depression** There have been reports of mood changes and depression for people treated with isotretinoin; however, a causal link remains unproven. Acne itself can be a contributory factor in anxiety, depression and suicide.

The British Association of Dermatologists recommends that a direct enquiry about previous psychiatric health should be made of any patient who is being considered for isotretinoin treatment and the facts recorded fully in the patient’s notes. In addition, all patients — and their parents in the case of minors and adolescents — should be made aware of the potential for mood change in a realistic, non-judgemental way. Patients should be advised to ask family and friends to tell them if they notice such changes and clinicians should enquire directly about psychological symptoms at each clinic visit.

If symptoms of depression or mood changes do occur then, ideally, isotretinoin treatment should be discontinued.

---

**Isotretinoin treatment — pharmacy checklist**

The following points should be followed for patients treated with isotretinoin (Roaccutane or generic product):

- For female patients, the pregnancy prevention programme detailed in the product’s summary of product characteristics and Medicines and Healthcare products Regulatory Agency guidance must be followed rigidly
- Isotretinoin prescriptions for women of childbearing age should be limited to 30 days of treatment
- Ideally, pregnancy testing, issuing a prescription and dispensing of isotretinoin should occur on the same day
- Dispensing of isotretinoin should occur within a maximum of seven days of the prescription being issued
- Patients should not give blood during and for one month after stopping therapy, due to the potential risk to the fetus of a pregnant transfusion recipient
- Patients should return any unused isotretinoin capsules to the pharmacist for safe disposal
- Vitamin A supplements or other retinoids should be avoided while receiving isotretinoin to avoid the risk of hypervitaminosis A

**Side effects**

- The most commonly reported side effects of isotretinoin are dryness of the skin and dryness of the mucosae (eg, of the lips, nasal mucosa and eyes)
- Patients taking retinoids are at risk of sunburn and should be warned to avoid sunbeds and excessive exposure to sunlight, and advised to use suncreams (SPF 15 or higher)
- Decreased night vision sometimes occurs during treatment and might affect driving ability at night
However, some patients, after discussion, may wish to continue with the medicine because of the benefit to their skin. In such cases, specialist psychiatric support should be arranged.10

**Antiandrogenic medicines**

Antiandrogen treatment may be useful for women with acne that appears to be related to hormonal events. For example, it can benefit women who have:

- Failed to respond to other treatments
- Acne that began or worsened in adulthood
- Premenstrual flares of acne
- Excessive facial oiliness
- Inflammatory acne limited to the "beard area"
- Acne accompanied by hirsutism

Antiandrogen therapy is also useful for women with acne when oral contraception or period regulation is required.

Cyproterone acetate is an androgen-receptor blocker that is available for the treatment of acne in combination with ethinylestradiol (co-cyprindiol; eg, Dianette). This is licensed for the treatment of severe acne in women refractory to prolonged oral antibacterial therapy, and for moderately severe hirsutism. However, experts suggest it may be appropriate to use it for certain women before antibiotics are tried, and this is done commonly in practice.1

Co-cyprindiol can take two to six months to produce an improvement in acne and carries all the cardiovascular risks of combined oral contraceptive treatments. It is believed to act by reducing sebum secretion. Co-cyprindiol is not licensed for the sole purpose of contraception and should be discontinued three to four menstrual cycles after the woman's acne has resolved.

Drospirenone, a derivative of spironolactone, is the progestogen in Yasmin — which is now recommended by some dermatologists for acne management.11 Yasmin is not licensed for the treatment of acne in the UK.

**Other treatments**

Nicotinamide has exhibited potent anti-inflammatory activity in vitro, but there are few data to support its topical use in acne.

There is insufficient evidence of effectiveness to support recommendation of light treatment including lasers or complementary therapies such as tea tree oil.

**Focus on mild-to-moderate disease**

Two recent studies have provided evidence that can help to guide treatment choice for mild-to-moderate cases.

The first study involved 649 patients and compared the relative efficacy and cost-effectiveness of five of the most commonly used antimicrobial preparations for treating mild-to-moderate facial acne in the community.12 The regimens were:

- Oral oxytetracycline 500mg twice daily + topical vehicle control twice daily
- Oral minocycline (Minocin MR) 100mg once daily + topical vehicle control twice daily
- Topical erythromycin 3% with benzoyl peroxide 5% (Benzamycin) twice daily + oral placebo once daily
- Topical erythromycin 2% (Stiemycin) once daily + topical benzoyl peroxide 5% (Panoxyl Aquagel) once daily + oral placebo once daily
- Topical benzoyl peroxide 5% (Panoxyl Aquagel) twice daily + oral placebo once daily (the active comparator group)

The results showed that all the treatments were similarly effective in improving acne: 54–66% had at least a moderate improvement at 18 weeks. Topical antimicrobial treatment performed at least as well as oral antibiotics. The combination of benzoyl peroxide and erythromycin, whether as a combined product (such as Benzamycin gel, which was discontinued in the UK in March 2007) or separate products used together, was the most effective. Benzoyl peroxide was deemed the most cost-effective treatment and minocycline the least cost-effective.

Systemic adverse effects occurred most frequently with oral antibiotics and local irritation (stinging and burning) was most common with benzoyl peroxide. Patients experienced less local irritation when benzoyl peroxide was used together with erythromycin. For all regimens the biggest improvement was seen in the first six weeks.

The study also showed that the two regimens including topical erythromycin produced the largest reductions in the numbers of cutaneous propionibacteria, including antibiotic-resistant variants, and these regimens were equally effective for participants with and without erythromycin-resistant propionibacteria.

In the second study a benzoyl peroxide plus clindamycin combination product was compared with adapalene in mild-to-moderate acne over a 12-week period.13 The results showed that the combination was

---

“Soap can dry the skin too much — a gentle cleanser should be recommended”

—— A DIRECT ENQUIRY ABOUT PREVIOUS PSYCHIATRIC HEALTH SHOULD BE MADE OF ANY PATIENT WHO IS BEING CONSIDERED FOR ISOTRETINOIN TREATMENT
more effective than adapalene, had a more rapid onset of action and had a better safety profile.

In this study the differences in response were evident from the first week of treatment. Benzoyl peroxide with clindamycin caused less irritation than did adapalene and the authors suggested that this might be due to the moisturiser incorporated into the gel formulation of the combination product and to the direct anti-inflammatory action of clindamycin.

**In practice** The practical implications of these studies are that patients with mild-to-moderate inflammatory acne can be advised to use benzoyl peroxide 5% in the first instance and that if this is not well tolerated or not effective then treatment with a combination product containing benzoyl peroxide and clindamycin (ie, Ducan Once Daily gel) would be a logical next choice. The rapid onset of action and low frequency of irritant skin reactions with the combination product are factors that could help to promote good adherence to the treatment regimen.

**When to refer to a doctor**

Many people respond to topical over-the-counter treatments. Those whose acne does not respond should be referred to their doctor, particularly people who:

- Have numerous inflamed spots
- Have obviously deep lesions
- Show evidence of scarring
- Seem overly anxious about their spots

Patients who have used benzoyl peroxide correctly for six weeks with no benefit should also be referred.

**When to refer to a specialist**

The National Institute for Health and Clinical Excellence recommends referral to a specialist for patients who:*†‡

- Have a very severe form of acne, such as fulminating acne with systemic symptoms (acne fulminans)§
- Have severe acne or painful, deep nodules or cysts (nodulocystic acne) and could benefit from oral isotretinoin
- Have severe social or psychosocial problems, including a morbid fear of deformity (dysmorphophobia)
- Are at risk of, or are developing, scarring despite treatment in primary care
- Have moderate acne that has failed to respond to treatment that should generally include several courses of both topical and systemic medicines over a period of at least six months. Failure is probably best based upon subjective assessment by the patient
- Are suspected of having an underlying endocrinological cause for the acne (such as polycystic ovary syndrome) that needs assessment

* Arrangements should be made so the patient is seen urgently
† Arrangements should be made so the patient is seen soon
‡ Arrangements should be made so the patient has a routine appointment

---

**Help patients get the most out of treatment**

Pharmacists can play an important role in helping people manage their acne and adhere to acne treatments.

- Be supportive, not dismissive — ongoing patient education, follow-up and encouragement, as well as maintaining a positive approach, are vital
- Reassure patients that acne is not caused by poor hygiene, diet or infection
- When assessing acne, ask about the back and chest — teenage boys especially can be reticent about discussing the full extent of their acne
- Advise that gentle washing with mild products is needed — soap and abrasives can be too drying and cause further damage
- Advise on suitable over-the-counter benzoyl peroxide products — gels are good for greasy skin, creams for normal skin
- Use make-up is not forbidden — non-comedogenic products are ideal
- Manage expectations — patients who expect an instant response could be disappointed and may stop using treatment; a 50% improvement in two months is a realistic expectation
- Encourage proper use of medicines and encourage patients to report back and discuss progress
- Remember that patient perception of improvement is the best measure of successful treatment