Psoriasis management

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Psoriasis is primarily treated in primary care, with referrals to secondary care occurring when the condition is severe or uncontrolled. Therefore, pharmacists in both sectors are likely to encounter patients with psoriasis.

In most cases, psoriasis is treated topically first line. In selecting a topical treatment, patient preference, the areas of skin affected, cosmetic acceptability of treatment (e.g., some patients may not want to use a greasy preparation on their face) and the extent of disease should be considered.

Emollients

The mainstay of topical treatment for many skin conditions is a suitable emollient. Emollients should be applied liberally and as often as possible. During flare-ups, patients may require several applications per day; between flare-ups, regular emollient use should still be encouraged. The British National Formulary suggests suitable quantities to prescribe based on how much of the body is affected. For example, larger patients with an acute flare of psoriasis affecting the whole body might need to use as much as 500g of emollient per day.

The best way to maintain compliance with treatment is to offer patients a selection of emollients so they can choose the preparations they prefer. Oily or greasy emollients are generally better moisturisers, but some patients struggle to use them during the day because they can be difficult to rub in and can damage clothing and furniture. Some patients benefit from using a lighter emollient during the day and a greasier one at night.

Although aqueous cream is still widely used as an emollient, it has a low lipid content and can cause the skin to dry excessively after application. It should not be used as a “leave on” emollient but can be a useful soap substitute. Preparations that do not contain sodium lauryl sulphate — an excipient that can irritate the skin — should be supplied.

Local formularies need to include a wide range of emollients. Wholesale switches of emollient therapy (which have been driven by some primary care organisations in recent years) are discouraged because they risk disengaging patients from treatment. Offering generic options (e.g., emulsifying ointment, hydrous ointment) as first-line treatments can help keep costs down.

Vitamin D analogues and corticosteroids

Vitamin D analogues have been the cornerstone of psoriasis treatment in primary care for many years. The three options currently available in the UK are:

- Calcipotriol — available alone or in combination with betametasone (the gel preparation of which can be used on the scalp)
- Calcitriol — the only vitamin D analogue licensed to treat flexural psoriasis
- Tacalcitol

Topical preparations can be effective at controlling the symptoms of psoriasis and keeping flare-ups at bay. Systemic treatments, such as biologics, may also be needed to prevent repeated exacerbations of the condition.
Psoriasis guidelines, published by the National Institute for Health and Care Excellence in October 2012, specify how vitamin D analogues should be used in conjunction with topical corticosteroids. Figure 1 summarises these recommendations for first-line topical treatment of psoriasis. When these treatment options are insufficient, or when patients are unable to manage acute exacerbations, referral to a dermatologist is usually necessary.

Topical dithranol (see below) can be used by patients in primary care. However, this is rarely prescribed without the involvement of a dermatology specialist.

**Specialist treatments**

Treatments prescribed by a dermatologist can be administered at home, at a day care treatment unit (where topical treatment can be applied by nursing staff once a day and combined with ultraviolet light treatment if indicated; see Box 1) or on an inpatient ward.

For patients with scaly psoriatic plaques, a descaling preparation (eg, salicylic acid 2% in white soft paraffin) should be used first. This normally removes the scale within a day or two, allowing further active treatments to be used. If a patient has large areas of erythematous skin, using an emollient every two hours, or a moderate corticosteroid (eg, clobetasone butyrate 0.05%) twice a day, should help settle the inflammation within a couple of days.

Dithranol, coal tar or hyperkeratotic preparations may then be prescribed by a dermatologist to control skin symptoms and an antihistamine prescribed to alleviate itching (see Box 2, p143).

For patients whose psoriasis remains uncontrolled, or whose flare-ups become too regular, a systemic treatment may be prescribed to try to keep psoriasis in remission, as described below.

**Methotrexate**

The antimitabolite methotrexate has been used for many decades. It is cheap and effective and the side effects are well known (as is the monitoring required for detecting them).

It is also effective against rheumatoid arthritis and Crohn’s disease, which are common comorbidities for patients with psoriasis.

Methotrexate is typically the first systemic treatment to be considered.

**Monitoring**

Renal and hepatic function should be assessed as baseline — treatment should be cautioned if there is impairment of either. Concern over liver function might warrant a liver biopsy to assess damage.

A full blood count (FBC) and liver function tests (LFTs) should be performed weekly for the first month of treatment and for a month after each dose change and then monthly thereafter. Urea and electrolytes should be checked every six to 12 months.

![Box 1: Phototherapy](image)

UVA light and narrow-band UVB light slow the rate of skin cell turnover and are established treatments for psoriasis. Patients are exposed to UV light in a phototherapy cabinet for set durations over a course of treatment. A course usually involves two or three treatments per week for up to nine weeks.

Patients receiving UVA treatment must either take methoxypсорalen orally two hours before treatment or immerse their skin in a psoralen solution 15 minutes before treatment. Psoralen sensitises the skin to the effects of UVA light; it is not required for UVB to be effective.

Compared with narrow-band UVB, psoralen plus UVA (PUVA) is believed to clear psoriasis in fewer sessions and provide longer lasting clearance. However, narrow-band UVB is easier to administer and appears to be safer in the long term, particularly in relation to skin cancer risk.

It can be offered to patients with plaque or guttate psoriasis that is not controlled with topical treatment alone.

NICE recommends that PUVA be considered for patients with localised pustular psoriasis. However, patients should be aware of the skin cancer risk associated with PUVA — a risk that is increased by subsequent use of ciclosporin. PUVA can be combined with acitretin for greater efficacy.
Timing is everything

Now indicated post-ADT failure

ZYTIGA® is now indicated with prednisolone for patients with metastatic castration-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) in whom chemotherapy is not yet clinically indicated.1

In a Phase III study of 1,088 men with asymptomatic or mildly symptomatic mCRPC, Zytiga® plus prednisolone vs. placebo plus prednisolone delivered:

- 8.2 month increase in the median time to radiographic progression (HR=0.53 (95% CI: 0.45-0.62), p<0.0001).1,2
- 5.2 month increase in median overall survival (HR=0.79 (95% CI: 0.66 – 0.95), p=0.015); this did not meet the specified significance boundary of p=0.0035).1,2,3
- 9.7 months increase in median time to chemotherapy initiation (HR=0.61 (95% CI: 0.51-0.72), p=0.0001) and statistically significant improvements in all other secondary endpoints.1,2,3

ZYTIGA® also offers once-daily oral dosing, and with prednisolone is generally well tolerated.1

References

Find out the latest on Zytiga at www.zytiga.co.uk

Prescribing information can be found overleaf. SmPC is available on request.
Methotrexate is unsuitable for use by patients who are:

- Pregnant or considering pregnancy (including men wishing to father a child) — methotrexate should be stopped for at least six months before attempting conception
- Breastfeeding
- Drinking excessive alcohol
- Experiencing blood dyscrasias (eg, anaemia, thrombocytopenia)

Side effects

The most troublesome side effects of methotrexate are nausea, diarrhoea and mouth ulcers. Others include leucopenia (and other blood dyscrasias), eye irritation and impotence.

Patients should report any sore throat, fever, breathlessness or unexplained bruising or bleeding to their doctor — these can be early signs of serious side effects and may warrant discontinuation or dose reduction.

If gastrointestinal side effects are particularly troublesome, antiseptics can help. Injectable methotrexate is also worth avoiding. Although more expensive than tablets, subcutaneous methotrexate injections can be a worthwhile investment when the drug has previously proven effective.

Dose

A test dose of 2.5mg is given to identify any potential idiosyncratic reaction to the drug. Assuming no adverse effects occur, treatment is normally started at 7.5—10mg once a week. The dose is adjusted according to response and tolerability, to a maximum of 10mg weekly. An effect should be seen in three to 12 weeks; six weeks is average.

To counteract certain side effects, folinic acid is prescribed. Although practices vary, this is never taken on an empty stomach.
Box 2: Treatments for acute exacerbations of psoriasis

**Dithranol** Dithranol has been used to treat psoriasis for over 70 years. Although its exact mechanism of action is not fully understood, it is believed to inhibit DNA replication and slow skin cell turnover.

Dithranol stains skin, clothing and other fabric (eg, furniture) and so can be too messy for many patients to apply in their own homes. In addition, treatment regimens are complicated and application often requires admission to a dermatology ward. A treatment course of dithranol starts at 0.1% w/w and is increased every two to three days to 2%, which is the highest licensed strength of dithranol available. If skin begins to burn, treatment is stopped and restarted at a previously tolerated strength once any soreness has settled.

Higher strengths are often needed if psoriasis is severe or widespread. Some special manufactures supply dithranol at concentrations up to 15% w/w — either in salicylic acid and emulsifying ointment, or in a zinc and salicylic acid paste (also known as Lassar’s paste). The latter has a thicker consistency and, once applied to plaques, is less likely to run onto surrounding skin. Usually, dithranol 8–10% is enough to clear most plaques. It takes two to three weeks to reach this strength so inpatient stays can last up to a month.

Dithranol is initially applied as short contact treatment: applied for 30 minutes and then washed off. The duration of contact can be increased to up four to hours as patients become accustomed to treatment. If a Lassar’s paste formulation is used, the product is often difficult to wash off with water — arachis oil or vegetable oil can help.

Dithranol must only be applied to psoriatic plaques. Healthy skin tends to burn and requires a moderately potent corticosteroid to alleviate the irritation.

**Coal tar** Coal tar has been used to treat psoriasis for over 75 years. Although its is not as effective as dithranol, it still has a place in therapy — eg, when distinguishing between eczema and psoriasis is difficult or when plaques are numerous and small (and it is difficult to apply other products accurately). There are several licensed coal tar products. To treat psoriatic flares, stronger, unlicensed preparations (up to 10% crude coal tar in yellow soft paraffin) are often required, and can be obtained from some special manufactures. Again, this is best used under dermatology ward supervision.

**Hyperkeratotic preparations** Flares of psoriasis are often accompanied by a considerable thickening of the skin on the palms and soles of the feet. When hardened skin cracks, it can become painful and infected. High strengths of topical salicylic acid, a hyperkeratotic preparation, can be used to remove hardened skin. A 5% preparation (in emulsifying ointment) can be sufficient but typically 20% strengths are required (although these can be costly to obtain in primary care). Care should be taken not to apply such ointments to healthy skin.

**Antihistamines** Itching can be especially aggravating for patients during a psoriasis flare-up. Although the regular application of an emollient is often helpful (and should always be tried in the first instance), systemic treatment is often required.

Sedating antihistamines are usually tried first. These treat itch better than the non-sedating alternatives (although some patients report success with cetirizine, loratadine or fexofenadine). Chlorphenamine, hydroxyzine and alimemazine should be used sequentially until the itch is relieved. Where antihistamines fail, amitriptyline, ondansetron, mirtazapine and doxepin can all be considered (although such use is off-licence).

**Ciclosporin** Ciclosporin is the best option for rapid or short-term control of psoriasis. This is because it usually becomes effective within one to two weeks (less in some patients). Ciclosporin is the first-line option for patients with localised pustular psoriasis, and for patients who are considering conception in the near future.

Continuous, long-term treatment with ciclosporin can lead to increased blood pressure or renal impairment. Although these effects are reversible, they typically lead to cessation of treatment or dose reduction. Therefore ciclosporin is only appropriate for short-term therapy (a few months to a year). For patients with pre-existing renal impairment or uncontrolled hypertension, ciclosporin should be avoided.

**Monitoring** An FBC should be performed before starting treatment. Creatinine, urea and electrolytes, LFTs and fasting lipids should also be measured. Blood pressure should be measured on at least two occasions, and female patients should have an up-to-date cervical smear.

During treatment, FBC, creatinine, urea, potassium and blood pressure should be taken weekly for one month, fortnightly for two months then monthly thereafter (if stable). Dose reduction or treatment cessation is required if:

- Serum creatinine rises to >30% above baseline
- The patient’s blood pressure is persistently above 140/90mmHg despite antihypertensive treatment (amlodipine or felodipine are first choice for patients with psoriasis)

Should this happen, the patient should be referred to a dermatologist for review. A 25mg reduction of the daily dose may be warranted ahead of the patient’s appointment.
Dose  Ciclosporin is started at 2.5–3mg/kg/day, given in two divided doses. If rapid control is required, a dose of 5mg/kg/day can be prescribed. The lowest effective dose should be used to maintain disease control and the dose should not exceed 5mg/kg/day.

Side effects  As well as its hypertensive and renal side effects, ciclosporin can also cause:

- Increased susceptibility to infection
- Dyslipidaemia
- Tremor
- Headache (including migraine)
- Some types of cancer — particularly skin cancer (patients taking ciclosporin should limit their sun exposure)
- Gum hyperplasia

Pharmacist input  Ciclosporin is metabolised by the cytochrome p450 isoenzyme CYP3A4, and is itself an inhibitor of CYP3A4 and P-glycoprotein; therefore there is a greater likelihood for drug interactions. Concomitant use of tacrolimus or rosuvastatin is contraindicated.

When used to treat psoriasis, ciclosporin brands can be switched. However, brand switching can lead to a change in the required dose and this is best done under the supervision of a dermatologist.

Other oral agents  Acitretin  The retinoid acitretin can be used when methotrexate and ciclosporin have failed or are unsuitable. It is particularly effective at treating psoriasis associated with hyperkeratosis.

Acitretin is highly teratogenic; women prescribed it should not conceive during treatment or for two years after. Common side effects are dose-related and reversible. They include an increase in serum cholesterol and triglycerides and drying of the mucous membranes (eg, mouth, lips, eyes, nostrils) that can cause pain or discomfort. Lip balm and hydrating eye drops can be beneficial should these drying effects occur. Acitretin can only be dispensed by hospital pharmacies.

Fumaric acid esters  In Germany, fumaric acid esters are widely prescribed for psoriasis; however, they are not licensed in the UK. Dose escalation is complicated and involves slow titration over at least nine weeks starting at 30mg once daily and increasing to 240mg three times a day. Side effects include flushing, nausea, stomach cramps, flatulence and diarrhoea. These usually become less frequent over time but can limit the use of higher doses.

Fumaric acid esters should not be used unless all licensed options have been considered. Consequently, they are often used to treat resistant psoriasis, which might make them appear less effective than they actually are.

Hydroxycarbamide  Although only licensed for certain haematological disorders, hydroxycarbamide has been used to treat psoriasis for many years. It is slow to act (usually taking six to eight weeks) and its use is often limited by side effects.

Biologics  Biologic treatments for psoriasis are relatively new. They consist of the tumour necrosis factor inhibitors adalimumab, etanercept and infliximab, and the interleukin inhibitor ustekinumab. Since they cost over £8,000 per year, NICE stipulates that patients should only be prescribed these treatments if they meet all of the following criteria:

- A psoriasis area severity index (PASI) score of 10 or more (20 or more for infliximab)
- A dermatology life quality index (DLQI) score of more than 10 (more than 18 for infliximab)
- The psoriasis has not responded to ciclosporin, methotrexate and psoralen plus UVA, or the patient is intolerant of or has a contraindication to these treatments

Selection  NICE has concluded that there are insufficient data to recommend one biologic over another; choice therefore depends on patient and prescriber preference. Factors to consider when choosing which biologic is most suitable include:

- Route of administration — all biologics are given subcutaneously except for infliximab, which is given by intravenous infusion
Assessing efficacy The efficacy of treatment must be assessed at a set point in time. Adalimumab and ustekinumab are assessed after 16 weeks, etanercept after 12 weeks and infliximab after 10 weeks. For treatment to continue, patients must have experienced either of the following:

- A 75% reduction in PASI score (known as PASI 75)
- A 50% reduction in PASI score (PASI 50) and a five-point reduction in DLQI

A second biologic can be offered to any patient for whom treatment is ineffective at this first evaluation, for those whose treatment fails at a later stage and for those who cannot tolerate treatment.

When switching between biologics, a wash-out period should be considered before the second biologic is started. The British Association of Dermatologists recommends this period be equivalent to four half-lives of the drug being discontinued. As a result, the following wash-out periods are recommended:

- Etanercept — 12 days
- Adalimumab — 56 days
- Infliximab — 36 days
- Ustekinumab — 84 days

Practically, this can result in a treatment break that might seem intolerable for patients experiencing an acute flare of psoriasis. If consultants choose to start the second biologic earlier than recommended, patients should be monitored closely for signs of infection.

In summary

Treatments for psoriasis progress from topical to oral and then to parenteral medicines as the severity of the condition progresses. At every stage, there are opportunities for pharmacists to interact with patients and ensure they are using their treatments effectively.

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References