



Beyond
Expectations

Psoriasis Treatment Guide

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The past and present of psoriasis treatment

Psoriasis is one of the oldest documented health conditions that exists in recorded human history, and is even mentioned in the Bible. Ancient treatments for the condition included highly toxic substances such as arsenic and mercury-based ointments, which were both dangerous as well as ineffective; while other sources mention use of coal tar, which is still present today in the landscape of psoriasis treatment.¹⁻²

Despite its tenure in history, psoriasis was a largely misunderstood skin condition until the 1970s when its cause was linked to dysfunction in the immune system, which in turn, led to the development of the first systemic immune-regulating therapy, methotrexate.³ As we learned more about how psoriasis works, treatments have become even more targeted to the workings of the immune system, far less burdensome and as such, much more effective.⁴

Nowadays, patients have around 20 different treatment options to choose from.⁵ In particular, great strides have been made in the last 20 years with the development of target-specific, antibody-based drugs, known as biologics, which allow healthcare professionals to treat even the most severe cases of psoriasis. Within the treatment landscape, three broad classes of options exist, the choice of which is very personal to each person. While one person may prefer oral medication, another might instead opt for topical creams, or even non-pharmacological treatment options (e.g. ultraviolet (UV) therapy). There are now more options than ever before, transforming psoriasis from a misunderstood disease a mere 50 years ago, to one of the most treatable immune-mediated conditions to date.⁶

The PASI score and what it means^{7,8}

The goal of psoriasis treatment is to allow patients to achieve maximal skin clearance, usually measured on the Psoriasis Area Severity index (PASI). This index takes into account the percentage of the affected areas as well as the redness, thickness and scaliness of plaques.



There are three main groups of treatment and a doctor will decide which to choose based on different factors such as the severity of the psoriasis.⁹⁻¹⁰

1. Topical treatments

applied to skin, these are available via the pharmacy ('over the counter') or prescribed by a doctor

Creams, ointment and gels

2. Phototherapy

natural ultraviolet (UV) light from the sun and controlled delivery or artificial UV light are administered by a doctor

UV therapy

3. Systemic treatment

prescribed by a doctor, commonly taken as a tablet or given in hospital via drip or injected at home

Orals

Injectables

- Biologics
- Other



1. Topical treatments

Topical treatments are a common first-line approach to psoriasis management as they are widely available, effective and simple to use. They can be prescribed or available over-the-counter, depending on their strength and how they work.¹⁰⁻¹¹

■ Corticosteroids

- Corticosteroids or steroids, the most common treatment for psoriasis, are made from natural hormones that control inflammation.¹¹
- They have been shown to reduce the inflammation associated with psoriatic skin lesions.¹¹
- There is a large variety of steroid medications and they are usually combined with other topicals like salicylic acid. Prescription will depend on the required strength, from Class 1 steroids (superpotent) to Class 7 (least potent).¹¹⁻¹²
- It is important to use steroids exactly as instructed by your healthcare professional, as abrupt changes to steroid use can cause psoriasis flare-ups.¹³

■ Vitamin A and D analogues^{12,14}

- Through the regulation of immune T-cells and keratin-producing skin cells, vitamin D analogues function to improve the signs and symptoms of psoriasis by reducing the inflammation associated with psoriatic lesions, and slowing down skin growth to minimise the scaling associated with psoriatic plaques.
- Vitamin D analogues are generally well tolerated. However, like many other topical treatments, vitamin D can cause mild skin irritation.
- Retinoids, a type of vitamin A, act on skin cells to slow their growth, thereby reducing the signs and symptoms of psoriasis.
- Retinoids are commonly associated with dose-dependent local irritation, itching, burning and erythema; and may increase sensitivity to sunlight, so patients should be advised to apply sunscreen before going outdoors.
- Retinoids are not recommended during pregnancy, whilst breast-feeding, or if you intend to become pregnant.¹⁵

■ Salicylic acid¹⁶

- Salicylic acid of mild-to-moderate strength is available from the pharmacy and stronger preparations are available on prescription. It is used to encourage the shedding of the outer layers of the skin. This helps to soften and eventually remove the scales of plaques.

■ Tar (coal or wood)¹⁶

- Tar has been used for many centuries in the treatment of psoriasis, helping to slow skin cell growth and reduce the inflammation, itching and scaling associated with the condition.
- Caution must be taken when using tar, as it can cause, local irritation, photosensitivity, and can be messy, malodourous and can cause staining of clothing, bed linen or lighter-coloured hair.

Topical treatments are often considered a first line of defence and are usually used to treat mild psoriasis.^{11,12} However, many topical treatments are not considered adequate to control the symptoms of moderate-to-severe plaque psoriasis, and may be combined with other treatments, such as systemic treatments.¹⁰



2. Phototherapy¹⁷

Ultraviolet (UV) phototherapy or light therapy can be used to treat psoriasis that cannot be controlled with other treatments alone. This treatment involves exposing the skin to controlled UVA and/or UVB light in order to help slow the growth of psoriatic skin cells. UVA and UVB therapy can be administered using natural sources of light from the sun, in which a doctor will recommend a specific exposure time outdoors, or via specialised devices that produce artificial UVB rays, under the supervision of a healthcare professional. When used in conjunction with other treatments, phototherapy may help improve the outcomes of certain psoriasis medications; however, UV exposure may increase your risk of skin burns (e.g. sunburn) and skin cancer, and therefore phototherapy is not recommended in patients who suffer from conditions associated with photosensitivity, such as lupus or porphyria, or for patients who are taking photosensitising medication.



3. Systemic treatments

Oral medication

Systemic means that the medication might reach all parts of the body, usually achieved via injection into the veins or orally.¹⁸



■ Cyclosporine¹⁹

- Cyclosporine is administered orally in a capsule format or as a liquid diluted in water, and acts as an immunosuppressant that reduces the activity of certain immune cells, thereby slowing the growth of skin cells.
- Cyclosporine is not suitable for patients with compromised immune systems; cancer or a history of cancer; impaired organ function; abnormal kidney function; uncontrollable hypertension; active, serious infections; severe gout; or patients who are breast-feeding or undergoing radiation treatment.

- **Methotrexate**²⁰
 - Methotrexate can be administered orally, acting as an anti-inflammatory that works by inhibiting the production of key immune mediators associated with inflammation.
 - Methotrexate is not suitable for patients at risk of liver or kidney damage, such as those who are alcohol-dependent, or who have a hepatitis infection. Since it interferes with the production of new cells, pregnant women or those planning pregnancy (both men and women) should also not take methotrexate.
- **Oral vitamin A analogues**²¹
 - Vitamin A analogues can also be administered in pill format, such as acitretin.
 - Much like topical vitamin A analogues, oral administration can help to control the rate of skin cell growth and proliferation.
 - Oral retinoids are not suitable for patients with severe liver or kidney disease or uncontrollable hyperlipidaemia. Additionally, due to the risk of birth-defects, retinoids are contraindicated for use in pregnant women, or women who might become pregnant.
- **Apremilast**
 - Apremilast is administered orally, acting as an immunosuppressant which inhibits an enzyme known to contribute to inflammation, leading to the improvement of symptoms in the skin.²²
 - Apremilast is not suitable for patients who are underweight, have symptoms of depression, pregnant or those planning pregnancy.²³

Systemic treatments are usually used to treat moderate-to severe psoriasis.¹⁹⁻²¹ They may also be prescribed to patients who have responded to or were unable to tolerate other treatments.¹⁸ If these systemic treatments do not work for you, combining treatments may be an option. Alternatively, your doctor may suggest biologic treatments as a next step.¹⁹⁻²¹

Biologic treatments

As the latest innovation to join psoriasis' therapeutic landscape, biologics are used if you have severe psoriasis that has not responded to other treatments, or if you cannot use other treatments.²⁴ Derived from living cells, biologics are antibody-based drugs that exclusively target specific chemicals associated with psoriatic disease, thereby preventing their function in



the pathogenesis of psoriasis. These chemicals, also known as cytokines, include the cell-to-cell messenger molecules tumour necrosis factor alpha (TNF- α) and the interleukins (ILs), all of which play important roles in the mediation of the inflammatory immune response and skin cell proliferation²⁵

There are a number of different biologic options for the treatment of psoriasis, some of which target different cytokines or a combination of cytokines, depending on the type of antibody used in the development of the drug.²⁵

1 T-cell inhibitors²⁶

- T-cell inhibitors represent the oldest group of biologics used in the treatment of psoriasis, which function by specifically blocking the activation and migration of T-cells associated with the inflammatory immune response.
- E.g. **Alefacept**: approved by the FDA in 2003, alefacept represents the first ever biologic to revolutionise the standard of care in the treatment of psoriasis. In subsequent years, as our understanding of psoriasis improved, alefacept became inferior for the treatment of psoriasis in relation to some of the newer biologics available. Later being deemed the least cost-effective option, alefacept was withdrawn from the market in 2011.

2 TNF- α inhibitors²⁶

- TNF- α inhibitors function to block the activity of TNF- α , a protein-based cytokine that stimulates immune cells to release other proteins that activate the inflammatory immune response.
- E.g. **Infliximab**: approved by the FDA in 2006, infliximab is the first chimeric monoclonal antibody to target TNF- α in the treatment of psoriasis.

Safe administration of injectable medicines

If you are prescribed injectable medicines, you may be shown how to carefully self-administer the treatment. If you need help from a carer, both you and your carer must feel completely comfortable with the process and its requirements. It is completely acceptable to ask for more information if you have any concerns. Speak to your doctor about the best way forward, or refer to our **Psoriasis Carer guide**.

3 IL-12/23 inhibitors²⁶

- IL-12/23 inhibitors block the activity of both IL-23 and IL-12, two cytokines believed to be important in the maturation of immune T-cells, which in turn migrate to the skin where they release cytokines that initiate the inflammatory immune response, and stimulate keratin-producing skin cells to proliferate.
- E.g. **Ustekinumab**: approved by the FDA in 2009, ustekinumab is a human monoclonal antibody that targets a shared protein subunit of the IL-23 and IL-12 cytokines, thereby inhibiting the action of both cytokines. In comparison to TNF- α inhibitors used in the treatment of psoriasis prior to 2009, real world data suggests that ustekinumab demonstrates significantly longer drug survival vs infliximab and other similar biologics of the same class.

4 IL-17 inhibitors²⁶

- IL-17 is a cytokine secreted by immune cells during an inflammatory immune response. IL-17 is found in high proportions in psoriatic plaques, and as such is thought to be integral to the pathogenesis of psoriasis.
- E.g. **Secukinumab**: approved by the FDA in 2015, secukinumab was the first IL-17 inhibitor to be used in the treatment of psoriasis, demonstrating improved efficacy compared some earlier biologics, with a faster onset of action.

5 IL-23 inhibitors

- IL-23 inhibitors are the latest development in the biologic treatment landscape, exclusively targeting IL-23, independent of IL-12. Whilst both cytokines target the maturation of T cells, recent studies have differentiated their roles, with only IL-12 directly promoting T-cell maturation.²⁶⁻²⁷
- Fewer side effects are to be expected with IL-23 inhibitors in comparison to its predecessors IL-12/23 inhibitors, as the T-helper cell response is left intact for bacterial or viral defence with the direct activity of IL-12.²⁶
- E.g. **Guselkumab**: approved by the FDA in 2017, is a monoclonal antibody that target IL-23. It has been shown to have efficacy through five years of continuous use.^{26,28,29}
- E.g. **Risankizumab**: approved by the FDA in 2019 for the treatment of moderate to severe psoriasis, risankizumab specifically targets the p19 subunit of IL-23, thus inhibiting its pro-inflammatory activity.³⁰

Biologics have revolutionised the treatment landscape for psoriasis, improving outcomes for patients since 2003, especially for those who suffer from moderate-to-severe forms of the condition.²⁶ Despite this, side effect-free treatment can never be guaranteed, and because biologic treatments directly interact with the immune system, it is common for patients on biologics to suffer from more infections than would otherwise be expected. For this reason, patients with weakened immune systems, or an active infection should not take these kind of treatments. Your doctor will always recommend the option that is most suitable for you.²⁵

Other treatment

■ Methotrexate⁴

- Methotrexate can also be administered intramuscularly via injection, as previously mentioned it inhibits the production of immune mediators associated with inflammation.

The importance of taking your treatment as instructed

Patients with poor adherence have worse treatment outcomes and higher healthcare costs when medication is taken sub-optimally. Despite this, up to 25% of patients across all medical conditions do not take their medication at all, and only 50% of moderate-to-severe psoriasis patients always take their medication as prescribed because of:³¹⁻³²

- Forgetfulness
- Ill-health
- Too busy to take/source medication
- Belief that medication is no longer required
- Side effects
- Running out
- Expense

The vast majority of these causes could be avoided. If you are struggling to follow the medical advice you were given about your treatment, or believe you need to change something about your treatment, arrange an appointment with your doctor to discuss your concerns. In the meantime, do not stop taking your medication as prescribed.

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EM-49443 February 2021