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# BIOLOGIC AND TARGETED SYSTEMIC THERAPIES FOR MODERATE-TO-SEVERE PLAQUE PSORIASIS IN EUROPE: A REVIEW OF MECHANISMS, EFFICACY, SAFETY, AND CLINICAL POSITIONING

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**ABSTRACT**

Major advances in the understanding of psoriasis immunopathogenesis have reshaped the treatment of moderate-to-severe plaque psoriasis. Identification of tumor necrosis factor-α (TNF-α) and the IL-23/Th17 axis as central drivers of disease has led to the development of biologic and targeted systemic therapies capable of achieving substantially improved disease control and patient outcomes.

This review examines the principal biologic and targeted systemic therapies currently used in Europe, including TNF-α, IL-12/23, IL-17, and IL-23 inhibitors, as well as apremilast. We discuss their mechanisms of action, clinical efficacy, durability of response, safety profiles, and therapeutic positioning on the basis of pivotal trials, extension studies, network meta-analyses, and real-world evidence.

Among currently available agents, IL-17 and IL-23 inhibitors generally provide the greatest levels of skin clearance, whereas TNF-α inhibitors continue to occupy an important place in selected clinical contexts, particularly in patients with concomitant psoriatic arthritis. Ustekinumab remains a well-established option with durable efficacy and convenient administration, while apremilast retains relevance in patients for whom an oral non-biologic approach is preferred.

Taken together, current evidence supports a shift from broad immunosuppression toward mechanism-based, individualized therapy. In contemporary psoriasis care, treatment selection should be guided not only by efficacy, but also by long-term safety, durability, comorbidities, and patient-specific considerations.

**KEYWORDS**

Psoriasis, Plaque Psoriasis, Biologic Therapy, Targeted Therapy, TNF-A Inhibitors, IL-17 Inhibitors, IL-23 Inhibitors

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## 1. Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by erythematous, scaly plaques and a relapsing clinical course. (Gao et al., 2025) (Sharma et al., 2022)

The disease affects a substantial proportion of the European population and is associated with a marked burden on quality of life, as well as multiple systemic comorbidities, including psoriatic arthritis, metabolic syndrome, and cardiovascular disease. (Ponikowska et al., 2025) (Almenara-Blasco et al., 2024) (Langenbruch et al., 2023) (Acioly et al., 2024) (Jiang et al., 2023) The heterogeneity of clinical presentation and the presence of associated comorbidities make individualized systemic treatment a central component of contemporary psoriasis management.

Advances in the understanding of psoriasis pathogenesis have highlighted the central role of dysregulated immune pathways, particularly those involving tumor necrosis factor-α (TNF-α) and the IL-23/Th17 axis, which have become major therapeutic targets in contemporary systemic treatment. (Sieminska et al., 2024) (Sharma et al., 2022) (Potestio et al., 2024)

Over the past two decades, these insights have led to the development of several targeted biologic and small-molecule therapies that have substantially improved treatment outcomes in patients with moderate-to-severe psoriasis. (Sbidian et al., 2025) (Jiang et al., 2023)

In addition to established biologic classes such as TNF-α inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors, newer targeted approaches, including phosphodiesterase-4 (PDE-4) inhibitors, have further broadened the therapeutic landscape. (Sbidian et al., 2025)

This review provides an overview of the major classes of biologic and targeted systemic therapies currently used in Europe for the treatment of moderate-to-severe psoriasis. The mechanisms of action, long-term efficacy, and safety profiles of these therapies are discussed with primary reference to pivotal clinical trials, pooled analyses, network meta-analyses, and longer-term observational studies.

## 2. Methodology

This article was prepared as a structured narrative review of targeted therapies approved in Europe for the treatment of psoriasis. The literature search was conducted primarily in the PubMed database and focused on publications concerning biologic agents and apremilast currently registered for clinical use in Europe.

The evidence base was built mainly on phase III randomized clinical trials, meta-analyses, and European clinical guidelines, as these sources were considered the most reliable for assessing efficacy, safety, and the current therapeutic role of individual agents. In addition, landmark and highly cited studies were reviewed to ensure inclusion of publications that have had a major impact on the evolution of psoriasis treatment and on the interpretation of clinical outcomes in both trial settings and routine practice.

Publications were selected according to their relevance to the topic, methodological rigor, and clinical applicability. Particular attention was paid to studies addressing comparative efficacy, long-term response, safety profile, and treatment positioning in moderate-to-severe psoriasis. Long-term extension studies and real-world data were also included when they provided clinically meaningful information not fully captured in pivotal trials.

Because this was a narrative review, no formal systematic-review framework, PRISMA flow diagram, or quantitative evidence synthesis was employed.

## 3. Discussion

### 3.1. TNF-α inhibitors

Tumor necrosis factor alpha (TNF-α) antagonists represent the first generation of targeted biologic therapies introduced for the treatment of moderate-to-severe plaque psoriasis and have played a pivotal role in transforming the systemic treatment of moderate-to-severe psoriasis. Their introduction in the early 2000s marked one of the earliest successful applications of targeted immunotherapy in psoriasis and contributed substantially to a redefinition of systemic treatment standards in dermatology. (Rønholt & Iversen, 2017; Wcisło-Dziadecka et al., 2016)

TNF-α is a key pro-inflammatory cytokine involved in both the initiation and maintenance of psoriatic inflammation. It promotes activation of dendritic cells, drives differentiation of Th1 and Th17 lymphocytes, enhances endothelial expression of adhesion molecules (including ICAM-1 and VCAM-1), stimulates angiogenesis, and induces keratinocyte proliferation and aberrant differentiation through activation of the NF-κB and MAPK signaling pathways. (Lowes et al., 2014)

Overexpression of TNF-α in psoriatic skin has been consistently demonstrated in immunohistochemical and molecular studies, which revealed significantly increased TNF-α mRNA and protein levels within psoriatic plaques compared with non-lesional skin. Neutralization of TNF-α also contributes to downregulation of the IL-23/Th17 axis, likely through reduced IL-23 production by dendritic cells and decreased downstream expression of IL-17- and IL-22-associated inflammatory pathways. This results in normalization of keratinocyte proliferation, reduction of epidermal hyperplasia, and attenuation of inflammatory cellular infiltrates within psoriatic lesions. (Menter et al., 2021) (Lowes et al., 2013)

The clinical efficacy of TNF-α inhibitors has been confirmed in randomized placebo-controlled trials and network meta-analyses. Compared with placebo, these agents significantly increase the likelihood of achieving clinically meaningful PASI responses during induction therapy. However, in comparative network meta-analyses, the overall efficacy of TNF-α inhibitors in achieving higher response thresholds, particularly PASI90, is generally lower than that reported for IL-17 and IL-23 inhibitors, reflecting the evolution of biologic therapy toward more selective targeting of psoriatic inflammatory pathways. (Sbidian et al., 2023) (Armstrong et al., 2021) (Reich et al., 2005) (Menter et al., 2008)

Beyond PASI-based endpoints, clinical trials consistently demonstrate reductions in body surface area involvement and clinically meaningful improvements in patient-reported outcomes, including DLQI, indicating that TNF-α blockade translates into both objective disease control and improved health-related quality of life. (Lebwohl et al., 2025) (de Ruiter & Rustemeyer, 2022)

Currently approved TNF-α inhibitors for the treatment of psoriasis in Europe include adalimumab, infliximab, etanercept, and certolizumab pegol, each of which differs in molecular structure, pharmacokinetics, dosing strategy, and clinical profile. (Nast et al., 2020)

### 3.1.1. Adalimumab

Adalimumab, a fully human IgG1 monoclonal antibody targeting both soluble and membrane-bound TNF-α, remains one of the most extensively studied inhibitors of this cytokine in the treatment of moderate-to-severe plaque psoriasis. Its efficacy has been demonstrated in pivotal phase III trials, including REVEAL and CHAMPION, in which PASI75 responses at week 16 were achieved in 71–80% of patients and PASI90 responses in 45–49%, with statistically significant superiority over both placebo and methotrexate. (Saurat et al., 2008) (Papp et al., 2015)

Adalimumab treatment is also associated with substantial reductions in the extent of skin involvement and marked improvements in health-related quality of life. Mean reductions in the Dermatology Life Quality Index (DLQI) have been reported in the range of approximately 9–12 points, well above the minimal clinically important difference (de Ruiter & Rustemeyer, 2022). Furthermore, a significant proportion of patients achieve DLQI scores indicating minimal impact of disease on daily functioning (Mrowietz et al., 2013), confirming that adalimumab provides both robust objective disease control and meaningful patient-reported outcomes (Revicki et al., 2008).

Long-term data support the durability of response to adalimumab. In an open-label extension of the REVEAL study, patients with sustained initial PASI75 responses maintained high rates of response over 3 years, with approximately 76% retaining PASI75 and 50% retaining PASI90 at 160 weeks of continuous therapy. Real-world registry analyses, including BADBIR, demonstrate favorable treatment persistence of adalimumab in clinical practice, with loss of efficacy representing one of the most common reasons for discontinuation. (Gordon et al., 2012) (Alabas et al., 2023)

The safety profile of adalimumab is well established; the most frequently reported adverse events include injection-site reactions and mild infections, while meta-analyses and pooled long-term studies have not demonstrated a significant increase in serious adverse events. Pre-treatment screening for latent tuberculosis remains essential due to the risk of reactivation, whereas current evidence does not indicate a clear increase in the incidence of solid malignancies. (Dommasch et al., 2011) (Semble et al., 2014)

Owing to its documented efficacy in psoriatic arthritis, including inhibition of radiographic progression, adalimumab represents a particularly appropriate therapeutic option for patients with concomitant joint involvement. Its systemic anti-inflammatory activity also supports its use in individuals with extensive cutaneous disease (high BSA) or significant nail involvement. Overall, adalimumab remains a well-established therapy with robust long-term efficacy and a predictable safety profile and remains an important reference agent in comparative evaluations of newer biologic therapies. (Mease et al., 2009)

### 3.1.2. Infliximab

Infliximab is a chimeric IgG1 monoclonal antibody composed of human and murine sequences that targets TNF-α and is one of the most effective TNF-α inhibitors in short-term induction therapy for moderate-to-severe plaque psoriasis. Its efficacy is characterized by a rapid onset of action, which is particularly relevant for patients with severe and extensive disease. In pivotal phase III trials, including EXPRESS and EXPRESS II, PASI75 responses were achieved in 80–88% of patients by week 10, while PASI90 responses were observed in 55–60%, supporting the view that infliximab is among the most rapidly acting TNF-α inhibitors and achieves high short-term response rates. (Reich et al., 2005) (Gottlieb et al., 2004)

Reductions in body surface area (BSA) averaged over 75%, and improvements in health-related quality of life, assessed by the Dermatology Life Quality Index (DLQI), ranged from 10 to 13 points, with approximately half of patients achieving DLQI 0/1. (Feldman et al., 2005)

Observational studies suggest that clinical benefit may be maintained long term in selected patients, although treatment persistence is limited in routine practice by loss of efficacy and immunogenicity. (Mourad & Gniadecki, 2021) (Warren et al., 2015) (Iskandar et al., 2017)

Due to its chimeric structure, infliximab exhibits higher immunogenicity compared with fully human antibodies, which may result in the formation of neutralizing anti-drug antibodies and necessitate dose escalation or concomitant conventional therapy. (Thomas et al., 2015)

The safety profile of infliximab includes similar adverse events as other TNF-α inhibitors, such as infusion reactions, upper respiratory tract infections, and mild opportunistic infections. Pre-treatment screening for latent tuberculosis is essential due to the risk of reactivation. Long-term data do not indicate a significant increase in solid malignancy risk, although rare cases of lymphoma have been reported. (Dommasch et al., 2011) (Leman & Burden, 2008)

Infliximab is particularly relevant in patients with severe, extensive plaque psoriasis (high BSA) and those requiring rapid therapeutic effect. Its efficacy in psoriatic arthritis, including inhibition of radiographic progression, also makes it suitable for patients with concomitant joint involvement. The combination of rapid onset, high efficacy, and well-characterized safety profile supports its role as an important therapeutic option in patients with severe disease. (Reich et al., 2005) (Antoni et al., 2005) (Van Der Heijde et al., 2007)

### 3.1.3. Etanercept

Etanercept is a recombinant fusion protein composed of the extracellular domain of the human tumor necrosis factor (TNF) receptor linked to the Fc portion of human IgG1. It exerts its therapeutic effect by acting as a soluble TNF receptor fusion protein that binds TNF and thereby neutralizes its pro-inflammatory activity.

Etanercept is approved for the treatment of moderate-to-severe plaque psoriasis, and its efficacy has been demonstrated in randomized phase III trials. PASI75 response rates of approximately 47–59% have been reported between weeks 12 and 24, whereas PASI90 responses are generally lower, typically ranging from 20% to 28%, and remain below those observed with monoclonal anti-TNF antibodies such as infliximab and adalimumab. (C. L. Leonardi et al., 2003)(Tyring et al., 2006). Nevertheless, etanercept remains a clinically relevant option because of its well-established safety profile and convenient subcutaneous administration.

In addition to improvements in PASI scores, treatment with etanercept has also been associated with reductions in the extent of skin involvement and significant improvements in health-related quality of life. Improvements in Dermatology Life Quality Index (DLQI) scores have been consistently reported in clinical trials, indicating a meaningful reduction in the impact of psoriasis on daily functioning and well-being. (Reich et al., 2009) Long-term studies further suggest that clinical responses can be maintained during extended treatment periods, with sustained PASI improvements and stable safety outcomes observed for up to 96 weeks of therapy (Long-Term Safety and Efficacy of Etanercept in Patients with Psoriasis: An Open-Label Study - PubMed, n.d.)

Long-term data indicate that etanercept can maintain efficacy over several years; however, European registry analyses suggest lower drug survival than with adalimumab, and comparable or only slightly better persistence than with infliximab, with secondary loss of efficacy and adverse events being the most common reasons for discontinuation (Warren et al., 2015)(Mourad & Gniadecki, 2021). The safety profile of etanercept is well established; the most frequent adverse events include injection-site reactions and mild upper respiratory tract infections, while meta-analyses have not shown a significant increase in serious adverse events compared with controls (Sbidian et al., 2023a) (Jain & Singh, 2013) As with other TNF-α inhibitors, pre-treatment screening for latent tuberculosis is required.(Smolen et al., 2017)

Etanercept remains a useful option in patients with moderate-to-severe psoriasis, particularly when a subcutaneous, weekly dosing regimen is preferred or when long-term therapy with predictable administration is required. It also demonstrates efficacy in psoriatic arthritis. (Mease et al., 2004) With a favorable safety profile and consistent clinical effects, etanercept remains a valuable therapeutic option among TNF-α inhibitors.

### 3.1.4. Certolizumab pegol

Certolizumab pegol is a PEGylated, Fc-free Fab′ fragment of a humanized monoclonal antibody that selectively binds TNF-α and neutralizes its pro-inflammatory activity. Unlike other TNF-α inhibitors, it lacks an Fc fragment, which results in the absence of Fc-mediated effector functions and is associated with minimal placental transfer. The drug is approved for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis. (Dattola et al., 2017)

Efficacy has been demonstrated in pivotal phase III trials, including CIMPASI-1 and CIMPASI-2. By week 16, PASI75 responses were achieved in 75–82% of patients, and PASI90 responses in 45–52%, placing certolizumab among the TNF-α inhibitors with high short-term efficacy (Gottlieb et al., 2018)

Treatment was also associated with substantial reductions in the extent of skin involvement and significant improvements in Dermatology Life Quality Index (DLQI) scores, with a substantial proportion of patients achieving DLQI 0/1. (Gottlieb et al., 2018)

Long-term follow-up studies have demonstrated sustained efficacy during several years of treatment. Its safety profile is broadly consistent with that of the TNF-α inhibitor class, with the most commonly reported adverse events including mild infections and injection-site reactions; long-term analyses have not identified unexpected safety signals. (Blauvelt et al., 2021)

Available evidence does not indicate an increased incidence of serious adverse events or solid malignancies. As with other TNF-α inhibitors, screening for latent tuberculosis is required before therapy initiation. (Nast et al., 2020)

Certolizumab pegol is particularly relevant when biologic treatment is required during pregnancy, as minimal placental transfer was demonstrated in the prospective CRIB pharmacokinetic study. Moreover, the CRADLE study showed minimal to no transfer into breast milk, further supporting the relevance of certolizumab pegol during lactation and in the broader perinatal setting. (Mariette et al., 2018) (Clowse et al., 2017)

Clinically, certolizumab is especially useful in patients requiring a rapid therapeutic response, including those with severe or extensive plaque psoriasis, joint or nail involvement, and situations where treatment during pregnancy is necessary. Consequently, certolizumab pegol represents an important TNF-α inhibitor option, combining high short-term efficacy with a distinctive pharmacokinetic profile that may be particularly advantageous when treatment during pregnancy is required. (Dattola et al., 2017)

### 3.1.5. A summary of TNF-α inhibitors

In summary, TNF-α inhibitors represent an effective and well-established therapeutic option for the treatment of moderate-to-severe psoriasis; however, individual agents differ in their clinical profiles. (Sbidian et al., 2020) (Smith et al., 2020)

Infliximab is associated with a particularly rapid onset of action and high short-term PASI75 and PASI90 response rates, as demonstrated in the pivotal EXPRESS trial and supported by subsequent comparative meta-analyses. (Reich et al., 2005) (Signorovitch et al., 2015)

Adalimumab, while providing robust induction efficacy, has shown favorable long-term drug survival in registry-based and meta-analytic studies, with higher treatment persistence than etanercept and infliximab in several real-world analyses. (Gniadecki et al., 2015) (Warren et al., 2015) (Mourad & Gniadecki, 2021)

Etanercept is characterized by a stable safety profile and a convenient subcutaneous dosing regimen, although comparative analyses suggest slightly lower efficacy and treatment persistence than adalimumab. (Warren et al., 2015) (Long-Term Safety and Efficacy of Etanercept in Patients with Psoriasis: An Open-Label Study - PubMed, n.d.)

Certolizumab pegol combines high clinical efficacy with a distinctive pharmacokinetic profile related to the absence of an Fc fragment, resulting in minimal placental transfer and supporting its consideration when biologic therapy is required during pregnancy. (M. Lebwohl et al., 2018) (Mariette et al., 2018)

In light of available meta-analyses, long-term extension studies, and real-world registry data, selection of a specific TNF-α inhibitor should be individualized according to the required speed of response, expected treatment persistence, safety considerations, comorbid psoriatic arthritis, and reproductive context. (Sbidian et al., 2020)

### 3.2. IL-17 inhibitors

Interleukin-17 inhibitors represent a distinct class of biologic therapies that play a pivotal role in the contemporary management of psoriasis. They are currently positioned among first-line biologic therapies for the treatment of moderate-to-severe psoriasis in patients eligible for systemic therapy. The development of IL-17 inhibitors represented a further step in the evolution of biologic therapies for psoriasis, following the earlier introduction of TNF-α and IL-12/23 inhibitors and reflecting an improved understanding of the IL-23/Th17 inflammatory pathway.

IL-17 inhibitors have substantially improved treatment efficacy in psoriasis, with PASI 90 and PASI 100 responses now achieved in a significantly larger proportion of patients.(Abrouk et al., 2017) Prior to the availability of this class of agents, attaining such levels of response was considerably more difficult, and PASI 75 was more commonly regarded as the standard efficacy endpoint. Consequently, the therapeutic goals in psoriasis have evolved, shifting toward near-complete or complete skin clearance as a realistic and clinically meaningful objective in the management of moderate-to-severe psoriasis. Moreover, IL-17 inhibitors are characterized by a rapid onset of action, with clinically meaningful responses often observable as early as 2–4 weeks after treatment initiation. Those improvement translate into a significant enhancement in patients' quality of life, as demonstrated by marked reductions in Dermatology Life Quality Index (DLQI) scores (Kruczek et al., 2025)

An additional advantage of IL-17 inhibitors is their high efficacy in the treatment of nail psoriasis (Yan et al., 2025), as well as in other difficult-to-treat disease locations, including genital psoriasis, palmoplantar psoriasis, and scalp psoriasis. Notably, in the latter indication, clinical study has demonstrated superior efficacy of IL-17 inhibitors compared with another highly effective biologic class, IL-23 inhibitors (Mastorino et al., 2023).

Regarding the mechanism of action, the interleukin-17 (IL-17) family is a group of pro-inflammatory cytokines that play a central immunopathogenic role in psoriasis by driving cutaneous inflammation (Martin et al., 2013). IL-17A and IL-17F, the most biologically active members of this family, are produced mainly by Th17 cells and other immune subsets, and they stimulate keratinocytes to express pro-inflammatory cytokines, chemokines, and antimicrobial peptides, amplifying local inflammatory networks within psoriatic lesions (Sánchez-Rodríguez & Puig, 2023).

Binding of IL-17 cytokines to the IL-17 receptor complex, predominantly IL-17RA/RC on epithelial cells, triggers intracellular signaling pathways such as NF-κB and MAP. This activation leads to up-regulation of genes involved in inflammation and recruitment of immune cells. (Vidal et al., 2021)

This IL-17 signaling in psoriatic lesions establishes a self-reinforcing inflammatory loop. Activation of IL-17 receptors on keratinocytes induces the expression of pro-inflammatory cytokines, chemokines, and antimicrobial peptides, which recruit neutrophils and additional IL-17-producing immune cell and contribute to the local inflammatory environment characteristic for psoriatic plaques (Vidal et al., 2021). In addition, IL-17 acts synergistically with other pro-inflammatory cytokines such as TNF-α, to further enhance expression of inflammatory mediators and sustain tissue inflammation (Blauvelt & Chiricozzi, 2018).

In Europe, four IL-17 inhibitors are currently approved for the treatment of moderate-to-severe plaque psoriasis — secukinumab, ixekizumab, brodalumab, and bimekizumab — which differ mechanistically in their target specificity within the IL-17 pathway (Armstrong & Read, 2020) (Simopoulou et al., 2023)

#### 3.2.1. Secukinumab

Secukinumab is a fully human IgG1κ monoclonal antibody administered subcutaneously and approved for the treatment of moderate-to-severe plaque psoriasis. It selectively binds and neutralizes interleukin-17A (IL-17A), thereby preventing IL-17A from interacting with its receptor, without directly blocking the IL-17 receptor itself or significantly affecting IL-17F (Vidal et al., 2021). The efficacy and safety of secukinumab were demonstrated in the pivotal phase III ERASURE and FIXTURE trials, which evaluated its superiority over placebo (and additionally over etanercept in FIXTURE) in reducing disease severity.

In ERASURE, secukinumab produced markedly higher rates of clinical response at week 12 than placebo, with PASI 75 achieved by 81.6 % (300 mg) and 71.6 % (150 mg) versus 4.5 % for placebo. (Langley et al., 2014) Secondary endpoints further demonstrated that PASI 90 was reached by 59.2 % and 39.1 %, and other efficacy endpoint - PASI 100 by 28.6% and 12,8%, compared with ~1 % in the placebo group, reflecting profound skin clearance.

Similarly, in the FIXTURE trial, secukinumab was superior to both placebo and the TNF-α inhibitor - etanercept, with PASI 75 rates of 77.1 % and 67.0 % for 300 mg and 150 mg, compared with 44.0 % for

etanercept and 4.9 % for placebo (Langley et al., 2014), and PASI 90 responses of 54.2 % and 41.9 % versus 20.7 % for etanercept and 1.5 % for placebo, again as secondary endpoints. PASI 100 was reached by 24,1% and 14,4% versus 4,3% for Etanercept.

Beyond its pronounced effects on skin clearance, secukinumab demonstrated significant improvements in patient-reported quality of life, as evidenced in the phase II study where the early regimen led to 40.8 % of patients achieving DLQI 0/1 at week 12, compared with 1.6 % in the placebo group. (Augustin et al., 2015)

Long-term studies of secukinumab have demonstrated sustained efficacy and a favorable safety profile in patients with moderate-to-severe plaque psoriasis. (Langley et al., 2023) In the 5-year extension of the pivotal ERASURE and FIXTURE trials, high rates of PASI 75, PASI 90, and PASI 100 responses were maintained and also improvements in quality of life (DLQI 0/1) persisted throughout the observation period.(Langley et al., 2023) Also real-world data support these findings, showing durable effectiveness and tolerability for up to 6 years of continuous treatment (Galluzzo et al., 2024). Pediatric studies indicate similar long-term efficacy and quality-of-life benefits for up to 236 weeks,(Kaszuba et al., 2025) with a safety profile consistent with adult populations(Sticherling et al., 2023).

Secukinumab has a favorable long-term safety profile in patients with moderate-to-severe plaque psoriasis, with low rates of serious adverse events and no apparent increase over up to 5 years of treatment(Gottlieb et al., 2022). The most common adverse events were mild infections, such as nasopharyngitis and upper respiratory tract infections (Langley et al., 2023). Serious infections, opportunistic infections, malignancies, and major cardiovascular events were rare and did not increase in incidence over time (Gottlieb et al., 2022). Cases of inflammatory bowel disease, including Crohn's disease, ulcerative colitis, and unclassified IBD were uncommon, with exposure-adjusted incidence rates remaining low and stable over time (Schreiber et al., 2019).

Overall, secukinumab is a highly effective, well tolerated therapeutic option for patients with moderate-to-severe plaque psoriasis, and has a stable safety profile supported by both clinical trials and real-world evidence.

### 3.2.2. Ixekizumab

Ixekizumab is a humanized IgG4 monoclonal antibody administered subcutaneously that, similarly to secukinumab, selectively binds to and neutralizes interleukin-17A (IL-17A), targeting a key pro-inflammatory cytokine central to psoriasis pathogenesis (K. B. Gordon et al., 2016). In Europe, It has been approved for the treatment of adult moderate-to-severe plaque psoriasis, active psoriatic arthritis, axial spondyloarthritis and additional inflammatory indications. (*Taltz | European Medicines Agency (EMA)*, n.d.)

The efficacy of ixekizumab in adults with moderate-to-severe plaque psoriasis was demonstrated in the phase III UNCOVER-1, UNCOVER-2, and UNCOVER-3 trials, which evaluated two dosing regimens of ixekizumab and compared them against placebo in all three studies, and additionally against etanercept (tumor necrosis factor-α inhibitor) in UNCOVER-2 and UNCOVER-3 (Farahnik, Beroukhim, Zhu, et al., 2016). At week 12, treatment responses with ixekizumab were consistently high across the UNCOVER program, with the percentages below reflecting the range observed across all three individual trials. PASI 75 — indicating at least 75 % improvement in psoriasis severity — was achieved by approximately 77 % to 90 % (depending on a study and dosing frequency) of patients treated with ixekizumab compared with 2–8% in the placebo groups and 41–53% in the etanercept groups (Farahnik et al., 2016). PASI 90 responses ranged from 59 % to 71 % with ixekizumab versus <1–3% with placebo and 19–26% with etanercept. (Farahnik et al., 2016) Complete skin clearance (PASI 100) was observed in approximately 30–41% of ixekizumab-treated patients, compared with 0–1% receiving placebo and 5–7% receiving etanercept. Patient-reported quality of life, as measured by the proportion achieving DLQI 0/1, was also consistently greater with ixekizumab (~60–64 %) than with placebo (~6–8 %) and with etanercept (~34–44 %) at week 12 (Farahnik, Beroukhim, Zhu, et al., 2016). These data underscore the high level of clinical benefit with ixekizumab in psoriasis in both comparisons - to placebo and to a TNF inhibitor.

Long-term extension studies of the UNCOVER program show that the high efficacy of ixekizumab achieved during the 12-week induction phase is maintained over several years of continuous therapy. At week 60, PASI 75, PASI 90, and PASI 100 responses were approximately 95 %, 85 %, and 62 %, respectively, and at year 5 these responses remained high- 90 %, 71 %, and 46 % (C. Leonardi et al., 2020). Similarly, in UNCOVER-3, responses at week 204 (~4 years) ranged from 83–98 % for PASI 75, 66–88 % for PASI 90, and 48–67 % for PASI 100, depending on the analysis method (M. G. Lebwohl et al., 2020). These data indicate that deep and durable skin clearance can be sustained for up to 4–5 years with continuous ixekizumab therapy.

Ixekizumab has generally demonstrated a favorable safety profile, consistent with IL-17A inhibition. In the UNCOVER-1, -2, and -3 trials, the most common adverse events were nasopharyngitis, upper respiratory tract infections, injection-site reactions, and headache, with serious events being uncommon (Farahnik, Beroukhim, Zhu, et al., 2016). Mild mucocutaneous candidiasis and occasional neutropenia were reported but were generally manageable. Long-term data from extension studies with follow-up of up to 4–5 years demonstrate a stable safety profile of ixekizumab, with no new safety signals and low rates of serious infections, supporting its tolerability during prolonged therapy (M. G. Lebwohl et al., 2020).

Overall, ixekizumab is a highly effective and well-tolerated therapeutic option for patients with moderate-to-severe plaque psoriasis, providing rapid and sustained skin clearance and improvements in quality of life, with an established long-term efficacy and safety profile supported by pivotal clinical trials and extended follow-up data.

### 3.2.3. Brodalumab

Brodalumab is a fully human monoclonal antibody that targets the interleukin-17 A receptor (IL-17RA), thereby blocking the biological activity of multiple IL-17 cytokines, including IL-17A, IL-17F, and IL-17A/F heterodimers. By inhibiting IL-17RA signaling, brodalumab suppresses downstream IL-17–mediated inflammatory pathways involved in the pathogenesis of plaque psoriasis. It is approved in Europe for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy (Farahnik, Beroukhim, Abrouk, et al., 2016).

The efficacy of brodalumab in adults with moderate-to-severe plaque psoriasis was demonstrated in the pivotal phase III AMAGINE-1, AMAGINE-2, and AMAGINE-3 trials, which compared brodalumab with placebo in all three studies and with ustekinumab ( IL-12/23 inhibitor) in AMAGINE-2 and AMAGINE-3 (M. Lebwohl et al., 2015). At the primary efficacy time point of week 12, PASI 75 was achieved by approximately 67–86% of patients receiving brodalumab across dose groups and trials, compared with 6–8 % in the placebo groups and 69–70 % in the ustekinumab groups (AMAGINE-2 and -3) (M. Lebwohl et al., 2015).

Complete skin clearance (PASI 100) at week 12 was observed in approximately 37–44 % of patients treated with brodalumab 210 mg, compared with 0–1 % with placebo and 19–22 % with ustekinumab (M. Lebwohl et al., 2015). Patient-reported quality of life outcomes measured by DLQI were assessed in integrated analyses of the AMAGINE-2 and AMAGINE-3 trials, showing that a significantly greater proportion of patients treated with brodalumab achieved DLQI 0/1 compared with ustekinumab at week 12 and this difference persisted at week 52 (Lambert et al., 2021).

Long-term extension analyses from the AMAGINE clinical program demonstrate that the high levels of skin clearance achieved with brodalumab are sustained through extended treatment periods beyond the initial 12-week induction phase. In the AMAGINE-2 open-label extension through 120 weeks, patients receiving brodalumab 210 mg every 2 weeks maintained robust responses, with approximately 84.4 % achieving PASI 75, 75.6 % achieving PASI 90, and 61.1 % achieving PASI 100 at week 120 in observed data analyses (continuous therapy)(Puig et al., 2020). Post-hoc pooled analyses of AMAGINE-2 and AMAGINE-3 similarly demonstrated sustained efficacy through week 120, with high proportions of patients achieving PASI 90 and PASI 100 during long-term treatment, indicating that deep skin clearance can be maintained for more than 2 years with continuous brodalumab exposure (Reich et al., 2022). These findings support the long-term durability of brodalumab efficacy in moderate-to-severe plaque psoriasis, with many patients maintaining clinically meaningful improvements in disease severity over extended treatment periods.

Brodalumab has shown a generally well-tolerated safety profile in the phase III AMAGINE-1, -2, and -3 trials, with the most common adverse events being nasopharyngitis, upper respiratory tract infections, headache, arthralgia, and injection-site reactions (M. Lebwohl et al., 2015). Rates of serious infections were low, and long-term follow-up through week 120 showed no new safety signals (Puig et al., 2020)(Reich et al., 2022). Rare cases of suicidal ideation and behavior have been reported, however, a causal relationship has not been established, highlighting the need for appropriate monitoring (M. Lebwohl et al., 2025).

### 3.2.4. Bimekizumab

Bimekizumab is a humanized IgG1 monoclonal antibody that targets the interleukin-17 (IL-17) pathway by selectively neutralizing both IL-17A and IL-17F, as well as the IL-17A/F heterodimer, thereby preventing their interaction with the IL-17 receptor complex. This dual blockade differentiates bimekizumab from other IL-17 inhibitors. Preclinical and early clinical studies indicate that simultaneous neutralization of IL-17A and IL-17F may result in a more profound suppression of inflammatory cytokine responses and related inflammatory processes than blocking IL-17A alone, providing a mechanistic rationale for broader inhibition of IL-17-mediated inflammation in immune-mediated diseases such as psoriasis and psoriatic arthritis (Glatt et al., 2018).

Bimekizumab is approved in Europe for the treatment of plaque psoriasis, psoriatic arthritis, axial spondyloarthritis, and moderate-to-severe hidradenitis suppurativa (Bimzelx | European Medicines Agency (EMA), n.d.)

Clinical efficacy of bimekizumab in treating plaque psoriasis has been demonstrated across few pivotal, phase III trials, including the BE VIVID, BE SURE, and BE RADIANT trials, in which the drug was evaluated against placebo as well as against ustekinumab (IL-12/23 inhibitor), adalimumab (TNF alpha inhibitor), and secukinumab (IL-17 inhibitor) (Reich, Papp, et al., 2021); (Warren et al., 2021).

At week 16, achievement of PASI 90—a primary or co-primary endpoint in these trials - occurred in 85 % of patients in BE VIVID compared with 50 % receiving ustekinumab and 5 % receiving placebo (Reich, Papp, et al., 2021). In BE SURE, 86.2 % of patients achieved PASI 90 versus 47.2 % with adalimumab (Warren et al., 2021).

Rates of complete skin clearance (PASI 100) were similarly high, reaching 59 % in BE VIVID versus 21% with ustekinumab and 0 % with placebo (Reich, Papp, et al., 2021), and 60.8 % in BE SURE versus 23.9 % with adalimumab (Warren et al., 2021). In BE RADIANT, responses were 61.7 % with bimekizumab compared with 48.9 % with secukinumab (Reich, Warren, et al., 2021). Bimekizumab was also associated with substantial improvements in patient-reported outcomes, including superior dermatology-specific quality-of-life benefits compared with placebo and active comparators, with these effects maintained over time. (Reich, Warren, et al., 2021)(A. Armstrong et al., 2026).

Long-term studies have confirmed the durable efficacy of bimekizumab in adults with moderate-to-severe plaque psoriasis. In the BE RADIANT open-label extension, complete skin clearance (PASI 100) was maintained in approximately 68.8 % of patients at 3 years (Warren et al., 2025). In the BE BRIGHT extension, 80.8 % of patients sustained PASI 100 and also high PASI 90 responses were preserved through 3 years (Strober et al., 2023), while four-year follow-up showed that approximately 64.7 % of patients maintained PASI 100 through week 196 (Blauvelt et al., 2025). Real-world evidence supports these findings, with 72.1% of patients achieving PASI 100 and 93.3 % achieving DLQI 0/1 after 52 weeks of continuous Bimekizumab therapy (Hagino et al., 2025). Across long-term studies, patient-reported outcomes remained robust, with DLQI= 0 responses sustained at high levels (65.5–94.8 %) through 4 years, confirming lasting improvements in quality of life (A. Armstrong et al., 2026).

Bimekizumab, has been shown in pooled phase II/III clinical trials to exhibita generally acceptable safety profile in patients with moderate-to-severe plaque psoriasis, with treatment-emergent adverse events (TEAEs) consistent over time and not increasing with longer exposure. The most common TEAEs reported across trials were nasopharyngitis, upper respiratory tract infections, and oral candidiasis, with oral candidiasis occurring at a notable exposure-adjusted incidence but being predominantly mild to moderate and only very rarely leading to treatment discontinuation (K. B. Gordon et al., 2022). In the phase IIIb BE RADIANT head-to-head trial, which compared bimekizumab with the IL-17A inhibitor secukinumab, oral candidiasis was observed more frequently in the bimekizumab group (~19.3 %) than in the secukinumab group (~3.0 %) further supporting the signal for increased mucocutaneous Candida infections with dual IL-17A/F blockade (Reich, Warren, et al., 2021). Overall, serious adverse events including serious infections and inflammatory bowel disease events occurred at low rates, and no new safety signals emerged over longer follow-up (up to 2–3 years in extension periods), indicating sustained tolerability under clinical trial conditions. (Warren et al., 2025)

### 3.3. IL-23 inhibitors

Interleukin-23 (IL-23) inhibitors represent an important class of biologic therapies for the treatment of moderate-to-severe plaque psoriasis, addressing one of the central cytokines involved in the pathogenesis of the disease and achieving high and sustained levels of skin clearance. Selective IL-23p19 inhibition has been shown in clinical trials and systematic analyses to result in high PASI90 and PASI100 responses that are maintained over extended treatment periods, reflecting both robust efficacy and long-term disease control across this class of agents (Megna et al., 2026). Improvements in psoriasis are accompanied by substantial gains in patient-reported quality of life, with large proportion of patients achieving Dermatology Life Quality Index (DLQI) scores indicating minimal or no impact on daily functioning.

While IL-23 inhibitors generally provide a strong and sustained clinical response, studies examining time to meaningful improvement note that IL-17 inhibitors may show the fastest onset of action in psoriasis, followed closely by IL-23 inhibitors; nonetheless, IL-23 inhibitors still achieve meaningful PASI responses in the early weeks of therapy and remain among the faster biologic options overall for achieving significant clinical improvements. (Aggarwal & Fleischer, 2024)(Egeberg et al., 2020)

Importantly, real-world registry data indicate that IL-23 inhibitors also have very favorable long-term drug survival, supporting durable effectiveness with lower likelihood of discontinuation due to loss of response compared with many other biologic classes (Motedayen Aval et al., 2025).

Targeting the IL-23 pathway may also be particularly advantageous in patients with concomitant inflammatory bowel disease; selective IL-23 blockade has demonstrated clinical benefit in Crohn's disease, in contrast to IL-17 blockade, which has been associated with potential exacerbations of IBD in some contexts, highlighting clinically relevant differences in immunologic effects beyond the skin (Vuyyuru et al., 2023) (B. Gao et al., 2023). IL-23 inhibitors are also effective in psoriatic arthritis (Huang et al., 2023), though some comparative analyses suggest other classes, particularly IL-17 inhibitors, may show more rapid improvement in joint symptoms during the early weeks of treatment (S. Gao et al., 2025).

When it comes to the mechanism of action, IL-23 inhibitors act by selectively binding the p19 subunit of IL-23, disrupting a key upstream step in the IL-23/Th17/IL-17 inflammatory axis. IL-23 is essential for the expansion, survival, and pathogenic activity of Th17 cells, which produce effector cytokines such as IL-17A, IL-17F and IL-22 that drive keratinocyte hyperproliferation and sustained cutaneous inflammation in psoriasis (Girolomoni et al., 2017a) (T. Liu et al., 2020). By targeting this upstream cytokine, IL-23 inhibitors reduce downstream effector signals and interrupt the chronic inflammatory feedback loop characteristic of psoriatic plaques. This selective mechanism helps explain both the high efficacy in skin clearance and the favorable safety profile observed in clinical studies of IL-23 inhibitors (J. J. Crowley et al., 2019).

In Europe, three selective IL-23p19 inhibitors are currently approved for the treatment of psoriasis: risankizumab, guselkumab, and tildrakizumab.

#### 3.3.1. Risankizumab

Risankizumab is a humanized IgG1 monoclonal antibody that selectively binds to the p19 subunit of interleukin-23, thereby inhibiting IL-23–mediated Th17 signaling implicated in the pathogenesis of moderate-to-severe plaque psoriasis. It is approved in Europe for moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy, as well as for active psoriatic arthritis in adults, and also more recently for Crohn's disease and ulcerative colitis based on regulatory extensions of indication. (Skyrizi | European Medicines Agency (EMA), n.d.)

The clinical efficacy of risankizumab in moderate-to-severe plaque psoriasis was demonstrated in the pivotal Phase III trials UltIMMa-1 and UltIMMa-2, which were randomized, double-blind studies including placebo and ustekinumab as comparators. In both trials PASI 90 at week 16 was a co-primary endpoint, and risankizumab achieved significantly higher levels of skin clearance than placebo (approximately 75% versus ~2–5%) and ustekinumab (~42–48%) at week 16 (K. B. Gordon et al., 2018). In addition, a higher proportion of patients treated with risankizumab reached PASI 100 (complete skin clearance) by week 16 compared with both placebo and ustekinumab (35,9%-50,7% of patients treated with risankizumab vs 12%-24% with ustekinumab and 0-2% on placebo), reflecting deeper levels of clinical response (K. B. Gordon et al., 2018). Analysis of patient-reported outcomes from these trials showed that a significantly greater proportion of risankizumab-treated patients achieved DLQI 0/1 (indicating no impact of psoriasis on quality of life) at week 16 versus both ustekinumab and placebo, with these quality-of-life improvements sustained through week 52(Augustin et al., 2020).

Long-term continuous treatment with risankizumab has demonstrated robust and durable efficacy. In the pivotal Phase III UltIMMa-1 and UltIMMa-2 trials, clinical responses were maintained through week 52, with PASI 90 achieved in approximately 81–82% of patients and PASI 100 in 56-60%, confirming sustained high levels of skin clearance over one year of therapy (K. B. Gordon et al., 2018). These findings are further supported by results from the Phase III open-label extension LIMMitless study, which demonstrated that at week 304 (~6 years), 86.0% of patients maintained PASI 90 responses (observed cases), 54.2% maintained PASI 100, and 76,3% achieved DLQI 0/1, indicating durable long-term skin clearance and sustained quality-of-life improvement with prolonged IL-23p19 inhibition (K. A. Papp et al., 2025).

The safety profile of risankizumab in psoriasis is favorable and consistent across studies; in UltIMMa-1 and UltIMMa-2 the frequency of treatment-emergent adverse events was similar between risankizumab, ustekinumab, and placebo with no unexpected safety signals. The most commonly observed events include infections (primarily mild upper respiratory tract infections), headache, and injection-site reactions, with low rates of serious adverse events reported through 52 weeks of treatment. (K. B. Gordon et al., 2018)

In conclusion, risankizumab represents a highly effective IL-23p19 inhibitor for moderate-to-severe psoriasis in Europe, with an evidence of high level skin clearance, quality-of-life improvement,and sustained efficacy through 52 weeks, underpinned by a consistent safety profile in the pivotal phase III studies (K. B. Gordon et al., 2018)

### 3.3.2. Guselkumab

Guselkumab is a recombinant, fully human monoclonal antibody of the IgG1λ subclass that specifically targets the p19 subunit of interleukin-23 (IL-23), thereby selectively inhibiting the IL-23–driven inflammatory pathway central to the pathogenesis of several immune-mediated diseases including psoriasis. In Europe, guselkumab is authorized for the treatment of moderate-to-severe plaque psoriasis in adults who are eligible for systemic therapy, for active psoriatic arthritis in adults, and for moderately to severely active ulcerative colitis and Crohn's disease. (Tremfya | European Medicines Agency (EMA), n.d.)

The efficacy of guselkumab in plaque psoriasis was established in pivotal phase III trials VOYAGE 1 and VOYAGE 2. In those trials, guselkumab demonstrated superior clinical efficacy compared with placebo and adalimumab - TNF alpha inhibitor - in adults with moderate-to-severe plaque psoriasis. In VOYAGE 1, at week 16 the proportion of patients achieving PASI 90 was 73.3 % with guselkumab versus 2.9 % for placebo and 49.7 % for adalimumab (Blauvelt et al., 2017). In VOYAGE 2, at week 16 PASI 90 was achieved by 70.0 % of patients treated with guselkumab versus 2.4 % with placebo and 46.8 % with adalimumab (Reich et al., 2017). Complete skin clearance (PASI 100) was formally assessed at week 24, with a greater proportion of guselkumab-treated patients achieving PASI 100 than adalimumab in both VOYAGE 1 and VOYAGE 2 (Blauvelt et al., 2017); (Reich, Armstrong, et al., 2017). Dermatology Life Quality Index (DLQI) 0/1 responses were significantly higher in guselkumab-treated patients compared with placebo at week 16, and meaningful improvement versus adalimumab was observed at week 24 (Blauvelt et al., 2017); (Reich, Armstrong, et al., 2017)

Long-term extension data from the VOYAGE 1 trial indicate that the clinical benefits of guselkumab are sustained with continued treatment in adults with moderate-to-severe plaque psoriasis. In patients who remained on guselkumab, robust rates of PASI 75, PASI 90, and PASI 100 were observed through week 52, reflecting durable skin clearance with ongoing therapy (Griffiths et al., 2022). Extended efficacy data from long-term analysis through week 100 confirm that high levels of clinical response are maintained with continued guselkumab treatment: proportions of patients achieving PASI 75, PASI 90, and PASI 100 remained robust at week 100 in all treatment groups, including those initially randomized to placebo or adalimumab who later switched to guselkumab (Long-Term Efficacy of Guselkumab for the Treatment of Moderate-to-Severe Psoriasis: Results from the Phase 3 VOYAGE 1 Trial Through Two Years - PubMed, n.d.). Furthermore, a post-hoc analysis of VOYAGE 1 reported that a substantial proportion of patients maintained complete skin clearance for ≥ 156 consecutive weeks, demonstrating sustained long-term resolution of disease with ongoing guselkumab therapy (Puig et al., 2024).

Guselkumab demonstrated a favorable safety profile that was generally consistent across short-term and long-term follow-up. In the 16-week placebo-controlled period of phase III trials, adverse events were comparable to placebo, with mild infections such as upper respiratory tract infections being most common (M. G. Lebwohl et al., 2023). Long-term analyses from VOYAGE 1 and VOYAGE 2 through 100 weeks and pooled data up to 5 years show that serious infections, malignancies, and discontinuations due to AEs remained low, with no new safety signals identified (Reich, Papp, et al., 2019)(M. G. Lebwohl et al., 2023). Injection-

site reactions and mild infections were among the most frequently reported events. Overall, guselkumab's safety is manageable and stable over both short- and long-term treatment.

Guselkumab is a highly effective and selective IL-23p19 inhibitor with rapid onset, superior short-term efficacy compared with placebo and adalimumab in pivotal trials, durable long-term PASI responses, and a favorable safety profile.

### 3.3.3. Tildrakizumab

Tildrakizumab is a humanized IgG1κ monoclonal antibody targeting the p19 subunit of interleukin-23 (IL-23). In the European Union, it is approved for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy. (Ilumetri | European Medicines Agency (EMA), n.d.)

In the pivotal phase III reSURFACE 1 and reSURFACE 2 trials, tildrakizumab demonstrated significantly greater efficacy than placebo and, in reSURFACE 2, superior PASI 75 responses compared with the active comparator etanercept (TNF alpha inhibitor). Two doses of Tildrakizumab (100 mg and 200 mg) were evaluated. The co-primary endpoint was the proportion of patients achieving ≥75 % improvement (PASI 75) at week 12. In reSURFACE 1, PASI 75 at week 12 was achieved by approximately 62–64 % of patients receiving tildrakizumab compared with 6 % receiving placebo. In reSURFACE 2, PASI 75 at week 12 was achieved by approximately 61–66 % of patients treated with tildrakizumab compared with 6 % with placebo and 48 % with etanercept (Reich, Papp, et al., 2017). PASI 90, a key secondary endpoint, was assessed in both trials at week 12 and achieved by approximately 35-39 % of patients receiving tildrakizumab versus 1–3 % with placebo. (Reich, Papp, et al., 2017) Continued treatment through week 28 led to further improvements. PASI 75 response rates increased to 80.4–81.9% in reSURFACE 1 and 72.6–73.5% in reSURFACE 2, while PASI 90 response rates reached 51.6–59.0% and 55.5–57.7%, respectively. Improvements in health-related quality of life paralleled clinical efficacy, as reflected by DLQI 0/1 responses in 41.5–47.4% of tildrakizumab-treated patients at week 12, compared with 5.3–8.0% with placebo, and in 52.4–65.0% at week 28. Collectively, these findings demonstrate statistically significant and clinically meaningful efficacy of tildrakizumab through 28 weeks in patients with moderate-to-severe plaque psoriasis. (Reich, Papp, et al., 2017) (L. Gao et al., 2020) (Blauvelt et al., 2019a)

Longer-term analyses indicate that the efficacy of tildrakizumab is durable with continued treatment. In pooled analyses of reSURFACE 1 and reSURFACE 2, patients who achieved at least a PASI 50 response at week 28 and continued treatment generally maintained or further improved their clinical responses through week 52, with corresponding maintenance or improvement in DLQI 0/1 responses (Blauvelt et al., 2019b). In addition, longer-term pooled data through 148 weeks showed that tildrakizumab was well tolerated and that efficacy was maintained in week-28 responders who remained on therapy (Reich, Warren, et al., 2019).

Pooled analyses of the reSURFACE 1 and reSURFACE 2 trials indicate that the efficacy of tildrakizumab is durable with continued therapy in patients with moderate-to-severe plaque psoriasis. Among patients who achieved PASI >50 at week 28 and continued the same tildrakizumab dose, mean PASI improvement was maintained or further improved through week 52. Sustained benefits in health-related quality of life were also observed, with DLQI 0/1 responses being maintained or improved during follow-up. These findings support the durability of clinical response and quality-of-life improvement with continued tildrakizumab treatment. (Blauvelt et al., 2019b)

Tildrakizumab demonstrated a favourable safety profile in the phase III reSURFACE 1 and reSURFACE 2 trials, with overall adverse event rates comparable to placebo and the active comparator etanercept (Reich, Papp, et al., 2017). The most frequently reported adverse events included nasopharyngitis and upper respiratory tract infections, which were generally mild to moderate in severity (Reich, Papp, et al., 2017). Pooled safety analyses confirmed that the incidence of serious adverse events remained low during longer-term treatment, and no new safety signals were identified with continued therapy (Reich et al., 2020)

### 3.4. IL-12/IL-23 (p40) inhibitors

With the advancement of knowledge regarding the immunopathogenesis of psoriasis and the recognition of the IL-23/Th17 axis as a central driver of chronic inflammation, the development of biologic therapies targeting more specific immune pathways became possible. Interleukin-12 and interleukin-23 are heterodimeric cytokines primarily produced by dendritic cells and macrophages. They share a common p40 subunit, while differing in their respective p35 (IL-12) and p19 (IL-23) subunits. IL-12 is involved in Th1 differentiation and interferon-γ production, whereas IL-23 plays a crucial role in the stabilization and maintenance of Th17 cells, which produce IL-17 and IL-22—cytokines directly implicated in keratinocyte proliferation and the perpetuation of cutaneous inflammation. Inhibition of the shared p40 subunit therefore results in simultaneous modulation of both Th1 and Th17 pathways, leading to clinically meaningful suppression of disease activity. (Lowes et al., 2013) (Girolomoni et al., 2017b) (Fitch et al., 2007)

Ustekinumab is currently the only approved IL-12/IL-23 (p40) inhibitor for the treatment of moderate-to-severe plaque psoriasis. It is a fully human IgG1κ monoclonal antibody directed against the p40 subunit. Its efficacy was demonstrated in the pivotal phase III PHOENIX 1 and PHOENIX 2 trials, in which PASI75 responses at week 12 were achieved in 66–76% of patients, and PASI90 responses in 42–51%, significantly outperforming placebo. (C. L. Leonardi et al., 2008) (Papp et al., 2008).

Long-term extension data confirmed sustained PASI75 responses for up to 5 years with continuous treatment (Kimball et al., 2013). In the head-to-head ACCEPT trial, ustekinumab demonstrated superior efficacy compared with etanercept in achieving PASI75 at week 12 (67% vs 57%; $p = 0.01$), underscoring its robust clinical effectiveness relative to certain TNF-α inhibitors (Griffiths et al., 2010).

Treatment was also associated with substantial reductions in affected body surface area (BSA) and marked improvements in health-related quality of life, with mean DLQI reductions of 9–11 points and approximately 40–50% of patients achieving DLQI 0/1 (M. Lebwohl et al., 2010).

Beyond randomized controlled trials, real-world evidence further supports the effectiveness and durability of ustekinumab therapy. Data from the prospective PsABio study demonstrated comparable 1-year and 3-year treatment persistence between ustekinumab and TNF-α inhibitors in patients with psoriatic arthritis, with similar effectiveness outcomes after adjustment for baseline characteristics (Menter et al., 2016) (Mourad & Gniadecki, 2021).

Registry-based analyses in psoriasis populations have likewise reported favorable drug survival rates and sustained clinical responses over time, often comparable to or exceeding those observed with first-generation TNF-α inhibitors. (Mourad & Gniadecki, 2021)

According to European (EDF/EADV) and international guidelines, ustekinumab is indicated for adult patients with moderate-to-severe psoriasis who have had an inadequate response, contraindication, or intolerance to conventional systemic therapies such as methotrexate, cyclosporine, or acitretin (Nast et al., 2020).

It may also be considered following failure of TNF-α inhibitors or in patients for whom a less frequent dosing schedule is preferred, given its administration every 12 weeks after the induction phase.

The safety profile of ustekinumab is well established in both clinical trials and post-marketing surveillance. The most commonly reported adverse events include mild upper respiratory tract infections and injection-site reactions. Large meta-analyses and long-term safety evaluations have not demonstrated a significant increase in the risk of serious infections, malignancies, or major adverse cardiovascular events compared with placebo or background population rates (Papp et al., 2013) (Sbidian et al., 2023b) (Nast et al., 2020).

In contrast to TNF-α inhibitors, no clearly increased risk of tuberculosis reactivation has been consistently demonstrated with ustekinumab, although routine pre-treatment screening remains mandatory (Nast et al., 2020) (Tsai et al., 2012).

In summary, IL-12/IL-23 (p40) inhibition, represented clinically by ustekinumab, constitutes an effective and well-tolerated therapeutic strategy for moderate-to-severe psoriasis. By simultaneously modulating Th1 and Th17 pathways, this approach provides high rates of clinical response, significant improvement in quality-of-life measures, and durable long-term disease control in both randomized and real-world settings. Within current treatment algorithms, ustekinumab maintains a well-established position as a post-conventional systemic option and as an alternative to TNF-α inhibitors, particularly in patients requiring predictable and convenient long-term therapy.

### 3.5. PDE-4 inhibitors

Phosphodiesterase 4 (PDE4) inhibitors constitute a class of orally administered small-molecule agents that modulate intracellular inflammatory signaling through inhibition of cyclic adenosine monophosphate (cAMP) degradation. Increased intracellular cAMP levels result in downregulation of multiple pro-inflammatory mediators relevant to psoriasis pathogenesis, including TNF-α, IL-17, and IL-23, alongside enhanced production of anti-inflammatory cytokines such as IL-10. In contrast to biologic agents that selectively neutralize extracellular cytokines, PDE4 inhibitors exert broader intracellular immunomodulatory effects. (Gooderham & Papp, 2015) (Schafer, 2012) (Mechanisms Underlying the Clinical Effects of Apremilast for Psoriasis - PubMed, n.d.)

At present, apremilast is the only systemic PDE4 inhibitor approved in Europe for the treatment of moderate-to-severe plaque psoriasis. Its efficacy and safety were established in the pivotal phase III ESTEEM 1 and ESTEEM 2 randomized controlled trials. At week 16, PASI75 responses were achieved in approximately 28–33% of patients receiving apremilast 30 mg twice daily, compared with 5–6% in the placebo groups (K. Papp et al., 2015) (Paul et al., 2015)

In addition to improvements in overall disease activity, clinically meaningful benefits were also observed in difficult-to-treat localizations, including scalp and nail involvement, assessed using dedicated tools (Rich et al., 2016). Subsequent pooled analyses and meta-analyses confirmed that apremilast significantly increases the likelihood of achieving PASI75 compared with placebo, without a statistically significant increase in serious adverse events (Y. Liu et al., 2023). Although response rates at higher thresholds, particularly PASI90 and PASI100, are lower than those reported for IL-17 or IL-23 inhibitors, apremilast consistently provides clinically meaningful improvements in quality of life, with mean reductions in DLQI of approximately 6–7 points at week 16 (K. Papp et al., 2015) (Paul et al., 2015).

Long-term extension studies indicate sustained efficacy in a subset of responders for up to 3–5 years, with no emergence of new safety signals over prolonged exposure (J. Crowley et al., 2017). Real-world observational data further corroborate the effectiveness and favorable tolerability profile of apremilast in routine clinical practice, particularly in patients with moderate disease severity or contraindications to biologic therapy (Papadavid et al., 2018).

The safety profile of apremilast is well characterized and generally favorable. The most frequently reported adverse events include transient gastrointestinal symptoms (diarrhea and nausea), headache, and modest weight loss, typically occurring during the initial weeks of therapy (K. Papp et al., 2015). Importantly, pooled safety analyses have not demonstrated an increased risk of serious infections, malignancy, or major adverse cardiovascular events compared with placebo (Mease et al., 2023) (K. Papp et al., 2015). Unlike biologic therapies, apremilast does not require laboratory monitoring for immunosuppression or screening for latent tuberculosis prior to treatment initiation (J. Crowley et al., 2017).

According to current European (EDF/EADV) guidelines, apremilast is recommended as a systemic treatment option for adult patients with moderate-to-severe psoriasis who have an inadequate response, intolerance, or contraindication to conventional systemic therapies, and it may be particularly considered in patients for whom biologic therapy is unsuitable or not preferred (Nast et al., 2020).

In summary, apremilast represents the sole approved systemic PDE4 inhibitor for psoriasis in Europe. While its efficacy in achieving high-level PASI responses is generally lower than that observed with biologic agents targeting TNF-α, IL-17, or IL-23, its oral administration, favorable safety profile, and absence of routine laboratory monitoring requirements define a distinct therapeutic niche within contemporary psoriasis treatment algorithms.

## 4. Conclusions

The treatment of moderate-to-severe psoriasis has been fundamentally transformed by advances in the understanding of disease immunopathogenesis and by the development of increasingly selective biologic and targeted systemic therapies. Agents directed against TNF-α, IL-12/23, IL-17, and IL-23, as well as targeted small-molecule therapies such as PDE-4 inhibitors, have substantially improved the ability to achieve sustained disease control, higher levels of skin clearance, and meaningful improvement in quality of life. At the same time, important differences remain between therapeutic classes and individual agents with respect to efficacy, durability of response, safety, route and frequency of administration, and suitability for specific clinical contexts. Although IL-17 and IL-23 inhibitors generally provide the highest levels of skin clearance, TNF-α inhibitors continue to play an important role in selected patients, particularly those with concomitant psoriatic arthritis, whereas ustekinumab and apremilast retain distinct value in appropriately selected clinical settings. Overall, contemporary psoriasis management has shifted from broad immunosuppression toward mechanism-based, individualized therapy, and optimal treatment selection should integrate comparative efficacy with long-term safety, comorbidity profile, practical treatment characteristics, and patient-related factors in order to achieve sustained long-term outcomes.

## REFERENCES


1. Abrouk, M., Nakamura, M., Zhu, T. H., Farahnik, B., Koo, J., & Bhutani, T. (2017). The impact of PASI 75 and PASI 90 on quality of life in moderate to severe psoriasis patients. *The Journal of Dermatological Treatment, 28*(6), 488–491. https://doi.org/10.1080/09546634.2016.1278198
2. Aggarwal, P., & Fleischer, A. B. (2024). IL-17 and IL-23 inhibitors have the fastest time to meaningful clinical response for plaque psoriasis: A network meta-analysis. *Journal of Clinical Medicine, 13*(17). https://doi.org/10.3390/jcm13175139
3. Armstrong, A., Papp, K. A., Lebwohl, M., Savage, L. J., Yamanaka, K., Vlase, D. E., Warham, R., Lambert, J., López Pinto, J. M., Wixted, K., & Thaçi, D. (2026). Bimekizumab impact on patient-reported outcomes in plaque psoriasis: 4-year results from BE SURE, BE VIVID, BE READY, and BE BRIGHT. *Dermatology and Therapy, 16*(1). https://doi.org/10.1007/s13555-025-01595-9
4. Armstrong, A. W., & Read, C. (2020). Pathophysiology, clinical presentation, and treatment of psoriasis: A review. *JAMA, 323*(19), 1945–1960. https://doi.org/10.1001/jama.2020.4006
5. Augustin, M., Abeysinghe, S., Mallya, U., Qureshi, A., Roskell, N., McBride, D., Papavassillis, C., & Gelfand, J. (2015). Secukinumab treatment of plaque psoriasis shows early improvement in DLQI response: Results of a phase 2 regimen-finding trial. *Journal of the European Academy of Dermatology and Venereology, 30*(4), 645. https://doi.org/10.1111/jdv.13478
6. Augustin, M., Lambert, J., Zema, C., Thompson, E. H. Z., Yang, M., Wu, E. Q., Garcia-Horton, V., Geng, Z., Valdes, J. M., Joshi, A., & Gordon, K. B. (2020). Effect of risankizumab on patient-reported outcomes in moderate to severe psoriasis: The UltIMMa-1 and UltIMMa-2 randomized clinical trials. *JAMA Dermatology, 156*(12), 1344–1353. https://doi.org/10.1001/jamadermatol.2020.3617
7. European Medicines Agency. (n.d.). *Bimzelx*. Retrieved March 13, 2026, from https://www.ema.europa.eu/en/medicines/human/EPAR/bimzelx
8. Blauvelt, A., & Chiricozzi, A. (2018). The immunologic role of IL-17 in psoriasis and psoriatic arthritis pathogenesis. *Clinical Reviews in Allergy & Immunology, 55*(3), 379. https://doi.org/10.1007/s12016-018-8702-3
9. Blauvelt, A., Langley, R. G., Lebwohl, M., Strober, B., Warren, R. B., Puig, L., Morita, A., Gordon, K. B., Fernandez-Peñas, P., Kavanagh, S., López Pinto, J. M., Lambert, J., Hoepken, B., Deherder, D., Cross, N., & Thaçi, D. (2025). Bimekizumab durability of efficacy through 196 weeks and safety through 4 years in patients with moderate to severe plaque psoriasis: Results from the BE BRIGHT open-label extension trial. *Journal of the American Academy of Dermatology, 93*(3), 644–653. https://doi.org/10.1016/j.jaad.2025.04.038
10. Blauvelt, A., Papp, K. A., Griffiths, C. E. M., Randazzo, B., Wasfi, Y., Shen, Y. K., Li, S., & Kimball, A. B. (2017). Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator trial. *Journal of the American Academy of Dermatology, 76*(3), 405–417. https://doi.org/10.1016/j.jaad.2016.11.041
11. Blauvelt, A., Paul, C., van de Kerkhof, P., Warren, R. B., Gottlieb, A. B., Langley, R. G., Brock, F., Arendt, C., Boehnlein, M., Lebwohl, M., & Reich, K. (2021). Long-term safety of certolizumab pegol in plaque psoriasis: Pooled analysis over 3 years from three phase III, randomized, placebo-controlled studies. *The British Journal of Dermatology, 184*(4), 640–651. https://doi.org/10.1111/bjd.19314
12. Blauvelt, A., Sofen, H., Papp, K., Gooderham, M., Tyring, S., Zhao, Y., Lowry, S., Mendelsohn, A., Parno, J., & Reich, K. (2019a). Tildrakizumab efficacy and impact on quality of life up to 52 weeks in patients with moderate-to-severe psoriasis: A pooled analysis of two randomized controlled trials. *Journal of the European Academy of Dermatology and Venereology, 33*(12), 2305. https://doi.org/10.1111/jdv.15862
13. Blauvelt, A., Sofen, H., Papp, K., Gooderham, M., Tyring, S., Zhao, Y., Lowry, S., Mendelsohn, A., Parno, J., & Reich, K. (2019b). Tildrakizumab efficacy and impact on quality of life up to 52 weeks in patients with moderate-to-severe psoriasis: A pooled analysis of two randomized controlled trials. *Journal of the European Academy of Dermatology and Venereology, 33*(12), 2305–2312. https://doi.org/10.1111/jdv.15862
14. Crowley, J. J., Warren, R. B., & Cather, J. C. (2019). Safety of selective IL-23p19 inhibitors for the treatment of psoriasis. *Journal of the European Academy of Dermatology and Venereology, 33*(9), 1676–1684. https://doi.org/10.1111/jdv.15653
15. Crowley, J., Thaçi, D., Joly, P., Peris, K., Papp, K. A., Goncalves, J., Day, R. M., Chen, R., Shah, K., Ferrándiz, C., & Cather, J. C. (2017). Long-term safety and tolerability of apremilast in patients with psoriasis: Pooled safety analysis for ≥156 weeks from 2 phase 3, randomized, controlled trials (ESTEEM 1 and 2). *Journal of the American Academy of Dermatology, 77*(2), 310–317.e1. https://doi.org/10.1016/j.jaad.2017.01.052
16. Dattola, A., Cannizzaro, M. V., Mazzeo, M., & Bianchi, L. (2017). Certolizumab pegol in the treatment of psoriasis and psoriatic arthritis: Preliminary real-life data. *Dermatology and Therapy, 7*(4), 485–492. https://doi.org/10.1007/s13555-017-0208-z
17. de Ruiter, C. C., & Rustemeyer, T. (2022). Biologics can significantly improve dermatology life quality index (DLQI) in psoriatic patients: A systematic review. *Psoriasis, 12*, 99–112. https://doi.org/10.2147/ptt.s356568

18. Dommasch, E. D., Abuabara, K., Shin, D. B., Nguyen, J., Troxel, A. B., & Gelfand, J. M. (2011). The risk of infection and malignancy with tumor necrosis factor antagonists in adult patients with psoriatic disease: A systematic review and meta-analysis of randomized controlled trials. *Journal of the American Academy of Dermatology, 64*(6), 1035. https://doi.org/10.1016/j.jaad.2010.09.734
19. Egeberg, A., Andersen, Y. M. F., Halling-Overgaard, A. S., Alignahi, F., Thyssen, J. P., Burge, R., & Mallbris, L. (2020). Systematic review on rapidity of onset of action for interleukin-17 and interleukin-23 inhibitors for psoriasis. *Journal of the European Academy of Dermatology and Venereology, 34*(1), 39–46. https://doi.org/10.1111/jdv.15920
20. Farahnik, B., Beroukhim, K., Abrouk, M., Nakamura, M., Zhu, T. H., Singh, R., Lee, K., Bhutani, T., & Koo, J. (2016). Brodalumab for the treatment of psoriasis: A review of phase III trials. *Dermatology and Therapy, 6*(2), 111. https://doi.org/10.1007/s13555-016-0121-x
21. Farahnik, B., Beroukhim, K., Zhu, T. H., Abrouk, M., Nakamura, M., Singh, R., Lee, K., Bhutani, T., & Koo, J. (2016). Ixekizumab for the treatment of psoriasis: A review of phase III trials. *Dermatology and Therapy, 6*(1), 25–37. https://doi.org/10.1007/s13555-016-0102-0
22. Feldman, S. R., Gordon, K. B., Bala, M., Evans, R., Li, S., Dooley, L. T., Guzzo, C., Patel, K., Menter, A., & Gottlieb, A. B. (2005). Infliximab treatment results in significant improvement in the quality of life of patients with severe psoriasis: A double-blind placebo-controlled trial. *The British Journal of Dermatology, 152*(5), 954–960. https://doi.org/10.1111/j.1365-2133.2005.06510.x
23. Galluzzo, M., Trovato, E., Talamonti, M., Caldarola, G., Di Nardo, L., Lazzeri, L., Mugheddu, C., Burlando, M., Balestri, R., Bernardini, N., Biondi, G., Vellucci, L., Russo, F., De Simone, C., Paganini, C., Rech, G., Cozzani, E. C., Atzori, L., Montesu, M. A., … Rubegni, P. (2024). Long-term persistence rate of secukinumab in psoriatic patients: A six-year multicenter, real-world experience, retrospective study. *Journal of Clinical Medicine, 13*(13). https://doi.org/10.3390/jcm13133864
24. Gao, B., Shentu, H., Sha, S., Wang, D., Chen, X., Huang, Z., Dong, N., Lai, H., Xu, J., & Zhou, X. (2023). Efficacy of IL-23 inhibitors and IL-12/23 inhibitors in the induction treatment of Crohn's disease: A meta-analysis based on randomized controlled trials. *Central-European Journal of Immunology, 48*(4), 301–310. https://doi.org/10.5114/ceji.2023.134257
25. Gao, L., Gu, L., Chen, Z., & Cao, S. (2020). Tildrakizumab: An evidence-based review of its use in the treatment of moderate-to-severe chronic plaque psoriasis. *Therapeutics and Clinical Risk Management, 16*, 903–916. https://doi.org/10.2147/TCRM.S227880
26. Gao, S., Xie, X., Fan, L., & Yu, L. (2025). Efficacy and safety of IL-17, IL-12/23, and IL-23 inhibitors for psoriatic arthritis: A network meta-analysis of randomized controlled trials. *Frontiers in Immunology, 16*. https://doi.org/10.3389/fimmu.2025.1654343
27. Gao, Y., Xu, T., Wang, Y., Hu, Y., Yin, S., Qin, Z., & Yu, H. (2025). Pathophysiology and treatment of psoriasis: From clinical practice to basic research. *Pharmaceutics, 17*(1), 56. https://doi.org/10.3390/pharmaceutics17010056
28. Girolomoni, G., Strohal, R., Puig, L., Bachelez, H., Barker, J., Boehncke, W. H., & Prinz, J. C. (2017a). The role of IL-23 and the IL-23/TH17 immune axis in the pathogenesis and treatment of psoriasis. *Journal of the European Academy of Dermatology and Venereology, 31*(10), 1616–1626. https://doi.org/10.1111/jdv.14433
29. Girolomoni, G., Strohal, R., Puig, L., Bachelez, H., Barker, J., Boehncke, W. H., & Prinz, J. C. (2017b). The role of IL-23 and the IL-23/TH17 immune axis in the pathogenesis and treatment of psoriasis. *Journal of the European Academy of Dermatology and Venereology, 31*(10), 1616. https://doi.org/10.1111/jdv.14433
30. Glatt, S., Baeten, D., Baker, T., Griffiths, M., Ionescu, L., Lawson, A. D. G., Maroof, A., Oliver, R., Popa, S., Strimenopoulou, F., Vajjah, P., Watling, M. I. L., Yeremenko, N., Miossec, P., & Shaw, S. (2018). Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: Evidence from preclinical experiments and a randomised placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation. *Annals of the Rheumatic Diseases, 77*(4), 523–532. https://doi.org/10.1136/annrheumdis-2017-212127
31. Gniadecki, R., Bang, B., Bryld, L. E., Iversen, L., Lasthein, S., & Skov, L. (2015). Comparison of long-term drug survival and safety of biologic agents in patients with psoriasis vulgaris. *The British Journal of Dermatology, 172*(1), 244–252. https://doi.org/10.1111/bjd.13343
32. Gooderham, M., & Papp, K. (2015). Selective phosphodiesterase inhibitors for psoriasis: Focus on apremilast. *BioDrugs, 29*(5), 327–339. https://doi.org/10.1007/s40259-015-0144-3
33. Gordon, K. B., Blauvelt, A., Papp, K. A., Langley, R. G., Luger, T., Ohtsuki, M., Reich, K., Amato, D., Ball, S. G., Braun, D. K., Cameron, G. S., Erickson, J., Konrad, R. J., Muram, T. M., Nickoloff, B. J., Osuntokun, O. O., Secrest, R. J., Zhao, F., Mallbris, L., & Leonardi, C. L. (2016). Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. *New England Journal of Medicine, 375*(4), 345–356. https://doi.org/10.1056/NEJMoa1512711
34. Gordon, K. B., Langley, R. G., Warren, R. B., Okubo, Y., Stein Gold, L., Merola, J. F., Peterson, L., Wixted, K., Cross, N., Deherder, D., & Thaçi, D. (2022). Bimekizumab safety in patients with moderate to severe plaque psoriasis: Pooled results from phase 2 and phase 3 randomized clinical trials. *JAMA Dermatology, 158*(7), 735–744. https://doi.org/10.1001/jamadermatol.2022.1185

35. Gordon, K. B., Strober, B., Lebwohl, M., Augustin, M., Blauvelt, A., Poulin, Y., Papp, K. A., Sofen, H., Puig, L., Foley, P., Ohtsuki, M., Flack, M., Geng, Z., Gu, Y., Valdes, J. M., Thompson, E. H. Z., & Bachelez, H. (2018). Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): Results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *The Lancet, 392*(10148), 650–661. https://doi.org/10.1016/S0140-6736(18)31713-6
36. Gordon, K., Papp, K., Poulin, Y., Gu, Y., Rozzo, S., & Sasso, E. H. (2012). Long-term efficacy and safety of adalimumab in patients with moderate to severe psoriasis treated continuously over 3 years: Results from an open-label extension study for patients from REVEAL. *Journal of the American Academy of Dermatology, 66*(2), 241–251. https://doi.org/10.1016/j.jaad.2010.12.005
37. Gottlieb, A. B., Blauvelt, A., Thaçi, D., Leonardi, C. L., Poulin, Y., Drew, J., Peterson, L., Arendt, C., Burge, D., & Reich, K. (2018). Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). *Journal of the American Academy of Dermatology, 79*(2), 302–314.e6. https://doi.org/10.1016/j.jaad.2018.04.012
38. Gottlieb, A. B., Deodhar, A., McInnes, I. B., Baraliakos, X., Reich, K., Schreiber, S., Bao, W., Marfo, K., Richards, H. B., Pricop, L., Shete, A., Trivedi, V., Keefe, D., Papavassilis, C. C., Jagiello, P., Papanastasiou, P., Mease, P. J., & Lebwohl, M. (2022). Long-term safety of secukinumab over five years in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis and ankylosing spondylitis: Update on integrated pooled clinical trial and post-marketing surveillance data. *Acta Dermato-Venereologica, 102*, 563. https://doi.org/10.2340/actadv.v102.563
39. Griffiths, C. E. M., Papp, K. A., Song, M., Miller, M., You, Y., Shen, Y. K., Han, C., & Blauvelt, A. (2022). Continuous treatment with guselkumab maintains clinical responses through 4 years in patients with moderate-to-severe psoriasis: Results from VOYAGE 1. *Journal of Dermatological Treatment, 33*(2), 1–9. https://doi.org/10.1080/09546634.2020.1782817
40. Griffiths, C. E. M., Strober, B. E., van de Kerkhof, P., Ho, V., Fidelus-Gort, R., Yeilding, N., Guzzo, C., Xia, Y., Zhou, B., Li, S., Dooley, L. T., Goldstein, N. H., & Menter, A. (2010). Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. *The New England Journal of Medicine, 362*(2), 118–128. https://doi.org/10.1056/NEJMoa0810652
41. Hagino, T., Saeki, H., Fujimoto, E., & Kanda, N. (2025). Effectiveness of long-term bimekizumab treatment and predictive factors for responders in moderate-to-severe psoriasis: A 52-week real-world study. *The Journal of Dermatology, 52*(2), 317–328. https://doi.org/10.1111/1346-8138.17532
42. Huang, X., Shentu, H., He, Y., Lai, H., Xu, C., Chen, M., & Zhu, H. (2023). Efficacy and safety of IL-23 inhibitors in the treatment of psoriatic arthritis: A meta-analysis based on randomized controlled trials. *Immunologic Research, 71*(4), 505–515. https://doi.org/10.1007/s12026-023-09366-4
43. European Medicines Agency. (n.d.). *Ilumetri*. Retrieved March 14, 2026, from https://www.ema.europa.eu/en/medicines/human/EPAR/ilumetri#overview
44. Jain, A., & Singh, J. A. (2013). Harms of tumor necrosis factor inhibitors in rheumatic diseases: A focused systematic review of the literature. *Immunotherapy, 5*(3), 265–293. https://doi.org/10.2217/imt.13.10
45. Kaszuba, A., Papanastasiou, P., Krasowska, D., De Lucas Laguna, R., Ziv, M., Ravichandran, S., Bansal, A., Dahale, S. S., Martin, R., Paguet, B., Magnolo, N., & Kingo, K. (2025). Long-term safety and efficacy of secukinumab in paediatric severe plaque psoriasis: 236-week phase 3 trial results. *Journal of the European Academy of Dermatology and Venereology*. Advance online publication. https://doi.org/10.1111/jdv.70155
46. Kimball, A. B., Papp, K. A., Wasfi, Y., Chan, D., Bissonnette, R., Sofen, H., Yeilding, N., Li, S., Szapary, P., & Gordon, K. B. (2013). Long-term efficacy of ustekinumab in patients with moderate-to-severe psoriasis treated for up to 5 years in the PHOENIX 1 study. *Journal of the European Academy of Dermatology and Venereology, 27*(12), 1535–1545. https://doi.org/10.1111/jdv.12046
47. Kruczek, W., Frątczak, A., Litwińska-Inglot, I., Polak, K., Pawlus, Z., Rutecka, P., Bergler-Czop, B., & Miziołek, B. (2025). Comparative analysis of the long-term real-world efficacy of interleukin-17 inhibitors in a cohort of patients with moderate-to-severe psoriasis treated in Poland. *Journal of Clinical Medicine, 14*(15). https://doi.org/10.3390/jcm14155421
48. Lambert, J., Hansen, J. B., Sohrt, A., & Puig, L. (2021). Dermatology life quality index in patients with moderate-to-severe plaque psoriasis treated with brodalumab or ustekinumab. *Dermatology and Therapy, 11*(4), 1265–1275. https://doi.org/10.1007/s13555-021-00545-5
49. Langley, R. G., Elewski, B. E., Lebwohl, M., Reich, K., Griffiths, C. E. M., Papp, K., Puig, L., Nakagawa, H., Spelman, L., Sigurgeirsson, B., Rivas, E., Tsai, T.-F., Wasel, N., Tyring, S., Salko, T., Hampele, I., Notter, M., Karpov, A., Helou, S., & Papavassilis, C. (2014). Secukinumab in plaque psoriasis: Results of two phase 3 trials. *The New England Journal of Medicine, 371*(4), 326–338. https://doi.org/10.1056/NEJMoa1314258
50. Langley, R. G., Sofen, H., Dei-Cas, I., Reich, K., Sigurgeirsson, B., Warren, R. B., Paul, C., Szepietowski, J. C., Tsai, T. F., Hampele, I., You, R., Charef, P., & Papavassilis, C. (2023). Secukinumab long-term efficacy and safety in psoriasis through to year 5 of treatment: Results of a randomized extension of the phase III ERASURE and FIXTURE trials. *The British Journal of Dermatology, 188*(2), 198–207. https://doi.org/10.1093/bjd/ljac040

51. Lebwohl, M., Blauvelt, A., Paul, C., Sofen, H., Węgłowska, J., Piguet, V., Burge, D., Rolleri, R., Drew, J., Peterson, L., & Augustin, M. (2018). Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). *Journal of the American Academy of Dermatology, 79*(2), 266–276.e5. https://doi.org/10.1016/j.jaad.2018.04.013
52. Lebwohl, M. G., Carvalho, A., Asahina, A., Zhang, J., Fazeli, M. S., Kasireddy, E., Serafini, P., Ferro, T., Gogineni, R., & Thaçi, D. (2025). Biologics for the treatment of moderate-to-severe plaque psoriasis: A systematic review and network meta-analysis. *Dermatology and Therapy, 15*(7), 1633–1656. https://doi.org/10.1007/s13555-025-01423-0
53. Lebwohl, M. G., Gordon, K. B., Gallo, G., Zhang, L., & Paul, C. (2020). Ixekizumab sustains high level of efficacy and favourable safety profile over 4 years in patients with moderate psoriasis: Results from UNCOVER-3 study. *Journal of the European Academy of Dermatology and Venereology, 34*(2), 301–309. https://doi.org/10.1111/jdv.15921
54. Lebwohl, M. G., Merola, J. F., Rowland, K., Miller, M., Yang, Y. W., Yu, J., You, Y., Chan, D., Thaçi, D., & Langley, R. G. (2023). Safety of guselkumab treatment for up to 5 years in patients with moderate-to-severe psoriasis: Pooled analyses across seven clinical trials with more than 8,600 patient-years of exposure. *The British Journal of Dermatology, 189*(1), 42–52. https://doi.org/10.1093/bjd/ljad115
55. Lebwohl, M., Papp, K., Han, C., Schenkel, B., Yeilding, N., Wang, Y., & Krueger, G. G. (2010). Ustekinumab improves health-related quality of life in patients with moderate-to-severe psoriasis: Results from the PHOENIX 1 trial. *The British Journal of Dermatology, 162*(1), 137–146. https://doi.org/10.1111/j.1365-2133.2009.09491.x
56. Lebwohl, M., Song, E. J., Bhutani, T., Green, L., & Jacobson, A. (2025). Real-world evidence of brodalumab safety for the treatment of psoriasis. *Journal of Psoriasis and Psoriatic Arthritis*. Advance online publication. https://doi.org/10.1177/24755303251382878
57. Lebwohl, M., Strober, B., Menter, A., Gordon, K., Weglowska, J., Puig, L., Papp, K., Spelman, L., Toth, D., Kerdel, F., Armstrong, A. W., Stingl, G., Kimball, A. B., Bachelez, H., Wu, J. J., Crowley, J., Langley, R. G., Blicharski, T., Paul, C., … Nirula, A. (2015). Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *The New England Journal of Medicine, 373*(14), 1318–1328. https://doi.org/10.1056/NEJMoa1503824
58. Leonardi, C. L., Kimball, A. B., Papp, K. A., Yeilding, N., Guzzo, C., Wang, Y., Li, S., Dooley, L. T., & Gordon, K. B. (2008). Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *The Lancet, 371*(9625), 1665–1674. https://doi.org/10.1016/S0140-6736(08)60725-4
59. Leonardi, C. L., Powers, J. L., Matheson, R. T., Goffe, B. S., Zitnik, R., Wang, A., & Gottlieb, A. B. (2003). Etanercept as monotherapy in patients with psoriasis. *The New England Journal of Medicine, 349*(21), 2014–2022. https://doi.org/10.1056/NEJMoa030409
60. Leonardi, C., Reich, K., Foley, P., Torii, H., Gerdes, S., Guenther, L., Gooderham, M., Ferris, L. K., Griffiths, C. E. M., ElMaraghy, H., Crane, H., Patel, H., Burge, R., Gallo, G., Shrom, D., Leung, A., Lin, C.-Y., & Papp, K. (2020). Efficacy and safety of ixekizumab through 5 years in moderate-to-severe psoriasis: Long-term results from the UNCOVER-1 and UNCOVER-2 phase 3 randomized controlled trials. *Dermatology and Therapy, 10*(3), 431–447. https://doi.org/10.1007/s13555-020-00367-x
61. Liu, T., Li, S., Ying, S., Tang, S., Ding, Y., Li, Y., Qiao, J., & Fang, H. (2020). The IL-23/IL-17 pathway in inflammatory skin diseases: From bench to bedside. *Frontiers in Immunology, 11*. https://doi.org/10.3389/fimmu.2020.594735
62. Liu, Y., Li, Y., & Du, H. (2023). Efficacy of apremilast for psoriasis: A meta-analysis of randomized controlled studies. *Postępy Dermatologii i Alergologii, 40*(1), 165–170. https://doi.org/10.5114/ada.2022.119081
63. *Long-term efficacy of guselkumab for the treatment of moderate-to-severe psoriasis: Results from the phase 3 VOYAGE 1 trial through two years*. (n.d.). PubMed. Retrieved March 14, 2026, from https://pubmed.ncbi.nlm.nih.gov/30124721/
64. *Long-term safety and efficacy of etanercept in patients with psoriasis: An open-label study*. (n.d.). PubMed. Retrieved March 13, 2026, from https://pubmed.ncbi.nlm.nih.gov/20684143/
65. Lowes, M. A., Russell, C. B., Martin, D. A., Towne, J. E., & Krueger, J. G. (2013). The IL-23/T17 pathogenic axis in psoriasis is amplified by keratinocyte responses. *Trends in Immunology, 34*(4), 174–181. https://doi.org/10.1016/j.it.2012.11.005
66. Lowes, M. A., Suárez-Fariñas, M., & Krueger, J. G. (2014). Immunology of psoriasis. *Annual Review of Immunology, 32*, 227–255. https://doi.org/10.1146/annurev-immunol-032713-120225
67. Mariette, X., Förger, F., Abraham, B., Flynn, A. D., Moltó, A., Flipo, R. M., Van Tubergen, A., Shaughnessy, L., Simpson, J., Teil, M., Helmer, E., Wang, M., & Chakravarty, E. F. (2018). Lack of placental transfer of certolizumab pegol during pregnancy: Results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Annals of the Rheumatic Diseases, 77*(2), 228–233. https://doi.org/10.1136/annrheumdis-2017-212196
68. Martin, D. A., Towne, J. E., Kricorian, G., Klekotka, P., Gudjonsson, J. E., Krueger, J. G., & Russell, C. B. (2013). The emerging role of IL-17 in the pathogenesis of psoriasis: Preclinical and clinical findings. *Journal of Investigative Dermatology, 133*(1), 17–26. https://doi.org/10.1038/jid.2012.194

69. Mastorino, L., Burzi, L., Frigatti, G., Fazio, A., Celoria, V., Macagno, N., Rosset, F., Passerini, S. G., Roccuzzo, G., Verrone, A., Stroppiana, E., Ortoncelli, M., Dapavo, P., Quaglino, P., & Ribero, S. (2023). Clinical effectiveness of IL-17 and IL-23 inhibitors on difficult-to-treat psoriasis areas (scalp, genital, and palmoplantar sites): A retrospective, observational, single-center, real-life study. *Expert Opinion on Biological Therapy, 23*(9), 929–936. https://doi.org/10.1080/14712598.2023.2236023
70. Mease, P. J., Hatemi, G., Paris, M., Cheng, S., Maes, P., Zhang, W., Shi, R., Flower, A., Picard, H., & Stein Gold, L. (2023). Apremilast long-term safety up to 5 years from 15 pooled randomized, placebo-controlled studies of psoriasis, psoriatic arthritis, and Behçet's syndrome. *American Journal of Clinical Dermatology, 24*(5), 809–820. https://doi.org/10.1007/s40257-023-00783-7
71. Mease, P. J., Kivitz, A. J., Burch, F. X., Siegel, E. L., Cohen, S. B., Ory, P., Salonen, D., Rubenstein, J., Sharp, J. T., & Tsuji, W. (2004). Etanercept treatment of psoriatic arthritis: Safety, efficacy, and effect on disease progression. *Arthritis & Rheumatism, 50*(7), 2264–2272. https://doi.org/10.1002/art.20335
72. Mease, P. J., Ory, P., Sharp, J. T., Ritchlin, C. T., Van Den Bosch, F., Wellborne, F., Birbara, C., Thomson, G. T. D., Perdok, R. J., Medich, J., Wong, R. L., & Gladman, D. D. (2009). Adalimumab for long-term treatment of psoriatic arthritis: 2-year data from the Adalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT). *Annals of the Rheumatic Diseases, 68*(5), 702–709. https://doi.org/10.1136/ard.2008.092767
73. Megna, M., D'Agostino, M., Feo, F., Ventura, V., Tommasino, N., & Potestio, L. (2026). IL-23 inhibitors in psoriasis: What have we learnt so far? *Journal of Inflammation Research, 19*. https://doi.org/10.2147/JIR.S540848
74. Menter, A., Krueger, G. G., Paek, S. Y., Kivelevitch, D., Adamopoulos, I. E., & Langley, R. G. (2021). Interleukin-17 and interleukin-23: A narrative review of mechanisms of action in psoriasis and associated comorbidities. *Dermatology and Therapy, 11*(2), 385–403. https://doi.org/10.1007/s13555-021-00483-2
75. Menter, A., Papp, K. A., Gooderham, M., Pariser, D. M., Augustin, M., Kerdel, F. A., Fakharzadeh, S., Goyal, K., Calabro, S., Langholff, W., Chavers, S., Naessens, D., Sermon, J., & Krueger, G. G. (2016). Drug survival of biologic therapy in a large, disease-based registry of patients with psoriasis: Results from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *Journal of the European Academy of Dermatology and Venereology, 30*(7), 1148–1158. https://doi.org/10.1111/jdv.13611
76. Motedayen Aval, L., Yiu, Z. Z. N., Alabas, O. A., Griffiths, C. E. M., Reynolds, N. J., Hampton, P. J., Smith, C. H., & Warren, R. B. (2025). Drug survival of IL-23 and IL-17 inhibitors versus other biologics for psoriasis: A British Association of Dermatologists Biologics and Immunomodulators Register cohort study. *Journal of the European Academy of Dermatology and Venereology, 39*(10), 1785–1795. https://doi.org/10.1111/jdv.20739
77. Mourad, A. I., & Gniadecki, R. (2021). Biologic drug survival in psoriasis: A systematic review and comparative meta-analysis. *Frontiers in Medicine, 7*. https://doi.org/10.3389/fmed.2020.625755
78. Mrowietz, U., Kragballe, K., Reich, K., Griffiths, C. E. M., Gu, Y., Wang, Y., & Rozzo, S. J. (2013). An assessment of adalimumab efficacy in three phase III clinical trials using the European Consensus Programme criteria for psoriasis treatment goals. *The British Journal of Dermatology, 168*(2), 374–380. https://doi.org/10.1111/j.1365-2133.2012.11214.x
79. Nast, A., Smith, C., Spuls, P. I., Avila Valle, G., Bata-Csörgö, Z., Boonen, H., De Jong, E., Garcia-Doval, I., Gisondi, P., Kaur-Knudsen, D., Mahil, S., Mälkönen, T., Maul, J. T., Mburu, S., Mrowietz, U., Reich, K., Remenyik, E., Rønholt, K. M., Sator, P. G., … Dressler, C. (2020). EuroGuiDerm guideline on the systemic treatment of psoriasis vulgaris—Part 1: Treatment and monitoring recommendations. *Journal of the European Academy of Dermatology and Venereology, 34*(11), 2461–2498. https://doi.org/10.1111/jdv.16915
80. Papadavid, E., Rompoti, N., Theodoropoulos, K., Kokkalis, G., & Rigopoulos, D. (2018). Real-world data on the efficacy and safety of apremilast in patients with moderate-to-severe plaque psoriasis. *Journal of the European Academy of Dermatology and Venereology, 32*(7), 1173–1179. https://doi.org/10.1111/jdv.14832
81. Papp, K. A., Griffiths, C. E. M., Gordon, K., Lebwohl, M., Szapary, P. O., Wasfi, Y., Chan, D., Hsu, M. C., Ho, V., Ghislain, P. D., Strober, B., & Reich, K. (2013). Long-term safety of ustekinumab in patients with moderate-to-severe psoriasis: Final results from 5 years of follow-up. *The British Journal of Dermatology, 168*(4), 844–854. https://doi.org/10.1111/bjd.12214
82. Papp, K. A., Lebwohl, M. G., Puig, L., Ohtsuki, M., Beissert, S., Gooderham, M., Amin, A. Z., Wu, T., Rubant, S., Bialik, B., Ashley, D., Soliman, A. M., Chen, M. M., & Blauvelt, A. (2025). Long-term safety and efficacy of risankizumab to treat moderate-to-severe plaque psoriasis: Final LIMMitless phase 3, open-label extension trial results. *American Journal of Clinical Dermatology, 26*(5), 829–841. https://doi.org/10.1007/s40257-025-00964-6
83. Papp, K., Reich, K., Leonardi, C. L., Kircik, L., Chimenti, S., Langley, R. G. B., Hu, C. C., Stevens, R. M., Day, R. M., Gordon, K. B., Korman, N. J., & Griffiths, C. E. M. (2015). Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (ESTEEM 1). *Journal of the American Academy of Dermatology, 73*(1), 37–49. https://doi.org/10.1016/j.jaad.2015.03.049
84. Ponikowska, M., Hill, L., Lee, C. S., Barisone, M., Ponikowski, P., Aldossary, H. M., Jędrzejczyk, M., Kubielas, G., & Uchmanowicz, I. (2025). Cardiovascular disease and psoriasis. *Dermatology and Therapy, 16*(1), 155. https://doi.org/10.1007/s13555-025-01566-0

85. Puig, L., Costanzo, A., de Jong, E. M. G. J., Torres, T., Warren, R. B., Wapenaar, R., Wegner, S., Gorecki, P., Gramiccia, T., Jazra, M., Buyze, J., & Conrad, C. (2024). Guselkumab-treated patients with plaque psoriasis who achieved complete skin clearance for ≥156 consecutive weeks: A post hoc analysis from the VOYAGE 1 clinical trial. *American Journal of Clinical Dermatology, 25*(2), 315–325. https://doi.org/10.1007/s40257-023-00816-1
86. Puig, L., Lebwohl, M., Bachelez, H., Sobell, J., & Jacobson, A. A. (2020). Long-term efficacy and safety of brodalumab in the treatment of psoriasis: 120-week results from the randomized, double-blind, placebo- and active comparator-controlled phase 3 AMAGINE-2 trial. *Journal of the American Academy of Dermatology, 82*(2), 352–359. https://doi.org/10.1016/j.jaad.2019.05.095
87. Reich, K., Armstrong, A. W., Foley, P., Song, M., Wasfi, Y., Randazzo, B., Li, S., Shen, Y. K., & Gordon, K. B. (2017). Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind VOYAGE 2 trial. *Journal of the American Academy of Dermatology, 76*(3), 418–431. https://doi.org/10.1016/j.jaad.2016.11.042
88. Reich, K., Iversen, L., Puig, L., Lambert, J., Mrowietz, U., Kaplan Saday, K., & Warren, R. B. (2022). Long-term efficacy and safety of brodalumab in moderate-to-severe plaque psoriasis: A post hoc pooled analysis of AMAGINE-2 and AMAGINE-3. *Journal of the European Academy of Dermatology and Venereology, 36*(8), 1275–1283. https://doi.org/10.1111/jdv.18068
89. Reich, K., Nestle, F. O., Papp, K., Ortonne, J. P., Evans, R., Guzzo, C., Li, S., Dooley, L. T., & Griffiths, C. E. M. (2005). Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: A phase III, multicentre, double-blind trial. *The Lancet, 366*(9494), 1367–1374. https://doi.org/10.1016/S0140-6736(05)67566-6
90. Reich, K., Papp, K. A., Armstrong, A. W., Wasfi, Y., Li, S., Shen, Y. K., Randazzo, B., Song, M., & Kimball, A. B. (2019). Safety of guselkumab in patients with moderate-to-severe psoriasis treated through 100 weeks: A pooled analysis from the randomized VOYAGE 1 and VOYAGE 2 studies. *The British Journal of Dermatology, 180*(5), 1039–1049. https://doi.org/10.1111/bjd.17454
91. Reich, K., Papp, K. A., Blauvelt, A., Langley, R. G., Armstrong, A., Warren, R. B., Gordon, K. B., Merola, J. F., Okubo, Y., Madden, C., Wang, M., Cioffi, C., Vanvoorden, V., & Lebwohl, M. (2021). Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): Efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo-controlled phase 3 trial. *The Lancet, 397*(10273), 487–498. https://doi.org/10.1016/S0140-6736(21)00125-2
92. Reich, K., Papp, K. A., Blauvelt, A., Tyring, S. K., Sinclair, R., Thaçi, D., Nograles, K., Mehta, A., Cichanowitz, N., Li, Q., Liu, K., La Rosa, C., Green, S., & Kimball, A. B. (2017). Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): Results from two randomised controlled, phase 3 trials. *The Lancet, 390*(10091), 276–288. https://doi.org/10.1016/S0140-6736(17)31279-5
93. Reich, K., Segaert, S., Van De Kerkhof, P., Durian, C., Boussuge, M. P., Paolozzi, L., Wajdula, J., & Boggs, R. (2009). Once-weekly administration of etanercept 50 mg improves patient-reported outcomes in patients with moderate-to-severe plaque psoriasis. *Dermatology, 219*(3), 239–249. https://doi.org/10.1159/000237871
94. Reich, K., Warren, R. B., Iversen, L., Puig, L., Pau-Charles, I., Igarashi, A., Ohtsuki, M., Falqués, M., Harmut, M., Rozzo, S., Lebwohl, M. G., Cantrell, W., Blauvelt, A., & Thaçi, D. (2019). Long-term efficacy and safety of tildrakizumab for moderate-to-severe psoriasis: Pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2) through 148 weeks. *The British Journal of Dermatology, 182*(3), 605. https://doi.org/10.1111/bjd.18232
95. Reich, K., Warren, R. B., Iversen, L., Puig, L., Pau-Charles, I., Igarashi, A., Ohtsuki, M., Falqués, M., Harmut, M., Rozzo, S., Lebwohl, M. G., Cantrell, W., Blauvelt, A., & Thaçi, D. (2020). Long-term efficacy and safety of tildrakizumab for moderate-to-severe psoriasis: Pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2) through 148 weeks. *The British Journal of Dermatology, 182*(3), 605–617. https://doi.org/10.1111/bjd.18232
96. Reich, K., Warren, R. B., Lebwohl, M., Gooderham, M., Strober, B., Langley, R. G., Paul, C., De Cuyper, D., Vanvoorden, V., Madden, C., Cioffi, C., Peterson, L., & Blauvelt, A. (2021). Bimekizumab versus secukinumab in plaque psoriasis. *The New England Journal of Medicine, 385*(2), 142–152. https://doi.org/10.1056/NEJMoa2102383
97. Revicki, D., Willian, M. K., Saurat, J. H., Papp, K. A., Ortonne, J. P., Sexton, C., & Camez, A. (2008). Impact of adalimumab treatment on health-related quality of life and other patient-reported outcomes: Results from a 16-week randomized controlled trial in patients with moderate to severe plaque psoriasis. *The British Journal of Dermatology, 158*(3), 549–557. https://doi.org/10.1111/j.1365-2133.2007.08236.x
98. Rich, P., Gooderham, M., Bachelez, H., Goncalves, J., Day, R. M., Chen, R., & Crowley, J. (2016). Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with difficult-to-treat nail and scalp psoriasis: Results of 2 phase III randomized, controlled trials (ESTEEM 1 and ESTEEM 2). *Journal of the American Academy of Dermatology, 74*(1), 134–142. https://doi.org/10.1016/j.jaad.2015.09.001
99. Rønholt, K., & Iversen, L. (2017). Old and new biological therapies for psoriasis. *International Journal of Molecular Sciences, 18*(11), 2297. https://doi.org/10.3390/ijms18112297

100. Sánchez-Rodríguez, G., & Puig, L. (2023). Pathogenic role of IL-17 and therapeutic targeting of IL-17F in psoriatic arthritis and spondyloarthropathies. *International Journal of Molecular Sciences, 24*(12). https://doi.org/10.3390/ijms241210305
101. Saurat, J. H., Stingl, G., Dubertret, L., Papp, K., Langley, R. G., Ortonne, J. P., Unnebrink, K., Kaul, M., & Camez, A. (2008). Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). *The British Journal of Dermatology, 158*(3), 558–566. https://doi.org/10.1111/j.1365-2133.2007.08315.x
102. Sbidian, E., Chaimani, A., Afach, S., Doney, L., Dressler, C., Hua, C., Mazaud, C., Phan, C., Hughes, C., Riddle, D., Naldi, L., Garcia-Doval, I., & Le Cleach, L. (2020). Systemic pharmacological treatments for chronic plaque psoriasis: A network meta-analysis. *Cochrane Database of Systematic Reviews, 2020*(1), Article CD011535. https://doi.org/10.1002/14651858.CD011535.pub3
103. Sbidian, E., Chaimani, A., Guelimi, R., Garcia-Doval, I., Hua, C., Hughes, C., Naldi, L., Kinberger, M., Afach, S., & Le Cleach, L. (2023). Systemic pharmacological treatments for chronic plaque psoriasis: A network meta-analysis. *Cochrane Database of Systematic Reviews, 2023*(7), Article CD011535. https://doi.org/10.1002/14651858.CD011535.pub6
104. Sbidian, E., Chaimani, A., Guelimi, R., Tai, C. C., Beytout, Q., Choudhary, C., Mubuanga Nkusu, A., Ollivier, C., Samaran, Q., Hughes, C., Afach, S., & Le Cleach, L. (2025). Systemic pharmacological treatments for chronic plaque psoriasis: A network meta-analysis. *Cochrane Database of Systematic Reviews, 2025*(8), Article CD011535. https://doi.org/10.1002/14651858.CD011535.pub7
105. Schreiber, S., Colombel, J. F., Feagan, B. G., Reich, K., Deodhar, A. A., McInnes, I. B., Porter, B., Das Gupta, A., Pricop, L., & Fox, T. (2019). Incidence rates of inflammatory bowel disease in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis treated with secukinumab: A retrospective analysis of pooled data from 21 clinical trials. *Annals of the Rheumatic Diseases, 78*(4), 473–479. https://doi.org/10.1136/annrheumdis-2018-214273
106. Sieminska, I., Pieniawska, M., & Grzywa, T. M. (2024). The immunology of psoriasis—Current concepts in pathogenesis. *Clinical Reviews in Allergy & Immunology, 66*(2), 164–184. https://doi.org/10.1007/s12016-024-08991-7
107. Simopoulou, T., Tsiogkas, S. G., Zafiriou, E., & Bogdanos, D. P. (2023). Secukinumab, ixekizumab, bimekizumab and brodalumab for psoriasis and psoriatic arthritis. *Drugs of Today, 59*(3), 135–167. https://doi.org/10.1358/dot.2023.59.3.3419557
108. European Medicines Agency. (n.d.). *Skyrizi*. Retrieved March 14, 2026, from https://www.ema.europa.eu/en/medicines/human/EPAR/skyrizi
109. Smolen, J. S., Landewé, R., Bijlsma, J., Burmester, G., Chatzidionysiou, K., Dougados, M., Nam, J., Ramiro, S., Voshaar, M., Van Vollenhoven, R., Aletaha, D., Aringer, M., Boers, M., Buckley, C. D., Buttgereit, F., Bykerk, V., Cardiel, M., Combe, B., Cutolo, M., … Van Der Heijde, D. (2017). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Annals of the Rheumatic Diseases, 76*(6), 960–977. https://doi.org/10.1136/annrheumdis-2016-210715
110. Sticherling, M., Nikkels, A. F., Hamza, A. M., Kwong, P., Szepietowski, J. C., El Sayed, M., Ghislain, P. D., Khotko, A. A., Patekar, M., Ortmann, C. E., Forrer, P., Papanastasiou, P., & Keefe, D. (2023). Secukinumab in pediatric patients with plaque psoriasis: Pooled safety analysis from two phase 3 randomized clinical trials. *American Journal of Clinical Dermatology, 24*(5), 821–835. https://doi.org/10.1007/s40257-023-00782-8
111. Strober, B., Tada, Y., Mrowietz, U., Lebwohl, M., Foley, P., Langley, R. G., Warren, R. B., Wang, M., Vanvoorden, V., Szilagyi, B., Ciaravino, V., & Paul, C. (2023). Bimekizumab maintenance of response through 3 years in patients with moderate-to-severe plaque psoriasis: Results from the BE BRIGHT open-label extension trial. *The British Journal of Dermatology, 188*(6), 749–759. https://doi.org/10.1093/bjd/ljad035
112. European Medicines Agency. (n.d.). *Taltz*. Retrieved March 13, 2026, from https://www.ema.europa.eu/en/medicines/human/EPAR/taltz
113. Thomas, S. S., Borazan, N., Barroso, N., Duan, L., Taroumian, S., Kretzmann, B., Bardales, R., Elashoff, D., Vangala, S., & Furst, D. E. (2015). Comparative immunogenicity of TNF inhibitors: Impact on clinical efficacy and tolerability in the management of autoimmune diseases. A systematic review and meta-analysis. *BioDrugs, 29*(4), 241–258. https://doi.org/10.1007/s40259-015-0134-5
114. European Medicines Agency. (n.d.). *Tremfya*. Retrieved March 14, 2026, from https://www.ema.europa.eu/en/medicines/human/EPAR/tremfya
115. Tyring, S., Gottlieb, A., Papp, K., Gordon, K., Leonardi, C., Wang, A., Lalla, D., Woolley, M., Jahreis, A., Zitnik, R., Cella, D., & Krishnan, R. (2006). Etanercept and clinical outcomes, fatigue, and depression in psoriasis: Double-blind placebo-controlled randomised phase III trial. *The Lancet, 367*(9504), 29–35. https://doi.org/10.1016/S0140-6736(05)67763-X
116. Vidal, S., Puig, L., Carrascosa-Carrillo, J. M., González-Cantero, Á., Ruiz-Carrascosa, J. C., & Velasco-Pastor, A. M. (2021). From messengers to receptors in psoriasis: The role of IL-17RA in disease and treatment. *International Journal of Molecular Sciences, 22*(13). https://doi.org/10.3390/ijms22136740

117. Vuyyuru, S. K., Solitano, V., Hogan, M., MacDonald, J. K., Zayadi, A., Parker, C. E., Sands, B. E., Panaccione, R., Narula, N., Feagan, B. G., Singh, S., Jairath, V., & Ma, C. (2023). Efficacy and safety of IL-12/23 and IL-23 inhibitors for Crohn's disease: Systematic review and meta-analysis. *Digestive Diseases and Sciences, 68*(9), 3702–3713. https://doi.org/10.1007/s10620-023-08014-z
118. Warren, R. B., Blauvelt, A., Bagel, J., Papp, K. A., Yamauchi, P., Armstrong, A., Langley, R. G., Vanvoorden, V., De Cuyper, D., Cioffi, C., Peterson, L., Cross, N., & Reich, K. (2021). Bimekizumab versus adalimumab in plaque psoriasis. *The New England Journal of Medicine, 385*(2), 130–141. https://doi.org/10.1056/NEJMoa2102388
119. Warren, R. B., Lebwohl, M., Thaçi, D., Gooderham, M., Pinter, A., Paul, C., Gisondi, P., Szilagyi, B., White, K., Deherder, D., Staelens, F., Lambert, J., & Strober, B. (2025). Bimekizumab efficacy and safety through 3 years in patients with moderate-to-severe plaque psoriasis: Long-term results from the BE RADIANT phase IIIb trial open-label extension period. *The British Journal of Dermatology, 193*(1), 44–55. https://doi.org/10.1093/bjd/ljaf032
120. Warren, R. B., Smith, C. H., Yiu, Z. Z. N., Ashcroft, D. M., Barker, J. N. W. N., Burden, A. D., Lunt, M., McElhone, K., Ormerod, A. D., Owen, C. M., Reynolds, N. J., & Griffiths, C. E. M. (2015). Differential drug survival of biologic therapies for the treatment of psoriasis: A prospective observational cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). *Journal of Investigative Dermatology, 135*(11), 2632–2640. https://doi.org/10.1038/jid.2015.208
121. Wcisło-Dziadecka, D., Zbiciak-Nylec, M., Brzezińska-Wcisło, L., & Mazurek, U. (2016). TNF-α in a molecularly targeted therapy of psoriasis and psoriatic arthritis. *Postgraduate Medical Journal, 92*(1085), 172–178. https://doi.org/10.1136/postgradmedj-2015-133419
122. Yan, X., Shi, M., Wang, B., Zeng, L., Wang, H., Shi, J., Cui, Y., & Hou, S. (2025). Targeting nail psoriasis: IL-17A inhibitors demonstrate site-specific superiority over IL-23 inhibitor in a 24-week dermoscopy-guided real-world cohort. *Frontiers in Immunology, 16*. https://doi.org/10.3389/fimmu.2025.1573715