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Pharmaceutical Biotechnology and Comparative Efficacy of Biologic Therapies in Patients with Moderate-To-Severe Psoriasis: An Evaluation of Clinical Outcomes and Therapeutic Response

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ABSTRACT: Background. Moderate-to-severe plaque psoriasis is a chronic, immune-mediated inflammatory disease driven by the interleukin (IL)-23/IL-17 axis. Advances in pharmaceutical biotechnology have delivered successive generations of monoclonal antibodies that selectively neutralise tumour necrosis factor (TNF)- α , the shared p40 subunit of IL-12/IL-23, IL-17A, IL-17A/F and the p19 subunit of IL-23, transforming therapeutic expectations from partial improvement to complete skin clearance.

Objective. To synthesise and critically appraise the comparative efficacy of biologic therapies in adults with moderate-to-severe psoriasis, with emphasis on head-to-head randomised trials, network meta-analyses and the biotechnological rationale underlying each drug class.

Methods. A systematic literature review was conducted following PRISMA principles, searching the scientific discovery engines Scite and Consensus (indexing Semantic Scholar, OpenAlex and PubMed). Clinical response was appraised using validated outcomes —PASI 75/90/100, IGA/sPGA 0/1 and the Dermatology Life Quality Index (DLQI). An analytical corpus of 46 peer-reviewed studies (2007–2026) was retained.

Results. Head-to-head trials and network meta-analyses establish a broadly consistent efficacy hierarchy: IL-23p19 inhibitors (risankizumab, guselkumab) and the dual IL-17A/F inhibitor bimekizumab achieve the highest rates of PASI 90 and PASI 100, outperforming IL-12/23 inhibition (ustekinumab), TNF inhibitors and, for durability of response, the IL-17A inhibitors. IL-17A inhibition provides the most rapid onset, whereas IL-23 inhibition offers superior maintenance of response with infrequent dosing. Safety profiles are generally favourable and class-dependent.

Conclusions. Selective cytokine inhibition has made complete or near-complete skin clearance a realistic treatment target. Drug positioning should integrate speed of onset,

durability, safety, comorbidities and patient-reported outcomes; the emergence of biosimilars is expected to broaden access, a consideration of particular relevance to resource-constrained settings.

1. INTRODUCTION

Psoriasis vulgaris is one of the most common organ-specific immune-mediated diseases, affecting approximately 2% of the population and imposing a substantial burden on quality of life, with frequent depression, anxiety and stigmatisation, as well as systemic comorbidities such as psoriatic arthritis, cardiovascular disease and metabolic syndrome (Hawkes et al., 2018; Georgescu et al., 2019). Over the last two decades, research has unequivocally shown that psoriasis is a T cell-mediated disease driven by pathogenic T cells that produce high levels of IL-17 in response to IL-23, a discovery that produced a major paradigm shift in the pathogenic model of the condition (Hawkes et al., 2017; Kim et al., 2017).

This mechanistic understanding, coupled with advances in pharmaceutical biotechnology and recombinant monoclonal antibody (mAb) engineering, has transformed the therapeutic landscape. Where conventional systemic agents offered modest and often toxic improvement, successive generations of biologic agents now selectively neutralise defined cytokines, and psoriasis has become arguably the most effectively treated human autoimmune disease, with high-level clinical improvement achievable in roughly 90% of patients using drugs that target the IL-23/type-17 T-cell axis (Kim et al., 2017). The therapeutic target itself has shifted: from the historical benchmark of a 75% reduction in the Psoriasis Area and Severity Index (PASI 75) toward complete skin clearance (PASI 100).

As the therapeutic armamentarium has expanded to encompass TNF- α inhibitors, the IL-12/23 inhibitor ustekinumab, IL-17 pathway inhibitors (secukinumab, ixekizumab and the dual IL-17A/F inhibitor bimekizumab) and IL-23p19 inhibitors (guselkumab, risankizumab, tildrakizumab and mirikizumab), clinicians increasingly require robust comparative evidence to guide selection. Placebo-controlled trials no longer suffice; head-to-head randomised controlled trials (RCTs) and network meta-analyses (NMAs) have become the reference standard for establishing relative efficacy (Sawyer et al., 2019; Armstrong et al., 2020; Sbidian et al., 2025).

This article aims to synthesise and critically appraise the comparative efficacy of biologic therapies in adults with moderate-to-severe psoriasis. The specific objectives are: (i) to summarise the biotechnological rationale underlying each therapeutic class; (ii) to evaluate efficacy by drug class against validated clinical outcomes; (iii) to analyse the evidence from head-to-head RCTs and NMAs in order to derive an efficacy hierarchy; and (iv) to appraise safety, durability, drug survival and patient-reported outcomes that inform therapeutic positioning. Three questions guide the review: (RQ1) how do the biologic classes compare in the magnitude and speed of clinical response? (RQ2) how do they compare in the durability of that response and in safety? and (RQ3) what factors beyond efficacy—including biosimilars and access—should inform drug positioning?

2. METHODS

2.1 Design and information sources

An integrative systematic literature review was conducted following the principles of the PRISMA 2020 statement across the phases of identification, screening, eligibility and inclusion. Studies were identified using two next-generation scientific discovery engines, Scite and Consensus, which operate over large indices of peer-reviewed literature (Semantic Scholar, OpenAlex and PubMed) and return verifiable bibliographic metadata (authorship, year, journal and DOI). Scite additionally enabled examination of Smart Citations and verification of editorial notices of retraction or correction, strengthening the reliability of the corpus.

2.2 Search strategy and eligibility

Searches combined Boolean operators and phrase searching over terms for the disease ("moderate-to-severe plaque psoriasis"), the interventions (each biologic agent and cytokine target), the comparators ("head-to-head", "versus", "network meta-analysis") and the outcomes ("PASI 75", "PASI 90", "PASI 100", "IGA", "DLQI", "drug survival", "safety"). Medical mode and a peer-review filter were applied. Inclusion criteria were: (i) randomised controlled trials, systematic reviews or network meta-analyses in adults with moderate-to-severe plaque psoriasis; (ii) reporting of validated efficacy or safety

outcomes; and (iii) availability of a verifiable DOI. Mechanistic and pathogenesis studies were included where they informed the biotechnological rationale. An analytical corpus of 46 studies published between 2007 and 2026 was retained.

2.3 Outcome measures

Efficacy was appraised primarily through the proportion of patients achieving a 75%, 90% or 100% reduction from baseline in the Psoriasis Area and Severity Index (PASI 75/90/100) and a clear or almost-clear Investigator's/static Physician's Global Assessment (IGA/sPGA 0 or 1), the co-primary endpoints of most pivotal trials. Patient-reported outcomes were appraised using the Dermatology Life Quality Index (DLQI). This review synthesises published trial-level evidence and does not constitute clinical guidance for individual treatment decisions.

3. PHARMACEUTICAL BIOTECHNOLOGY AND THE IL-23/IL-17 AXIS

The biologic era in psoriasis is a direct product of pharmaceutical biotechnology: the capacity to engineer fully human or humanised recombinant monoclonal antibodies that bind defined cytokine targets with high affinity and specificity. The mechanistic rationale rests on the IL-23/type-17 inflammatory circuit. Under the regulation of IL-23, pathogenic T cells produce IL-17, generating a self-amplifying, feed-forward inflammatory response in keratinocytes that drives epidermal hyperplasia and the mature psoriatic plaque (Hawkes et al., 2017; Lowes et al., discussed in Hawkes et al., 2018). IL-17A acts on keratinocytes, neutrophils, endothelial cells and fibroblasts to amplify inflammation, which provides the biological rationale for targeting the IL-17 cytokine family (IL-17A, IL-17F and the IL-17 receptor) (Blauvelt & Chiricozzi, 2018). The divergent roles of the axis in skin versus joints help explain the heterogeneous efficacy of these agents across psoriatic phenotypes (Boutet et al., 2018).

Four principal molecular strategies have been realised as marketed biotechnological products. First, inhibition of TNF- α (etanercept, adalimumab, infliximab), the earliest biologic target. Second, inhibition of the shared p40 subunit of IL-12 and IL-23 by ustekinumab, whose proof of concept was established by an anti-IL-12/23 mAb that achieved PASI 75 in up to 81% of patients at week 12 (Krueger et al., 2007). Third, inhibition of IL-17 signalling, either by neutralising IL-17A (secukinumab, ixekizumab) or, more recently, by dual inhibition of IL-17A and IL-17F (bimekizumab). Fourth, selective inhibition of the p19 subunit of IL-23 (guselkumab, risankizumab, tildrakizumab, mirikizumab), which spares IL-12 and more precisely targets the apex of the pathogenic circuit (Hawkes et al., 2017). Single-cell and longitudinal studies now show that IL-23 blockade produces durable remodelling of the type-17 inflammatory circuit in lesional skin, offering a mechanistic explanation for the prolonged responses observed with this class (Kim et al., 2017; Blauvelt & Chiricozzi, 2018).

A further biotechnological frontier is the development of molecules with engineered properties—for example, extended half-life IL-23p19 antibodies—and of biosimilars, which reproduce reference biologics to reduce cost. The first comparative evidence for a secukinumab biosimilar in moderate-to-severe psoriasis has recently emerged (Chen et al., 2026), signalling a maturing market with important implications for access.

4. EFFICACY BY THERAPEUTIC CLASS

4.1 TNF- α inhibitors and the first biologic generation

TNF- α inhibitors established that selective cytokine blockade could produce meaningful disease control and remain active comparators in modern trials. However, their efficacy ceiling is lower than that of newer agents: in the FIXTURE trial, etanercept achieved PASI 75 in 44.0% of patients at week 12, substantially below the 77.1% achieved with secukinumab 300 mg (Langley et al., 2014). Adalimumab, the most efficacious TNF inhibitor in psoriasis, serves as the active comparator in the VOYAGE, IMMvent and BE SURE programmes, where it is consistently outperformed by IL-23 and IL-17A/F inhibitors (Blauvelt et al., 2017; Reich et al., 2019b; Warren et al., 2021).

4.2 IL-12/23 inhibition: ustekinumab

Ustekinumab, targeting the shared p40 subunit, marked a substantial advance over TNF inhibition. In PHOENIX 1, PASI 75 at week 12 was achieved by 67.1% (45 mg) and 66.4% (90 mg) of patients versus 3.1% with placebo, with efficacy maintained for at least one year under 12-weekly dosing (Leonardi et al., 2008). Its convenient dosing and strong long-term safety record made ustekinumab the reference active comparator for the IL-17 and IL-23 programmes; against those newer classes,

however, it is consistently outperformed on PASI 90 and PASI 100 (Thaçi et al., 2015; Reich et al., 2017a; Gordon et al., 2018).

4.3 IL-17 pathway inhibitors

IL-17A inhibitors are characterised by rapid onset and high response rates. In the pivotal ERASURE and FIXTURE trials, secukinumab 300 mg achieved PASI 75 in 81.6% and 77.1% of patients at week 12, with superiority over both placebo and etanercept (Langley et al., 2014); long-term data confirm sustained efficacy through five years (Langley et al., 2022). Ixekizumab demonstrated similarly high efficacy against placebo and etanercept in the UNCOVER programme (Griffiths et al., 2015; Gordon et al., 2016). Bimekizumab, which neutralises both IL-17A and IL-17F, represents the most recent evolution of this class and has achieved the highest rates of complete skin clearance reported in head-to-head trials, with efficacy sustained over three to four years (Warren et al., 2021; Warren et al., 2025).

4.4 IL-23p19 inhibitors

Selective IL-23p19 inhibitors target the apex of the pathogenic circuit while sparing IL-12. Guselkumab and risankizumab have shown high and notably durable responses. In the UltIMMa-1 and UltIMMa-2 trials, risankizumab met its co-primary PASI 90 and sPGA 0/1 endpoints with superiority over both placebo and ustekinumab (Gordon et al., 2018), and a review of the class documents its favourable efficacy-to-dosing ratio, with maintenance dosing every eight (guselkumab) to twelve (risankizumab) weeks (Blair, summarised in Gordon et al., 2021). Guselkumab demonstrated superiority over adalimumab in VOYAGE 1 and VOYAGE 2 (Blauvelt et al., 2017; Reich et al., 2017b). The defining feature of this class is the durability of response, which underpins its strong performance in long-term and maintenance analyses.

5. HEAD-TO-HEAD COMPARATIVE EFFICACY

Direct comparative trials provide the least biased evidence on relative efficacy and have progressively mapped the hierarchy among classes.

5.1 IL-17A and IL-23 inhibition versus IL-12/23 inhibition

Both newer classes are superior to ustekinumab. In IXORA-S, ixekizumab was superior to ustekinumab for PASI 90 at week 12 (72.8% vs 42.2%; difference 32.1%, $p < 0.001$), with superiority maintained through week 52 (Reich et al., 2017a; Paul et al., 2019). Secukinumab was likewise superior to ustekinumab in the CLEAR trial for PASI 90, both at week 16 and over 52 weeks (Thaçi et al., 2015; Blauvelt et al., 2016). Risankizumab demonstrated clear superiority over ustekinumab across the UltIMMa programme and an earlier phase-2 comparison (Papp et al., 2017; Gordon et al., 2018).

5.2 IL-23 inhibition versus TNF inhibition

IL-23p19 inhibitors outperform adalimumab. In IMMvent, risankizumab was superior to adalimumab, including among initial adalimumab responders who were re-randomised (Reich et al., 2019b). Guselkumab was superior to adalimumab in VOYAGE 1 and VOYAGE 2, with higher PASI 90 rates and durable maintenance (Blauvelt et al., 2017; Reich et al., 2017b).

5.3 IL-23 inhibition versus IL-17A inhibition

The comparison between the two dominant modern classes is the most clinically informative. In ECLIPSE—the first head-to-head trial of an IL-23 inhibitor against an IL-17A inhibitor—guselkumab was superior to secukinumab for the primary endpoint of PASI 90 at week 48 (84% vs 70%), reflecting the superior durability of IL-23 inhibition, even though secukinumab showed marginally faster early responses (Reich et al., 2019a). Conversely, in IXORA-R the faster-acting ixekizumab was superior to guselkumab for the early endpoint of PASI 100 at week 12 (Papp et al., 2019; Blauvelt et al., 2020), while risankizumab was superior to secukinumab at week 52 in IMMerge (Warren et al., 2020). Taken together, these trials delineate a consistent pattern: IL-17A inhibition confers the fastest onset, whereas IL-23 inhibition confers superior maintenance of response over the longer term.

5.4 Dual IL-17A/F inhibition versus established agents

Bimekizumab has been compared directly against an agent from each major class and was superior in every case: versus ustekinumab in BE VIVID (Reich et al., 2021b), versus adalimumab in BE SURE (Warren et al., 2021), and versus secukinumab in BE RADIANT (Reich et al., 2021a). In BE RADIANT, bimekizumab achieved higher rates of complete

clearance (PASI 100) than secukinumab, and pooled analyses report the highest concurrent skin-and-nail clearance of any comparator (Merola et al., 2025). The emergence of a more specific IL-23 inhibitor, mirikizumab, which was superior to secukinumab in a phase-3 comparison, further reinforces the strength of the IL-23 and dual IL-17A/F strategies (Papp et al., 2023).

6. NETWORK META-ANALYSES AND THE EFFICACY HIERARCHY

Because no single trial compares all available agents, NMAs are indispensable for ranking relative efficacy. Their findings are broadly concordant. A large meta-analysis of biologic and oral agents found that IL-23 and IL-17 inhibitors ranked highest for achievement of PASI 90/100 (Armstrong et al., 2020), and a dedicated NMA comparing IL-17 and IL-23 targeted treatments confirmed the leading position of these classes over earlier biologics (Sawyer et al., 2019). An updated NMA of biologic therapies similarly placed the IL-23p19 inhibitors and high-efficacy IL-17 agents at the top of the short-term efficacy ranking (Mahil et al., 2020), while analyses of cumulative clinical benefit over the first 16 weeks captured the trade-off between the rapid onset of IL-17 inhibition and the sustained response of IL-23 inhibition (Warren et al., 2019). Earlier quantitative syntheses had already established the superiority of the newer classes over the first biologic generation (Signorovitch et al., 2015; Jabbar-Lopez et al., 2017). The most recent Cochrane network meta-analysis, continuously updated, reaffirms that the IL-23 and IL-17 inhibitors are among the most effective systemic treatments for plaque psoriasis (Sbidian et al., 2025), and comparative analyses of the oral TYK2 inhibitor deucravacitinib position it below the leading biologics on PASI endpoints (Chen et al., 2025).

7. SAFETY AND TOLERABILITY

The high efficacy of modern biologics is accompanied by generally favourable and class-specific safety profiles. A network meta-analysis of benefit-risk found that the improved efficacy of newer agents was not offset by a proportionate increase in short-term harms (Shear et al., 2021). Pooled long-term data for secukinumab across ten phase II/III trials and dedicated long-term analyses documented a consistent safety profile, with mucocutaneous *Candida* infections being the most characteristic class-related event of IL-17A inhibition (van de Kerkhof et al., 2016; Deodhar et al., 2019). For IL-23p19 inhibition, integrated safety data for risankizumab from 17 clinical trials showed low rates of serious infections and no new safety signals over extended follow-up (Gordon et al., 2021). Because IL-17 inhibition can exacerbate inflammatory bowel disease and dual IL-17A/F inhibition is associated with a higher incidence of oral candidiasis, cytokine selectivity carries direct clinical consequences for patient selection (Blauvelt & Chiricozzi, 2018; Warren et al., 2021).

8. DURABILITY, DRUG SURVIVAL AND PATIENT-REPORTED OUTCOMES

Beyond short-term response, durability and real-world persistence are decisive for chronic disease. Drug survival—the time a patient remains on a given therapy—integrates effectiveness, safety and tolerability. Analysis of a large prospective register found that IL-23 inhibitors, led by guselkumab, had the highest drug survival among the newer agents, with risankizumab and ixekizumab also performing strongly (Yiu et al., 2022). Long-term extension data confirm sustained efficacy for secukinumab through five years (Langley et al., 2022) and for bimekizumab through three to four years (Warren et al., 2025). Patient-reported outcomes track these clinical gains: risankizumab produced significant improvements in DLQI and other patient-reported measures (Augustin et al., 2020), and the achievement of PASI 90/100 corresponds to markedly higher rates of DLQI 0/1, indicating resolution of disease impact on daily life (Reich et al., 2017a; Nast et al., 2015).

9. DISCUSSION

The convergence of head-to-head RCTs and NMAs supports a robust and reproducible efficacy hierarchy for moderate-to-severe psoriasis. At the apex, the IL-23p19 inhibitors and the dual IL-17A/F inhibitor bimekizumab deliver the highest rates of PASI 90 and PASI 100; IL-17A inhibitors follow closely with the fastest onset; ustekinumab occupies an intermediate position; and TNF inhibitors, though still useful, display the lowest efficacy ceiling (Sawyer et al., 2019; Armstrong et al., 2020; Mahil et al., 2020; Sbidian et al., 2025). This answers RQ1: the magnitude of response is greatest for IL-23 and dual IL-17A/F inhibition, while the speed of response favours IL-17 inhibition.

With respect to RQ2, the trials reveal a consistent dissociation between speed and durability. IL-17A inhibition acts rapidly but, as ECLIPSE demonstrated, is surpassed by IL-23 inhibition at later time points (Reich et al., 2019a), a pattern echoed by IMMerge and supported mechanistically by the durable circuit remodelling that follows IL-23 blockade (Warren et al., 2020;

Hawkes et al., 2017). Drug-survival data reinforce the long-term advantage of IL-23 inhibition in routine practice (Yiu et al., 2022). Safety profiles are favourable across classes but cytokine-specific: the candidiasis signal of IL-17 inhibition and the caution required in inflammatory bowel disease contrast with the particularly clean long-term profile of IL-23 inhibition (Deodhar et al., 2019; Gordon et al., 2021).

Regarding RQ3, efficacy alone cannot dictate drug positioning. The choice among high-performing agents should integrate speed of onset (favouring IL-17 inhibition when rapid control is critical), durability and dosing convenience (favouring IL-23 inhibition), comorbidities (psoriatic arthritis, inflammatory bowel disease, metabolic and cardiovascular risk) and patient-reported outcomes (Boutet et al., 2018; Augustin et al., 2020). Economic and access considerations are increasingly central: the arrival of biosimilars, including the first secukinumab biosimilar evaluated in psoriasis (Chen et al., 2026), is expected to lower costs and broaden access—a consideration of particular importance in resource-constrained and Latin American health systems, where access to high-cost biologics remains uneven.

Several limitations of the evidence base warrant caution. Cross-trial comparisons are complicated by heterogeneity in design, populations, placebo-arm responses and endpoint timing, which NMAs attempt but cannot fully resolve (Signorovitch et al., 2015; Ellis, as discussed in Mahil et al., 2020). Long-term comparative trials remain scarce and heterogeneous, head-to-head data for some agents are indirect, and most pivotal trials enrol selected populations that may not reflect routine practice. Finally, this review is itself conditioned by the indices searched and the interpretive selection inherent to any systematic review.

10. CONCLUSIONS

Advances in pharmaceutical biotechnology have transformed moderate-to-severe psoriasis from a difficult-to-control disease into one in which complete or near-complete skin clearance is a realistic therapeutic target. Comparative evidence from head-to-head RCTs and network meta-analyses converges on a clear hierarchy in which IL-23p19 inhibitors and the dual IL-17A/F inhibitor bimekizumab achieve the highest rates of PASI 90 and PASI 100, IL-17A inhibitors offer the most rapid onset, and IL-23 inhibitors offer the most durable response and the strongest real-world drug survival. Optimal therapeutic positioning therefore depends not on efficacy alone but on the integration of speed, durability, safety, comorbidity profile and patient-reported outcomes. The maturation of biosimilars is poised to improve the affordability and accessibility of these high-efficacy therapies. Future priorities include long-term head-to-head comparisons, the identification of predictive biomarkers of therapeutic response, and real-world effectiveness studies in under-represented populations and health systems.

Declarations

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Methodological note. Source identification and verification relied on the scientific discovery engines Scite and Consensus, which operate over peer-reviewed literature indexed in Semantic Scholar, OpenAlex and PubMed. All references include a DOI to ensure verifiability. This article is a review of published evidence and does not constitute clinical guidance for individual patients.

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