

Advances in Biologic Therapies for Moderate-to-Severe Psoriasis: Current Status and Future Directions

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by erythematous plaques with silvery scales, most commonly affecting the elbows, knees, scalp and lower back. Among its various clinical phenotypes, plaque psoriasis is the most prevalent and can range in severity from localized, mild lesions to extensive involvement causing profound physical discomfort and psychological distress. In moderate-to-severe cases, where topical therapies and phototherapy are inadequate, systemic treatments are warranted. Over the past two decades, there has been a significant transformation in the management of moderate-to-severe psoriasis with the advent of biologic therapies, which specifically target key immune pathways involved in disease pathogenesis. These therapies have not only improved disease outcomes but have also redefined treatment goals, shifting from basic control to complete or near-complete skin clearance. This article discusses the current status of biologic treatments for psoriasis and explores the future directions in the evolving therapeutic landscape [1].

The pathogenesis of psoriasis involves complex interactions between genetic susceptibility, environmental triggers and immune dysregulation. Central to this process is the activation of dendritic cells and T lymphocytes, leading to the release of pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin (IL)-23, IL-17 and IL-22. These cytokines contribute to keratinocyte hyperproliferation, epidermal thickening and the formation of psoriatic plaques. The discovery of these molecular targets has led to the development of biologic agents that inhibit specific cytokines or their receptors, resulting in more precise and effective treatment with fewer systemic side effects than traditional immunosuppressive agents.

Description

The first wave of biologics targeted TNF- α and included agents such as etanercept, infliximab and adalimumab. These drugs demonstrated substantial efficacy in reducing disease severity and improving quality of life. Etanercept, a soluble TNF receptor fusion protein and monoclonal antibodies like infliximab and adalimumab remain widely used in clinical practice, particularly in patients with coexisting psoriatic arthritis. However, limitations such as partial responses, secondary loss of efficacy and concerns over infection risks and immunogenicity prompted the development of next-generation biologics. Subsequent advancements focused on the IL-12/23 and IL-23 pathways. Ustekinumab, a monoclonal antibody targeting the p40 subunit shared by IL-12 and IL-23, was among the first in this category and offered improved disease control with quarterly dosing. More recently, selective IL-23 inhibitors such as guselkumab, tildrakizumab and risankizumab have emerged as highly effective options, with

many patients achieving a 90–100% reduction in Psoriasis Area and Severity Index (PASI) scores. These agents specifically block the p19 subunit of IL-23, thereby modulating the Th17 inflammatory axis while preserving IL-12-mediated immune surveillance, potentially reducing the risk of opportunistic infections. The IL-17 pathway has also become a pivotal target in psoriasis treatment. Secukinumab and ixekizumab are monoclonal antibodies that neutralize IL-17A, a key effector cytokine in psoriasis. Brodalumab, targeting the IL-17 receptor A, offers an alternative mechanism by blocking multiple IL-17 isoforms. These drugs demonstrate rapid onset of action, often resulting in substantial improvement within weeks. However, concerns about mucocutaneous candidiasis and potential exacerbation of inflammatory bowel disease necessitate careful patient selection [2].

The evolution of biologics has not only improved efficacy but also influenced treatment expectations. The concept of "treat to target," aiming for complete or near-complete skin clearance, has become the standard. This has prompted regular disease monitoring using validated tools such as PASI, the Dermatology Life Quality Index (DLQI) and patient-reported outcomes. Moreover, the extended dosing intervals of newer agents have enhanced treatment adherence and convenience. Despite the success of biologics, challenges remain. Primary and secondary non-response, immunogenicity, high cost and limited access in certain regions restrict their universal application. Biosimilars biologic products that are highly similar to approved reference agents offer a potential solution to cost-related barriers. Several biosimilars for adalimumab, infliximab and etanercept are now available and have demonstrated comparable efficacy and safety, increasing treatment accessibility in resource-limited settings.

Conclusion

Biologic therapies have revolutionized the treatment of moderate-to-severe psoriasis by offering targeted, effective and sustainable disease control. The current landscape includes a diverse array of agents targeting TNF- α , IL-12/23, IL-23 and IL-17 pathways, each with unique attributes suited to different patient needs. While significant strides have been made, ongoing research continues to refine therapeutic strategies, personalize care and improve long-term safety and efficacy. As innovation accelerates and accessibility expands, biologic therapy is poised to remain at the forefront of psoriasis management, offering hope for improved quality of life and long-term disease remission for patients worldwide.

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Conflict of Interest

None.

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