Psoriasis is a chronic multisystem inflammatory disorder with significant co-morbidities and also profound physical, emotional and social impact on quality of life. A wide array of treatment options are available including topical treatments, phototherapy, traditional systemic therapy and several biologic agents.

Despite these advances an effective long-term treatment of psoriasis remains a challenge and many patients are dissatisfied with the management of their disease and perceived lack of effect of their therapy. Adherence to treatment can be improved by considering individual preferences and including them in decision making.1

Psoriasis was traditionally viewed as a disorder affecting only the skin and in some patients the joints; however, recent evidence has shifted our perception and understanding of psoriasis to a more complex inflammatory disease. Patients with severe psoriasis have an increased risk of cardiovascular disease and this inherent risk is probably independent of conventional cardiovascular risk factors.2 It is therefore of paramount importance that primary-care physicians actively screen for and address obesity, hypertension, diabetes and dyslipidaemia in psoriasis patients, many of whom are young.3

Another aspect is an overall increased tendency towards unhealthy behaviour reflected in increased prevalence of smoking and alcohol consumption in the psoriatic population, and again early intervention and counselling are essential.

Finally psoriasis is strongly associated with anxiety and depression. This relationship is often overlooked and may play an important role in further nonadherence to prescribed treatment.

Topical preparations prescribed by a primary-care physician can effectively treat mild to moderate psoriasis. Treatment with traditional systemic agents or biologics required for moderate to severe psoriasis is initiated in the specialist setting, while...
primary-care physicians often participate in ongoing treatment monitoring.

**Topical therapy**

**Topical corticosteroids**

Topical corticosteroids are particularly useful in the treatment of patients with limited disease, such as on the scalp, palms, and soles. Steroid use is mainly limited by local cutaneous side-effects such as skin atrophy, telangiectasiae, purpura and striae and also rebound after abrupt discontinuation. Only lower-strength corticosteroids should be used on the face, flexural and genital areas and in children.

**Vitamin D analogues**

Vitamin D analogues are effective in the treatment of mild to moderate psoriasis. Lower radiation in the form of burning, peeling and pruritus can occur and excessive usage above the recommended dosage (100μg per week) can lead to hypercalcaemia. Vitamin D analogues can act as a corticosteroid-sparing agent and a combination product containing calcipotriol/betamethasone (Dovobet) is available.

**Coal tar**

Coal tar has been used in the treatment of psoriasis for over 80 years, often in combination with UV therapy. It is very effective in controlling disease activity in psoriasis and is especially indicated for scalp psoriasis, palmoplantar psoriasis and localized chronic plaque psoriasis. Coal tar formulations can be cosmetically less appealing to patients because of the odour and staining of clothes.

**Topical calcineurin inhibitors**

Tacrolimus and pimecrolimus (unlicensed indication) are used in facial and flexural psoriasis to avoid skin atrophy associated with use of topical corticosteroids in these areas.

**Dithranol**

Dithranol was a principal effective treatment for chronic stable plaque psoriasis for many years. However, skin irritation and staining have led to its declining use in recent years.

**Scalp psoriasis**

The scalp area is commonly affected in psoriasis and can be very difficult to treat. Hair prevents adequate application of creams and ointments, and specific formulations such as shampoo, gel, lotion, and mousse are often used instead. Scale builds up quickly and most treatments must be used on a regular basis. Scalp products usually contain coal tar, topical steroids, vitamin D analogues or salicylic acid and their combinations.

**Phototherapy**

**Narrowband UVB**

Narrowband UVB (311–313nm) has mainly replaced former broadband UVB treatment as it is less erythrogenic, has shorter clearing times and longer periods of remission. Patients usually attend three times per week and narrowband UVB can also be used in children and pregnant women.

**PUVA**

PUVA is a combination treatment with psoralen that temporarily makes skin more sensitive to subsequent irradiation with longer-wavelength UVA. Treatment is administered twice per week. Psoralen tablets can cause nausea and patients must also protect skin and eyes from sunlight on treatment days. Topical PUVA consists of applying psoralen paint directly to the skin or soaking in psoralen solution prior to UVA exposure.

Long-term PUVA therapy is associated with an increased risk of squamous cell carcinoma. PUVA treatment can therefore be combined with retinoids or vitamin D analogues in order to minimise the total dosage of PUVA.
**Targeted phototherapy**

Targeted phototherapy with an excimer laser emitting a wavelength of 308 nm has been found to be safe and effective in an early multicentre study and efficacy was also demonstrated for scalp and palmoplantar psoriasis. Therapy is delivered by a handheld device directed at the affected areas and risks to uninvolved skin are therefore limited.

**Traditional systemic therapy**

**Methotrexate**

Methotrexate is an antimetabolite that has been used in the treatment of psoriasis for many decades and remains one of the most effective as well as relatively low-cost therapies. Methotrexate is usually given as a single weekly oral dose and folic acid supplementation is used to reduce nausea and prevent bone marrow toxicity. Methotrexate use is associated with liver toxicity and regular liver function tests and serial serum procollagen III levels are used for monitoring therapy. Patients with pre-existing conditions including obesity, diabetes and alcohol use are at a higher risk for liver toxicity.

**Ciclosporin**

Ciclosporin is an immunosuppressive agent originally developed as an organ transplantation drug in the early 1970s and its efficacy in psoriasis was described shortly thereafter. It acts rapidly and it is excellent for short-term use due to its weak myelosuppressive effect. Long-term therapy is, however, limited by an increased risk of hypertension and nephrotoxicity.

**Oral retinoids**

Oral retinoids are particularly effective in pustular psoriasis (see Figure 1) but are also used for erythrodemic psoriasis and as a maintenance therapy in chronic plaque psoriasis.

Acitretin is prescribed as a single or divided dose of 10–50 mg per day, although lower doses of up to 25 mg daily are usually used to minimise mucocutaneous side-effects. Adverse effects include xerosis, pruritus, cheilitis, alopecia, dry mouth, hypertriglyceridaemia, abnormal liver function tests and teratogenicity. Acitretin cannot be given to women of child-bearing potential who may become pregnant within three years after discontinuation of treatment.

**Fumaric acid esters**

Fumaric acid esters (unlicensed indication) are currently used for psoriasis mainly in German-speaking countries and have a good and sustained clinical efficacy. Side-effects are common, including lymphopenia, gastrointestinal symptoms and flushing, but can be prevented or reduced by starting at a lower dose initially with gradual escalation.

**Biologics**

Biologics are immunomodulators that target specific components in the molecular pathogenesis of psoriasis. Unlike traditional systemic agents that suppress the entire immune
system, they specifically interfere with T-cell function and cytokine activity related to psoriasis.

**TNF antagonists**

Tumour necrosis factor (TNF) alpha is a proinflammatory cytokine that plays an important role in the pathogenesis of psoriasis and psoriatic arthritis. There are currently three approved agents that target TNF: adalimumab (Humira) and infliximab (Remicade) are monoclonal antibodies that target TNF-alpha and etanercept (Enbrel) is a soluble TNF-alpha receptor fusion protein.

The National Institute for Health and Care Excellence (NICE) recommends that patients being considered for treatment with biologics should have severe disease defined by a total psoriasis area and severity index (PASI) score of 10 or more (20 for infliximab) and also be ineligible for phototherapy or traditional systemic treatment due to contraindications, intolerance or previous treatment failure.4

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**Figure 3. Recommended stepwise management of psoriasis (BSA = body surface area)**

- **Localised or mild-to-moderate psoriasis (10–15% BSA)**
  - **Emollients**
    - Vitamin D analogue
    - Retinoid
    - Coal-tar preparation
    - Corticosteroid ointment/cream
    - Dithranol incremental strength, short contact
  - **If above measures fail, refer for dermatological opinion**

- **Widespread or moderate-to-severe psoriasis (15–20% BSA)**
  - **1st line**
    - Topical treatment as above
    - +/- dermatological referral
  - **2nd line**
    - nUVB/PUVA
    - Methotrexate
    - Ciclosporin
    - Acitretin
    - Fumaric acid esters
  - **3rd line**
    - Etanercept
    - Infliximab
    - Ustekinumab
    - Adalimumab

Possible psoriasis
Exclude other disorders – eczema, lichen planus, pityriasis rosea, tinea corporis, mycosis fungoides, cutaneous lupus erythematosus – and assess degree of psychosocial disability due to psoriasis

Emollients
- Vitamin D analogue
- Retinoid
- Coal-tar preparation
- Corticosteroid ointment/cream
- Dithranol incremental strength, short contact

Emollients
- Mild-to-moderate potency topical corticosteroid
- Vitamin D cream may be used with caution to the hairline and in flexures

Mild: tar shampoo
- Moderate: corticosteroid or calcipotriol scalp lotion or gel
- Severe: coal tar/salicylic acid/coconut oil ointment

If above measures fail, refer for dermatological opinion
Adalimumab is a fully human anti-TNF-alpha monoclonal antibody that induces a rapid response with maximum effect achieved between week 12 and 16. Given as a fortnightly injection, adalimumab has shown to maintain efficacy for up to three years.14

Etanercept is a recombinant human TNF-alpha receptor fusion protein licensed for use in moderate to severe psoriasis at 50mg subcutaneously twice weekly for the first three months followed by 50mg weekly thereafter.

Infliximab is a chimeric anti-TNF antibody with a rapid onset of action. Therapy is initiated at 5mg per kg at weeks 0, 2 and 6 and then every eight weeks. Loss of efficacy correlates with development of antibodies, which might be prevented by a combined therapy with methotrexate.15

Side-effects Potential side-effects of TNF antagonists include infections, reactivation of tuberculosis and hepatitis B, development of demyelinating disease and drug-induced lupus.

To assess the long-term safety of biologics the British Association of Dermatology Biologic Interventions Register (BAD-BIR) has been established. This web-based register compares adult patients with psoriasis treated with biologics versus patients treated with traditional systemic therapies.16

Interleukin antagonists Ustekinumab (Stelara) is a fully human monoclonal antibody that belongs to a new class of biologics targeting the p40 sub-unit of both interleukin (IL)-12 and IL-23. These cytokines play a role in the regulation of immune response and T-cell activation in psoriasis. The treatment is initiated with 45mg (or 90mg if >100kg) at weeks 0 and 4 and then every 12 weeks thereafter.

Ustekinumab is remarkably effective for treatment of chronic plaque psoriasis, with the onset of action evident as early as two weeks (see Figure 2). So far efficacy has been shown to be maintained up to three years.17

There is a relative lack of long-term safety data for ustekinumab but a recent pooled analysis of 3117 patients from phase 2/3 trials showed that ustekinumab was generally well tolerated for up to four years and rates of serious adverse events (serious infections, malignancies and major cardiovascular events) were consistent with those in the general psoriasis population.3

Future treatments Recent research suggests that the T helper 17 (Th17) lymphocyte subset, which produce the IL-17A cytokine, play a crucial role in psoriasis pathology and therapeutic approaches focused on this pathway have brought forward new drugs currently undergoing phase 2/3 studies. These include: brodalumab18 (anti-IL-17 receptor monoclonal antibody), ixekizumab19 (anti-IL-17A monoclonal antibody) and secukinumab20 (anti-IL-17A monoclonal antibody).

Results from short-term studies are promising but further trials are required to determine sustained efficacy and highlight potential side-effects of these new agents.

REFERENCES

Declaration of interests
None to declare.

Dr Dvorakova is a specialist registrar in dermatology and Dr Markham is consultant dermatologist at University Hospital Galway, Ireland.
Prescription review

GPs in England wrote 1.2 million scripts for psoriasis preparations in 2012, at a total cost of £48 million. Calcipotriol accounted for 77 per cent of volume and 90 per cent of spending, of which two-thirds of scripts and 80 per cent of costs were for Dovobet (calcipotriol/betamethasone) ointment and gel. By contrast, only 18 per cent of scripts were for calcipotriol ointment (Dovonex) 50µg per g, amounting to 10 per cent of spending.

Tar and Cocois (coal tar solution/salicylic acid/sulphur in coconut oil) products were the most frequently prescribed of the remaining preparations, at a cost of about £2.1 million.

Use of the retinoids acitretin (for resistant psoriasis), and tazarotene (for mild to moderate psoriasis; Zorac), and the vitamin D analogue tacalcitol (Curatoderm), was relatively low.

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Table 1. Number and cost of prescriptions for psoriasis preparations in England, 2012


Groups and organisations

Psoriasis Association. Tel: 0845 676 0076; e-mail: mail@psoriasis-association.org.uk; website: www.psoriasis-association.org.uk.

Psoriasis and Psoriatic Arthritis Alliance (PAPAA). Tel: 01923 672837; e-mail: info@papaa.org; website: www.papaa.org.

Websites

www.psoriasis.org. This site is provided by the National Psoriasis Foundation and gives information about psoriasis in general and also current research into psoriasis and treatments.

www.psoriasis-help.org.uk. The Psoriasis Help Organisation site contains information about treatments, and also provides a discussion forum for psoriasis sufferers to exchange views and advice on living with psoriasis.

Resources

Further reading

Guidelines


The assessment and management of psoriasis. CG153. NICE, October 2012.

Keeping up to date with the latest thinking in prescribing and therapeutics can be a challenge. However, it is a requirement for all health professionals to maintain their competency through continued professional development.

Learning Central provides automatically marked questions linked to articles that have been published in the journal.

Visit http://bit.ly/prescriberCPD to see the latest online modules.