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JAK INHIBITORS IN ATOPIC DERMATITIS: CURRENT EVIDENCE AND CLINICAL APPLICATIONS – A NARRATIVE REVIEW

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ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by epidermal barrier dysfunction, immune dysregulation, and severe pruritus that significantly impairs quality of life. In recent years, Janus kinase (JAK) inhibitors have emerged as an important therapeutic option for patients with moderate-to-severe AD due to their rapid onset of action and ability to inhibit multiple cytokine pathways involved in disease pathogenesis. This narrative review summarizes the current evidence regarding the mechanism of action, clinical efficacy, safety profile, and practical use of JAK inhibitors in AD. A literature search of recent clinical trials, systematic reviews, meta-analyses, and international guidelines was performed using PubMed, Scopus, and major dermatological journals. Available evidence demonstrates that selective JAK1 inhibitors such as upadacitinib and abrocitinib provide rapid reduction of pruritus and significant improvement in Eczema Area and Severity Index (EASI) scores. Baricitinib has also shown clinical benefit in selected patient populations. Despite strong efficacy, treatment with JAK inhibitors requires careful patient selection and monitoring because of potential risks including infections, laboratory abnormalities, cardiovascular events, and thromboembolic complications. Current evidence supports JAK inhibitors as valuable systemic therapies for patients with moderate-to-severe AD, particularly when rapid disease control is required. Long-term studies and real-world evidence remain essential for further optimization of treatment strategies and safety assessment.

KEYWORDS

Atopic Dermatitis, JAK Inhibitors, Upadacitinib, Abrocitinib, Baricitinib, Biologic Therapy

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1. Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease characterized by intense pruritus, recurrent eczematous lesions, xerosis, and substantial impairment in quality of life [1–4]. The prevalence of AD has increased significantly over recent decades, particularly in industrialized countries, making it one of the most common chronic inflammatory skin disorders worldwide [1,2]. It is estimated that AD affects approximately 15–20% of children and 2–10% of adults, although prevalence varies depending on geographic region, age, environmental exposure, and socioeconomic factors [1,2].

The disease imposes a considerable burden not only on patients but also on healthcare systems and caregivers. Persistent itching, sleep disturbance, visible skin lesions, and chronic relapsing symptoms often lead to psychological distress, reduced work productivity, impaired social functioning, and decreased overall well-being [3]. In many patients, AD is also associated with other atopic conditions, including asthma, allergic rhinitis, and food allergies, further increasing disease complexity [4].

The pathogenesis of AD is multifactorial and involves complex interactions between epidermal barrier dysfunction, immune dysregulation, environmental triggers, microbiome alterations, and genetic susceptibility [4,5]. One of the most important pathogenic mechanisms is type 2 helper T-cell (Th2)-mediated inflammation, particularly involving cytokines such as interleukin (IL)-4, IL-13, and IL-31 [5,6]. These cytokines contribute to epidermal barrier impairment, increased immunoglobulin E (IgE) production, eosinophilic inflammation, and severe pruritus [6].

Many cytokines implicated in AD pathogenesis exert their effects through intracellular signaling pathways mediated by Janus kinases (JAKs) and signal transducer and activator of transcription (STAT) proteins [7,8]. Dysregulation of the JAK-STAT pathway has therefore become an important therapeutic target in modern dermatology. Unlike biologic therapies that target single cytokines or receptors, JAK inhibitors interfere with intracellular signaling pathways shared by multiple cytokines involved in disease progression [8,9].

Conventional treatment strategies for AD include topical corticosteroids, topical calcineurin inhibitors, phototherapy, and systemic immunosuppressive agents such as cyclosporine, methotrexate, and azathioprine [4]. However, these therapies are often limited by inadequate long-term efficacy, adverse effects, or poor tolerability. In recent years, the introduction of targeted therapies, including biologics and JAK inhibitors, has significantly changed the therapeutic landscape of moderate-to-severe AD [9,10].

JAK inhibitors have emerged as promising systemic treatment options because of their rapid onset of action, oral administration, and ability to simultaneously inhibit multiple inflammatory pathways [8,10]. Clinical trials have demonstrated rapid reduction of pruritus, improvement in Eczema Area and Severity Index (EASI) scores, and enhancement of patient-reported quality-of-life outcomes [17–25]. Nevertheless, concerns remain regarding long-term safety, particularly risks of infections, cardiovascular events, venous thromboembolism, and laboratory abnormalities [27–31].

This narrative review summarizes current evidence regarding the role of JAK inhibitors in atopic dermatitis, focusing on disease pathophysiology, mechanism of action, clinical efficacy, safety profile, practical use, and future therapeutic perspectives.

2. Methodology

This narrative review was based on analysis of current literature regarding Janus kinase inhibitors in atopic dermatitis. Relevant publications were identified through searches of PubMed, Google Scholar, and clinical trial databases. Articles focusing on pathophysiology, efficacy, safety, and practical application of JAK inhibitors were included.

3. Pathophysiology of Atopic Dermatitis

3.1 Epidermal Barrier Dysfunction

Atopic dermatitis (AD) is strongly associated with significant impairment of epidermal barrier integrity involving both structural and functional abnormalities of the skin [4,10]. The epidermis in patients with AD demonstrates altered lipid composition, reduced ceramide levels, impaired keratinocyte differentiation, and abnormalities in the organization of the stratum corneum, all of which compromise its protective function [4].

One of the most important pathogenic factors is mutation of the filaggrin gene (FLG), which encodes a key structural protein responsible for epidermal barrier formation and maintenance of skin hydration [10]. Loss-of-function mutations in the filaggrin gene contribute to impaired keratinocyte differentiation, decreased natural moisturizing factor levels, and increased transepidermal water loss (TEWL), resulting in excessive skin dryness and enhanced skin permeability [10].

As a consequence, patients with AD demonstrate increased susceptibility to penetration of allergens, irritants, microorganisms, and environmental antigens through the epidermis [4]. This promotes activation of cutaneous immune responses and contributes to initiation and persistence of chronic skin inflammation [4,5]. Barrier dysfunction therefore represents not only a structural abnormality but also a major driver of immune activation and disease progression in AD.

Furthermore, epidermal barrier disruption contributes to microbial dysbiosis, particularly colonization with Staphylococcus aureus, which may additionally exacerbate inflammation through production of toxins and superantigens [5]. Repetitive scratching induced by severe pruritus further aggravates epidermal damage and perpetuates the inflammatory cycle characteristic of chronic AD [3,11].

3.2 Immune Dysregulation and Th2 Response

Immune dysregulation plays a central role in the pathogenesis of AD and involves complex interactions between innate and adaptive immune pathways [5]. The disease is characterized predominantly by activation of type 2 helper T-cell (Th2)-mediated immune responses, particularly during the acute phase of inflammation [5,6].

Th2 cytokines, especially interleukin (IL)-4 and IL-13, contribute significantly to disease development by promoting B-cell class switching toward immunoglobulin E (IgE) production, amplifying inflammatory responses, and further impairing epidermal barrier integrity [6]. These cytokines also suppress antimicrobial peptide production, thereby increasing susceptibility to bacterial and viral infections [6].

The predominance of Th2-mediated inflammation contributes to IgE-mediated hypersensitivity and impaired cellular immunity. However, AD is increasingly recognized as a heterogeneous and dynamic disease involving multiple inflammatory pathways [5]. In chronic disease stages, additional activation of Th1, Th17, and Th22 immune responses may occur, contributing to epidermal hyperplasia, chronic inflammation, and disease persistence [5].

These overlapping immune mechanisms partly explain the substantial clinical heterogeneity observed among patients with AD, including differences in disease severity, lesion morphology, treatment response, and chronic relapsing course.

3.3 Role of Cytokines

Cytokines are key mediators involved in both inflammation and symptom development in AD [5,6]. Among them, IL-4 and IL-13 are considered the principal drivers of type 2 inflammation and are directly associated with epidermal barrier dysfunction, increased IgE production, eosinophilic inflammation, and amplification of inflammatory signaling pathways [6].

IL-31 is strongly associated with pruritus, which represents one of the most burdensome and characteristic symptoms of AD [11]. IL-31 interacts directly with sensory neurons and contributes to chronic itch signaling, thereby worsening scratching behavior, epidermal damage, sleep disturbance, and overall disease severity [11].

Additional cytokines, including IL-21, IL-25, IL-33, and thymic stromal lymphopoietin (TSLP), may further modulate immune responses and contribute to disease progression [5]. These mediators not only sustain inflammation but also interact with neural pathways involved in itch perception and chronic neuroimmune dysregulation.

The complex cytokine network involved in AD pathogenesis highlights the multifactorial nature of the disease and provides the rationale for targeted therapeutic approaches aimed at interrupting inflammatory signaling pathways.

3.4 JAK-STAT Signaling Pathway

The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway plays a fundamental role in intracellular signaling involved in immune regulation, cytokine activity, and inflammation [7,8]. Numerous cytokines implicated in AD pathogenesis, including IL-4, IL-13, IL-31, interferons, and several other interleukins, signal through JAK-mediated pathways [7,8].

Following cytokine binding to its receptor, JAK kinases become activated through phosphorylation, subsequently leading to phosphorylation and activation of STAT proteins [7]. Activated STAT proteins dimerize and translocate into the nucleus, where they regulate transcription of genes associated with inflammatory and immune responses [7,13].

Dysregulation and excessive activation of the JAK-STAT pathway contribute to chronic inflammation, epidermal barrier dysfunction, and amplification of pruritus in AD [8]. Consequently, the JAK-STAT pathway represents a major therapeutic target and provides the biological rationale for the use of JAK inhibitors in patients with moderate-to-severe AD [8,12].

Unlike biologic therapies targeting individual cytokines or receptors, JAK inhibitors interfere with intracellular signaling pathways shared by multiple cytokines simultaneously [8]. This broader mechanism of action may explain their rapid clinical efficacy, particularly regarding itch reduction and improvement in inflammatory skin lesions.

3.5 Impact of Atopic Dermatitis on Quality of Life

Atopic dermatitis is not only a chronic inflammatory skin disorder but also a condition associated with substantial psychosocial, emotional, and functional burden [3,25]. Persistent pruritus, visible skin lesions, sleep disturbance, and recurrent disease exacerbations significantly impair quality of life in both pediatric and adult populations [3,25]. The chronic relapsing nature of the disease frequently affects daily functioning, social interactions, and long-term psychological well-being.

Pruritus is considered one of the most distressing symptoms of AD and represents a major contributor to reduced quality of life [11]. Severe itch often leads to chronic sleep deprivation, fatigue, irritability, impaired concentration, and decreased work or school productivity [3,11]. Repetitive scratching further worsens epidermal barrier dysfunction and perpetuates the inflammatory cycle, resulting in increased disease severity and psychological distress [4,11].

Patients with moderate-to-severe AD are also at increased risk of anxiety, depression, stress-related disorders, and social isolation [3]. Visible skin lesions may negatively affect self-esteem, body image, interpersonal relationships, and participation in social or professional activities. In children and adolescents, AD may additionally impair school performance and emotional development, while adult patients frequently report reduced occupational productivity and impaired social functioning [3,25].

The burden of AD extends beyond patients themselves and significantly affects caregivers and family members. Parents of children with severe AD often experience sleep disturbance, emotional stress, and financial burden associated with long-term treatment requirements and repeated medical consultations [3]. The need for continuous skincare routines, lifestyle modifications, and avoidance of environmental triggers may additionally reduce overall quality of life for both patients and caregivers.

Several studies have demonstrated that the impact of AD on quality of life may be comparable to or even greater than that observed in other chronic systemic diseases, including diabetes mellitus and cardiovascular disorders [3,25]. Consequently, assessment of patient-reported outcomes and quality-of-life measures should represent an integral component of clinical evaluation and treatment monitoring in patients with AD [25].

Effective disease control, particularly rapid reduction of pruritus and improvement of sleep quality, may substantially improve overall patient well-being and psychosocial functioning. In this context, targeted therapies such as JAK inhibitors may provide clinically meaningful benefits extending beyond improvement of skin lesions alone, particularly due to their rapid antipruritic effects and favorable impact on patient-reported outcomes [17–25].

4. Mechanism of Action of JAK Inhibitors

Janus kinase (JAK) inhibitors represent a novel class of targeted therapies that interfere with intracellular signaling pathways critically involved in the pathogenesis of atopic dermatitis (AD) [7,8,12]. Their mechanism of action is based on selective inhibition of JAK enzymes, which play a central role in mediating cytokine-driven inflammatory responses and immune regulation [7,13].

The JAK-STAT signaling pathway is activated by a broad range of cytokines implicated in AD pathogenesis, including interleukins, interferons, thymic stromal lymphopoietin (TSLP), and other inflammatory mediators [5–8]. Following cytokine binding to type I or type II cytokine receptors located on the cell surface, associated JAK kinases become activated through phosphorylation [7]. Activated JAK enzymes subsequently phosphorylate signal transducer and activator of transcription (STAT) proteins, which dimerize and translocate into the nucleus, where they regulate transcription of genes involved in inflammation, immune responses, and epidermal barrier regulation [7,12,13].

JAK inhibitors act by blocking the catalytic activity of JAK enzymes, thereby preventing phosphorylation and activation of STAT proteins and interrupting downstream intracellular signaling [8,13]. As a result, transcription of pro-inflammatory genes is suppressed, leading to reduced cytokine production, attenuation of inflammatory responses, and decreased immune cell activation [8,14].

One of the principal advantages of JAK inhibitors is their ability to simultaneously inhibit signaling from multiple cytokines involved in AD pathogenesis [8,14]. In contrast to biologic therapies that target a single cytokine or receptor, JAK inhibitors interfere with several inflammatory pathways at the intracellular level, including those mediated by IL-4, IL-13, IL-31, interferon-γ, and other cytokines [6,8]. This broader mechanism of action allows for more comprehensive suppression of inflammation and may partly explain the high clinical efficacy observed in moderate-to-severe AD [14,15].

Inhibition of IL-4 and IL-13 signaling contributes to reduction of Th2-mediated inflammation, decreased IgE production, and partial restoration of epidermal barrier integrity [6]. Blockade of IL-31 signaling is particularly important because IL-31 plays a major role in chronic pruritus, one of the most burdensome symptoms of AD [11]. Consequently, JAK inhibitors are often associated with rapid antipruritic effects observed shortly after treatment initiation [15,17].

Additionally, JAK inhibition may indirectly improve epidermal barrier function by decreasing inflammatory damage to keratinocytes and restoring normal skin homeostasis [5,15]. Reduced inflammatory signaling also contributes to decreased recruitment and activation of immune cells within the skin, leading to reduction of erythema, lichenification, edema, and excoriations characteristic of chronic AD lesions [14,16].

At the cellular level, JAK inhibitors reduce activation of T lymphocytes, dendritic cells, eosinophils, and other inflammatory cells involved in AD pathogenesis [5,14]. Suppression of cytokine signaling also decreases expression of chemokines responsible for inflammatory cell migration into the skin. These combined effects contribute to rapid clinical improvement and reduction of disease severity.

Importantly, the pharmacodynamic properties of JAK inhibitors enable rapid onset of therapeutic action. Clinical improvement, particularly regarding pruritus reduction, is frequently observed within days to weeks after treatment initiation [15,17]. This rapid response distinguishes JAK inhibitors from many conventional

systemic therapies and some biologic agents, which may require longer periods to achieve maximal efficacy [17–20].

Another important aspect is selectivity among different JAK inhibitors. Upadacitinib and abrocitinib primarily inhibit JAK1-dependent signaling pathways, whereas baricitinib inhibits both JAK1 and JAK2 [16–21]. Differences in selectivity may influence efficacy, safety profile, and risk of adverse effects. Greater selectivity toward JAK1 may theoretically allow stronger suppression of inflammatory signaling while minimizing hematologic adverse events associated with JAK2 inhibition [8,14].

Overall, the mechanism of action of JAK inhibitors provides a strong biological rationale for their use in moderate-to-severe atopic dermatitis. By targeting a central intracellular signaling pathway shared by multiple cytokines, these agents offer an effective and versatile therapeutic approach that addresses several key components of disease pathogenesis simultaneously [8,12,14].

5. Available JAK Inhibitors in Atopic Dermatitis

Several Janus kinase (JAK) inhibitors have been developed and approved for the treatment of moderate-to-severe atopic dermatitis (AD) [15–24]. Although these agents share a common mechanism of interfering with intracellular cytokine signaling pathways, they differ in their selectivity profiles, pharmacokinetic properties, clinical efficacy, and safety characteristics [8,14]. Currently available oral JAK inhibitors used in AD include upadacitinib, abrocitinib, and baricitinib, each targeting specific components of the JAK-STAT signaling pathway involved in disease pathogenesis.

The development of JAK inhibitors has significantly expanded therapeutic options for patients with moderate-to-severe AD, particularly for individuals who do not achieve adequate disease control with topical therapies, conventional systemic immunosuppressants, or biologic agents [15–24]. Their rapid onset of action, oral administration, and strong antipruritic effects represent important clinical advantages in dermatological practice.

5.1 Upadacitinib

Upadacitinib is an oral selective JAK1 inhibitor designed to maximize anti-inflammatory efficacy while minimizing off-target effects associated with broader JAK inhibition [16,18]. By selectively targeting JAK1-dependent cytokine signaling pathways, including those mediated by IL-4, IL-13, IL-31, and interferons, upadacitinib effectively suppresses Th2-driven inflammation and reduces disease activity in AD [6,18].

Clinical efficacy of upadacitinib has been demonstrated in several phase III randomized controlled trials, including the Measure Up 1, Measure Up 2, and AD Up studies [17–20]. These trials reported significant improvements in Eczema Area and Severity Index (EASI) scores, Investigator's Global Assessment (IGA) responses, reduction of pruritus, and enhancement of quality-of-life outcomes compared with placebo [19,20].

One of the most important advantages of upadacitinib is its rapid onset of action. Clinical improvement, particularly regarding itch reduction, may occur within the first days to weeks of treatment initiation [20]. In comparative studies, upadacitinib demonstrated faster symptom relief and superior efficacy in certain clinical outcomes compared with dupilumab, especially regarding rapid reduction of pruritus [33].

The most commonly reported adverse events associated with upadacitinib include acne, upper respiratory tract infections, nasopharyngitis, headache, and laboratory abnormalities such as elevated creatine phosphokinase and lipid levels [27–31]. Despite these concerns, overall tolerability has generally been favorable in appropriately selected patients.

5.2 Abrocitinib

Abrocitinib is another oral selective JAK1 inhibitor approved for the treatment of moderate-to-severe AD [19–22]. Similar to upadacitinib, abrocitinib selectively inhibits cytokine signaling pathways involved in type 2 inflammation, resulting in suppression of inflammatory activity and rapid reduction of disease symptoms [21].

Clinical efficacy of abrocitinib has been demonstrated in multiple randomized controlled trials included in the JADE clinical trial program, such as JADE MONO-1, JADE MONO-2, JADE COMPARE, and JADE TEEN [19–22]. These studies showed significant improvements in EASI scores, reduction of itch severity, and improved patient-reported quality-of-life outcomes compared with placebo [20–22].

A particularly important clinical characteristic of abrocitinib is its rapid antipruritic effect [20]. Reduction of itch intensity may occur within several days of therapy initiation, which significantly improves

sleep quality and overall patient well-being [20,22]. Because pruritus represents one of the most burdensome symptoms of AD, rapid itch control is considered a major therapeutic advantage.

In comparative analyses, higher-dose abrocitinib demonstrated efficacy comparable to or greater than certain biologic therapies in selected clinical endpoints [35]. Commonly reported adverse effects include nausea, headache, acne, herpes simplex infection, and transient laboratory abnormalities [27–30]. As with other JAK inhibitors, careful patient monitoring remains necessary during treatment.

5.3 Baricitinib

Baricitinib is an oral inhibitor of both JAK1 and JAK2, resulting in broader cytokine pathway inhibition compared with highly selective JAK1 inhibitors [21–24]. By inhibiting multiple inflammatory signaling pathways, baricitinib reduces cytokine-mediated inflammation associated with AD pathogenesis [23].

Clinical efficacy of baricitinib has been demonstrated in phase III studies such as the BREEZE-AD clinical trial program [21,23]. Patients treated with baricitinib experienced significant improvement in skin lesions, pruritus, sleep disturbance, and overall disease severity compared with placebo [22,23]. Improvement in patient-reported outcomes and quality-of-life measures was also observed [23].

Although the onset of action of baricitinib may be somewhat slower compared with highly selective JAK1 inhibitors such as upadacitinib or abrocitinib, it remains an effective therapeutic option for selected patients with moderate-to-severe AD [21–24]. Its broader cytokine inhibition profile may be beneficial in certain clinical scenarios involving complex inflammatory pathways.

The safety profile of baricitinib is generally consistent with other JAK inhibitors and includes increased risk of infections, laboratory abnormalities, and potential thromboembolic complications [27–31]. Careful patient selection and monitoring are therefore essential.

5.4 Emerging and Future JAK Inhibitors

In addition to currently approved therapies, several emerging JAK inhibitors and topical formulations are under investigation for the treatment of AD [36,37]. Topical JAK inhibitors may provide targeted anti-inflammatory effects with reduced systemic exposure and potentially improved safety profile [37].

Ongoing research focuses on improving selectivity, minimizing adverse effects, and optimizing long-term safety outcomes. Personalized treatment strategies based on disease phenotype, biomarkers, and patient-specific risk factors may further improve therapeutic outcomes in the future [36].

Overall, currently available JAK inhibitors provide effective and versatile treatment options for patients with moderate-to-severe atopic dermatitis [17–25]. Differences in selectivity, efficacy, pharmacodynamics, and safety profiles allow for individualized therapeutic approaches tailored to patient characteristics, comorbidities, and treatment goals.

6. Clinical Efficacy of JAK Inhibitors in Atopic Dermatitis

Janus kinase (JAK) inhibitors have demonstrated substantial clinical efficacy in the treatment of moderate-to-severe atopic dermatitis (AD) [17–35]. Their therapeutic effect results from inhibition of intracellular cytokine signaling pathways involved in type 2 inflammation, chronic pruritus, immune dysregulation, and epidermal barrier dysfunction [6–8]. Data from randomized clinical trials, extension studies, and meta-analyses consistently indicate that JAK inhibitors significantly improve both objective disease severity scores and patient-reported outcomes in patients with AD [23–26].

A major efficacy endpoint used in clinical trials is improvement in the Eczema Area and Severity Index (EASI), particularly achievement of EASI-75 and EASI-90 responses [23–26]. These endpoints represent at least 75% or 90% improvement from baseline disease severity and are widely accepted as markers of clinically meaningful treatment response. Available evidence demonstrates that oral JAK inhibitors significantly increase the proportion of patients achieving EASI-75 and EASI-90 responses compared with placebo [23–27].

Improvement in EASI scores reflects reduction in erythema, edema, excoriations, lichenification, and affected body surface area [25]. Significant improvements have also been observed in Investigator's Global Assessment (IGA) scores, Scoring Atopic Dermatitis (SCORAD) indices, and Dermatology Life Quality Index (DLQI) outcomes [25,26].

One of the most clinically important advantages of JAK inhibitors is their rapid onset of action [15,17,20]. Reduction in pruritus may occur within the first days or weeks after treatment initiation, which is particularly relevant because itch is one of the most burdensome symptoms of AD and strongly affects sleep quality, emotional well-being, work productivity, and daily functioning [3,11,25]. The rapid antipruritic effect

of JAK inhibitors is thought to result primarily from inhibition of IL-31-mediated signaling pathways involved in itch transmission [11,15].

Upadacitinib has demonstrated particularly robust efficacy in patients with moderate-to-severe AD [17–20]. Phase III trials, including Measure Up 1, Measure Up 2, and AD Up, reported significant improvements in EASI responses, Investigator's Global Assessment outcomes, reduction of pruritus, and improvement in quality-of-life measures compared with placebo [17–20]. In comparative analyses, upadacitinib also demonstrated rapid clinical responses and, in certain endpoints, superior efficacy compared with dupilumab [33].

Abrocitinib has likewise shown clinically meaningful improvements in disease severity, itch intensity, and patient-reported outcomes in randomized controlled trials included in the JADE clinical trial program [19–22]. Studies such as JADE MONO and JADE COMPARE demonstrated substantial improvement in EASI scores and rapid reduction in pruritus compared with placebo [20–22]. The rapid itch reduction associated with abrocitinib represents an important therapeutic advantage because persistent pruritus significantly contributes to sleep disturbance and impaired quality of life [3,25].

Baricitinib, a less selective inhibitor targeting both JAK1 and JAK2 pathways, has also demonstrated efficacy in moderate-to-severe AD [21–24]. Clinical trials reported improvement in disease severity, reduction of inflammatory skin lesions, and enhancement of patient-reported outcomes [21–24]. Although baricitinib is generally considered somewhat less potent than highly selective JAK1 inhibitors, it remains an effective therapeutic option for selected patient populations [23,24].

In addition to objective clinical improvement, JAK inhibitors substantially improve patient quality of life [3,25]. Reduction in pruritus, improvement in sleep quality, and better disease control may significantly decrease psychological burden, fatigue, anxiety, and social impairment associated with chronic AD [25,28]. These effects are particularly important in patients with moderate-to-severe disease, in whom persistent symptoms frequently impair occupational productivity, social relationships, and emotional well-being.

Increasing attention has also been directed toward the durability of therapeutic response during long-term treatment [41,49,50]. Available extension studies suggest that clinical improvements achieved during the initial treatment phase may be maintained over prolonged periods, particularly with continuous therapy [41]. Sustained reductions in EASI scores, persistent itch control, and long-term improvement in patient-reported outcomes have been observed in extension trials evaluating upadacitinib and abrocitinib [41,49].

However, differences between individual JAK inhibitors have been reported [32,35,50]. Selective JAK1 inhibitors such as upadacitinib and abrocitinib generally appear to produce faster and more pronounced clinical responses compared with less selective agents such as baricitinib [32,35]. These differences may be related to stronger inhibition of cytokines predominantly involved in type 2 inflammation and itch signaling [6,8].

Dose-dependent effects have also been observed in clinical studies [17–22]. Higher doses of JAK inhibitors are usually associated with greater efficacy and faster improvement of symptoms; however, increased efficacy may also be accompanied by higher incidence of adverse events [27–31]. Consequently, treatment decisions should balance therapeutic efficacy against potential safety concerns.

Emerging evidence further suggests that JAK inhibitors may be particularly beneficial in patients with severe disease or in individuals who previously failed conventional systemic therapies or biologic treatment [52]. Their rapid onset of action, oral administration, and broad anti-inflammatory effects make them especially useful in patients with substantial disease burden and urgent need for symptom control [17–25].

Long-term extension studies indicate that sustained disease control can be achieved with continued therapy, although relapse after treatment discontinuation has been observed in some patients [41,53]. These findings emphasize the importance of individualized maintenance strategies and long-term treatment planning in chronic AD management [53].

Overall, current evidence strongly supports JAK inhibitors as highly effective systemic therapies for moderate-to-severe atopic dermatitis [17–35]. Their ability to rapidly reduce pruritus, improve inflammatory skin lesions, and enhance patient quality of life has established them as an important component of modern targeted therapy in dermatology.

7. Safety and Adverse Effects of JAK Inhibitors in Atopic Dermatitis

The safety profile of Janus kinase (JAK) inhibitors in atopic dermatitis (AD) has been extensively evaluated in randomized clinical trials, meta-analyses, extension studies, and emerging real-world evidence [27–41]. Overall, these agents are considered effective and generally well tolerated in appropriately selected patients; however, because of their systemic immunomodulatory mechanism, careful assessment of potential risks remains essential before and during therapy [27,28,35].

The most commonly reported adverse events associated with JAK inhibitor therapy include upper respiratory tract infections, nasopharyngitis, headache, nausea, acne, and laboratory abnormalities [27–30]. Herpes simplex virus reactivation and herpes zoster infection have also been observed and are considered clinically important adverse effects associated with JAK inhibition [30,35,37]. The increased susceptibility to viral infections is biologically plausible because the JAK-STAT signaling pathway plays a central role in antiviral immune responses and interferon-mediated immunity [7,8].

Most infectious complications reported during clinical trials have been mild to moderate in severity [27–30]. Nevertheless, serious infections may occur, particularly in patients with advanced age, significant comorbidities, concomitant immunosuppressive therapy, or impaired immune function [35,36]. Consequently, baseline screening for tuberculosis, hepatitis B and C infection, and other infectious risk factors is recommended prior to treatment initiation [43,47].

Laboratory abnormalities are another important aspect of JAK inhibitor safety monitoring [36,38]. Reported changes include alterations in lipid profiles, elevations of liver enzymes, increased creatine phosphokinase levels, neutropenia, lymphopenia, and mild anemia [36,38]. Although many of these abnormalities are clinically manageable and often reversible, routine laboratory assessment is necessary to ensure patient safety during long-term therapy [38,47]. Monitoring is particularly important in patients with preexisting metabolic disorders, hepatic dysfunction, or cardiovascular comorbidities.

A major safety concern associated with systemic JAK inhibitors is the potential risk of serious infections, malignancy, major adverse cardiovascular events (MACE), and venous thromboembolism (VTE) [31,39,42]. Regulatory warnings were introduced following safety signals observed primarily in patients with rheumatoid arthritis receiving tofacitinib therapy; however, because several JAK inhibitors share similar intracellular mechanisms of action, caution has been extended to the entire drug class [31,39].

The U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) recommend individualized risk assessment prior to treatment initiation, especially in patients with cardiovascular risk factors, smoking history, previous thromboembolic events, advanced age, or history of malignancy [31,39]. Although current evidence suggests that these severe complications appear less frequent in patients with atopic dermatitis compared with rheumatologic populations, careful patient selection remains essential [35,42].

Long-term safety considerations are particularly important because AD often requires prolonged systemic therapy [35,41]. While randomized controlled trials provide valuable short-term safety data, real-world evidence and long-term extension studies are increasingly important for evaluating chronic treatment outcomes in broader patient populations [40,41]. Such studies may better reflect routine clinical practice and include patients with comorbidities frequently excluded from clinical trials.

Differences in selectivity among JAK inhibitors may also influence their safety profiles [8,14]. Selective JAK1 inhibitors such as upadacitinib and abrocitinib are generally considered to demonstrate more favorable safety characteristics compared with less selective agents because they may reduce off-target effects associated with inhibition of JAK2 or JAK3 pathways [14]. However, additional long-term comparative studies remain necessary to confirm these observations.

Vaccination status should be carefully assessed before initiation of JAK inhibitor therapy, particularly regarding herpes zoster vaccination [43,55]. Preventive strategies, including appropriate immunization and patient education, may reduce the risk of treatment-related infectious complications. Patients should also be informed about symptoms suggestive of infection, thrombosis, or cardiovascular events and advised to seek medical attention promptly if such symptoms occur [47,48].

Patient selection is especially important in individuals with significant cardiovascular disease, metabolic syndrome, obesity, smoking history, or previous thromboembolic events [42,54]. In these populations, clinicians should carefully evaluate the benefit-risk balance and consider alternative treatment strategies or intensified monitoring when appropriate [42].

Despite these concerns, the overall benefit-risk profile of JAK inhibitors remains favorable for many patients with moderate-to-severe AD, particularly in those who have failed topical therapies, conventional systemic agents, or biologic treatment [17–25]. Their rapid antipruritic effects, oral administration, and strong

clinical efficacy may significantly improve quality of life and disease control in appropriately selected individuals.

As real-world evidence continues to accumulate, a more comprehensive understanding of long-term safety outcomes will emerge [40,41]. These data will be essential for refining treatment guidelines, improving patient selection, and optimizing monitoring strategies for the use of JAK inhibitors in routine dermatological practice.

8. Patient Selection and Practical Use of JAK Inhibitors in Atopic Dermatitis

Appropriate patient selection is essential for optimizing both the therapeutic efficacy and safety of Janus kinase (JAK) inhibitors in atopic dermatitis (AD) [44–48]. These agents are primarily indicated for patients with moderate-to-severe disease who demonstrate inadequate response, intolerance, or contraindications to conventional topical therapies and, in many cases, to systemic immunosuppressive treatments or biologic agents [44,45].

Moderate-to-severe AD is typically defined using a combination of objective clinical scores and patient-reported outcomes, including elevated Eczema Area and Severity Index (EASI) scores, extensive body surface area involvement, severe pruritus, sleep disturbance, and substantial impairment of quality of life [3,25,44]. Patients experiencing persistent symptoms despite optimized topical treatment are considered appropriate candidates for systemic therapy, including JAK inhibitors [44].

One of the major clinical advantages of JAK inhibitors is their rapid onset of action, particularly regarding itch reduction [17–25]. For this reason, these agents may be considered as first-line systemic therapy in selected patients requiring rapid disease control, including individuals with severe pruritus, acute exacerbations, or widespread inflammatory skin lesions [17,18,20]. Rapid symptom improvement may significantly improve sleep quality, psychological well-being, and overall patient functioning.

When selecting between JAK inhibitors and biologic therapies, several factors should be considered, including disease phenotype, comorbidities, patient preferences, treatment accessibility, and individual risk profile [32,44–46]. Oral administration represents an important practical advantage of JAK inhibitors and may be preferred by patients who wish to avoid injectable therapies [32]. Conversely, biologic therapies such as dupilumab may be more appropriate in patients with significant cardiovascular risk factors, previous thromboembolic events, or concerns regarding systemic immunomodulation [42,46].

Baseline evaluation prior to initiation of JAK inhibitor therapy is essential for minimizing treatment-related complications [43,47,48]. Comprehensive assessment should include detailed medical history, evaluation of cardiovascular and thromboembolic risk factors, previous malignancy, smoking status, chronic infections, and concomitant medications [42,47]. Laboratory investigations typically include complete blood count, liver function tests, renal function assessment, lipid profile, and screening for infectious diseases such as tuberculosis, hepatitis B, and hepatitis C [43,47].

Monitoring during therapy is equally important to ensure long-term safety [47,48]. Periodic laboratory testing should be performed to detect potential abnormalities including lymphopenia, neutropenia, elevated liver enzymes, and dyslipidemia [42,47]. Clinical monitoring should additionally focus on symptoms suggestive of infection, thromboembolic complications, cardiovascular events, or other adverse effects associated with JAK inhibition [31,42].

Vaccination status should also be evaluated prior to treatment initiation [43]. In particular, vaccination against herpes zoster may be considered in selected patients because JAK inhibitors have been associated with increased risk of viral reactivation [30,43]. Preventive strategies and patient counseling may substantially reduce the likelihood of treatment-related complications and improve overall safety outcomes.

Certain patient populations require special caution when considering JAK inhibitor therapy [31,42]. Older adults, patients with significant cardiovascular disease, history of malignancy, previous thromboembolic events, or multiple cardiovascular risk factors may require closer monitoring or alternative therapeutic approaches [42]. Shared decision-making between physician and patient therefore remains crucial to balance potential therapeutic benefits against possible risks [46].

Treatment adherence and patient education are additional important aspects of successful clinical management. Patients should be informed about possible adverse effects, importance of regular laboratory monitoring, and the need to promptly report concerning symptoms such as fever, dyspnea, chest pain, or signs of infection [47,48]. Effective communication may improve treatment adherence, patient satisfaction, and long-term therapeutic outcomes.

In routine clinical practice, JAK inhibitors are often incorporated into broader management strategies that include topical therapies, skin barrier repair, trigger avoidance, and lifestyle modifications [44]. Combination treatment approaches may improve disease control while reducing the need for prolonged high-dose systemic therapy. Ultimately, individualized treatment planning remains essential and should account for disease severity, patient expectations, comorbidities, previous treatment response, and long-term management goals.

Overall, JAK inhibitors represent a valuable addition to the therapeutic armamentarium for moderate-to-severe atopic dermatitis [17–25]. Careful patient selection, comprehensive baseline evaluation, appropriate monitoring, and individualized treatment strategies are essential for maximizing therapeutic benefits while minimizing potential risks in everyday clinical practice.

9. Comparison with Biologic Therapies

The development of biologic therapies and Janus kinase (JAK) inhibitors has significantly transformed the management of moderate-to-severe atopic dermatitis (AD) over recent years [32–46]. Biologic agents, particularly dupilumab, represented the first targeted systemic therapies approved specifically for AD and remain an important component of current treatment strategies [44–46]. However, JAK inhibitors provide a fundamentally different therapeutic approach by targeting intracellular cytokine signaling pathways shared by multiple inflammatory mediators involved in AD pathogenesis [8,42].

Dupilumab is a monoclonal antibody directed against the interleukin-4 receptor alpha (IL-4Rα) subunit, thereby inhibiting signaling mediated by IL-4 and IL-13, two key cytokines involved in type 2 inflammation [6,44]. In contrast, JAK inhibitors interfere with intracellular signaling downstream of multiple cytokine receptors, including pathways involving IL-4, IL-13, IL-31, interferons, and additional inflammatory mediators [7,8]. This broader mechanism of action may partly explain the rapid and extensive clinical responses observed with JAK inhibitors, particularly regarding reduction of pruritus [8,42,43].

One of the most clinically relevant differences between these therapeutic classes is the speed of treatment response [17–25]. Several studies suggest that selective JAK1 inhibitors may provide faster improvement of symptoms compared with biologic therapies, particularly regarding itch reduction [33,35,43]. In a head-to-head clinical trial, upadacitinib demonstrated superior efficacy compared with dupilumab over a 16-week treatment period in adults with moderate-to-severe AD, with greater improvement in EASI scores and more rapid reduction of pruritus [33]. Similarly, abrocitinib demonstrated rapid itch improvement compared with dupilumab in selected clinical endpoints, especially at higher therapeutic doses [35,44].

Rapid antipruritic effects represent an especially important advantage because chronic itch substantially contributes to sleep disturbance, fatigue, impaired concentration, emotional distress, and reduced quality of life in patients with AD [3,11,25]. Consequently, JAK inhibitors may be particularly beneficial in patients with severe pruritus or acute disease exacerbations requiring rapid symptom control [17–25].

Despite these efficacy advantages, biologic therapies generally appear to demonstrate a more favorable long-term safety profile compared with systemic JAK inhibitors [42,46]. Dupilumab is most commonly associated with injection-site reactions, conjunctivitis, and transient eosinophilia, whereas JAK inhibitors may be associated with infections, herpes zoster reactivation, laboratory abnormalities, and rare but potentially serious complications such as thromboembolic and cardiovascular events [27–31,42].

Another important difference concerns monitoring requirements. Biologic therapies usually do not require extensive laboratory monitoring during treatment, while systemic JAK inhibitors necessitate regular assessment of blood counts, liver enzymes, lipid profiles, and additional safety parameters [38,47]. As a result, biologics may be preferred in patients with increased cardiovascular risk, previous thromboembolic events, or concerns regarding systemic immunomodulation [42].

Route of administration also represents a clinically relevant factor influencing treatment selection [32,44]. JAK inhibitors are administered orally, which many patients may prefer due to convenience and avoidance of injections. Oral administration may additionally improve treatment adherence in selected individuals. In contrast, biologics require subcutaneous administration at regular intervals, although their longer dosing schedules may be advantageous for some patients [44].

Treatment selection should therefore remain highly individualized and account for disease severity, previous treatment response, patient preference, comorbidities, safety considerations, accessibility, and feasibility of long-term monitoring [42,44–46]. Patients requiring rapid symptom control, particularly rapid itch reduction, may benefit more from JAK inhibitors, whereas biologic therapies may be preferable in individuals with increased cardiovascular or thromboembolic risk profiles [42].

Importantly, biologic therapies and JAK inhibitors should not necessarily be viewed as competing treatment modalities but rather as complementary therapeutic options within an increasingly personalized treatment landscape [36,46]. The growing availability of targeted therapies allows clinicians to tailor treatment strategies according to individual patient characteristics and therapeutic goals.

As understanding of AD pathogenesis continues to evolve, future treatment algorithms will likely become increasingly personalized, integrating biomarkers, disease phenotype, comorbidities, and patient-specific risk factors into therapeutic decision-making [36]. Both biologics and JAK inhibitors are expected to remain central components of modern systemic therapy for moderate-to-severe atopic dermatitis.

10. Limitations of Current Evidence

Despite substantial progress in the development and clinical evaluation of Janus kinase (JAK) inhibitors for atopic dermatitis (AD), several important limitations of the current evidence should be acknowledged [40,41,49,50]. Although available studies demonstrate high efficacy and generally acceptable safety profiles, many unresolved questions remain regarding long-term outcomes, optimal treatment strategies, and safety in broader patient populations.

One of the major limitations is that the majority of currently available evidence originates from randomized controlled trials with relatively short follow-up periods [17–35]. While these studies consistently demonstrate significant short-term efficacy regarding reduction of disease severity and pruritus, long-term data concerning sustained therapeutic response, relapse rates after treatment discontinuation, and cumulative safety risks remain limited [41,49]. Because atopic dermatitis is a chronic relapsing disease often requiring prolonged systemic treatment, understanding the long-term consequences of continuous JAK inhibition is essential for future therapeutic decision-making.

Real-world safety outcomes may differ from those observed in controlled clinical trials [40,49]. Trial populations are typically highly selected and frequently exclude patients with significant cardiovascular disease, malignancy history, chronic infections, metabolic syndrome, or elevated thromboembolic risk [42]. Consequently, clinical trial findings may not fully reflect outcomes in routine dermatological practice, where patients often present with multiple comorbidities and more complex clinical characteristics [40].

Another important limitation is the heterogeneity of study design across available clinical trials [23–35]. Differences in inclusion criteria, baseline disease severity, prior treatment exposure, dosing regimens, concomitant topical therapy, and outcome assessment methods may complicate direct comparisons between studies and therapeutic agents. Although standardized endpoints such as EASI-75, EASI-90, Investigator's Global Assessment (IGA), and Dermatology Life Quality Index (DLQI) are commonly used, variability in study methodology remains a challenge for interpretation of comparative efficacy data [25,26].

Head-to-head comparative studies between individual JAK inhibitors and between JAK inhibitors and biologic therapies also remain relatively limited [32–35]. Although available evidence suggests that selective JAK1 inhibitors may provide faster symptom control than some biologics, more robust comparative studies are necessary to determine optimal positioning of these agents within treatment algorithms [33,35]. Additional research comparing long-term efficacy, treatment persistence, relapse frequency, and safety profiles would significantly improve evidence-based therapeutic decision-making.

Long-term safety concerns continue to represent one of the most important unresolved issues associated with JAK inhibitor therapy [31,39,42]. Potential risks including serious infections, herpes zoster reactivation, malignancy, major adverse cardiovascular events (MACE), and venous thromboembolism (VTE) require ongoing investigation [31,42]. Although current evidence suggests that these complications appear relatively uncommon in patients with AD, the relatively young age and lower comorbidity burden of trial populations may partially underestimate real-world risks [40,41].

In addition, the influence of differences in JAK selectivity on long-term efficacy and safety remains incompletely understood [8,14]. Selective JAK1 inhibitors are generally considered to demonstrate more favorable efficacy and safety profiles compared with less selective agents; however, direct comparative evidence remains limited [14,32]. Future studies are needed to better define the clinical implications of selective versus nonselective JAK inhibition in dermatological practice.

Another significant limitation is the lack of validated biomarkers capable of reliably predicting treatment response, adverse events, or long-term outcomes [36]. Atopic dermatitis is a highly heterogeneous disease involving multiple inflammatory pathways and clinical phenotypes. Consequently, patients may demonstrate substantial variability in response to systemic therapy. Identification of predictive biomarkers could facilitate

personalized treatment selection and improve therapeutic outcomes while minimizing unnecessary exposure to ineffective therapies.

Economic considerations also represent an important limitation influencing access to treatment [44–46]. JAK inhibitors and biologic therapies remain expensive treatment options in many healthcare systems, potentially limiting their availability for some patient populations. Cost-effectiveness analyses and healthcare policy considerations may therefore influence future positioning of these therapies in clinical practice.

Furthermore, limited evidence is currently available regarding the use of JAK inhibitors in specific populations such as pregnant women, elderly patients with multiple comorbidities, pediatric populations, and individuals with severe immunologic or oncologic conditions [42]. Additional studies focusing on these vulnerable patient groups are necessary to better establish safety and efficacy profiles in real-world clinical settings.

Despite these limitations, current evidence strongly supports JAK inhibitors as highly effective targeted therapies for moderate-to-severe atopic dermatitis [17–35]. Nevertheless, further long-term studies, pharmacovigilance programs, biomarker research, and real-world observational data remain essential for optimizing patient selection, improving safety monitoring, and refining future treatment algorithms.

Overall, while JAK inhibitors represent a major therapeutic advancement in modern dermatology, continued research will be crucial to better define their long-term role in the management of atopic dermatitis and to further improve individualized patient care.

11. Future Perspectives

Future management of atopic dermatitis (AD) will likely focus on increasingly personalized therapeutic strategies, optimization of long-term safety, earlier disease control, and integration of targeted therapies into comprehensive patient-centered management plans [36,47]. The rapidly expanding number of biologic therapies and Janus kinase (JAK) inhibitors has significantly transformed the therapeutic landscape of AD and created new opportunities for individualized treatment selection based on disease phenotype, severity, comorbidities, patient preferences, and specific therapeutic goals.

One of the most important future directions involves the development of more selective JAK inhibitors with improved efficacy and safety profiles [8,14]. Greater selectivity toward JAK1-dependent signaling pathways may allow stronger suppression of cytokines involved in type 2 inflammation while minimizing off-target effects associated with inhibition of other JAK isoforms [14]. Improved selectivity could potentially reduce the incidence of hematologic abnormalities, thromboembolic complications, and other systemic adverse events.

Another promising area of research is the development of topical JAK inhibitor formulations [37,48]. Topical therapies may provide effective local suppression of inflammation while reducing systemic drug exposure and minimizing systemic adverse effects. This approach may be especially beneficial for patients with mild-to-moderate disease, localized lesions, or contraindications to systemic therapy [37]. Topical JAK inhibitors may also become useful components of combination treatment strategies together with systemic therapies and skin barrier repair approaches.

An additional important direction involves identification of biomarkers capable of predicting treatment response and long-term outcomes [36,47]. Atopic dermatitis is a clinically and immunologically heterogeneous disease characterized by substantial interindividual variability in inflammatory pathways and therapeutic response. Biomarker-guided treatment strategies could allow clinicians to more precisely select between biologic therapies, JAK inhibitors, and emerging targeted agents according to patient-specific disease characteristics [36].

Advances in molecular medicine and immunophenotyping may facilitate development of precision medicine approaches in AD management. Future therapeutic algorithms may incorporate genomic, transcriptomic, and immunologic profiling to optimize treatment selection and reduce unnecessary exposure to ineffective therapies. Such approaches could improve clinical efficacy, minimize adverse events, and reduce healthcare costs associated with chronic disease management.

Long-term safety monitoring will remain critically important for the future use of systemic JAK inhibitors [31,39,42]. Although current clinical trials demonstrate strong efficacy and generally manageable safety profiles, ongoing pharmacovigilance programs and real-world observational studies remain necessary to better characterize risks associated with infections, malignancy, cardiovascular events, and venous thromboembolism in broader patient populations [40,41,49]. Future data will be essential for refining patient selection criteria and optimizing long-term monitoring strategies.

Further research is also needed regarding treatment sequencing and combination therapy [44–46]. It remains unclear which patients may benefit most from early use of JAK inhibitors compared with biologics or conventional systemic therapies. Future studies comparing treatment algorithms, maintenance strategies, and switching approaches between targeted therapies may significantly improve evidence-based clinical decision-making.

Another important perspective concerns pediatric populations and early intervention strategies. Increasing evidence suggests that early and effective control of inflammation may influence long-term disease progression and potentially reduce development of the so-called "atopic march," including asthma and allergic rhinitis [4]. Consequently, future studies may investigate whether earlier introduction of targeted therapies could modify long-term disease outcomes in selected high-risk patients.

In addition to pharmacological advances, future management strategies will likely emphasize comprehensive multidisciplinary care integrating systemic therapy, topical treatment, skin barrier repair, lifestyle modification, trigger avoidance, psychological support, and patient education [44]. The ultimate therapeutic goal extends beyond simple reduction of skin lesions and includes sustained disease control, reduction of pruritus, improvement of sleep quality, psychosocial well-being, and overall quality of life [3,25].

Digital medicine and teledermatology may also become increasingly important in long-term AD management. Remote monitoring tools, electronic patient-reported outcomes, and digital adherence tracking could improve disease monitoring and facilitate individualized treatment adjustments in routine clinical practice.

Overall, the future of atopic dermatitis management is likely to become increasingly personalized, multidisciplinary, and biomarker-driven [36,47]. Continued advances in targeted therapy and precision medicine may substantially improve long-term disease control, patient safety, and quality of life for individuals affected by moderate-to-severe atopic dermatitis.

12. Conclusions

Janus kinase (JAK) inhibitors represent a major therapeutic advancement in the management of moderate-to-severe atopic dermatitis (AD) [17–35]. By targeting intracellular cytokine signaling through the JAK-STAT pathway, these agents directly interfere with key mechanisms involved in inflammation, pruritus, immune dysregulation, and disease progression [7,8,12]. Their introduction has substantially expanded the therapeutic landscape of AD and contributed to the development of more individualized and targeted treatment strategies in modern dermatology.

Current evidence strongly supports the efficacy of JAK inhibitors in improving disease severity, reducing itch intensity, and enhancing patient quality of life [17–35]. Significant improvements in Eczema Area and Severity Index (EASI) responses, Investigator's Global Assessment outcomes, sleep quality, and patient-reported symptoms have been consistently demonstrated in randomized clinical trials and meta-analyses [23–26]. In particular, their rapid antipruritic effects represent one of the most clinically meaningful advantages of this therapeutic class [15,17,20].

Unlike conventional systemic immunosuppressive therapies, JAK inhibitors provide targeted modulation of inflammatory pathways directly involved in AD pathogenesis [8,14]. Furthermore, their ability to inhibit signaling from multiple cytokines simultaneously may explain their broad clinical efficacy and rapid symptom control compared with therapies targeting a single cytokine pathway [8,42]. Oral administration additionally represents a practical advantage for many patients, particularly individuals who prefer noninjectable treatment options or require rapid disease control [32].

From a clinical perspective, one of the most important therapeutic benefits of JAK inhibitors lies in their ability to address both objective inflammatory skin lesions and subjective symptoms, especially chronic pruritus [11,25]. In many patients with moderate-to-severe AD, itch is the dominant symptom and is strongly associated with sleep disturbance, impaired daily functioning, anxiety, depression, and reduced overall quality of life [3,25]. Consequently, rapid control of pruritus should be considered not only symptomatic improvement but also a major therapeutic goal in long-term disease management.

The availability of oral JAK inhibitors provides clinicians with an important additional therapeutic option for patients who fail topical therapies, conventional systemic agents, or biologic treatment [17–25]. This is particularly relevant for patients requiring rapid onset of action, individuals with severe inflammatory disease burden, or those who prefer oral administration [32]. However, therapeutic flexibility must always be balanced with careful assessment of individual patient risk factors and long-term safety considerations.

Despite their substantial efficacy, the use of JAK inhibitors requires careful evaluation of potential adverse effects, including infections, laboratory abnormalities, cardiovascular complications, malignancy risk, and thromboembolic events [27–31,39,42]. Appropriate patient selection, baseline screening, regular laboratory monitoring, and long-term follow-up remain essential components of safe and effective therapy [43,47,48].

Importantly, JAK inhibitors should not necessarily be viewed as universal replacements for biologic therapies but rather as complementary therapeutic options within a broader and increasingly personalized treatment landscape [42,46]. Biologic therapies may remain preferable in selected patients because of their favorable long-term safety profiles, whereas JAK inhibitors may offer important advantages in patients requiring rapid symptom relief or more extensive cytokine suppression [32,42]. These considerations emphasize the importance of shared decision-making between clinicians and patients, taking into account disease severity, comorbidities, previous treatment response, monitoring feasibility, and patient preferences [46].

As understanding of atopic dermatitis continues to evolve, future therapeutic strategies will likely focus increasingly on personalized medicine approaches integrating clinical phenotype, biomarker profiling, immunologic characteristics, and individualized therapeutic selection [36,47]. Continued advances in precision medicine may improve identification of patient subgroups most likely to benefit from specific targeted therapies while minimizing unnecessary exposure to ineffective or potentially harmful treatments.

Further long-term clinical studies, pharmacovigilance programs, and real-world observational data remain essential for clarifying the optimal role of JAK inhibitors within future treatment algorithms and better characterizing their long-term safety profiles [40,41,49,50]. Additional research evaluating comparative efficacy, treatment sequencing, biomarker-guided therapy, and maintenance strategies will likely further refine their use in clinical practice.

Ultimately, JAK inhibitors have emerged as highly promising therapeutic agents capable of substantially improving disease control and patient quality of life in moderate-to-severe atopic dermatitis [17–35]. Their introduction represents an important step toward more precise, effective, and patient-centered management of chronic inflammatory skin disease in contemporary dermatology. Continuous evaluation of efficacy, safety, and patient-reported outcomes will remain essential to optimize long-term therapeutic success in everyday clinical practice.

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