APJAI
Asian Pacific Journal of
Allergy and Immunology

REVIEW ARTICLE

An updated review for management of atopic dermatitis

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Abstract

This review focuses on the updated knowledge of atopic dermatitis (AD) through collaboration between the Dermatological Society of Thailand, the Allergy, Asthma, and Immunology Association of Thailand, and the Pediatric Dermatological Society of Thailand. As AD is a chronic condition that significantly impacts quality of life and affects a large population worldwide, this review aims to provide an updated overview of the disease, including its prevalence, pathogenesis, diagnosis, and current treatment strategies. Continuous updates in that knowledge, especially the treatment guidelines, are necessary to provide proper management for both general practitioners and specialists who care for patients with AD. This also helps establish standards and improve the management of AD.

Key words: atopic dermatitis, update guideline, prevalence of atopic dermatitis, pathogenesis of atopic dermatitis, diagnosis of atopic dermatitis, treatment of atopic dermatitis

Citation:
Tuchinda, P., Nanthapisal, S., Nitiyarom, R., Vichyanond, P., Singalavanija, S., Rajatanavin, N., Wananukul, S., Limpongsanurak, W., Aunhachoke, K., Wisuthsarewong, W., Sangsupawanich, P., Chatchatee, P., Wattanakrai, P., Jirapongsananuruk, O., Chantaphakul, H., Thongngarm, T., Chularojanamontri, L., Kamchaisatian, W., Chatproedprai, S., Laisuan, W., Limphoka, P., Manuskiatti, P., Noppakun, N., Kulthanan, K. (2025). An updated review for management of atopic dermatitis. *Asian Pac J Allergy Immunol*, 43(4), 963-983. https://doi.org/10.12932/ap-211225-2192

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Introduction

This review of atopic dermatitis (AD), developed through a collaborative effort among the Dermatological Society of Thailand, the Allergy, Asthma, and Immunology Association of Thailand, and the Pediatric Dermatological Society of Thailand.[1] This review was updated to ensure its relevance, update, and to establish comprehensive knowledge of AD, including prevalence, pathogenesis, diagnosis, and treatment of AD.

Definition

Atopic dermatitis is a chronic, relapsing inflammatory skin disease, and the most common form of eczema, characterized by intense pruritus, xerosis, and eczematous lesions with age-specific distribution, arising from a complex interplay of epidermal barrier dysfunction, immune dysregulation (predominantly type 2 inflammation), genetic susceptibility (such as filaggrin mutations), and environmental factors, and it is frequently associated with other atopic conditions including asthma, allergic rhinitis, and food allergy, leading to substantial impairment in quality of life for patients and families.[2,3]

Epidemiology

AD is a common chronic inflammatory disease with substantial global variation in prevalence, age distribution, and disease severity. (**Figure 1**) Reported prevalence ranges from 1% to 20% worldwide, with the greatest burden occurring in childhood and adolescence, although adult disease contributes significantly to morbidity, particularly in urbanized and high-income settings.[4] The Global Burden of Disease (GBD) Study 2017 identified AD as a major contributor to disability-adjusted life years (DALYs), with peak burden in early childhood and higher prevalence among females. Disease burden is greatest in high-income countries, likely reflecting both epidemiologic differences and diagnostic recognition, while lower rates are reported in South Asia. Despite rising absolute case numbers, age-standardized prevalence has stabilized or declined in some regions.[5,6]

Large international datasets illustrate this heterogeneity. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three, encompassing over one million children across 98 countries, reported eczema symptom prevalence ranging from 0.9% in India to 22.5% in Ecuador among children aged 6–7 years, and from 0.2% in China to 24.6% in Colombia among adolescents aged 13–14 years.[7] GBD analyses further indicate that the fastest increases and a growing share of AD-related DALYs are occurring in rapidly urbanizing regions, particularly in Asia and Latin America. Several Latin American countries report among the highest childhood prevalence globally, and clinic-based studies consistently show a high proportion of moderate-to-severe disease (65–87%), reflecting substantial healthcare utilization and unmet treatment needs.[8]

In Europe, population-based studies report high childhood prevalence, often approaching 15–20% in Northern and Western countries, while adult prevalence is lower and more heterogeneous, typically 2–10%.[9] A persistent North–South gradient is observed, with lower prevalence historically reported in Southern Europe,

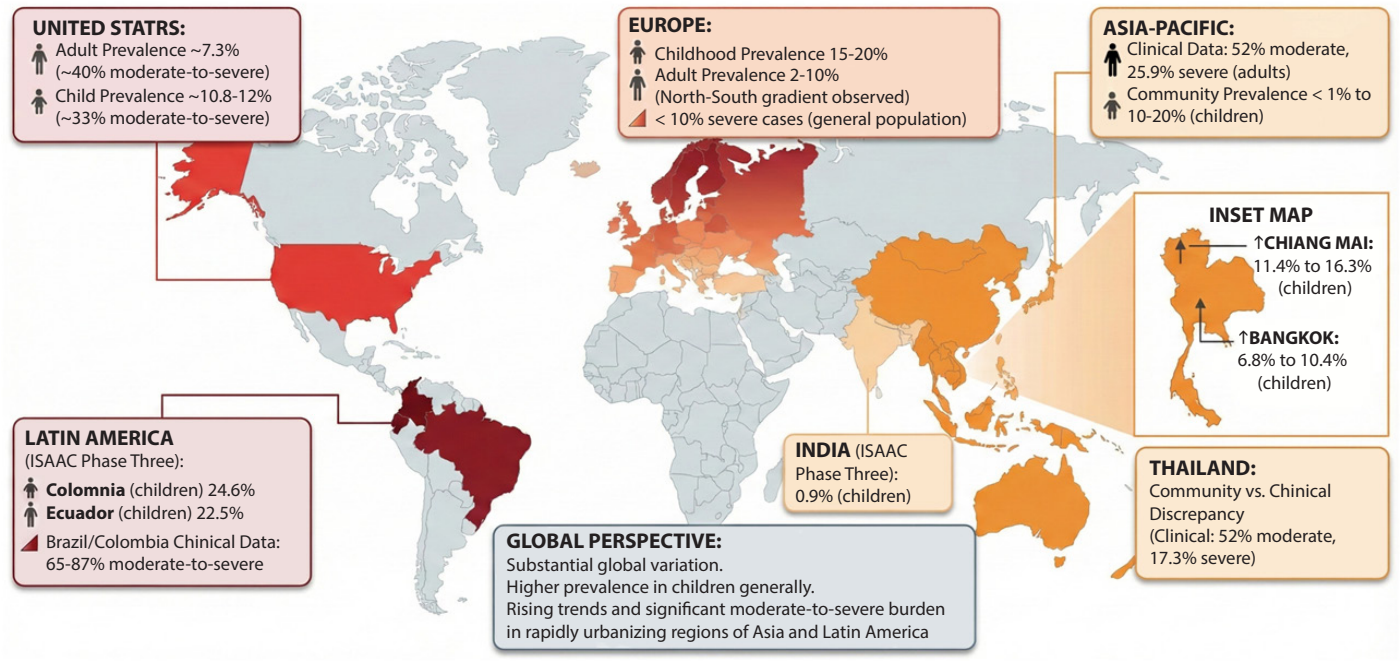


Figure 1. Geographic variation in Atopic Dermatitis prevalence and severity. Data indicates substantial global variation, with high childhood prevalence reported in Europe (15-20%) and Latin America. In the Asia-Pacific region, a discrepancy is observed between varying community prevalence and a high proportion of moderate-to-severe cases in clinical settings. The rising prevalence globally is closely linked to urbanization and environmental factors affecting disease expression.

although EAACI-associated data suggest increasing diagnosis and awareness in recent years.[9,10] Across Europe, fewer than 10% of cases are classified as severe in population studies, consistent with GBD severity weighting showing that most DALYs are attributable to mild-to-moderate disease rather than severe AD.[11,12]

The Asia-Pacific region demonstrates wide variation in prevalence and severity, reflecting heterogeneous genetic backgrounds and socioeconomic transitions. Population-based pediatric prevalence ranges from less than 1% in parts of South Asia to 10–20% in more urbanized settings, whereas clinical cohorts—particularly among adults—show a predominance of moderate-to-severe disease.[13,14] Thailand exemplifies the divergence between community-level burden and clinical severity: while ISAAC-based surveys indicate predominantly mild pediatric disease in the general population, multicenter tertiary-care data show that nearly 70% of referred children meet criteria for moderate-to-severe AD. National data also demonstrate a rising prevalence, with increases among older children in Bangkok (6.8% to 10.4%) and younger children in Chiang Mai (11.4% to 16.3%).[7,15]

Multiple factors contribute to the evolving epidemiology of AD. Genetic susceptibility and family history of atopy remain key determinants, while environmental exposures such as air pollution, urbanization, and reduced early-life microbial exposure are increasingly recognized.[16,17] Socioeconomic and lifestyle transitions, including smaller family size, higher socioeconomic status, and westernized diets, further contribute, particularly in rapidly developing regions.[18,19] Together, these data highlight that global variation in AD prevalence reflects the complex interplay between intrinsic susceptibility and extrinsic environmental pressures.

Pathogenesis

Atopic dermatitis (AD) arises from a tightly interconnected network of epidermal barrier fragility, immune dysregulation, microbial imbalance, epigenetic regulation, and neuroimmune activation. (**Figure 2**) A pivotal advance in understanding AD pathogenesis was the identification of loss-of-function filaggrin (FLG) mutations, which established that intrinsic epidermal defects can serve as primary drivers of disease.[20,21] Filaggrin is essential for proper stratum corneum maturation,

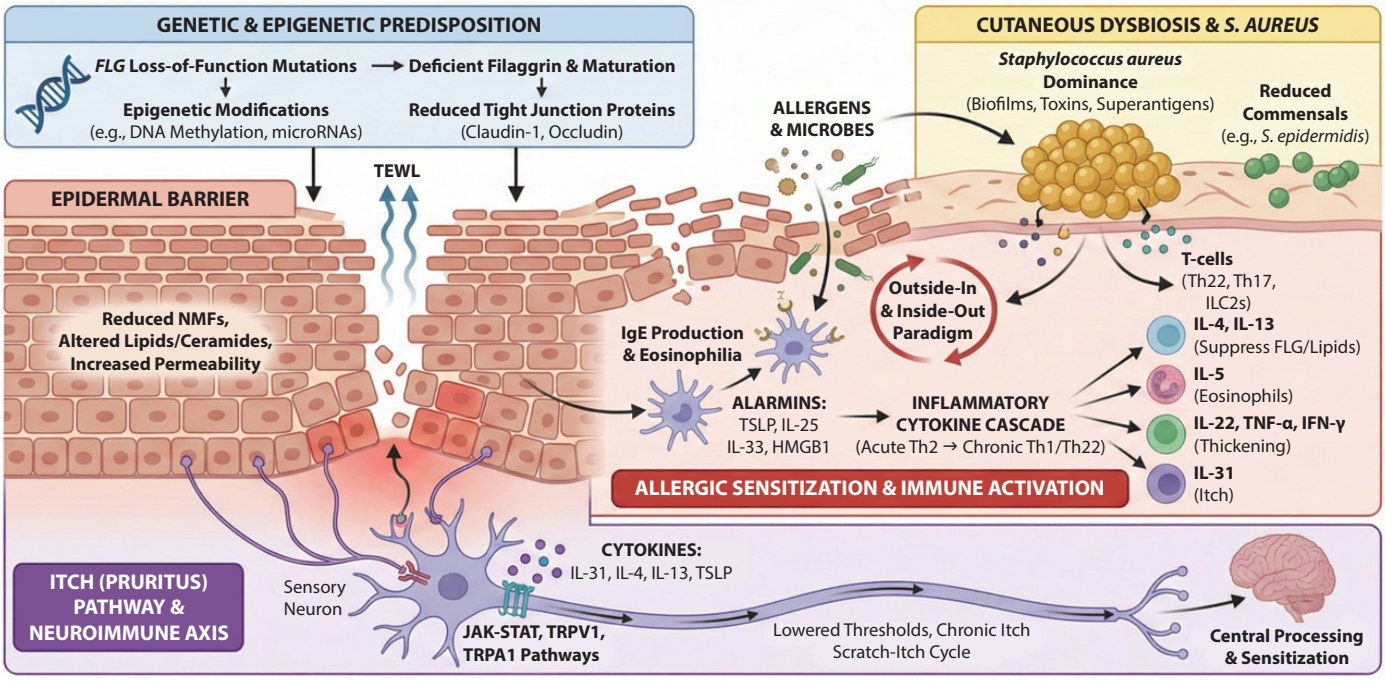


Figure 2. The complex interconnected pathophysiology of Atopic Dermatitis (AD). The pathogenesis involves a cyclic interaction between four key domains: (1) Epidermal Barrier Fragility: Genetic predisposition (*FLG* loss-of-function mutations) and epigenetic factors (e.g., DNA methylation, miR-155) compromise tight junctions and lipids, leading to increased transepidermal water loss (TEWL) and allergen penetration. (2) Cutaneous Dysbiosis: A shift in the microbiome towards *Staphylococcus aureus* dominance releases toxins and superantigens that further damage the barrier and amplify inflammation. (3) Immune Dysregulation: Barrier disruption triggers alarmins (TSLP, IL-25, IL-33), initiating an acute Th2-driven response (IL-4, IL-13) which may progress to a chronic Th1/Th22 phenotype. Notably, Asian and pediatric phenotypes often exhibit stronger Th17/IL-23 signatures. (4) Neuroimmune Activation: Pruritogenic cytokines, particularly IL-31, activate sensory neurons via JAK-STAT and TRPV1 pathways, causing central sensitization and driving the "itch-scratch cycle," which perpetuates the "Outside-In" and "Inside-Out" inflammatory loops.

*AD, atopic dermatitis; FLG, filaggrin; NMFs, natural moisturizing factors; TEWL, transepidermal water loss; *S. aureus*, *Staphylococcus aureus*; TSLP, thymic stromal lymphopoietin; IL, interleukin; Th, T helper; JAK–STAT, Janus kinase–signal transducer and activator of transcription; TRP, transient receptor potential (ion channels)

contributing to hydration, pH regulation, and generation of natural moisturizing factors; when filaggrin is reduced, either by genetic defects or cytokine-mediated suppression, the epidermis becomes more permeable, with increased transepidermal water loss and enhanced penetration of allergens and microbes.[22,23] Nevertheless, FLG mutations account for only part of AD heterogeneity, as many patients without FLG defects still develop disease, and type 2 cytokines such as IL-4 and IL-13 further compromise the barrier by downregulating filaggrin, loricrin, and involucrin and by perturbing ceramide synthesis and lipid metabolism.[24-27] Additional structural defects, including reduced expression of tight junction proteins such as claudin-1 and occludin, further weaken barrier function, while emerging evidence shows that epigenetic mechanisms (for example, DNA methylation and microRNAs such as miR-155 and miR-146a) modulate both barrier integrity and immune signaling.[28,29] Collectively, these findings support the view that barrier dysfunction in AD is both a heritable vulnerability and an inflammation-driven, dynamically maintained defect, providing a logical bridge to more detailed discussions of immune pathways, microbiome changes, and neuroimmune circuits in subsequent sections.

The immunologic landscape of atopic dermatitis (AD) is dynamic, varying with disease stage, ethnicity, and age to produce distinct phenotypes and endotypes.[30,31] Acute lesions are dominated by type 2 (Th2) pathways, with IL-4, IL-5, IL-13, IL-31 and epithelial alarmins such as TSLP driving IgE class switching, eosinophilia, pruritus, and dendritic-cell activation.[32,33] With chronicity, Th1 and Th22 responses become more prominent; interferon-γ, TNF-α, and IL-22 promote keratinocyte activation, epidermal hyperplasia, and lichenification.[30,34] Th17/IL-23 activity is especially accentuated in Asian and early-onset pediatric AD, where stronger Th17/Th22 signatures than in European adults define characteristic "Asian" and childhood endotypes with psoriasiform features.[35-37] Keratinocytes act as key immune sentinels by releasing TSLP, IL-25, and IL-33 in response to barrier damage and microbes, thereby activating dendritic cells and ILC2s and reinforcing type 2 inflammation, while reciprocal cytokine-mediated barrier injury sustains the classic "outside-in" and "inside-out" loop of AD pathophysiology.[25,31,32,38]

Cutaneous dysbiosis is a third key axis in atopic dermatitis (AD) pathophysiology, alongside barrier dysfunction and immune skewing.[39] Compared with healthy skin, AD lesions show reduced microbial diversity and frequent overgrowth of *Staphylococcus aureus*, particularly during flares.[40,41] *S. aureus*–derived toxins, proteases, and superantigens damage keratinocytes, disrupt tight junctions, and amplify type 2 and Th17/Th22 inflammation.[42,43] In contrast, commensals such as *Staphylococcus epidermidis*, *Staphylococcus hominis*, and *Cutibacterium* spp. produce antimicrobial factors that constrain *S. aureus* and help maintain microbial and barrier homeostasis.[44-46] Prospective microbiome studies indicate that reduced early-life microbial diversity can precede and predict later AD, supporting dysbiosis as a driver of disease risk.[47,48] These insights underpin emerging microbiome-directed therapies, including topical bacteriotherapy and live biotherapeutic products designed to restore protective commensals and reduce pathogenic *Staphylococcus* burden.

The neuroimmune axis is central to the hallmark symptom of itch in atopic dermatitis, linking immune mediators to peripheral sensory nerves and the central nervous system.[32] Pruritogenic cytokines such as IL-31, IL-4, IL-13, TSLP, and IL-33 activate cutaneous neurons through JAK–STAT signaling and ion channels including TRPV1 and TRPA1, thereby lowering activation thresholds and eliciting pruritus.[32,49,50] IL-31, produced mainly by Th2 cells and ILC2s, plays a pivotal role on neurons to drive chronic itch.[51,52] Neurotrophic factors like nerve growth factor and keratinocyte-derived pruritogens promote epidermal hyperinnervation and neuronal hypersensitivity, while central changes in itch-related brain networks support combined peripheral and central sensitization.[51-53] The modest antipruritic effect of antihistamines versus the marked itch relief achieved with IL-4Rα blockers (dupilumab, lebrikizumab), JAK inhibitors, and IL-31 antagonists such as nemolizumab illustrates how delineation of these neuroimmune pathways has translated into effective targeted therapies.[53-56]

Collectively, these interacting pathways position atopic dermatitis as a systems-level inflammatory disorder driven by reciprocal interactions among barrier dysfunction, immune skewing, microbial imbalance, and neuroimmune activation. This integrated model explains the clinical and biological heterogeneity of AD and supports an endotype-based approach to management. Crucially, delineation of these mechanisms has enabled a shift from broad immunosuppression to targeted therapies that interrupt key pathogenic circuits, providing a foundation for precision treatment and durable disease control.

Approaches to the Diagnosis of Atopic Dermatitis

The diagnosis of AD is predominantly established through a comprehensive evaluation of the patient's medical history and characteristic clinical features, particularly the morphology and age-specific anatomical distribution of cutaneous lesions. The diagnostic criteria for AD proposed by Hanifin and Rajka in 1980 encompass four major and twenty-three minor features. The diagnosis requires the presence of a minimum of three of four major and three of twenty-three minor criteria.[57] Due to the limitations of the original Hanifin and Rajka criteria—such as the complexity of assessment and the inclusion of certain features that are infrequently observed—Several international groups in various countries have proposed revised diagnostic criteria for AD.[58-60] A notable example is the UK Working Party's Diagnostic Criteria, which simplified the diagnostic process by requiring only one major and five minor criteria. These include pruritus as the essential major criterion, along with 1) a history of flexural eczema, 2) a personal history of asthma or allergic rhinitis, 3) a history of generally dry skin in the past year, 4) onset of symptoms before the age of two,

and 5) visible flexural eczema or involvement of the cheeks, forehead, and extensor surfaces in children under the age of four.[60,61] Subsequently, a 2003 consensus conference organized by the American Academy of Dermatology proposed another revised version of the Hanifin and Rajka criteria, aiming to enhance diagnostic efficiency and ensure applicability across all age groups affected by AD.[59,62] In addition, according to the 2018 revised the Japanese Dermatological Association (JDA) guideline, a diagnosis can be made regardless of disease severity when all three essential features are present: 1) itchy skin, 2) characteristic morphology and distribution of eczema, and 3) a chronic or chronically relapsing disease course.[63] Currently, the most widely accepted and commonly used diagnostic criteria for AD are the Hanifin and Rajka Criteria (1980) and the UK Working Party's Diagnostic Criteria (1994).[63,64] It is important to rule out other dermatologic conditions that present with clinical features similar to AD, including scabies, seborrheic dermatitis, allergic contact dermatitis, ichthyoses, cutaneous lymphoma, psoriasis, and some immunodeficiency disorders.

Laboratory investigations such as serum IgE, potassium hydroxide (KOH) preparation, and patch testing are not considered essential for establishing a diagnosis of AD. However, they may be useful in excluding other dermatologic conditions or identifying associated comorbidities. Currently, there are no specific biomarkers available for the diagnosis of AD or for the assessment of its disease severity.[59,65] In cases where patients do not respond adequately to appropriate and standard treatment, or when disease severity worsens, further laboratory investigations may be considered on an individual basis to identify potential triggering factors that may contribute to disease exacerbation. Assessment of potential allergic trigger factors can be performed using skin prick test, or through in vitro methods that measure specific IgE antibodies to specific relevant allergens.[66,67] It is important for clinicians to recognize that food allergies are frequently associated with AD in children under five years of age, particularly in those with moderate to severe disease. Therefore, food allergy testing may be considered in this patient population when the disease does not adequately respond to appropriate treatment.[65,68] Oral food challenges still remain the gold standard for the diagnosis of food allergy.[69,70]

Disease Severity and Clinical Outcome Assessment

Multiple assessment tools have been developed and are currently utilized to evaluate the severity and overall burden of AD. However, no specific diagnostic tests are available, and none of the existing assessment tools have achieved universal acceptance.[59] Consequently, clinical evaluation remains the principal approach for evaluating treatment outcomes. The assessment of AD can be categorized into objective and subjective components.

Objective measurements

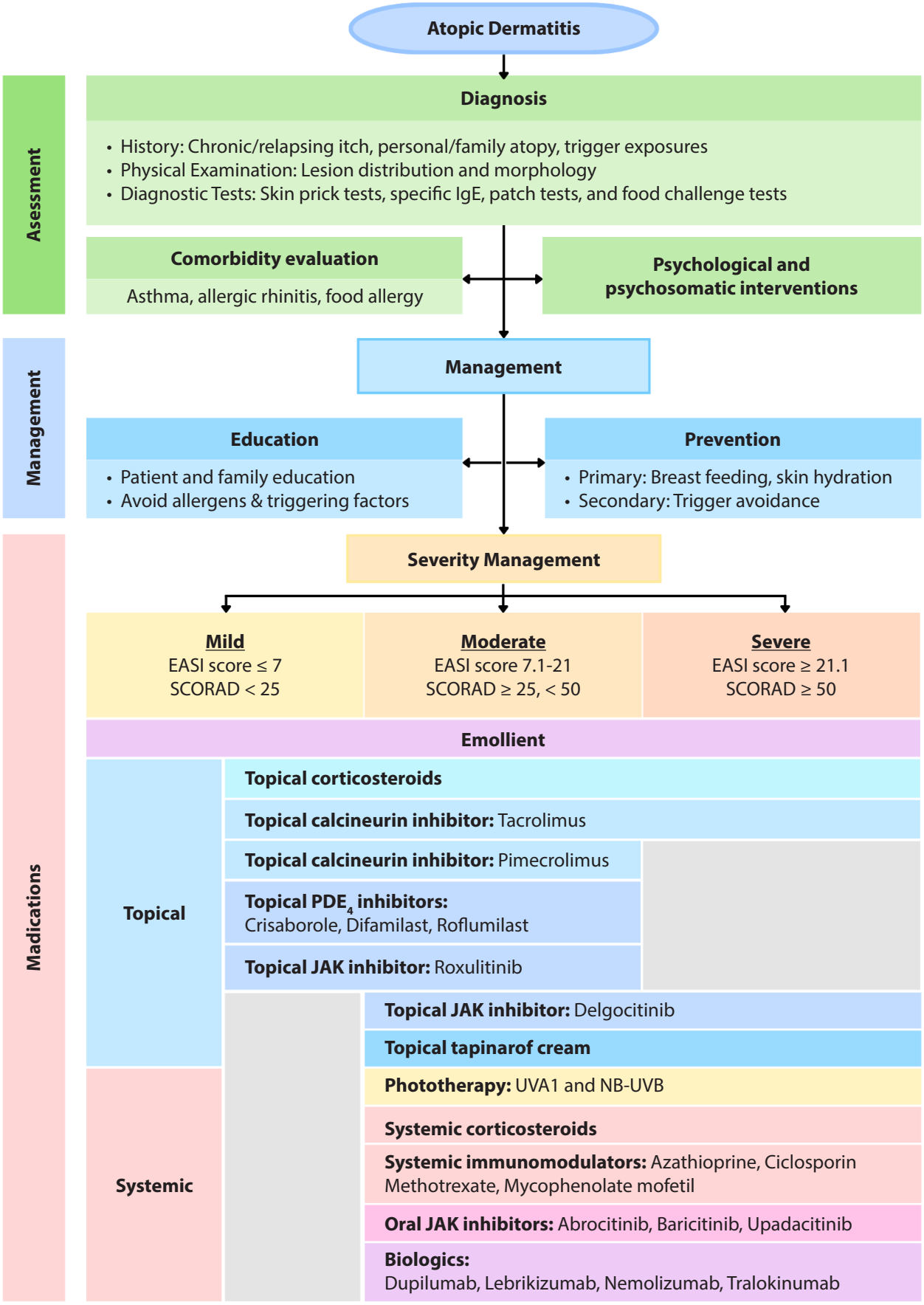
Objective measurements involve the assessment of visible clinical manifestations of the disease, including estimations of body surface area (BSA) involvement.[71] Examples of tools used for objective measurement in AD are SCORing Atopic Dermatitis (SCORAD) index, Eczema Area and Severity Index (EASI), Rajka & Langeland severity score, Physician Global Assessment (PGA), Six Area Six Sign Atopic Dermatitis index (SASSAD), Atopic Dermatitis Severity Index (ADSI), Atopic Dermatitis Area and Severity Index (ADASI), Nottingham Eczema Severity Score (NESS), Costa's Simple Scoring System, Total Body Severity Assessment (TBSA).[71] Although a variety of assessment tools are currently available, the SCORAD index, EASI, IGA, and SASSAD score remain among the most widely used instruments for evaluating disease severity in AD.[59] Among these, EASI and SCORAD are recommended as valid, reliable, and unbiased measures of objective disease severity and are commonly used in clinical trials.[72-74] The EASI score is based solely on objective physician assessments of disease extent and severity, whereas SCORAD combines these objective evaluations along with patient-reported measures of pruritus and sleep disturbance.[75,76]

Subjective measurements

Subjective measurements are based on patient-reported outcomes, with a focus on symptoms such as pruritus, sleep disturbance, and the overall impact of the disease on quality of life. Subjective assessment tools commonly used in AD include the Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), Children's Dermatology Life Quality Index (CDLQI), Infant's Dermatitis Quality of Life Index (IDQOL), Dermatitis Family Impact (DFI), and the Pruritus Numerical Rating Scale (NRS). Among these tools, the POEM is commonly used to assess the impact of AD on patients' quality of life.[59]

Guidelines for the Management of Patients with Atopic Dermatitis

Appropriate management of AD can help prevent disease flares, improve quality of life, and enable patients to participate in social activities. A stepwise treatment framework based on disease severity. Management of AD should be individualized and escalated in a stepwise manner, with continuous reassessment of disease control, treatment burden, and safety. All patients, regardless of disease severity, should receive foundational treatment to restore and maintain skin barrier function, including regular use of emollients, trigger avoidance, appropriate bathing, and patient and family education. Topical treatment is recommended for the management of mild disease and localized flares. For patients with moderate to severe disease or those who do not achieve adequate control with optimized topical treatment, systemic therapy or phototherapy may be considered. When disease control is achieved, tapering systemic therapy should be considered when appropriate. The standard therapeutic approach comprises the following key steps, as illustrated in **Figure 3**.



EASI: Eczema Area and Severity Index, JAK: Janus Kinase, PDE_4: phosphodiesterase-4, SCORAD: SCORing Atopic Dermatitis

Figure 3. An overview of the diagnosis and management of atopic dermatitis

*EASI, Eczema Area and Severity Index; SCORAD, Scoring Atopic Dermatitis; JAK, Janus kinase

The currently approved non-conventional topical and systemic treatments for atopic dermatitis were demonstrated in **Figure 4** and **Table 1**. The goals of treatment are adequate disease control, long term reduction of disease severity, effect control of pruritus, prevention of flare, and improvement of patients' quality of life.

1. Patient and Family Education

Patient and family education should be provided with adequate and proper information regarding the nature of the disease, its clinical course, appropriate skin care, preventive measures, and the importance of treatment adherence. This promotes long-term disease control and encourages active involvement of patients and families in disease management.

2. Assessment of Disease Severity

Disease severity as well as psychological aspects may be evaluated using the tools mentioned. Severity of AD is categorized as mild, moderate, or severe.

Individual assessment of disease severity is crucial for guiding treatment planning. This helps provide clinical decision-making as well as the consideration of choosing appropriate laboratory investigations.

3. Allergen and Trigger Avoidance

Identifying and avoiding trigger factors are essential in management of AD. Patients should be advised to minimize exposure to known or suspected allergens and triggers. Factors that may exacerbate AD include irritants, sweat, some relevant dietary component (such as egg, cow's milk, wheat, peanut, soy, and seafood), environmental changes (including seasonal variation such as spring, summer, or winter), showering, skin friction, aeroallergen (such as house dust mite or pollens) and psychological stress.[77-79] In Germany, the current S3 Guideline for atopic disease prevention also recommends limiting exposure to tobacco smoke and traffic-related air pollution.[80]

In both pediatric and adult populations with atopic dermatitis (AD), routine elimination diets are discouraged in favor of optimized topical and skin-directed therapies. Dietary interventions should be reserved exclusively for patients with a clinical history suggestive of food allergy and objective diagnostic confirmation, rather than being based solely on skin prick testing (SPT) or serum-specific IgE (sIgE) sensitization. While short, hypothesis-driven elimination diets (2–4 weeks) may be considered for infants and young children with moderate-to-severe or treatment-refractory disease, true food triggers are uncommon in adults.

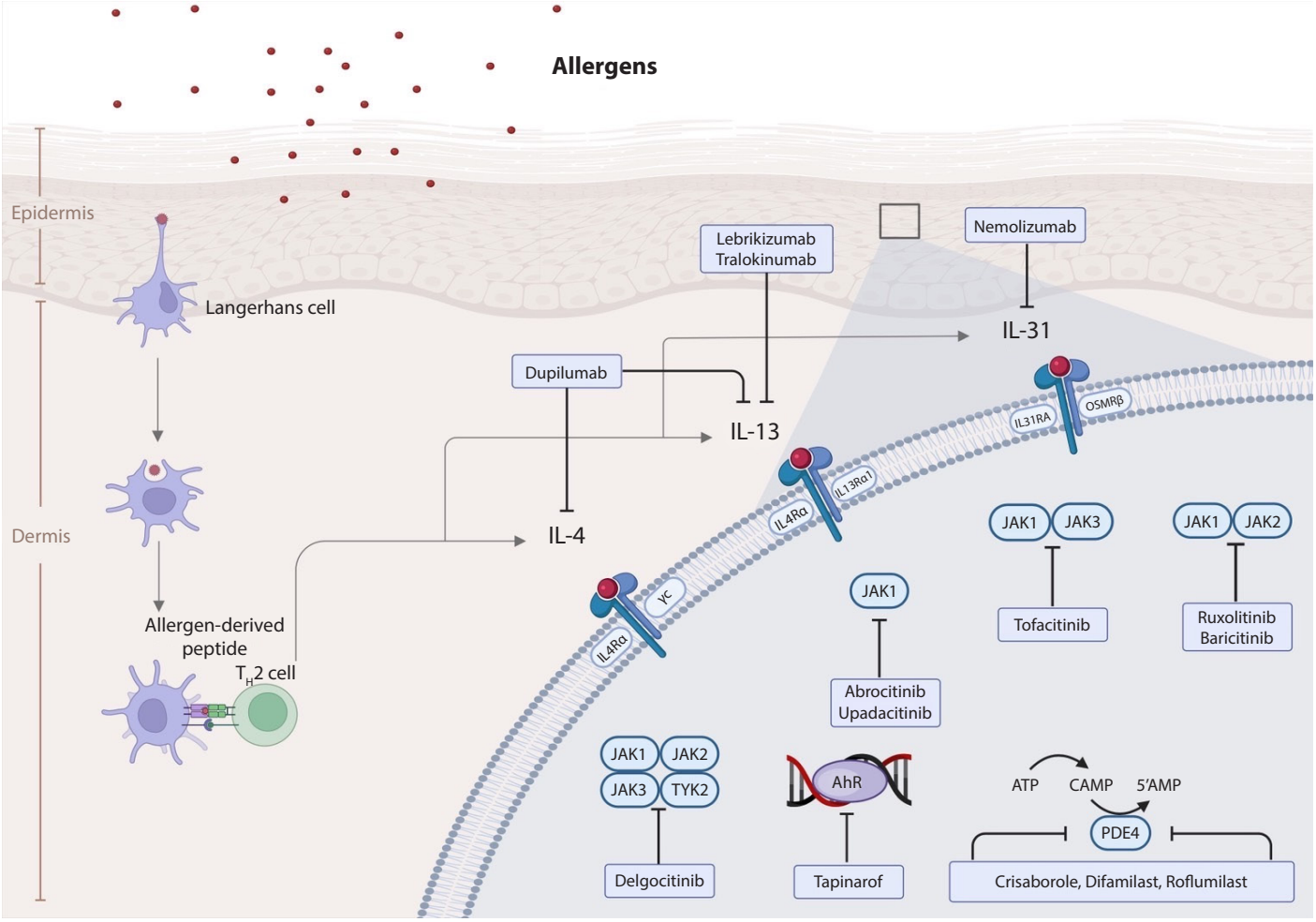


Figure 4. Mechanisms of action of currently approved non-conventional topical and systemic therapies for atopic dermatitis

IL, interleukin; JAK, Janus kinase; AhR, Aryl Hydrocarbon Receptor; ATP, adenosine triphosphate; PDE, phosphodiesterase; CAMP, cyclic adenosine monophosphate; Th, T helper

Table 1. Non-conventional topical and systemic treatment approved for atopic dermatitis.

Drug	Mechanism of action	Indication	Approved age	Administration		Approved region			
						US-FDA	EMA	PMDA (Japan)	Thai-FDA
Topical PDE-4 inhibitors									
Crisaborole	PDE-4 inhibitor	Mild to moderate AD	≥ 3 months	Twice daily		✓			✓
Difamilast	Highly selective inhibitor of PDE4 subtype B	Mild to moderate AD	≥ 2 years	Twice daily				✓	
Roflumilast	PDE-4 inhibitor	Mild to moderate AD	≥ 6 years	Once daily		✓			
Topical JAK inhibitors									
Delgocitinib	Pan-JAK inhibitor	Moderate to severe AD	≥ 2 years	Twice daily				✓	
Ruxolitinib	Selective JAK 1/2 inhibitor	Mild to moderate AD	≥ 12 years	Twice daily		✓			
Topical Tapinarof									
Tapinarof	Aryl hydrocarbon receptor agonist	Moderate to severe AD	≥ 2 years	Once daily		✓		✓	
Biologics									
				Loading Dose	**Maintenance Dose**				
Dupilumab	IL-4Rα antagonist	Moderate to severe AD	≥ 6 months	Adult ≥ 18 years: 600 mg SC Children age: - 6 month- 5 years <5- <15 kg: 200 mg SC 15-30 kg: 300 mg SC - 6-17 years 15-<30 kg: 600 mg SC 30-60 kg: 400 mg SC ≥ 60 kg: 600 mg SC	Adult ≥ 18 years: 300 mg SC every 2 weeks Childeren age: - 6 month- 5 years <5- 15 kg: 200 mg SC every 4 weeks 15-30 kg: 300 mg SC every 4 weeks - 6-17 years 15-<30 kg: 300 mg SC every 4 weeks 30-60 kg: 200 mg SC every 2 weeks ≥ 60 kg: 300 mg SC every 2 weeks	✓	✓	✓	✓
Lebrikizumab	IL-13 inhibitor	Moderate to severe AD	≥ 12 years and ≥ 40 kg	500 mg SC at week 0, 2	250 mg SC every 2 weeks through week 16 (or until response), then 250 mg SC every 4 weeks	✓	✓	✓	
Nemolizumab	IL-31RA antagonist	Moderate to severe AD	≥ 12 years	60 mg SC	30 mg SC every 4 weeks	✓	✓	✓	
Tralokinumab	IL-13 inhibitor	Moderate to severe AD	≥ 12 years	Adult: 600 mg SC Children age: 12-17 years 300 mg SC	Adult: 300 mg SC every 2 weeks Children age: 12-17 years 150 mg SC every 2 weeks	✓	✓	✓	
Oral JAK inhibitors									
Abrocitinib	Selective, reversible JAK 1 inhibitor	Moderate to severe AD	≥ 12 years	100–200 mg once daily		✓	✓	✓	✓
Baricitinib	Selective JAK 1/2 inhibitor	Moderate to severe AD	≥ 2 years	4 mg once daily Children weight: ≥ 30 kg: 4 mg once daily 10-30 kg: 2 mg once daily			✓	✓	✓
Upadacitinib	Selective, reversible JAK 1 inhibitor	Moderate to severe AD	≥ 12 years	15–30 mg once daily		✓	✓	✓	

*AD, Atopic Dermatitis; EMA, European Medicines Agency; FDA, Food and Drug Administration; JAK, Janus kinase; IL, interleukin; PDE-4, phosphodiesterase 4; PMDA, Pharmaceuticals and Medical Devices Agency; SC, subcutaneous

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Asian Pac J Allergy Immunol 2025;43:963-983 DOI 10.12932/AP-211225-2192

Indiscriminate or prolonged elimination is discouraged, as these practices pose significant nutritional risks and may lead to a potential loss of oral tolerance. Ultimately, dietary modifications must be guided by a consistent clinical history and confirmed through oral food challenges when clinically indicated.[64,68,81]

4. *Management of AD*

4.1 General recommendations for AD patients

Patients should avoid wearing coarse-textured, large fiber textiles or irritating fabrics such as wool or synthetic materials. Lightweight, breathable clothing made from soft fabrics, such as cotton, is recommended to promoter ventilation and minimize sweat accumulation. Exposure to excessive heat and other environmental triggers should be avoided. Additionally, patients should keep fingernails short and minimize scratching or exposure to irritants.

4.2 Bathing

Bathing helps to hydrates the skin while effectively removing scales, crusts, irritants, and allergens. It is recommended to use a gentle, non-irritating, hypoallergenic cleanser, and bathing should be limited to 5-10 minutes. Lukewarm or room-temperature water, ideally between 27–30°C should be used. After bathing, the skin should be gently patted dry with a towel and immediately apply an emollient to maximize moisture retention.[76,82] Caution is advised when using cleansing products containing food-derived ingredients, such as wheat flour,[83] rice starch, or rice bran,[84] as these may induce epicutaneous food sensitization, particularly in individuals with skin barrier dysfunction, and may contribute to the subsequent development of food allergies.[85] In addition, products containing antiseptic agents should be avoided, as these may cause skin irritation.

In patients with recurrent bacterial skin infections or moderate to severe AD, bleach baths may be considered as an adjunctive therapy.[86] A dilute sodium hypochlorite solution with a final concentration of 0.006% can be prepared by mixing 10 mL of 6% sodium hypochlorite in 10 liters of water. Patients should soak affected areas for 5–10 minutes, two to three times per week, followed by rinsing with clean water. Some studies have reported improvements in eczema severity, reduced use of topical corticosteroids and antibiotics, and a reduced risk of secondary skin infection.[86-89] However, current systematic reviews and meta-analyses have not demonstrated significant superiority over regular bathing.[90] Therefore, bleach baths should be recommended only under specialist supervision.

4.3 Moisturizers

Regular use of appropriate emollients is considered to be the first-line and effective treatment for AD. Routine application of moisturizers can reduce topical corticosteroid use and help maintain long-term disease stability.[91] Emollients can maintain skin hydration for approximately 2 to 6 hours, depending on the formulation. Emollient formulations generally contain a humectant, such as urea or glycerol, to enhance hydration of the stratum corneum, in combination with an occlusive agent, such as lipids or petrolatum to reduce transepidermal water loss.[68,82] Use of simple emollient ointments with minimal ingredients is recommended to minimize the risk of contact allergy. Emollients containing potential food allergens, such as peanut or oatmeal, should be avoided, as they may induce epicutaneous sensitization and increase the risk of subsequent food allergy.[68,92,93] Formulations should exclude common sensitizers, such as emulsifiers, preservatives, and fragrances, as these substances are frequently associated with type IV hypersensitivity reactions.[68] Using an adequate amount is recommended to ensure efficacy: approximately 100 grams per week for infants and young children, 150–200 grams per week for older children, and 250 grams per week for adults.[94,95] Generally, patients should apply cream- or lotion-based emollients before applying topical medications on the inflamed skin. However, if an ointment-based emollient is used, the topical medications should be applied first, followed by the emollient. A short interval should be allowed between the application of the products.[67]

The use of emollients containing bacterial components has been evaluated. In some randomized controlled trials, certain formulations have shown benefit in selected patients. However, no systematic reviews or meta-analyses are currently available, and further research is still needed to establish their efficacy and safety.[96-99]

Currently, certain emollients have been formulated with additional active anti-inflammatory ingredients such as flavonoids (e.g., licochalcone A), saponins, ceramide, and riboflavins.[82] These components are intended to enhance skin hydration, reduce inflammation, and alleviate pruritus.[100] As a result, such emollients may serve as part of the therapeutic strategy and potentially reduce the need for topical corticosteroids. However, these advanced moisturizing formulations are often expensive.

4.4 Topical corticosteroids (TCS)

TCS are effective in treating flare-ups of AD by applying a low- to medium-potency corticosteroid twice daily on acute inflamed skin lesions.[82] The frequency of application should be gradually reduced or discontinued when the disease is under control. Intermittent use may be considered as a maintenance strategy. The lowest potency corticosteroid that effectively controls the disease should be used to minimize potential side effects.

The prolonged continuous use of high-potency topical corticosteroids (> 4 weeks) should be avoided, and their application should be limited to sensitive areas such as the face, neck, groin, and skin folds.[64] Using multiple potencies of topical corticosteroids in either different body sites or disease severity should be done with caution to avoid the risks associated with polypharmacy.[64]

The use of mild potency TCS twice weekly on previously affected areas—known as proactive therapy—has been shown to be effective in preventing disease flares in patients with AD.[64] Clinical studies have demonstrated that proactive therapy with moderately potent TCS, such as fluticasone propionate cream and mometasone furoate cream, significantly reduces relapse rates compared to placebo.[101,102] Proactive therapy with intermittent TCS is therefore strongly recommended as a maintenance strategy to prevent disease flare.[64]

Continuous, prolonged use of TCS may lead to adverse effects. Local complications include skin atrophy, striae, telangiectasia, purpura, hypopigmentation, acneiform eruptions, steroid-induced rosacea, hypertrichosis, and secondary superimposed bacterial infection. Allergic contact dermatitis may result from the corticosteroid itself or from other components in the topical formulation, such as preservatives. Systemic effects, though less common, include glaucoma, cataract formation, hypothalamic-pituitary-adrenal (HPA) suppression, Cushing's syndrome, and impaired growth in children.[100,103]

4.5 Wet wrap therapy

Wet wrap therapy method involves applying a topical medication to the skin, then covering it with damp materials—such as bandages, gauze, or a cotton garment—followed by a dry outer layer. In cases of more widespread involvement, two layers of soft, non-irritating clothing can be used in the same manner.[100] This technique improves the efficacy of topical therapies by promoting greater skin penetration and reducing transepidermal water loss.[64] For AD patients who remain unresponsive to mid- to high-potency topical treatments, a short course of either low- to mid-potency or diluted topical corticosteroids (cream or ointment) under occlusion (wet wrap therapy) may be considered.[82,86,100] The duration of such therapy may range from a minimum of 1 hour to overnight, depending on patient tolerance.[64] Caution is advised when using mid- to high-potency corticosteroids beneath occlusive wraps, as enhanced absorption may increase the risk of adverse effects. Nevertheless, this therapeutic approach has not yet been formally standardized.

4.6 Topical calcineurin inhibitors (TCI)

TCI is considered second-line therapy for the treatment of AD, which may reduce the need for TCS. It has demonstrated good efficacy and safety in maintaining prolonged disease remission, and in preventing flare-ups.[76] These agents are particularly appropriate for use on sensitive areas where TCS should be avoided, such as the face, skin folds, and genital regions. The application should begin twice daily at the onset of symptoms, then reduce to once daily as lesions improve, and discontinue once the skin has cleared.

Adverse side effects of TCI include transient burning or erythema, tingling at the application site, particularly during the first week of treatment.[76] These symptoms are usually self-limited and resolve within one week. A temporary exacerbation of skin symptoms may occur in some patients. To reduce local site reactions, initiating treatment with TCS may be appropriate in patients with acute flares of skin lesions.[104] Secondary infections, particularly bacterial and viral, are commonly observed in AD. In these cases of viral infections, such as herpes simplex or eczema herpeticum, TCI should be discontinued during the active infection. In cases of mild bacterial infection, TCI may be continued alongside appropriate antimicrobial treatment. However, in severe bacterial infections or in pediatric patients, TCI should be withheld until the infection is adequately treated. Unlike TCS, TCI does not induce skin atrophy or ocular complications such as glaucoma or cataract.[76] Patients should be advised to avoid direct or intense sunlight during treatment. TCI is contraindicated in pregnant women and individuals with immunodeficiency.[105]

Medications in this group include:

- Tacrolimus ointment (0.03%, 0.1% strength) can be used to treat AD across all levels of disease severity. Tacrolimus 0.03% is indicated for children aged 2 to 16 years, while tacrolimus 0.1% is approved for patients 16 years of age and older and adults. Evidence suggests that tacrolimus 0.1% has comparable efficacy to moderate-to-potent TCS and is more effective than both tacrolimus 0.03% and pimecrolimus.[106] Tacrolimus 0.03% has not shown significantly superior efficacy compared to pimecrolimus; however, some studies have reported that, compared to mild-potency topical corticosteroids, 0.03% tacrolimus demonstrates statistically significant clinical improvement.[106-109] There are also reports supporting the efficacy and safety of tacrolimus in children under 2 years of age,[110,111] as well as long-term safety data supporting its use as monotherapy for up to 4 years.[112] Another study demonstrated that patients with AD who received topical tacrolimus during the initial 4 years experienced sustained treatment efficacy over a 10-year follow-up period.[113] Proactive therapy using topical tacrolimus, which is applied twice weekly to previously affected areas, has been shown to effectively reduce disease flares in patients with severe disease and having frequently relapsing course.[114] This approach may serve as a beneficial option for maintaining disease control and improving patients' quality of life.

- Pimecrolimus cream (0.1% strength) is indicated for the treatment of mild to moderate AD, particularly on the face and other sensitive areas. Pimecrolimus can be used in children aged 3 months and older. Long-term safety data support the use of pimecrolimus as monotherapy for up to 5 years.[115] The efficacy is comparable to low- to mid-potency topical corticosteroids.

4.7 Topical phosphodiesterase-4 (PDE-4) inhibito

i) Crisaborole ointment (2% strength) acts through inhibition of PDE-4, responsible for the degradation of cyclic adenosine monophosphate (cAMP), thereby modulating both pro-inflammatory and anti-inflammatory cytokine production.[64] It has been approved for the treatment of mild to moderate AD in patients 3 months of age and older, especially in alleviating symptoms and reducing itch.[82,86,105] Twice-daily application of crisaborole resulted in a higher proportion of patients achieving improvement in ISGA scores, with a greater percentage reaching clear or almost clear status.[116] A study showed that long-term use of once-daily crisaborole for 52 weeks was effective and safe, leading to fewer flares.[117] Reported adverse effects are generally mild and infrequent, and may include burning, erythema, or swelling at the application site.

ii) Difamilast ointment (0.3%, 1% strength) is a highly selective inhibitor of PDE4 subtype B.[118] This drug is approved for use in mild to moderate AD patients 2 years of age and older.[119] The 0.3% strength is recommended for pediatric patients (aged 2-14 years), while the 1% formulation is recommended for adult patients (aged 15-70 years). Several studies have demonstrated that difamilast ointment applied twice daily achieved significantly greater efficacy than vehicle, while remaining well tolerated.[120-124] Most treatment-emergent adverse events reported were of mild to moderate severity. Remarkably, the study revealed that, unlike other PDE4 inhibitors, difamilast was not associated with local irritation, including burning or stinging sensations.[120] To date, difamilast has been approved only in Japan.

iii) Roflumilast cream (0.15% strength), a PDE-4 inhibitor, is currently approved for patients with mild to moderate AD in patients 6 years of age and older.[125,126] In two phase 3 studies revealed that roflumilast cream 0.15% applied once daily showed superior efficacy over vehicle cream, with an acceptable safety profile including headache, nausea, mild to moderate application site pain, and nasopharyngitis.[127,128]

4.8 Antimicrobial therapy

In cases of secondary bacterial infection, the use of topical or oral antibiotics effective against *Staphylococcus aureus* and *Streptococcus pyogenes*, is recommended.[82] The appropriate treatment duration is generally 1–2 weeks.[68] According to a Cochrane review, the use of antibiotics is not recommended in the treatment of AD without clinical signs of bacterial infection.[64,82,129]

4.9 Topical coal-tar derivatives

Coal tar preparations may be effective in controlling disease flares in some adult patients. However, studies on the efficacy of coal tar in the treatment of AD remain limited.[68,130]

4.10 Topical JAK inhibitors

i) Delgocitinib ointment (0.25%, 0.5% strength), a pan-Janus kinase (JAK) inhibitor, simultaneously suppressing JAK1, JAK2, JAK3, and TYK2.[64,131,132] Both formulations can be used in pediatric patients 2 years of age and older.[119,133] Delgocitinib is recommended for twice-daily application. In phase 3 RCT, delgocitinib demonstrated a least-squares mean reduction from baseline in mEASI score of 44.3% compared with 1.7% with vehicle at week 4 in adults and 39.3% compared with 10.9% in patients aged 2-15 years. Delgocitinib achieved greater reduction in pruritus NRS scores than vehicle as early as week 1, with sustained effect through week 4. A further study involving infants aged 6 months to 2 years demonstrated that delgocitinib maintained therapeutic benefits and has favorable tolerability over a 52-week treatment period.[133] Delgocitinib 0.5% ointment may provide higher efficacy than the 0.25% formulation in patients with mild severity. Reported adverse effects include nasopharyngitis, eczema herpeticum, acne, dental caries, and paronychia, most of which were mild in severity. No severe adverse events were observed.[134]

ii) Ruxolitinib cream (1.5% strength), a selective JAK1 and JAK2 inhibitor, is indicated for the short-term and intermittent treatment of mild to moderate AD in patients 12 years of age and older when other topical prescription therapies are ineffective or inappropriate.[86,135] It should be applied twice daily to affected areas, and not exceeding 20% of BSA with a maximum of 60 grams per week. In phase 3 RCTs, topical ruxolitinib demonstrated significant efficacy. Approximately 51-54% of patients achieved IGA 0/1 at week 8. Significant itch reduction was observed within 12 hours following the first application.

Treatment should be discontinued once clinical signs have resolved. The concomitant use of ruxolitinib cream with biologics, other JAK inhibitors, or potent immunosuppressants (e.g., ciclosporin, azathioprine) is not recommended. It is also not recommended in patients with underlying immunocompromised, have risk of infection, or cancer.[64] Local application site reactions were uncommon, and no patients experienced serious adverse events.[136]

4.11 Topical Tapinarof Cream

Topical tapinarof cream (1% strength) is a nonsteroidal medication that functions as an aryl hydrocarbon receptor agonist that simultaneously suppresses pro-inflammatory cytokines (IL-17, IL-4/13), restores the skin barrier through filaggrin production, and boosts antioxidant defenses via the Nrf2 pathway. Tapinarof cream has been approved for treating moderate to severe AD individuals 2 years of age and older.[137] It was applied once daily. Long-term use of topical Tapinarof 1% revealed continued improvement in efficacy outcomes, which were maintained throughout the 52-week treatment period.[138] Folliculitis, acne, headache, and nasopharyngitis, which were mild, were among the most frequently observed adverse events.[138,139]

4.12 Phototherapy

Medium-dose UVA1 and narrowband UVB phototherapy may be used for the treatment of moderate to severe AD in adult patients by inducing apoptosis of inflammatory T-cells, suppressing pro-inflammatory cytokines, and strengthening the skin barrier while reducing *Staphylococcus aureus* colonization, and topical therapies should be continued concurrently during the initial phase of phototherapy to reduce flare-up of skin lesions.[68,76,80,82,140-142] UV phototherapy should not be initiated during acute disease flares which should first be managed with standard treatment.[68] Counseling should include a discussion of the risk of cutaneous malignancy and photoaging. However, updated American Academy of Dermatology (AAD) guidelines acknowledge the effectiveness of phototherapy (especially NB-UVB) for moderate to severe AD in both adults and children, often recommending it as a second-line option.[103]

4.13 Systemic steroids

Oral or intramuscular corticosteroids may be considered in cases of severe acute exacerbation of AD who are unresponsive to topical therapy. Short-term use of systemic corticosteroids, such as prednisolone at a dose of 0.5–1 mg/kg/day for up to 2 weeks, may be considered. Abrupt discontinuation of short courses of systemic corticosteroids may result in a high risk of disease relapse or rebound.[63,68,140,143,144] However, their use is associated with significant systemic adverse effects, including suppression of the HPA axis and impaired growth in children. Therefore, systemic corticosteroids are not recommended for routine treatment of AD in pediatric patients.

4.14 Systemic antihistamine

Currently, there is insufficient evidence to support the beneficial and efficacy of systemic antihistamines in patients with AD;[105] however, they are commonly used during acute flares to manage pruritus. Short-term use of sedating antihistamines may be considered, under appropriate supervision, especially for patients with eczema where pruritus significantly impairs sleep.[63,105,140,142,145] In addition, systemic antihistamines may be considered for use in patients with other atopy comorbidities such as dermographism, allergic rhinitis, or asthma, where additional symptomatic benefit may be achieved.[145] However, long-term treatment of pruritus in AD with systemic antihistamines—regardless of generation—is not advised.[80]

4.15 Systemic immunosuppressive drugs

i) Ciclosporin which selectively inhibits calcineurin to block T-cell activation and the production of pro-inflammatory cytokines like IL-2, may be considered as a first-line treatment in moderate to severe AD patients aged 16 and older (or younger when used off-label) who are unresponsive, refractory, or intolerant to other conventional therapies. It is recommended at a dose of 3–5 mg/kg/day, which may be divided into a morning and an evening dose.[63,64,68,142,143,146,147] Ciclosporin can be prescribed at either low doses (2–3 mg/kg/day) or high doses (4–5 mg/kg/day). The duration remains controversial, varying from 3 months to 2 years.[64,68] The decision should be individualized based on several factors—such as the current severity of disease and the urgency of symptom control—while carefully weighing the potential risks associated with higher dosages. The goal is to use the lowest effective dose that provides clinical improvement while minimizing the risk of adverse effects.[64,144] Adverse events include hypertension, nephrotoxicity, increased risk of infection, hypertrichosis, or gum hypertrophy.[64] Ciclosporin may be considered as a treatment option for pregnant women with severe AD.[143] Ciclosporin should not be used in combination with phototherapy.

ii) Azathioprine which acts as a purine analogue to inhibit DNA and RNA synthesis, thereby suppressing the proliferation of T and B lymphocytes, may be used as a second-line treatment for moderate to severe AD patients aged 6 years and older (or younger when used off-label). The recommended dosage is 1–2 mg/kg/day in children and 1–3 mg/kg/day in adults, with an initial dose is 50 mg/day for 1-2 weeks.[68,76,95,147] Azathioprine should be discontinued if no clinical improvement within 3 months of treatment initiation.[143] Possible adverse effects include gastrointestinal side effects, hepatotoxicity, hematological abnormalities, idiosyncratic hypersensitivity reactions, an increased risk of non-melanoma skin cancer, and non-Hodgkin lymphoma.[68,143]

iii) Methotrexate which acts as a folic acid antagonist that competitively inhibits dihydrofolate reductase to disrupt DNA synthesis and promote the release of anti-inflammatory adenosine may be considered in moderate to severe refractory AD patients aged 2 years and older (off-label). The recommended starting dose is 5–15 mg per week; maximum dose of 25 mg/week in adults and 10–15 mg/m² per week in children.[76,95,143,147] Optimal therapeutic outcomes with methotrexate are expected after 8–12 weeks of continuous use. Combination with other therapies, including TCS, TCI, or phototherapy, is recommended. Using methotrexate with ciclosporin is a relative contraindication.[143] Methotrexate must not be used during pregnancy and is contraindicated in both male and female patients with plans for conception.[64] Reported adverse effects of methotrexate include hepatotoxicity, susceptibility to infections, gastrointestinal side effects, and bone marrow suppression.[64,140]

iv) Mycophenolate mofetil which acts as a selective inhibitor of inosine monophosphate dehydrogenase to disrupt de novo purine synthesis, thereby specifically blocking the proliferation of T and B lymphocytes may be considered as an alternative immunosuppressive agent in patients with moderate to severe AD patients aged 2 years and older (off-label) who do not respond or are contraindicated to other immunosuppressive agents.[68,95] In children, the recommended dose is 600–1,200 mg/m²/day, divided into two daily doses, with a maximum dose of 2 grams per day. In adults, the dose should not exceed 2 grams per day. Mild gastrointestinal disturbance, headache, fatigue, and myelosuppression may occur.[63,68]

4.16 Biologics

i) Dupilumab is a fully human monoclonal antibody that binds to IL-4Rα subunit, which inhibits signaling of interleukin-4 and interleukin-13. It was approved for use in patients 6 months of age and older for the treatment of moderate to severe AD that is inadequately controlled by topical therapies, and has not responded to systemic therapies.[64,86,141] Evidence from Phase 3 randomized controlled trials (RCTs) has established dupilumab as a cornerstone treatment for adults, adolescents, and children as young as 6 months.[148-150] In pivotal trials, dupilumab demonstrated significant and sustained skin clearance and itch reduction, with approximately 40% of adult patients achieving clear or almost clear skin (IGA 0/1) by week 16.[126,151] In adolescent-specific RCTs, weight-based dosing led to similar efficacy profiles, with nearly 42% of patients achieving EASI-75.[152] In clinical practice, dupilumab is positioned as a first-line advanced systemic therapy for patients inadequately controlled by topicals; its targeted nature makes it preferable for long-term use over toxic, broad immunosuppressants like ciclosporin. Practical management focuses on a 16-week assessment, where achieving an EASI-50 or significant quality-of-life improvement (DLQI) warrants continued treatment.[1,153] The recommended dose of dupilumab depends on the patient's age and weight. The approved adult dosage of dupilumab is a 600 mg subcutaneous loading dose, followed by 300 mg every other week. For children, the recommended dosage of dupilumab is based on age and body weight. For children aged 6 months to 5 years who weigh between 5 to less than 15 kilograms should receive 200 mg every 4 weeks. For children weighing 15 to 30 kilograms, the dosage is 300 mg every 4 weeks. In patients aged 6 to 17 years with a body weight between 15 to less than 30 kilograms, an initial dose of 600 mg should be administered, followed by 300 mg every 4 weeks. For those weighing 30 to less than 60 kilograms, the treatment should begin with a 400 mg loading dose, followed by 200 mg every 2 weeks. In those weighing 60 kilograms or more, an initial dose of 600 mg should be given, followed by 300 mg every 2 weeks. Treatment with dupilumab should be used as an add-on therapy in conjunction with the patient's current topical regimen. Side effects include injection site reactions, transient conjunctivitis or blepharitis, occurring in roughly 10-15% of AD patients, and a paradoxical head and neck erythema.[143] Routine laboratory monitoring is not required during dupilumab therapy.[143] Dupilumab may provide additional clinical benefits in AD patients with other comorbidities, including asthma, nasal polyposis, and eosinophilic esophagitis.[143,144]

ii) Lebrikizumab, a human monoclonal antibody that selectively binds to soluble IL-13 with high affinity, preventing the IL-4Rα/IL-13Rα1 heterodimerization and subsequent downstream signaling, is effective and approved in adults and children with moderate to severe AD 12 years of age and older with a body weight of ≥ 88 pounds (40 kg) who are not adequately controlled with topical treatments or who cannot use topical medications.[154] Evidence from Phase 3 randomized controlled trials has established lebrikizumab as an effective therapy for adults and adolescents with over 50% of patients achieving EASI-75 by week 16.[154,155] Lebrikizumab binds IL-13 with high affinity and a slow dissociation rate, a pharmacologic property thought to support its durable clinical effects.[156] In long-term extension studies of week-16 responders, roughly 80% of patients who had achieved deep responses such as EASI-90 maintained near-clear or clear skin for up to three years of continuous lebrikizumab treatment.[157] In clinical practice, lebrikizumab is positioned as a first-line advanced systemic therapy or an alternative for those who have failed at least one other systemic agent. Loading begins with two 250 mg subcutaneous injections (500 mg total) at week 0, followed by 250 mg every two weeks through week 16.

At this critical 16-week assessment, responders achieving at least EASI-50 and significant quality-of-life improvements may transition to a convenient monthly maintenance dose (250 mg every four weeks). Conversely, partial responders may maintain the biweekly schedule to maximize further clinical gains before attempting to reduce dosing frequency. Continuous administration helps sustain improvements in the signs and symptoms of the disease while maintaining a favorable safety profile.[158] The most frequently reported side effects—mostly mild—included conjunctivitis, nasopharyngitis. Injection site reactions were infrequent.[158]

iii) Nemolizumab is a humanized monoclonal antibody that targets IL-31RA, a neuroimmune cytokine involved in the pathogenesis of chronic pruritic skin diseases, particularly AD.[64,144] Nemolizumab was approved for the treatment of pruritus associated with AD in adults and adolescents 12 years of age and older.[64] Phase 3 RCTs demonstrated statistically significant improvements in skin clearance and pruritus with approximately 40% of patients achieving IGA 0/1 by week 16 and a rapid onset of antipruritic effect, with significant reductions in itch scores and sleep disturbance observed within the first week of treatment.[159,160] In clinical practice, nemolizumab, combined with topical corticosteroids and/or calcineurin inhibitors, is indicated for moderate-to-severe atopic dermatitis inadequately controlled by topicals and is particularly attractive when severe pruritus dominates the disease burden. Treatment is initiated with a 60 mg subcutaneous injection at baseline, followed by 30 mg administered every 4 weeks as maintenance therapy. Clinical decision-making centers on a 16-week assessment; responders may transition to maintenance dosing every 4 or 8 weeks. A long-term extension study involving pediatric patients aged 6–12 years demonstrated continued improvement through week 68. Sustained clinical benefits were observed after treatment cessation, along with a favorable safety profile.[161] The reported adverse events include injection-site reactions, upper respiratory infections, nasopharyngitis, peripheral edema, and elevations in creatine phosphokinase levels.[64]

iv) Tralokinumab is a fully human monoclonal IgG4 antibody which targets IL-13, inhibiting its interaction between the IL-13Rα1 and IL-4Rα1 receptor complex.[86,162] Tralokinumab was approved for the treatment of refractory moderate-to-severe AD in patients 12 years of age and older.[64,86,144,163] In Phase 3 RCTs, tralokinumab demonstrated significant improvements in skin clearance, with 25–33% of subjects achieving EASI-75 by week 16.[164] Long-term extension data show durable disease control, with most initial responders maintaining clinical targets for up to 3–4 years of continuous therapy.[165] Although onset is progressive, overall efficacy is further enhanced when tralokinumab is given in combination with topical corticosteroids.[166] The recommended dosing regimen is 600 mg as an initial loading dose, followed by 300 mg every two weeks.[144] In pediatric patients aged 12 to 17 years, the initial dose is 300 mg subcutaneously, followed by 150 mg subcutaneously every two weeks. Conjunctivitis can be reported in patients using tralokinumab.[64,86,167]

4.17 Oral JAK inhibitors

i) Abrocitinib is a JAK1 inhibitor that has been approved for use in AD patients aged 12 years and older with moderate to severe severity.[64,86,168] The recommended dosage of abrocitinib is 100-200 mg/day. Dose adjustment is recommended in certain patient populations. For patients aged ≥ 65 years, treatment should be initiated at a lower dose of 100 mg/day. In patients with moderate to severe renal impairment, the recommended dose is 50-100 mg/day. For patients who are taking medications that inhibit cytochrome P450 (CYP) enzymes or receiving potent CYP2C19 inhibitors such as fluconazole, fluvoxamine, fluoxetine, and ticlopidine, a reduced starting dose of 50 mg/day is recommended. In phase 3 RCTs, abrocitinib showed significant efficacy at week 12 with approximately 61-63% of patients treated with 200 mg achieving EASI-75, and 40-44% of patients treated with 100 mg achieving EASI-75. Initiation with a 200 mg resulted in faster clinical improvement and a greater proportion of responders compared with the 100 mg regimen. Rapid improvement in pruritus severity was observed.[169,170] Abrocitinib also demonstrated good efficacy in adolescents. An EASI-75 response was achieved by 72% of patients receiving 200 mg and 68.5% receiving 100 mg.[171,172] Sustained efficacy was observed. An EASI-75 response was achieved by 85% (200mg/d) and 67% (100 mg/d).[173] Dose reduction should be considered in patients with adverse events. Dose adjustment based on clinical response may be considered during treatment. In long-term management, dose adjustment may require multiple dose modifications in cases of disease exacerbations and remission. Patients who achieve adequate disease control may be maintained on the lowest effective dose, while those with insufficient response to 100 mg may require an increase to 200 mg.[174] The data from post hoc analyses indicated that moderate disease severity AD patients with marked improvement during the induction phase may be suitable for dose reduction.[175] Abrocitinib is contraindicated in patients with a history of allergy to the drug or any of its components, those with severe infections, severe hepatic dysfunction, severe cytopenia, or those who are pregnant or breastfeeding.[64] Upper respiratory tract infections were among the most commonly observed adverse effects.[68] A transient, dose-dependent thrombocytopenia was observed,

typically resolving to baseline levels within four weeks.[68] Long-term integrated safety data from the JADE clinical development program, with follow-up to almost 4 years, demonstrate a consistent safety profile of abrocitinib. Patients aged≥ 65 years have a higher risk of low platelet and absolute lymphocyte count, serious infections, nonmelanoma skin cancers, malignancy excluding nonmelanoma skin cancers, major adverse cardiovascular events, venous thromboembolism, pulmonary embolism, and herpes zoster infection. Current or former smokers have a higher risk of nonmelanoma skin cancers.[176]

ii) Baricitinib is an oral selective JAK 1 and JAK 2 inhibitor that has been approved for the treatment of moderate to severe AD in patients aged 2 years and older.[86] The recommended dosage of baricitinib is 4 mg per day.[143] For pediatric patients, the recommended dose of baricitinib is typically 4 mg once daily for those weighing 30 kg or more, and 2 mg once daily for those weighing between 10 kg and less than 30 kg. Consider reducing the dose to 2 mg/day in patients with impaired kidney function (eGFR 30-60 mL/min), those taking probenecid, or in patients aged 75 years and older with a history of recurrent infections or those receiving organic anion transporter 3 inhibitors. In phase 3 RCTs, baricitinib demonstrated significant efficacy at week 16 with 13.8-16.8% of patients treated with 4 mg achieving IGA 0/1 and 10.6-11.4% of patients treated with 2 mg achieving vIGA-AD 0/1. Reduction in pruritus was observed as early as week 1 with 4 mg and by week 2 with 2 mg dose.[177] In pediatric patients age 2 to < 18 years, 41.7% of patients treated with 4 mg equivalent achieving vIGA-AD 0/1. vIGA-AD responses at week 16 were consistent across age and weight subgroups.[178] In long-term extension study, sustained clinical efficacy was observed among responder and partial responder patients receiving 4 mg or 2 mg. Achievement of vIGA-AD 0/1 was observed in 47.1% of 4 mg group and 59.3% in 2 mg group at week 68.[179] In the pediatric population, 56.8% of the 4 mg equivalent group achieved vIGA-AD 0/1 at week 52.[180] Data from clinical studies demonstrated that patients who underwent downtitration, a substantial proportion were able to maintain clinical response over 16 weeks. Notably, most of patients who experienced flare following dose reduction or treatment withdrawal were able to recapture treatment response upon resuming their prior dose.[181] Baricitinib should not be used in patients who have a history of hypersensitivity to the drug or its components, those with severe infections, significant hepatic or renal dysfunction, severe cytopenia, or individuals who are pregnant or breastfeeding. Frequent adverse effects observed were upper respiratory tract infections, headaches, and increased serum creatine kinase.[68] Integrated safety data from the clinical development program, with up to 3.9 years of exposure, demonstrated a stable and consistent safety profile in adults. The incidence rate of serious adverse events was low. The major adverse cardiovascular events, venous thromboembolism, malignancies, gastrointestinal perforation, and death were uncommon. No report of deep vein thrombosis or tuberculosis.[182]

iii) Upadacitinib is a selective reversible JAK1 inhibitor. It has been approved for the treatment of moderate to severe AD in patients aged 12 years and older.[64,86,143] Upadacitinib is recommended at a daily dose of 15–30 mg. In phase 3 RCTs, upadacitinib demonstrated significant efficacy. EASI-75 responses were achieved by 60-70% of patients receiving 15 mg and 73-80% of patients receiving 30 mg at week 16.[183] Pruritus improved as early as week 1, and the responses increased over time and were sustained through week 16.[184] At week 48, EASI-75 responses were achieved in 87.6%. Clinical responses did not show significant differences between patients treated with 15 mg and 30 mg.[185] In adolescence, EASI-75 response rates were maintained, indicating sustained disease control with long-term treatment. EASI-75 response was achieved by approximately 84-89% of patient receiving 15 mg and 82-96% of those receiving 30 mg.[186] Re-treatment following treatment interruption was not associated with a loss of efficacy.[185] While both doses are effective, clinical studies suggest that the higher dose may offer superior therapeutic outcomes, although it is also associated with an increased risk of adverse events.[64,168] In patients with severe renal impairment or those aged 65 years and older, 15 mg once daily is advised. For patients receiving potent CYP3A4 inhibitors (e.g., itraconazole, ritonavir, clarithromycin), the starting dose should be 15 mg once daily. Concomitant use with CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin) may reduce upadacitinib plasma concentrations and impact efficacy. Upper respiratory tract infections and acne were the most commonly reported adverse events.[187] In a real-world cohort, upadacitinib was generally well tolerated over 48 weeks of follow-up. Most of the reported adverse events were classified as mild to moderate severity and did not lead to treatment withdrawal.[185] In adolescences, long-term safety outcomes through 76 weeks demonstrated that upadacitinib was well-tolerated.[186] Like baricitinib, upadacitinib is also approved in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.[143]

Currently, there are no validated biologic or molecular biomarkers available to reliably predict treatment response to approved biologics or oral JAK inhibitors. Adverse events associated with oral JAK inhibitors include an increased risk of malignancy, serious infections, venous thromboembolism, arterial thrombosis, cardiovascular events, as well as renal and hepatic impairment.[64,168] Comprehensive counseling, pre-treatment screening, age-appropriate cancer screening, infection screening and control and vaccination, along with routine blood monitoring, are critical for the safe administration of oral JAK inhibitors.[64,143,144] Oral JAK inhibitors are contraindicated during pregnancy and lactation.[64] Oral JAK inhibitors may be particularly beneficial in patients with comorbid conditions for which these agents are also indicated, such as rheumatologic diseases or alopecia areata.

4.18 Allergen-specific immunotherapy/ specific desensitization

Allergen-specific immunotherapy may be considered in patients with moderate to severe AD, particularly those with comorbid allergic conditions such as allergic rhinitis or asthma.[64,68,80,86,105,188] This treatment approach may be beneficial for patients with clearly identified allergic sensitizations, as demonstrated by a history of symptom flares upon exposure to allergens, or by positive results from relevant specific IgE testing or skin prick testing—particularly in those sensitized to aeroallergens (e.g., house dust mites or pollen) or domestic animal allergens (e.g., cat and/or dog).[68,82,188-192] Allergen-specific immunotherapy is done by gradually increasing doses of the allergen to modulate the immune response and promote tolerance. Treatment modalities include subcutaneous immunotherapy and sublingual immunotherapy. Allergen-specific immunotherapy has been shown to improve quality of life in patients with AD, reduce disease severity and extent, and decrease the need for topical corticosteroids.[64,82,86,188,193] However, such therapy should be performed under the guidance of a specialist.[86]

Conclusion

Atopic dermatitis (AD) is a chronic, heterogeneous inflammatory skin disease driven by the interplay between epidermal barrier dysfunction, Th2-mediated immune dysregulation, cutaneous dysbiosis, and neuroimmune activation. Improved understanding of these mechanisms has enabled a shift from nonspecific anti-inflammatory treatments toward targeted, mechanism-based therapies. This integrated model explains the clinical diversity of AD and provides the foundation for precision management.

In clinical practice, optimal management must be individualized and guided by established diagnostic criteria and standardized severity assessments such as EASI or SCORAD. The fundamental components of care remain the regular use of emollients to maintain the skin barrier, proactive anti-inflammatory therapy to prevent relapses, and the prompt treatment of acute flares. It is essential to engage in shared decision-making with patients and caregivers; we will commit to providing thorough and current review for the best possible AD care.

The therapeutic landscape for moderate-to-severe or refractory AD has expanded significantly with the availability of targeted biologic agents and Janus kinase (JAK) inhibitors. These advancements offer improved disease control and quality of life when tailored to specific patient factors such as age, comorbidities, and safety considerations. Ongoing updates to clinical guidelines and the integration of emerging evidence into routine practice are essential to optimize long-term outcomes and establish comprehensive standards of care for all patients.

Competing interests

- **Papapit Tuchinda** received educational speaker fees from Sanofi Genzyme, Beiersdorf, and Pfizer.
- **Sira Nanthapisal** received investigator fees from Amgen and Mylan and speaker fees from Eli Lilly, Leo Pharma, Pfizer, and Sanofi.
- **Rattanavalai Nitiyarom** received honoraria for scientific lectures from L'Oreal, Naos, Sanofi-Aventis, and Beiersdorf; advisory board from Zuellig Pharma and Viatris Pharmaceutical; investigator for Amgen Inc.
- **Siriwan Wananukul** received honoraria for scientific lectures from Beiersdorf, Zuellig Pharma, Pfizer.
- **Pantipa Chatchatee** received research grant from Amgen Inc.
- **Orathai Jirapongsananuruk** received honorarium for speaker from Menarini, DKSH, and Viatris.
- **Torpong Thongngarm** has received honoraria for scientific lectures from A.Menarini, Astra-Zeneca, GSK, Novartis, P & G, Sanofi, Takeda, and Viatris; research support from Abbott and Sanofi; has served on the advisory board for Astra-Zeneca, Sanofi and Viatris.
- **Kanokvalai Kulthanan** received educational speaker fees from Sanofi Genzyme, Pfizer, and Zuellig Pharma.
- The rest of the authors declare that they have no relevant conflicts of interest.

Funding/financial support

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

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