

## PLAIN LANGUAGE SUMMARY

# Biologics and small molecules for psoriasis: current and future progress

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## What is psoriasis?

Psoriasis is a common, chronic skin disease that significantly affects the quality of life of those who have it due to red, scaly patches on the skin and associated health issues like psoriatic arthritis and heart disease. While the exact cause isn't known, the IL-17–IL-23 axis – a pathway that drives chronic inflammation – is central to the disease.

Traditional treatments like topical creams, light therapy and older systemic drugs (for example, methotrexate) can be limited by effectiveness, tolerability and safety concerns. This has led to newer treatments with advanced systemic therapies, called biologics and small molecules.

## Biologic therapies

Biologics are targeted treatments that inhibit specific parts of the immune system's inflammatory response such as pro-inflammatory proteins (cytokines). They are a major advance for moderate-to-severe psoriasis.

## TNF inhibitors (targeting tumour necrosis factor)

This was the first class of biologics. They are effective and have a favourable long-term safety profile:

- **Etanercept:** Approved in 2004, it works well and maintains responses over years. Real-world studies confirm its long-term safety.
- **Infliximab:** Administered intravenously, it offers a rapid and high response rate, though some patients may develop resistance over time.
- **Adalimumab:** A fully human antibody, it provides rapid and sustained skin clearance and has an

extensively studied, robust safety record over many years.

- **Certolizumab pegol:** Unique for its minimal transfer across the placenta, making it suitable during pregnancy and breastfeeding. It has demonstrated strong efficacy in trials.

## IL-17 inhibitors (targeting IL-17)

These agents offer very high rates of skin clearance and rapid onset of action:

- **Secukinumab:** The first in its class, it provides durable, long-term responses and is effective on difficult areas like the nails and scalp.
- **Ixekizumab:** Shows rapid and significant clearance, often superior to older biologics and effective for difficult-to-treat areas.
- **Brodalumab:** Works by blocking the IL-17 receptor, providing very rapid and profound skin clearance.
- **Bimekizumab:** The newest, it blocks both IL-17A and IL-17F, demonstrating superior efficacy to other biologics in head-to-head trials, with high rates of complete skin clearance.

## IL-12/23 and IL-23 inhibitors

These target the upstream drivers of the inflammatory axis:

- **Ustekinumab:** Targets both IL-12 and IL-23. It is effective and has a convenient dosing schedule (every 12 weeks) and good long-term durability.
- **Guselkumab, risankizumab and tildrakizumab:** These newer agents specifically target only IL-23. They have demonstrated superior efficacy and sustained, long-term responses in clinical trials and real-world data,

with risankizumab, in particular, showing excellent long-term maintenance of clearance.

## Small molecules

These are orally administered drugs that target different inflammatory pathways:

- **Apremilast:** A PDE4 inhibitor that is a good option for patients who prefer an oral medication and has a generally mild safety profile.
- **Deucravacitinib:** A TYK2 inhibitor that offers high efficacy comparable to biologics, representing a significant step forward in oral treatment options.

## Challenges and future directions

While these advanced therapies have transformed psoriasis care, challenges remain, including treatment non-response, potential side effects, the development of immunity against the drug and high costs.

This review emphasizes that the current treatment landscape for psoriasis offers a diverse and highly effective range of options, particularly with the newer anti-IL-17 and anti-IL-23 biologics and small molecules, ensuring that most people with moderate-to-severe psoriasis can achieve and maintain clear skin.