What is the recommended treatment approach to psoriasis?

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Abstract
Psoriasis is a chronic, relapsing, immune-mediated disease that can have a profound negative impact on patients’ quality of life. Five different types of psoriasis have been characterised according to their clinical features. A working group sanctioned by the Dermatology Society of South Africa engaged in discussions which resulted in the development of guidelines for the diagnosis and management of psoriasis in the South African context. Healthcare professionals can use these recommended guidelines to promote a strategic evidence-based approach when treating patients with psoriasis to ensure optimal treatment outcomes. Topical agents are the mainstay of treatment in mild psoriasis, and phototherapy and systemic agents should be considered if the treatment is ineffective or the severity of the psoriasis heightened.

Introduction
Psoriasis is described as “a chronic, relapsing, immune-mediated, potentially devastating disease, influenced by genetic and environmental factors, that can cause substantial morbidity and psychological stress, and which has a profound negative impact on patients’ quality of life”.

Worldwide, approximately 2% of the population has psoriasis, of whom one third have moderate to severe psoriasis. Evidence suggests that the prevalence of psoriasis is equal in men and women. It was revealed in a 2013 systematic review of data published on the incidence and prevalence of psoriasis in the global population that this condition was more commonly seen in adults than in children, and a greater number of cases were reported in countries that are further away from the equator. Studies on the prevalence and incidence of psoriasis provide a better understanding of the epidemiological trends and burden of disease. The availability of such data in the South African context is limited. Consequently, there is a need for research in this area.

Pathophysiology and types
The pathophysiology of psoriasis has evolved from an understanding that the condition is a hyperkeratotic (involving a thickening of the stratum corneum, i.e. the outermost layer of the epidermis) disorder of keratinocytes (the predominant cell type in the epidermis), owing to a dysfunction of the immune system mediated by cytokines ("T-cell mediated disease"). External factors have also been shown to trigger the onset of psoriasis, including:

- Infections
- Skin injuries
- Stress
- Smoking
- Excessive alcohol consumption
- Medicines (lithium, chloroquine, beta blockers and angiotensin-converting enzyme inhibitors)
- Immunosuppression.

The diagnosis of psoriasis is usually made based on the clinical features. Five different types of psoriasis have been identified, and are summarised in Table I. Subcategories of these psoriasis types are mainly characterised according to their location on the body surface. Arthritis and changes in the nail structure may accompany psoriasis.

Treatment of psoriasis
A working group, consisting of eight South African dermatologists sanctioned by the Dermatology Society of South Africa, engaged in discussions which resulted in the development of guidelines for the diagnosis and management of psoriasis in South African patients. These evidence-based guidelines were formulated based on clinical practice and updated guidelines from the USA, UK, Germany, Canada and Finland. The recent South African guidelines apply to patients of all ages, with varying degrees of psoriasis severity.

To improve treatment outcomes, including the quality of life in patients with psoriasis, healthcare professionals need to select the appropriate treatment approach.
most appropriate treatment option that takes into account the various patient, disease and treatment factors (Table II).1

The conventional stepwise approach to treat psoriasis involves three steps:
• Step 1: Topical agents
• Step 2: Phototherapy
• Step 3: Systemic agents, including biological agents.

If treatment with topical agents fails, phototherapy and/or systemic agents should be considered.1 In practice, the choice of therapy for psoriasis is often determined by its location and the severity of the disease. Mild psoriasis is generally treated with topical agents, and as the severity increases (i.e. moderate to severe psoriasis), the need for phototherapy and/or systemic agents needs to be determined.1,7,9

**Topical agents**

Formulations that are applied directly to the skin constitute the first-line treatment of psoriasis.1,7 Several effective formulations are available either over-the-counter or on prescription.7

**Corticosteroids**

Corticosteroids are commonly used in the treatment of psoriasis, and have shown to be particularly effective in the treatment of mild to moderate psoriasis vulgaris.1 For example, twice-daily treatment with betamethasone dipropionate has been shown to improve and clear psoriasis-associated skin lesions in 46-56% of patients. The use of a more potent topical corticosteroid preparation, e.g. clobetasol-17-propionate, twice daily, resulted in a 68-89% improvement.1 The mechanism of action of topical corticosteroids includes anti-inflammatory, antiproliferative, immunosuppressant and vasoconstrictive.7 The choice of corticosteroid primarily depends on the location, severity, treatment duration and cost of the therapy. The beneficial clinical effects of corticosteroid therapy are seen after 1-2 weeks of use.1 Combination therapy with other topical formulations, including salicylic acid, vitamin D₃ derivatives or tar preparations, has been shown to enhance therapeutic outcomes.1,7 However, the long-term use of topical corticosteroids has several potential adverse effects, including skin atrophy and enlargement of the blood vessels (telangiectasia).1 Additionally, the use of topical corticosteroids is contraindicated in patients with skin infections, rosacea and perioral dermatitis.

<table>
<thead>
<tr>
<th>Table I: The five different types of psoriasis1,6-8</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Plaque psoriasis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• Plaque psoriasis is the most common type, accounting for 80-90% of cases • It is also called psoriasis vulgaris • It consists of well-defined plaques and thick silvery-white scaling lesions on the skin • Plaque psoriasis is commonly seen on the scalp, but involvement ranges from a few to numerous lesions that cover almost the entire body surface</td>
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<td><strong>Guttate psoriasis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• “Guttate” is derived from the Latin word, gutta, meaning drop • It is the second most common type of psoriasis • It is often triggered by an infection, such as streptococcal pharyngitis, otitis media, a urinary tract infection or dental caries • Guttate psoriasis consists of lesions that are widely distributed over the body surface • These lesions are much smaller than those seen in plaque psoriasis</td>
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<tr>
<td><strong>Pustular psoriasis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• Pustular psoriasis may be generalised or localised to the palms and soles • It is characterised by extensive pustular lesions on the skin surface, i.e. white pustules surrounded by red skin • It is often triggered by infections, pregnancy and the abrupt withdrawal of oral corticosteroids • Pustular psoriasis is usually accompanied by fever • Severe cases can result in mortality</td>
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<td><strong>Inverse psoriasis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• Inverse psoriasis is also known as flexural psoriasis • It mainly occurs in the skin fold areas, e.g. the navel, genitalocutural, axillae, armpits and submammary region, owing to the presence of moisture and friction • Inverse psoriasis is characterised by a uniform, red, glazed appearance • The typical silvery-white scaling may be absent</td>
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<tr>
<td><strong>Erythrodermic psoriasis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• Erythrodermic psoriasis is a generalised form of psoriasis and is the most difficult to treat • It is characterised by a red scaly appearance of the skin, which differs to other types of psoriasis • It is often accompanied by severe itching and pain • This type of psoriasis is rare, and occurs in less than 3% of patients with psoriasis • Generally, it presents as a result of unstable plaque psoriasis</td>
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Topical corticosteroids should be given under close supervision and with appropriate counselling.

**Salicylic acid preparations**

Salicylic acid preparations are topical agents that reduce binding between the keratinocytes, and lower the pH of the stratum corneum, which ultimately results in softening of the psoriatic plaques and reduced scaling. A concentration greater than 5% should be utilised to achieve effective therapeutic activity. Systemic absorption can occur when salicylic acid preparations are applied to more than 20% of the skin surface. This phenomenon is particularly problematic in children. Thus, treatment with this preparation should be avoided in children. Combination therapy with tar has been shown to improve effectiveness in adults, but this was not observed using a combination of salicylic acid and calcipotriol (synthetic vitamin D analogue) or ultraviolet (UV) B phototherapy.

**Topical vitamin D<sub>3</sub> preparations**

Topical vitamin D<sub>3</sub> preparations are used in the treatment of mild to moderate psoriasis, and are considered to be a first-line agent in psoriasis treatment owing to their limited toxicity and therapeutic efficacy. However, vitamin D<sub>3</sub> preparations can induce a burning sensation and irritation when used on the face and flexures. Calcipotriol is a vitamin D analogue that binds to the vitamin D receptors on the keratinocytes, and this assists in both the regulation of keratinocyte proliferation and T-cell activation. Usually, it is applied twice daily. The weekly dose should not exceed 100 g. Calcipotriol is cosmetically acceptable, but high costs may limit its use. A combination of calcipotriol and topical steroids or phototherapy has been shown to increase therapeutic efficacy in psoriasis.

**Tar preparations**

Tar preparations have keratoplastic, antipruritic and mild anti-inflammatory activity. There is limited evidence to support the efficacy of coal tar as a monotherapy. However, it is an inexpensive and widely used treatment. Coal tar preparations have been replaced with alternatives in many developed countries because of the colour and odour of the preparation which makes tar preparations cosmetically unappealing. A combination of coal tar and phototherapy (UVB) demonstrated enhanced treatment outcomes, with a 75% reduction (using the Psoriasis Area and Severity Index) seen in 45-80% of patients after 15-20 applications.

Calcineurin inhibitors, such as pimecrolimus and tacrolimus, tazarotene (a vitamin A derivative) and dithranol are other topical agents used in the treatment of psoriasis. Simple emollients are commonly prescribed as adjuncts in the treatment of psoriasis.

**Phototherapy**

Phototherapy was discovered through observation of the action of natural sunlight and its ability to induce the remission of various types of skin disorders. Phototherapy involves exposure of the affected areas to UV rays of a particular wavelength, specifically UVA and UVB. It has been shown to be effective in the management of moderate to severe psoriasis, especially in patients with widespread psoriasis. Clinical effects can be seen after 1-2 weeks of exposure. However, it is important that this treatment is not used for long periods as it can result in untoward effects, like erythema and skin carcinoma. Therefore, phototherapy is generally reserved for cases when patients are unresponsive to topical agents. The combination of phototherapy with topical vitamin D<sub>3</sub> analogues has been shown to improve treatment outcomes. Limited scientific data are available to support its combination with tar and corticosteroids, but clinical practice suggests the beneficial effects of these combinations. Phototherapy is contraindicated in patients with photosensitivity diseases, skin malignancies and immunosuppression. Erythema, itching, blistering and skin malignancies are some of the common side-effects associated with the use of phototherapy in the treatment of psoriasis. Nausea may occur with photochemotherapy, and specifically psoralen and UVA.

**Systemic therapies**

Systemic therapies are recommended in severe psoriasis characterised by extensive cutaneous lesions, and when the response to topical preparations has been poor. Methotrexate, ciclosporin and acitretin are oral systemic agents that have been shown to be effective in the treatment of psoriasis.

**Methotrexate**

Methotrexate is effective in the treatment of moderate to severe plaque psoriasis at a dose of 7.5-25 mg/week. However, its usage is limited owing to its side-effect and contraindication profile. Supplementary folic acid may reduce the risk of hepatotoxicity in...
psoriatic patients, but the introduction of folic acid has an impact on methotrexate efficacy. Monitoring is needed with the use of this agent.

**Ciclosporin**

Ciclosporin inhibits T-cell activation, in addition to having a possible direct effect on the keratinocytes. Ciclosporin is an effective remission induction therapy, indicated for all types of psoriasis. A dose of 2.5-5 mg/kg/day has been shown to be effective in moderate to severe plaque psoriasis. The use of ciclosporin is also limited by its side-effect profile, drug interactions and contraindications. Its treatment efficacy is comparable with that of methotrexate.1

**Acitretin (oral retinoids)**

The precise mechanism of action of vitamin A (retinol) and its derivatives (retinoids) in the management of psoriasis has not been elucidated, but these substances have been shown to modulate keratinocyte differentiation and proliferation. Retinoids are teratogenic and hepatotoxic. The use of retinoids in women of childbearing age is not recommended, and if treatment is taken, effective contraception should be ensured during treatment, and for a minimum of two years after stopping acitretin therapy. The use of acitretin does not result in immunosuppression. Thus, it is preferred in patients with co-morbidities that are accompanied or triggered by immunosuppression, such as human immunodeficiency virus and cancer.1,10

Studies suggest that the use of acitretin in combination with phototherapy (UVA and UVB), topical corticosteroids or topical calcipotriol is more effective than acitretin monotherapy. Retinoids are less effective than other systemic agents as monotherapy in the short-term treatment of moderate to severe plaque psoriasis. However, the clinical evidence suggests that they are effective in the management of erythrodermic and pustular psoriasis.1

Sulphasalazine, azathioprine, hydroxyurea, leflunomide, myco-phenolate mofetil and fumaric acid esters are other systemic therapies with variable clinical outcomes when used in the treatment of psoriasis.1,7

**Biological agents**

Biological agents comprise pharmacologically active proteins derived from two sources, namely extraction from animal tissue or through synthesis using recombinant DNA technology. They target specific steps in the immunopathogenesis of psoriasis, and an effect can be seen within four weeks of the initiation of therapy. Biological agents offer an alternative treatment option that is less toxic (nonteratogenic, with reduced liver, kidney and bone marrow toxicity). This has contributed to recent interest in the use of these agents in the treatment of moderate to severe psoriasis. In South Africa, adalimumab, infliximab and etanercept are tumour necrosis factor-alpha inhibitors that are registered for use in the treatment of psoriasis. They are particularly effective in the treatment of psoriasis with associated arthritis.7 Ustekinumab is the latest biological agent approved for the treatment of moderate to severe plaque psoriasis. The main target of this biological agent is the p40 subunit shared by two cytokines, interleukin 12 and 23. The high cost of these medicines and the possibility of reactivation of latent tuberculosis are limitations to the use of biological agents.1,10

**Conclusion**

Psoriasis has a major impact on patients’ quality of life. To ensure optimal treatment outcomes, healthcare professionals should use these recommended guidelines to ensure a strategic evidence-based approach when treating patients with psoriasis. It may be necessary to deviate slightly from these guidelines in certain cases, in order to provide the best treatment approach in alignment with the patient’s needs. Topical agents are the mainstay of treatment in mild psoriasis, and if the treatment is ineffective or the severity of psoriasis heights, phototherapy and/or systemic agents should be considered.

**References**