Treating moderate-to-severe atopic dermatitis in children and adolescents: Insights from the experts

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Understanding and assessing disease severity in children and adolescents with atopic dermatitis

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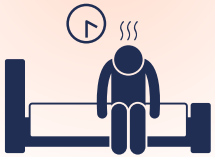
Symptom burden in paediatric populations with AD

CHRONIC PRURITUS[1–3]

SLEEP DISTURBANCE[1,2]



- **IMPAIRED QOL[1]**
- **COGNITIVE IMPAIRMENT[1]**
- **PSYCHOLOGICAL STRESS[1]**
- **IMPAIRED FAMILY RELATIONSHIPS[1,2]**
- **POOR SELF-ESTEEM[2]**
- **POOR SCHOOL PERFORMANCE[2]**
- **EMOTIONAL/ BEHAVIOURAL ISSUES[3]**
- **BURDENSOME TREATMENT (TIME/EXPENSE)[2]**

Symptom burden is particularly significant for patients with chronic hand dermatitis[4]

AD, atopic dermatitis; QoL, quality of life.

1. Cameron S, et al. *Allergy.* 2024;26–36; 2. Lyons JJ, et al. *Immunol Allergy Clin North Am.* 2015;35:161–83;
3. Drucker AM, et al. *J Investig Dermatol.* 2017;137:26e30; 4. Fowler JF, et al. *J Am Acad Dermatol.* 2006;54:448–57.

Considerations for the selection of systemic therapy for children and adolescents with moderate-to-severe atopic dermatitis

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Approved systemic therapies in moderate–severe AD

FDA

Monoclonal antibody

Dupilumab (anti-IL-4Rα)[1]
- Adult and paediatric patients aged ≥6 months

Tralokinumab (anti-IL-13)[2]
- Adult and paediatric patients aged ≥12 years

JAK inhibitor

Abrocitinib[6]
- Adult and paediatric patients aged ≥12 years

Upadacitinib[7]
- Adult and paediatric patients aged ≥12 years

EMA

Monoclonal antibody

Dupilumab (anti-IL-4Rα)[3]
- Adult and paediatric patients aged ≥12 years
- Children aged 6 months–11 years with severe AD

Lebrikizumab (anti-IL-13)[4]
- Adult and paediatric patients aged ≥12 years

Tralokinumab (anti-IL-13)[5]
- Adult and paediatric patients aged ≥12 years

JAK inhibitor

Abrocitinib[8]
- Adult and paediatric patients aged ≥12 years

Baricitinib[9]
- Adult and paediatric patients aged ≥2 years

Upadacitinib[10]
- Adult and paediatric patients aged ≥12 years

Agents used off-label for systemic therapy in paediatric patients with severe AD include methotrexate and cyclosporin A[11]

AD, atopic dermatitis; EMA, European Medicines Agency; FDA, US Food and Drug Administration; IL, interleukin; IL-4Ra, IL-4 receptor alpha; JAK, Janus kinase; pts, patients.

1. FDA. Dupilumab PI. 2024; 2. FDA. Tralokinumab PI. 2024; 3. EMA. Dupilumab SmPC. 2024; 4. EMA. Lebrikizumab. Summary of opinion. 2023. Available at: https://bit.ly/3WBCrkF (accessed 16 August 2024); 5. EMA. Tralokinumab SmPC. 2023; 6. FDA. Abrocitinib PI. 2023; 7. FDA. Upadacitinib PI. 2024; 8. EMA. Abrocitinib SmPC. 2024; 9. EMA. Baricitinib SmPC. 2024; 10. EMA. Upadacitinib SmPC. 2024; 11. Lockhart MK, Siegfried EC. *Dermatol Clin*. 2022;40:137–43.

All PIs available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. All SmPCs available at: www.ema.europa.eu/en/medicines; all URLs accessed 10 July–28 August 2024.

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Practical management of side effects of systemic treatments for moderate-to-severe atopic dermatitis

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Systemic therapies in paediatric AD: Notable side effects

Biologics[1]		JAK inhibitors[1]		
Dupilumab		**Abrocitinib**	**Baricitinib**	**Upadacitinib**
Lebrikizumab		1. Nausea 2. Acne (less than with upadacitinib) 3. ↑ upper respiratory tract & herpetic infections 4. Headache	1. Headache 2. ↑ upper respiratory and herpes simplex infections	1. Acne 2. Nasopharyngitis, ↑ upper respiratory tract and herpetic infections 3. Headache
Tralokinumab				
1. Conjunctivitis 2. Injection-site reactions		Abnormal haematologic counts, ↑ lipids & creatine phosphokinase levels[1]* Boxed warning[1] and PRAC recommendation[2] for JAK inhibitor agent class for theoretical risk of malignancy, cardiovascular disease, emboli, and serious infections		

Biologics are not associated with an increase in AEs/SAEs leading to discontinuation vs topical therapy alone[3]

The risk–benefit profile of **JAK inhibitors** should be considered when selecting an agent in clinical practice[3]

*Not clinically significant.

AD, atopic dermatitis; AE, adverse event; JAK, Janus kinase; PRAC, Pharmacovigilance Risk Assessment Committee; SAE, serious AE.

1. Butala S, Paller AS. *J Allergy Clin Immunol.* 2023;151:681–5; 2. EMA. 2023. Available at: https://shorturl.at/uXLcC (accessed 7 August 2024);
3. Chu DK, et al. *Ann Allergy Asthma Immunol.* 2024;132:274–312.

Long-term data: Systematic review and updates from EADV 2023

Long-term efficacy and safety data with systemic therapies for atopic dermatitis

Trial	Agent(s)	Outcomes	Conclusions
Systematic review of 33 publications on biologics and JAK inhibitors[1]	**Biologics:** Dupilumab Tralokinumab **JAK inhibitors:** Upadacitinib Baricitinib	**Efficacy (48–60 weeks)** • **Dupilumab** and **upadacitinib** achieved clinically superior efficacy outcomes (EASI 75 and vIGA-AD 0/1) • **Tralokinumab** data also highly satisfactory **Safety** • **Dupilumab (52-week treatment); tralokinumab (36-week maintenance)** showed the lowest risk of AEs; most discontinuations due to AD flares	Systematic review results like these may help inform treatment guidelines
Phase III Measure Up 1 study[2] Adults and adolescents aged ≥12 years with moderate-to-severe AD	**Upadacitinib (15 mg / 30 mg)** vs placebo Long-term efficacy and safety	Efficacy of both doses was consistently maintained for: • **Skin clearance** (EASI 75; EASI 90; vIGA-AD 0/1) and • **Symptom control** (WI-NRS 0/1) from week 16 **through week 140** **Safety consistent with the known upadacitinib safety profile, with no new safety signals observed**	Upadacitinib sustained skin clearance and itch with a consistent safety profile across 140 weeks

EASI, Eczema Area and Severity Index; JAK, Janus kinase; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS, Worst Itch Numerical Rating Scale.

1. Ayen-Rodriguez A, et al. *Life.* 2022;12:1159; 2. Silverberg JI, et al. *Br J Dermatol.* 2024;190(Suppl.2):ii8.

Latest data: Updates from AAD 2024 and AAAAI 2024

Long-term data for symptom improvement and disease control with systemic biological therapies

Trial	Agent	Outcomes	Conclusions
Phase III LIBERTY AD PED-OLE[1] Children and adolescents aged 0.5–17 yrs (N=763)	**Dupilumab** 300 mg Q4W (<60 kg) or 200/300 mg Q2W (≥60 kg)	**Weeks 4, 16, 28, 40 and 52** **EASI <7 maintained** in **≥4 of 5 timepoints** in most patients across ages (years): • 0.5–5, **63%** • 6–11, **58%** • 12–17, **50%**	Most patients achieved sustained and consistent improvements in signs and area affected by AD during 1 year of treatment with dupilumab
Phase III extension[2] Adults and adolescents with moderate-to-severe AD; week 16 responders (ADvocate1/2)	**Lebrikizumab** vs placebo	**At week 52** • EASI 75: **80%**; ≥4-point improvement in NRS: **84%** **Continuous maintenance of composite endpoint (EASI ≤7 or NRS ≤4) for 36 wks after Q2W to Q4W switch** **At week 52** **91%** of pts on Q4W regimen continued to maintain EASI ≤7 or NRS ≤4	Patients with moderate-to-severe AD switching to Q4W after Q2W induction maintain a response at week 52

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; NRS, pruritus Numeric Rating Scale; POEM, Patient-Oriented Eczema Measure; Q2W, every 2 weeks; Q4W, every 4 weeks.

1. Siegfried E, et al. *J Am Acad Dermatol.* 2024;91(Suppl.):AB188; 2. Stein Gold L, et al. *J Am Acad Dermatol.* 2024;91(Suppl.):AB58.