**Medical Science**

**To Cite:**
Kobrzyńska PA, Mogilany J, Ragan G, Korżel A, Cegielska N, Górowska K, Niedźwiecka J, Źródłowski K, Wojna E. New Therapies in Atopic Dermatitis: Biologic Agents and JAK Inhibitors - A Contemporary Literature Review. *Medical Science* 2026; 30: e15ms3803 doi: https://doi.org/10.54905/disssi.v30i167.e15ms3803

**Authors' Affiliation:**
[1]University Clinical Hospital No. 2 of the Medical University of Lodz: Łódź, ul. Stefana Żeromskiego 113, 90-549 Łódź, PL, Łódź, PL, E-mail: patrycja.kob27@gmail.com, 0009-0008-0476-5111
[2]Medical University of Lodz: Lodz, Łódź Voivodeship, PL, E-mail: jedrzej.mogilany@gmail.com, 0009-0001-6471-653X
[3]Medical University of Lodz, Al. Tadeusza Kościuszki 4, 90-419 Łódź, Poland, E-mail: gabriela.ragan@op.pl, 0009-0002-0869-6543
[4]Medical University of Lodz: Lodz, Łódź Voivodeship, PL, E-Mail: o.korzel@poczta.fm, 0009-0002-5388-9168
[5]Medical University of Lodz, Al. Tadeusza Kościuszki 4, 90-419 Łódź, Poland, E-mail: nataliacegielskaa@gmail.com, 0000-0002-2484-9637
[6]Medical University of Lodz: Lodz, Łódź Voivodeship, PL, E-mail: Karolina.gorowska@stud.umed.lodz.pl, 0009-0009-0088-6079
[7]Medical University of Lodz, Al. Tadeusza Kościuszki 4, 90-419 Łódź, Poland, E-mail: julianiedzwiecka1@gmail.com, my-orcid?orcid=0009-0002-8387-6085
[8]Medical University of Lodz: Lodz, Łódź Voivodeship, PL, E-mail: kamil.zrodlowski2@gmail.com, 0009-0001-1088-4853
[9]Medical University of Lodz: Lodz, Łódź Voivodeship, PL, E mail: ewelinawojna30@gmail.com 0009-0006-7049-5477

*Corresponding author:
Patrycja Anita Kobrzyńska, University Clinical Hospital No. 2 of the Medical University of Lodz: Łódź, ul. Stefana Żeromskiego 113, 90-549 Łódź, PL, Łódź, PL, E-mail: patrycja.kob27@gmail.com, 0009-0008-0476-5111

**Peer-Review History**
Received: 21 August 2025
Reviewed & Revised: 29/September/2025 to 07/January/2026
Accepted: 18 January 2026
Published: 27 January 2026

**Peer-review Method**
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367



DISCOVERY SCIENTIFIC SOCIETY

# New Therapies in Atopic Dermatitis: Biologic Agents and JAK Inhibitors - A Contemporary Literature Review

**Patrycja Anita Kobrzyńska[1*], Jędrzej Mogilany[2], Gabriela Ragan[3], Aleksandra Korżel[4], Natalia Cegielska[5], Karolina Górowska[6], Julia Niedźwiecka[7], Kamil Źródłowski[8], Ewelina Wojna[9]**

## ABSTRACT

Atopic Dermatitis is an inflammatory skin disease characterised by ongoing inflammation and a disrupted skin barrier. Advances in our knowledge of both have made possible the use of targeted systemic therapies to treat the disease. The following is a summary of current evidence on the use of biologic agents and Janus kinase (JAK) Inhibitors as treatment options for patients with Moderate-to-Severe Atopic Dermatitis, with emphasis on their efficacy, safety, and their place in treatment plans. The Researchers conducted a narrative literature review using studies on the epidemiology and pathophysiology of atopic dermatitis, along with results from clinical trials evaluating the use of systemic biologics and JAK inhibitors for its treatment. The Researchers used PubMed to search for all relevant articles published through today describing either the use of systemic biologic or JAK Inhibitor therapy for the treatment of moderate to severe atopic dermatitis. The available data support the use of biologic treatment as the preferred option for long-term disease control across all ages. At the same time, JAK inhibitors are alternative options for patients who require additional efficacy or symptom relief sooner than would typically occur with biologic therapy. Real-world data from long-term studies will provide vital information to refine treatment protocols and enable more individualised approaches to managing moderate to severe atopic dermatitis.

**Keywords:** atopic dermatitis; biologics; dupilumab; tralokinumab; JAK inhibitors; abrocitinib; upadacitinib; targeted therapy; IL-4/IL-13 blockade; immunomodulation

## 1. INTRODUCTION

Atopic dermatitis (AD) is a persistent, recurrent inflammatory skin condition characterised by pruritus, eczematous lesions, xerosis, and dysfunction of the skin barrier. It is one of the most prevalent dermatologic disorders in the world. Infects about 2 out of 10 children and 1 out of 10 adults, and the prevalence continues to

rise in most parts of the industrialised world (Migliavaca et al., 2025; Afshari et al., 2024). AD also has a substantial economic, psychological and physical impact on patients including impaired quality of life due to sleep disturbances, decreased productivity at home and/or at work, increased stress anxiety, and in health care utilisation (Elahi et al., 2024).

All the different factors that contribute to Atopic Dermatitis are interconnected and involve genetic predisposition and exposure to the environment daily, impairments of the epidermal barrier, disturbances in the microbiome of the skin, and changes in the immune system response to the body (Schuler et al., 2024; Yue et al., 2024). Breakdown of the skin's natural barrier function is an essential component of the disease process and is frequently due to mutations in filaggrin. Filaggrin mutations increase water loss from the skin and facilitate the entry of both allergens and microbes into the skin (Li et al., 2021). Additionally, Type II Inflammation, which is primarily mediated by IL-4, IL-13, and IL-31, and their respective signalling pathways, plays an essential role in establishing and maintaining the disease (Afshari et al., 2024).

Standard therapy for AD consists of emollients, topical corticosteroids, calcineurin inhibitors, and phototherapy. These treatments are still widely used, but several patients with moderate to severe AD either fail to reach disease control or develop side effects with prolonged systemic drugs like cyclosporine or methotrexate (Deva et al., 2024; Wollenberg et al., 2021). Such limitations created a need for more targeted, mechanism-based treatments with better efficacy and more acceptable safety over time.

Improved understanding of the immune pathways involved in AD has led to the development of biologic drugs and small-molecule inhibitors that selectively modulate key inflammatory signals. Dupilumab and tralokinumab, which are biologic agents that target IL-4 and IL-13 signaling, offer new treatment options for moderate to severe atopic dermatitis (AD) and provide a significant effect on reducing the overall severity of the disease, pruritus, and sleep disturbances as well as patients' self-assessed effects of the disease (Wollenberg et al., 2021; Simpson et al., 2016). Other biologic agents, such as lebrikizumab and nemolizumab, are emerging as new and effective treatments for various age groups and clinical phenotypes of AD (Reich et al., 2025; Paller et al., 2023).

As such, the JAK/STAT pathway is a major contributor to type 2 inflammatory responses in atopic dermatitis. Oral JAK inhibitors such as abrocitinib, upadacitinib, and baricitinib provide rapid relief of itch and skin inflammation by blocking multiple cytokine pathways (He et al., 2024; Yoon et al., 2024). Although several clinical trials and a few meta-analyses report good clinical responses with these drugs. The picture regarding long-term safety remains unclear, especially regarding infections and possible cardiovascular problems (Chen et al., 2023; Tarafdar et al., 2024).

With the growing number of available systemic options, there is a need for a concise overview of current evidence on biologics and JAK inhibitors to support treatment choices in everyday care. Therefore, the purpose of this review is to summarise recent evidence on the efficacy, safety, and clinical applications of developing systemic therapies for moderate to severe atopic dermatitis, based on randomised controlled trials, real-world studies, and revised international practice guidelines.

## 2. REVIEW METHODS

A narrative literature review was conducted using the PubMed database to identify studies published between 2016 and 2025 on systemic biologic and JAK-inhibitor therapies for moderate-to-severe atopic dermatitis. Search terms included combinations of atopic dermatitis, biologics, dupilumab, tralokinumab, JAK inhibitors, abrocitinib, upadacitinib, and systemic therapy. Eligible publications included clinical trials, meta-analyses, systematic reviews, long-term safety studies, and real-world evidence reports. Articles not focused on AD, non–peer-reviewed sources, and single case reports were excluded. Data from 35 relevant publications were synthesized qualitatively, focusing on efficacy, safety, and the clinical positioning of biologic agents and JAK inhibitors. The study method is shown in Figure 1.

## 3. RESULTS & DISCUSSION

Recently, treatment options for atopic dermatitis increased, altering what patients with moderate to severe disease can expect from their treatments. The systemic immunosuppressive drugs like methotrexate and cyclosporine are no longer a final option for treating atopic dermatitis. They serve as a transition between traditional immunosuppressive drugs and newer immune-targeted therapies. Compared with previous standards of care, both biologics and JAK inhibitors have demonstrated advantages in clinical efficacy, pruritus control, and overall quality of life. In addition, there is considerable variability among the different classes of agents in terms of mechanism of action, time to response, age approval status, and long-term safety considerations for patients.

Biological therapies, such as dupilumab and tralokinumab, are currently the primary biologic agents for the treatment of systemic atopic dermatitis. These treatments provide a durable level of disease control through the specific inhibition of inflammation caused by

IL-4/IL-13, require less laboratory testing than other biological treatments, and have the best long-term safety record of all systemic biologic treatments available (Wollenberg et al., 2021; Simpson et al., 2016; Reich et al., 2025). In addition to having the broadest spectrum of patients, dupilumab is also the first biologic agent that has been approved by the FDA for use in children under the age of one year (six months), which includes both infants and toddlers (Wang et al., 2024; Xu et al., 2023). Tralokinumab was not as broadly applicable as dupilumab, it has an excellent long-term tolerability, and has demonstrated considerable clinical benefit, particularly in adults and adolescents (Merola et al., 2023; Paller et al., 2023).

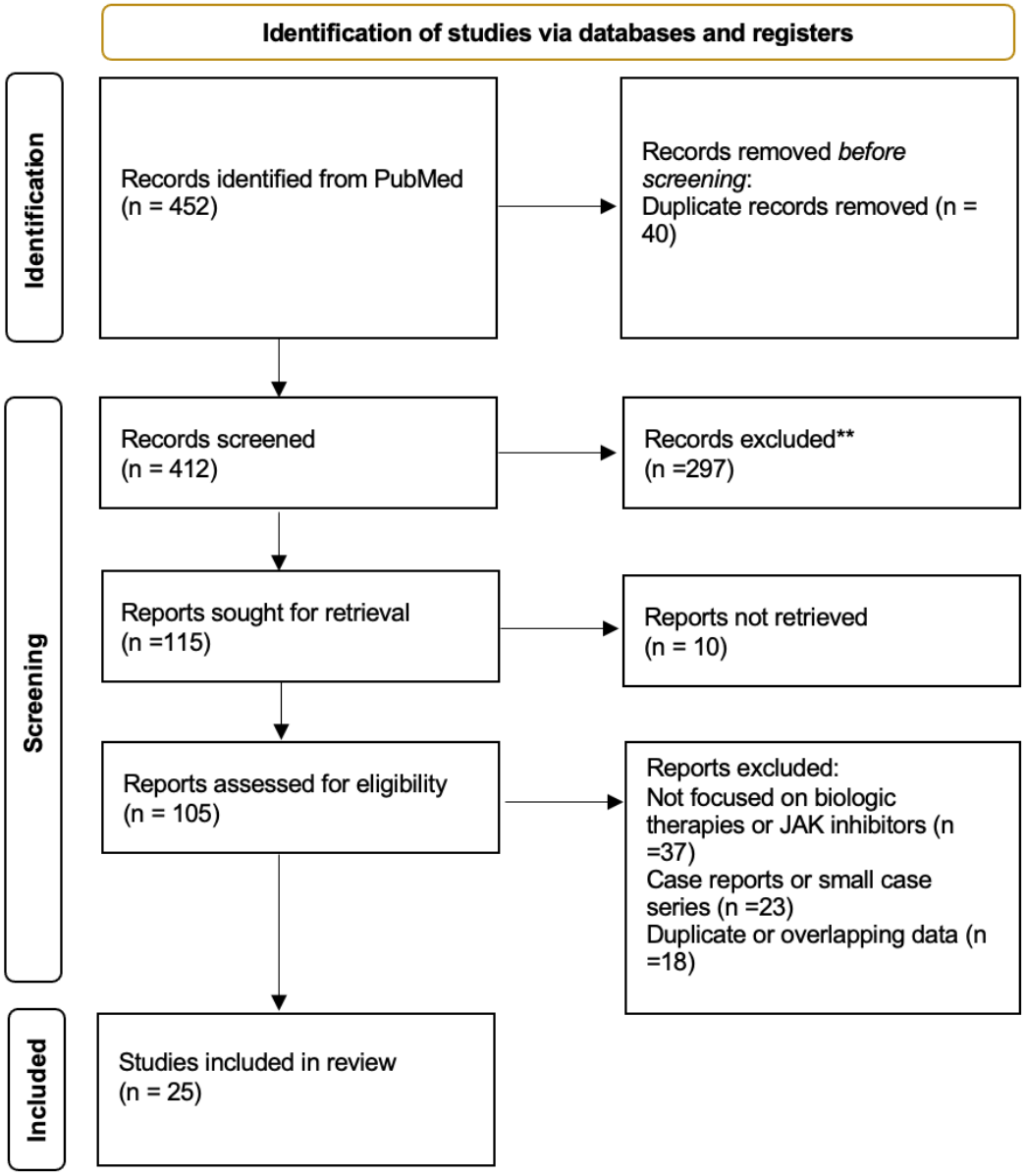


**Figure 1.** Flow chart

JAK inhibitors (abrocitinib, upadacitinib, baricitinib) can rapidly stop the intracellular signalling of many cytokines, which results in fast onset of itch relief, usually occurring by 24-48 hours - an advantage that is not common with biologic treatments (Simpson et al., 2020; Silverberg et al., 2020).

Upadacitinib has a very high chance of achieving EASI-90 and may provide greater benefit than many biologic agents in terms of both how quickly and to what degree patients experience relief from their psoriasis symptoms when rapid relief of symptoms is

essential (Simpson et al., 2022; Chen et al., 2023), making JAK inhibitors a viable treatment option for patients with severe pruritis or those that require rapid relief of their symptoms.

While they are also effective, the safety of a drug over time continues to be the primary method to differentiate drugs. According to the meta-analysis studies, there was a greater need for patient monitoring along with potential increased risk of specific adverse effects of prolonged use of these medications, such as herpes zoster, abnormal lab results, cardiovascular-related events, specifically for elderly or comorbidity involved individuals (Tarafdar et al., 2024; Irvine et al., 2025; Yoon et al., 2024). While real-world evidence continues to grow, biologics currently maintain a stronger long-term safety profile supported by years of follow-up exposure data (Kamata et al., 2021; Reich et al., 2025). In view of the above, most practitioners believe that biologics should be considered for first-line systemic therapy for all moderate to severe atopic dermatitis cases, and reserve the use of JAK inhibitors for rapidly needed symptom relief or for those atopic dermatitis cases that have been non-responsive to biologics, or have a primary skin symptom of intense itching.

One key factor that distinguishes the two forms of treatment is the patient's age. Dupilumab is one of the few biologic treatments prescribed to infants. In contrast, prescribing JAK inhibitor medications is limited only to patients within a specific age range and most commonly used as an adult treatment option (Xu et al., 2023; Zheng et al., 2024). For this reason, in the majority of cases, biologics are preferable to JAK inhibitors as a first line of treatment for children/adolescents. The choice of therapy should depend on the patient's individual needs.

Biologics are first-choice drugs for long-term disease management due to sustained efficacy, minimal monitoring, and robust safety. JAK inhibitors may be appropriate when rapid or high-level clearance is required -or if biologics fail to achieve adequate control. Optimal therapy will continue to evolve as emerging agents such as lebrikizumab and nemolizumab move toward wider clinical use. The summary points are mentioned in Table 1.

**Table 1**. Key discussion points on biologic therapies and JAK inhibitors in AD

| Aspect | Biologic therapies | JAK inhibitors | Clinical interpretation |
|---|---|---|---|
| Mechanism | Highly selective (IL-4/IL-13 blockade) | Broad cytokine pathway inhibition (JAK–STAT) | Selectivity favors long-term safety |
| Onset of action | Gradual (weeks) | Rapid (days) | JAK inhibitors useful when fast symptom relief is needed |
| Long-term efficacy | Sustained disease control | Effective, but long-term data limited | Biologics preferred for maintenance therapy |
| Safety profile | Favorable, minimal monitoring | Requires laboratory and risk monitoring | Patient risk profile should guide therapy choice |
| Pediatric patients | Approved across wide age range | Limited approvals | Biologics favored in children |
| Pruritus control | Progressive improvemen | Rapid and pronounced improvement | JAK inhibitors effective for severe itch |

**The Pathophysiology of Atopic Dermatitis**

The atopic dermatitis (AD) condition combines effects of an impaired epidermal barrier, an inappropriate or excessive immunologic response to allergens, genetic predisposition to the disease, disrupted skin micro-biome, and the presence of other environmental exposures which interact with each other to cause the chronic, recurring AD pattern and to develop a cycle of inflammation, pruritus, and impaired barrier function (Afshari et al., 2024; Yue et al., 2024). In contrast to previous perceptions that viewed atopic dermatitis as primarily an allergic disorder, the current view considers AD as an immunological cutaneous disorder involving both innate and adaptive immune systems.

*I. Epidermal Barrier Dysfunction*

The hallmark of AD is disruption of the skin's barrier function. The single most important genetic risk factor for AD is filaggrin deficiency due to loss-of-function mutations in the FLG gene, which impairs keratinocyte development and reduces the production of the natural moisturising factor, leading to desiccation and increased trans-epidermal water loss (Li et al., 2021). In addition to filaggrin deficiency, lower ceramide levels and altered lipid lamella arrangement contribute to weakened stratum corneum (Schuler et al., 2024). Disruption of the barrier increases the access of allergens, irritants, and microorganisms into the skin, leading to the activation of cutaneous immune cells and increased inflammation. Additionally, this barrier defect allows for increased colonisation by Staphylococcus aureus, a defining feature of AD flare-ups that promotes inflammation by secreting toxins and superantigens (Afshari et al., 2024). Therefore, impaired barrier function is both a contributing factor to AD inflammation and an outcome.

*II.Type 2 Immune Response*

AD immunopathogenesis is type 2 inflammation that is mediated by T helper 2 (Th2), group 2 innate lymphoid cells (ILC2s), mast cells, eosinophils, and basophils. The main cytokines - interleukin (IL)-4, IL-13, IL-5, and IL-31 provoke IgE synthesis, eosinophilic inflammation, barrier damage, and severe pruritus (Yue et al., 2024).

IL-4 and IL-13 decrease the production of filaggrin and structural components in the outermost layer of the skin (the epidermis), as well as the production of antimicrobial peptides. IL-4 and IL-13 caused an increase in the production of chemokines, leading to increased migration of inflammatory cells from the dermis into the epidermis (Schuler et al., 2024). IL-31 appears to play a part in chronic atopic dermatitis and elicits severe pruritus (itching), which could be due to cytokine interactions with the peripheral nervous system (Afshari et al., 2024). The reasons for this could be intense itching in some patients despite only minor skin inflammation. The immune response associated with chronic atopic dermatitis involves the Th2 pathway and other pathways. There is a distinct polarity in the immune reactions within chronic AD lesions; for example, IL-22 produced from Th22 results in acanthosis (hyperplasia of the epidermis), while Th1 and Th17 cytokines are found in the late stage of the disease, in specific subpopulations of atopic dermatitis (Asian atopic dermatitis) (Yue et al., 2024). This phenomenon illustrates considerable diversity in the immune response and significant variation in clinical manifestations among individual patients.

*III. JAK–STAT Signalling Pathway*

Several cytokines involved in AD pathology signal through the JAK/STAT pathway. These include IL-4, IL-13, IL-31, TSLP, and IFN; each uses one of several JAKs (JAK1, JAK2, JAK3, TYK2) to drive their downstream transcriptional responses that promote continued inflammation (He et al., 2024). Overexpression of the JAK-STAT pathway results in increased expression of inflammatory genes, decreased barrier function, and increased neuronal sensitivity, leading to chronic pruritus. The emphasis on the role of the JAK-STAT pathway in the pathogenesis of atopic dermatitis (AD) is key to supporting the rationale that JAK inhibitors, which can simultaneously inhibit the intracellular signalling of multiple cytokines (Yoon et al., 2024), will help treat AD. Moreover, the fast itch alleviation with JAK inhibitors is a reason to believe that the JAK-neural and JAK-inflammatory pathways contribute to the AD.

*IV. Microbiome Dysbiosis*

Patients with Alzheimer's disease exhibit marked differences in their microbiomes: reduced overall microbial diversity and increased Staphylococcus aureus (Yue et al., 2024). An increase in the number of these bacteria can stimulate an inflammatory response to exotoxins, proteases, and superantigens produced by S. aureus, thereby activating keratinocytes and other immune cells.

In addition, due to dysbiosis, the body has difficulty mounting an effective antimicrobial response and maintaining the structural integrity of tight junctions, both of which contribute to compromised barrier function (Afshari et al., 2024).

S. aureus flare episodes also often occur when there is an overgrowth of S. aureus, indicating that microbial factors play a crucial role in disease activity. Restoring the microbiome balance, improving barrier function, or providing targeted treatment for S. aureus overgrowth are emerging treatment options.

*V. Genetic and Environmental Factors*

Genetic susceptibility contributes significantly to AD risk. Studies have link FLG mutations, polymorphisms in cytokine genes (e.g. IL-4R$\alpha$, IL-13, TSLP) and immune regulatory pathways to the onset and severity of the disease (Schuler et al., 2024). Environmental exposures, e.g. pollution, cigarette smoke, household cleaning products, climate change and allergens stimulate the immune response

and worsen disease severity (Elahi et al., 2024). The combination of environmental triggers, the weakened state of the epithelial layer, and the immune system results in flare-ups of the disease; consequently, disease progression varies from person to person and from one geographic area to another.

*VI. The Barrier Immune Loop Concept*

Atopic dermatitis is an interlocking loop involving both barrier dysfunction and the immune response. Increased permeability to allergens and microorganisms is due to loss of barrier function leading to an increase in exposure to these substances, resulting in the activation of type 2 immunity as a response to this challenge through the generation of Th2 cytokines (IL-4, IL-13, and IL-31) from T helper cells that are then responsible for continued disruption of the skin's epidermal barrier, creating a self-perpetuating cycle of inflammation (Yue et al., 2024; Li et al., 2021).

Therefore, this conceptualisation of AD pathogenesis provides a basis for combining interventions that repair the barrier and selectively modulate the immune response to manage AD.

**Biologic Therapies in Atopic Dermatitis**

The treatment for atopic dermatitis now features a variety of "biologic" therapies, which represent a new class of mechanism-based treatments that target the immunological mechanisms involved in AD, rather than traditional systemic immunosuppressive therapy, which has a broader effect on the immune system. Biologic treatments have a selective mechanism that inhibits specific cytokines that drive type 2 inflammation. As a result of this mechanism of action, patients experience significant improvement in their clinical manifestations of atopic dermatitis (AD), including skin eruptions, itching, and disturbed sleep patterns, along with an overall improvement in quality of life. Currently, both the FDA and the EMA approve dupilumab and tralokinumab for the treatment of atopic dermatitis. Several other drugs are in the final stages of testing to be approved to treat AD, which include lebrikizumab and nemolizumab.

**Mechanism of Action of Biologic Therapies**

The Type 2 cytokine family (e.g., IL-4, IL-13, and IL-31) is an essential factor in the pathogenesis of Atopic Dermatitis by promoting disruption of the epidermal barrier, itching, and chronic inflammation. It may be possible to interrupt the inflammatory pathway of AD by targeting either one or more of these cytokines or their receptors, thereby restoring the equilibrium of normal skin function (Yue et al., 2024; Schuler et al., 2024).

- Dupilumab is a fully human monoclonal antibody targeting the IL-4 receptor alpha (IL-4R$\alpha$), thereby inhibiting signaling of both IL-4 and IL-13.
- Tralokinumab and lebrikizumab selectively neutralise IL-13.
- Nemolizumab targets IL-31 receptor A (IL-31RA), a key mediator of chronic pruritus.

These targeted mechanisms underpin the clinical precision and favourable safety profiles of biologics in comparison with traditional systemic therapies.

*I. Dupilumab*

As a treatment for atopic dermatitis (AD), Dupilumab works by blocking the action of interleukins 4 & 13 on their receptor (IL-4R$\alpha$) – which then prevents them from activating the Janus Kinase (JAK)-Signal Transducer and Activator of Transcription (STAT) pathway that produces type 2 inflammation (Schuler et al., 2024). Dupilumab was the first biologic approved as an option for moderate to severe AD, and it was tested more than all other biologics combined. Phase III studies (SOLO 1 and SOLO 2) showed that dupilumab resulted in significant reductions in eczema area and severity index (EASI) scores and in itching-related symptoms compared with placebo (Simpson et al., 2016). In another study (CHRONOS), dupilumab combined with topical steroids reduced the overall severity of AD disease for 52 weeks.

Dupilumab has shown efficacy in treating AD in both adults and children ≥6 months (Wang et al., 2024; Xu et al., 2023). A systematic review/meta-analysis concluded that dupilumab is safe and effective for the long-term treatment of AD in pediatric patients (Xu et al., 2023). Additional real-world evidence demonstrates that dupilumab also maintains its ability to treat AD for extended periods — especially for itching and involvement of the face, head, and neck regions (Kamata et al., 2021). Dupilumab appears to have few side effects. The most commonly reported are conjunctivitis, injection site reactions, and temporary increases in eosinophils.

Studies evaluating the long-term safety of dupilumab did not find an increase in the incidence of serious infections or malignancies (Kamata et al., 2021; Wang et al., 2024).

***II. Tralokinumab***

Tralokinumab is a human monoclonal antibody of the IgG4 class that specifically binds IL-13 and prevents it from binding to IL-13Rα1, thereby preventing the inflammatory reactions and barrier disruption caused by cytokines. In Phase 3 clinical studies ECZTRA 1 & ECZTRA 2, there was proof that tralokinumab resulted in a substantial improvement in EASI-75 scores, as well as symptomatically decreased itch and an improved quality of life for adult patients experiencing moderate to severe atopic dermatitis when compared to a control group receiving a placebo (Wollenberg et al., 2021) and continued over the course of long-term study extensions.

In adolescent populations, the ECZTRA 6 study demonstrated efficacy and safety outcomes comparable to those observed in adults (Paller et al., 2023). The results of the complete analysis of all participant data collected after participants received tralokinumab for up to 4.5 years indicated no evidence of an emerging or increased risk associated with this medication. There was also no increase in serious infection rates (Reich et al., 2025). Experts rate the treatment as both safe and tolerable. Side effects are primarily localised and/or secondary to drug administration and can occur at the injection site or due to reactions such as conjunctivitis. Data indicate consistent efficacy among elderly patients (Merola et al., 2023) and patients with predominant head-and-neck involvement (Chovatiya et al., 2025)

***III. Lebrikizumab***

Another monoclonal antibody against IL-13 with a mechanism of action similar to tralokinumab is lebrikizumab, which neutralises IL-13 by binding to distinct epitopes. Phase III studies have shown improved skin clearance and itch relief in patients treated every 2 weeks with lebrikizumab; a head-to-head network meta-analysis also indicated that, while lebrikizumab demonstrated slightly better results for skin symptoms than tralokinumab, both were viable options (Chen et al., 2023).

***IV. Nemolizumab***

Nemolizumab addresses the neuropathic component of AD associated with pruritus by targeting IL-31RA. It is well known that IL-31 plays a strong role in activating sensory nerves; therefore, Nemolizumab produces an anti-pruritic effect rapidly (often within days). While systematic review data support its potential utility in treating severe pruritus, there is no current widespread approval for AD (Yue et al., 2024)

Additional biologic agents are in earlier or later stages of clinical development, including anti-TSLP antibodies, anti-IL-22 agents targeting epidermal hyperplasia, and anti-OX40 monoclonal antibodies targeting T cell activation. Preliminary data from early-phase trials have shown positive results and will require longer-term studies to determine the clinical usage of these agents.

Biologics for AD generally exhibit favourable safety profiles compared with traditional immunosuppressants. In studies conducted to date, the two most common adverse events reported have been conjunctival inflammation and local injection site reactions. There has been no evidence of serious infections, malignancies, or other laboratory abnormalities indicative of an increased risk in either larger-scale clinical trials or long-term follow-up studies (Reich et al., 2025; Wollenberg et al., 2021; Simpson et al., 2016). Due to their better safety profile and predictable immunologic effects, clinicians recommend biologics for patients who require extended systemic therapy.

**JAK Inhibitors in Atopic Dermatitis**

JAK inhibitors comprise the second primary type of systemic targeted therapy for the treatment of moderate-to-severe atopic dermatitis (AD). They contrast with biologic therapies, which specifically inhibit individual cytokines by blocking the cell-surface receptors through which these cytokines interact with their target cells; JAK inhibitors are small-molecule drugs that can block intracellular signal transduction from a variety of cytokine receptors. These are receptors for Interleukins (IL)-4, IL-13, IL-31, interferons, and thymic stromal lymphopoietin (TSLP), which all contribute to the chronic inflammation, pruritus, and barrier dysfunction seen with atopic dermatitis (He et al., 2024). Three oral JAK inhibitors are currently in Phase 3 clinical trial testing for Atopic Dermatitis: abrocitinib, upadacitinib, and baricitinib. Abrocitinib and upadacitinib are highly selective for JAK1, whereas baricitinib inhibits both JAK1 and JAK2. These differences in JAK selectivity result in variations in efficacy, onset of action, and safety profiles.

**Mechanism of Action of JAK Inhibitors**

Cytokine signalling, which is critical in the pathogenesis of Alzheimer's disease (AD), utilises the JAK/STAT pathway. Cytokine signalling, which is vital to AD development, involves the JAK/STAT pathway. Activation of the JAK/STAT signalling pathway begins with the binding of a cytokine to its receptor, which then activates the JAK enzymes. Once activated, the JAK enzymes phosphorylate the STAT protein, allowing it to enter the cell nucleus. Within the nucleus, the STAT protein stimulates increased transcription of genes involved in inflammation (Yoon et al., 2024). This pathway can be blocked downstream and simultaneously block signalling for several cytokines, thereby rapidly reducing symptoms such as pruritus (often in days or less), decreasing inflammation, improving skin barrier function, and decreasing neuronal hypersensitivity. This broad mechanism explains the strong, rapid effects of JAK inhibitors in AD compared with those of biologics that target single cytokines.

***I. Abrocitinib***

Abrocitinib recently received approval as a selective JAK1 inhibitor for the treatment of adult and adolescent patients with moderate to severe atopic dermatitis (AD). Both the JADE MONO-1 and JADE MONO-2 phase 3 clinical trials provided proof of efficacy for both doses of abrocitinib (100mg & 200mg) by showing significant improvement in peak pruritus (itch) on the Numeric Rating Scale (NRS), Eczema Area Severity Index (EASI) score, and investigator global assessment (IGA) response vs. placebo (Silverberg et al., 2020; Simpson et al., 2020). Abrocitinib also has an advantage over other JAK inhibitors in terms of time to onset, as it relieved pruritus in a large number of patients within 24–48 hours of dosing.

Side effects: Abrocitinib is commonly associated with nausea, headaches, acne, and herpes zoster (the latter is dose-dependent). Meta-analyses have suggested that although a slightly higher early risk of nausea with abrocitinib seems to exist in comparison to other JAK inhibitors, the overall safety of this drug remains the same (Yoon et al., 2024).

***II. Upadacitinib***

Another selective JAK1 inhibitor used to treat AD is upadacitinib. Measure Up 1 and Measure Up 2 Phase III Clinical Trials showed that the upadacitinib once-daily doses of 15mg and 30mg were significantly better than placebo at improving patient response in all three endpoints: EASI-75, EASI-90, and IGA 0/1 (Simpson et al., 2022). In addition to potentially achieving faster onset of itch relief than biologics, upadacitinib achieved higher EASI-90 rates than dupilumab in some studies (Chen et al., 2023).

The side effects are similar to those of other JAK inhibitors, such as acne, nasopharyngitis, and herpes zoster. The higher doses (30 mg) are also associated with increased risks of laboratory abnormalities and infections (Tarafdar et al., 2024). A follow-up trial demonstrated that upadacitinib has a long-term effect of more than 140 weeks, and no safety concerns emerge (Irvine et al., 2025).

***III. Baricitinib***

Baricitinib, which targets both JAK1 and JAK2, may have a reduced availability in comparison to abrocitinib and upadacitinib for the treatment of AD. The effect size for baricitinib was slightly smaller than that of the other JAK inhibitors; however, baricitinib demonstrated clinical efficacy (EASI-75 & pruritus) at both 2mg and 4mg in adults (Yoon et al., 2024). Baricitinib in high-risk patients increased the prevalence rate of haematologic AEs and thromboembolic risk. Baricitinib has a similar amount of AEs as other JAK inhibitors (Tarafdar et al., 2024).

Studies conducted in real-world circumstances have demonstrated the high efficacy and rapid reduction in pruritus with JAK inhibitors, such as abrocitinib and upadacitinib (Zheng et al., 2024). There is considerable evidence across multiple studies using a network meta-analysis approach that JAKs may be superior to biologic agents for both time-to-relief and the degree of relief (Chen et al., 2023). However, biologics appear to be safer over the longer term than JAKs.

All class-wide safety issues associated with JAKs include Herpes zoster, rare but serious infections, lab abnormalities (lipid, platelet), rare venous thromboembolic events (dose-related), and major adverse cardiovascular events (MACE) - limited primarily to those at high risk. Overall, JAKs appear to be safe and well tolerated by the majority of AD patients without other severe comorbidities (Tarafdar et al., 2024; Yoon et al., 2024). In these patients, it is advisable to monitor blood lipid levels, complete blood counts (CBCs), liver function tests (LFTs), and cardiovascular risk factors.

## 4. CONCLUSION

The therapeutic landscape for atopic dermatitis has changed dramatically. From broad-acting immunosuppressive agents to targeted systemic treatments, how clinicians approach treatment has changed; as a result, treatment goals now include long-term disease control, reduction or elimination of pruritus, clear skin, and improved quality of life. The biologics and JAK inhibitors are the two most clinically essential developments in the treatment of atopic dermatitis; both have advantages and disadvantages, enabling clinicians to develop individualised treatment plans.

Due to the durable clinical responses that dupilumab, tralokinumab, and other biologic agents provide, as well as favourable terms of safety profiles, they are becoming a First-Line Systemic Therapeutic Option for atopic dermatitis patients who suffer from moderate to severe symptoms. Dupilumab is the most versatile across many age groups. Biologic agents are considered the optimal long-term maintenance therapy for patients with AD.

JAK inhibitors are faster acting, block several cytokine pathways and have higher capacity to reduce itching and achieve clear skin than biologics. Every JAK inhibitor requires ongoing risk assessment of adverse drug events, such as possible augmented infections and cardiovascular disease. The future of controlling atopic dermatitis will be a combination of both forms of therapy - Biologics for the long-term control of AD, and JAK Inhibitors as high-dose, short- to medium-term therapies to reduce inflammation quickly. Further studies are required to develop effective treatment sequences, continue surveillance, and conduct comparative effectiveness studies to continue improving the standard of care provided to individuals with atopic dermatitis.

**Acknowledgments**

The authors have no acknowledgments to disclose.

**Author's Contribution:**

Conceptualization: Aleksandra Korżel, Patrycja Kobrzyńska
Methodology: Julia Niedźwiecka, Natalia Cegielska
Formal Analysis: Jędrzej Mogilany, Gabriela Ragan
Sources: Natalia Cegielska, Kamil Źródłowski
Visualization: Ewelina Wojna, Aleksandra Korżel
Investigation: Gabriela Ragan, Karolina Górowska
Supervision: Patrycja Kobrzyńska, Jędrzej Mogilany
Validation: Kamil Źródłowski, Julia Niedźwiecka
Writing – Review & Editing: Karolina Górowska, Ewelina Wojna
Project administration: Patrycja Kobrzyńska, Jędrzej Mogilany
All authors have read and agreed with the published version of the manuscript.

**Informed consent**

Not applicable.

**Ethical approval**

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

**Funding**

This research did not receive any external funding like specific grant from funding agencies in the public, commercial, or nonprofit sectors.

**Conflict of interest**

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

**Data and materials availability**

All data associated with this study will be available based on reasonable request to the Corresponding Author.

## REFERENCES


1. Afshari M, Kolackova M, Rosecka M, Čelakovská J, Krejsek J. Unraveling the skin; a comprehensive review of atopic dermatitis, current understanding, and approaches. Front Immunol 2024;15:1361005. doi:10.3389/fimmu.2024.1361005
2. Chen Q, Cui L, Hu Y, Chen Z, Gao Y, Shi Y. Short-term efficacy and safety of biologics and Janus kinase inhibitors for patients with atopic dermatitis: A systematic review and meta-analysis. Heliyon 2023;9(11):e22014. doi:10.1016/j.heliyon.2023.e22014
3. Chovatiya R, Ribero S, Wollenberg A, Park CO, Silvestre JF, Hong HC, Seneschal J, Saeki H, Thyssen JP, Øland CB, Gjerum L, Maslin D, Blauvelt A. Long-Term Disease Control and Minimal Disease Activity of Head and Neck Atopic Dermatitis in Patients Treated with Tralokinumab up to 4 Years. Am J Clin Dermatol 2025;26(4):587-601. doi:10.1007/s40257-025-00931-1
4. Deva M, Netting MJ, Weidinger J, Brand R, Loh RK, Vale SL. A systematic review of guidelines for the management of atopic dermatitis in children. World Allergy Organ J 2024;17(12):100989. doi:10.1016/j.waojou.2024.100989
5. Elahi N, Astaneh ME, Ai J, Rizwan M. Atopic dermatitis treatment: A comprehensive review of conventional and novel bioengineered approaches. Int J Biol Macromol 2024;282(Pt 5):137083. doi:10.1016/j.ijbiomac.2024.137083
6. He Q, Xie X, Chen Q, Li W, Song Z, Wang X, Ma X, Zeng J, Guo J. Janus kinase inhibitors in atopic dermatitis: an umbrella review of meta-analyses. Front Immunol 2024;15:1342810. doi:10.3389/fimmu.2024.1342810
7. Irvine AD, Prajapati VH, Guttman-Yassky E, Simpson EL, Papp KA, Blauvelt A, Chu CY, Hong HC, Gold LFS, de Bruin-Weller M, Bieber T, Kabashima K, Rosmarin D, Sancho C, Calimlim BM, Grada A, Yang Y, Wu X, Levy G, Raymundo EM, Teixeira HD, Silverberg JI. Efficacy and Safety of Upadacitinib in Patients With Moderate-to-Severe Atopic Dermatitis: Phase 3 Randomized Clinical Trial Results Through 140 Weeks. Am J Clin Dermatol 2025;26(6):1003-1016. doi:10.1007/s40257-025-00975-3
8. Kamata M, Tada Y. A Literature Review of Real-World Effectiveness and Safety of Dupilumab for Atopic Dermatitis. JID Innov 2021;1(3):100042. doi:10.1016/j.xjidi.2021.100042
9. Li H, Zhang Z, Zhang H, Guo Y, Yao Z. Update on the Pathogenesis and Therapy of Atopic Dermatitis. Clin Rev Allergy Immunol 2021;61(3):324-338. doi:10.1007/s12016-021-08880-3
10. Merola JF, Butler DC, Mark T, Schneider S, Kim Y, Abuabara K. Safety and Efficacy of Tralokinumab in Older Adults with Moderate-to-Severe Atopic Dermatitis: A Secondary Analysis. JAMA Dermatol 2023;159(10):1119-1123. doi:10.1001/jamadermatol.2023.2626
11. Migliavaca CB, Lazzarini R, Stein C, Escher GN, de Gaspari CN, Dos Santos HWG, Myers DE, Lemeshow AR, Pinheiro MRT, Falavigna M, Pachito DV. Prevalence of Atopic Dermatitis: A Systematic Review and Meta-Analysis. Dermatitis 2025;36(6):575-582. doi:10.1089/derm.2024.0165
12. Paller AS, Flohr C, Cork M, Bewley A, Blauvelt A, Hong HC, Imafuku S, Schuttelaar MLA, Simpson EL, Soong W, Arlert P, Lophaven KW, Kurbasic A, Soldbro L, Vest NS, Wollenberg A. Efficacy and Safety of Tralokinumab in Adolescents With Moderate to Severe Atopic Dermatitis: The Phase 3 ECZTRA 6 Randomized Clinical Trial. JAMA Dermatol 2023;159(6):596-605. doi:10.1001/jamadermatol.2023.0627
13. Reich K, Langley RG, Salvador JFS, Staumont-Sallé D, Costanzo A, Pink AE, Paller AS, Katoh N, Wollenberg A, Warren RB, Blauvelt A, Øland CB, Tindberg AM, Gjerum L, Simpson EL. Safety of tralokinumab in patients with moderate-to-severe atopic dermatitis followed for up to 4.5 years: an integrated analysis of 8 clinical trials. Br J Dermatol 2025. doi:10.1093/bjd/ljaf309
14. Schuler CF 4th, Tsoi LC, Billi AC, Harms PW, Weidinger S, Gudjonsson JE. Genetic and Immunological Pathogenesis of Atopic Dermatitis. J Invest Dermatol 2024;144(5):954-968. doi:10.1016/j.jid.2023.10.019
15. Silverberg JI, Simpson EL, Thyssen JP, Gooderham M, Chan G, Feeney C, Biswas P, Valdez H, DiBonaventura M, Nduaka C, Rojo R. Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol 2020;156(8):863-873. doi:10.1001/jamadermatol.2020.1406
16. Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, Silverberg JI, Deleuran M, Kataoka Y, Lacour JP, Kingo K, Worm M, Poulin Y, Wollenberg A, Soo Y, Graham NM, Pirozzi G, Akinlade B, Staudinger H, Mastey V, Eckert L, Gadkari A, Stahl N, Yancopoulos GD, Ardeleanu M. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. N Engl J Med 2016;375(24):2335-2348. doi:10.1056/NEJMoa1610020
17. Simpson EL, Papp KA, Blauvelt A, Chu CY, Hong HC, Katoh N, Calimlim BM, Thyssen JP, Chiou AS, Bissonnette R, Stein

Gold LF, Wegzyn C, Hu X, Liu M, Liu J, Tenorio AR, Chu AD, Guttman-Yassky E. Efficacy and Safety of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis: Analysis of Follow-up Data From the Measure Up 1 and Measure Up 2 Randomized Clinical Trials. JAMA Dermatol 2022;158(4):404-413. doi:10.1001/jamadermatol.2022.0029

18. Simpson EL, Sinclair R, Forman S, Wollenberg A, Aschoff R, Cork M, Bieber T, Thyssen JP, Yosipovitch G, Flohr C, Magnolo N, Maari C, Feeney C, Biswas P, Tatulych S, Valdez H, Rojo R. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet 2020;396(10246):255-266. doi:10.1016/S0140-6736(20)30732-7
19. Tarafdar N, Sachdeva M, Dubale NM, Smythe C, Lytvyn Y, Maliyar K, Georgakopoulos JR, Mufti A, Yeung J. The Rate of Infections With Janus Kinase Inhibitor Treatment for Atopic Dermatitis: A Systematic Review and Meta-Analysis. J Cutan Med Surg 2024;28(1):83-85. doi:10.1177/12034754231211805
20. Wang M, Gao XH, Zhang L. A Review of Dupilumab in the Treatment of Atopic Dermatitis in Infants and Children. Drug Des Devel Ther 2024;18:941-951. doi:10.2147/DDDT.S457761
21. Wollenberg A, Blauvelt A, Guttman-Yassky E, Worm M, Lynde C, Lacour JP, Spelman L, Katoh N, Saeki H, Poulin Y, Lesiak A, Kircik L, Cho SH, Herranz P, Cork MJ, Peris K, Steffensen LA, Bang B, Kuznetsova A, Jensen TN, Østerdal ML, Simpson EL Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol 2021;184(3):437-449. doi:10.1111/bjd.19574
22. Xu Y, Guo L, Li Z, Wu S, Jiang X. Efficacy and safety profile of dupilumab for the treatment of atopic dermatitis in children and adolescents: A systematic review and meta-analysis. Pediatr Dermatol 2023;40(5):841-850. doi:10.1111/pde.15398
23. Yoon S, Kim K, Shin K, Kim HS, Kim B, Kim MB, Ko HC, Kim YH. The safety of systemic Janus kinase inhibitors in atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials. J Eur Acad Dermatol Venereol 2024;38(1):52-61. doi:10.1111/jdv.19426
24. Yue C, Zhou H, Wang X, Yu J, Hu Y, Zhou P, Zhao F, Zeng F, Li G, Li Y, Feng Y, Sun X, Huang S, He M, Wu W, Huang N, Li J. Atopic dermatitis: pathogenesis and therapeutic intervention. Med Comm 2024;5(12):e70029. doi:10.1002/mco2.70029
25. Zheng Y, Ding RL, Bu J. Effectiveness and safety of systemic therapy for moderate-to-severe atopic dermatitis in children and adolescent patients: a systematic review. Front Immunol 2024;15:1367099. doi:10.3389/fimmu.2024.1367099