Atopic dermatitis
New and emerging treatments

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Atopic dermatitis is a chronic relapsing and remitting disease. Patients typically receive treatment with counselling, trigger avoidance, emollients, wet dressings and topical corticosteroids. Conventional systemic agents may be required for severe disease but are often associated with significant adverse events. Recently, the treatment landscape for these patients has changed dramatically with the PBS listing of two targeted systemic treatments: dupilumab and upadacitinib. Other emerging treatments are on the horizon, offering promising options for those with severe recalcitrant disease.

KEY POINTS

- Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder worldwide, resulting from skin barrier disruption and a genetic predisposition.
- The mainstay of treatment for mild-to-moderate AD includes topical corticosteroids, topical calcineurin inhibitors and trigger avoidance.
- Conventional treatment of moderate-to-severe AD includes phototherapy and systemic immunosuppression.
- Novel systemic treatments that are PBS listed for moderate-to-severe AD include dupilumab (a human monoclonal antibody that blocks interleukin-4 and interleukin-13 signalling) and upadacitinib (a Janus kinase-1 selective small molecule inhibitor).
- Emerging targeted treatments offer promising options for patients with AD who have severe recalcitrant disease.

Atopic dermatitis (AD), also known as eczema, is the most common inflammatory skin condition worldwide, affecting about one in 10 individuals. It is a chronic relapsing and remitting condition seen in all age groups, although it tends to begin in infancy within the first year of life.[1] About 30% of infants and 10% of adults experience AD.[1-3] AD is often clustered with other allergic hypersensitivity diseases (allergic rhinitis and asthma, often known as the atopic triad), which all have similar mechanisms of pathogenesis.[4] Several longitudinal studies also provide evidence to support the atopic march – that is, the progressive development of AD, food allergy, allergic rhinitis and asthma throughout childhood.[5-7]

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Untreated symptomatic AD can have a negative impact on patients' quality of life. The unrelenting itch-scratch cycle leads to sleep disturbance and chronic fatigue. Continuous itch affects concentration and school performance in children. The mental health comorbidities of AD (e.g. attention deficit hyperactivity disorder, anxiety, depression, low self-esteem, conduct disorder and autism) are well established.[8-10] Importantly, school performance is compromised by chronic fatigue, behavioural issues and absenteeism, which severely impacts future life courses. Assertive proactive management of AD is paramount.

The past decade has seen an increase in advanced therapeutic options becoming available for AD in Australia through clinical trials and more recently listed on the PBS. This article provides an overview of treatment option pathways, which includes new topical and systemic agents and those on the near horizon. Many of these emerging therapies have surpassed phase 3 clinical trials and are already in use for patients overseas with chronic severe AD (Figure 1).[11-16]

Pathogenesis

The pathogenesis of AD is complex and multifactorial. AD is a result of both genetic and environmental factors and immune system dysregulation.[17,18] Evidence to date suggests that AD is

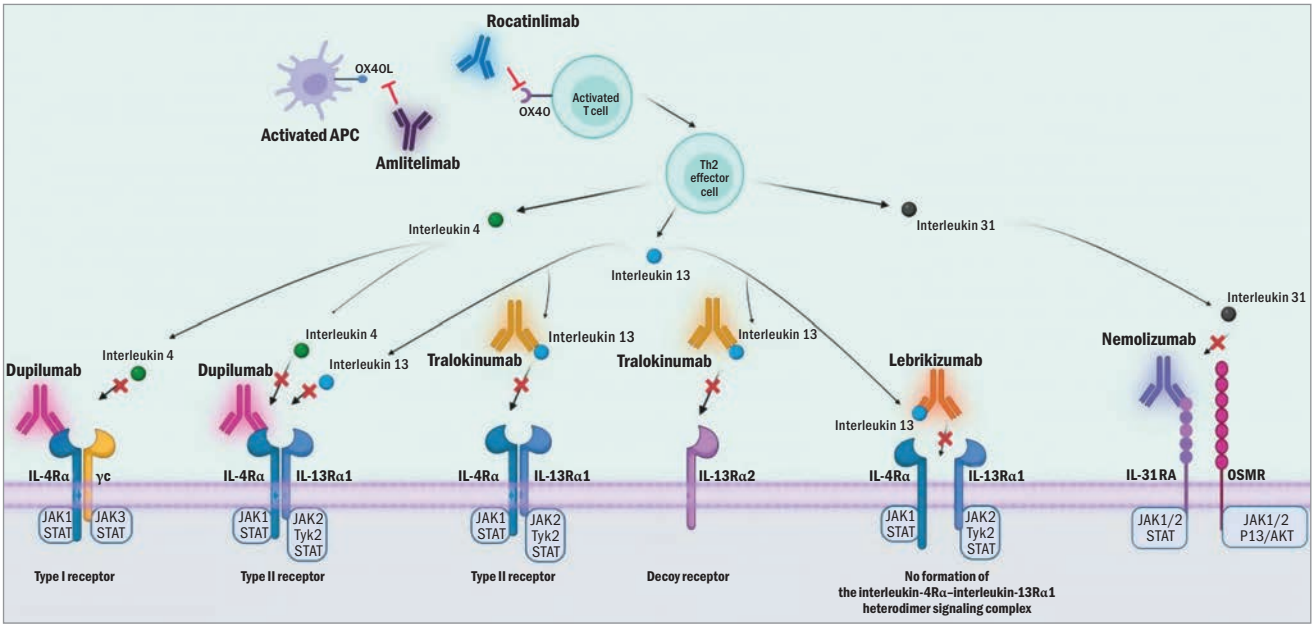

Figure 1. Mechanisms of action of biologic drugs for atopic dermatitis: dupilumab, tralokinumab, lebrikizumab, nemolizumab, rocatinlimab and amlitelumab.

Abbreviations: APC = antigen-presenting cell; IL-31RA = IL-31 receptor A; IL-4Rα = IL-4 receptor alpha chain; IL-13Rα1 = IL-13 receptor alpha 1 chain; IL-13Rα2 = IL-13 receptor alpha 2 chain; JAK = Janus kinase; OSMR = oncostatin M receptor; PI3/AKT = phosphoinositide 3-kinase/protein kinase B; STAT = signal transducer and activator of transcription; Th2 = T helper 2; Tyk2 = tyrosine kinase 2; γc = γc chain.

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driven by an overactive T helper 2 (Th2) response. This Th2 dominance leads to the production of various cytokines, such as interleukin (IL)-4, IL-5, IL-13 and IL-31, which contribute to a dysregulated inflammatory response, contributing to skin barrier disruption.[17] In response to the compromised skin barrier, keratinocytes produce cytokines such as thymic stromal lymphopoietin, IL-25 and IL-33, which further augments the Th2 response. These inflammatory cytokines also orchestrate the itch sensation by activating cutaneous sensory nerve fibres.[1,17]

Together, this heightened inflammatory cycle reduces the expression of filaggrin that maintains skin barrier integrity. There is a well-established association between filaggrin mutations and AD, although this is not a causal link, as many patients with filaggrin mutations do not develop AD.[17,18] Reduced levels of expression of other components of the epidermis, such as loricrin, involucrin and ceramides, also contribute to the skin barrier deficits that are a hallmark feature of AD.[17,19]

The impaired skin barrier in AD allows for increased transepidermal water loss, enabling allergens to enter more easily, triggering immunoglobulin E sensitisation.[19,20] Triggers for AD can include common allergens such as food, dust mites, environmental allergens (e.g. pollen, grass and mould), irritants (e.g. chlorine, sex hormones, latex) and even changes in weather can trigger an eczema flare.[20,21] A disrupted skin barrier also provides a portal for pathogen entry. Secondary skin infections with *Staphylococcus aureus* and herpes simplex virus further disrupt the skin barrier and further exacerbate AD.[20,21]

Clinical presentation

AD is generally a clinical diagnosis; however, the clinical presentation of AD varies tremendously. Infants can present with AD on the face and there can be extensor involvement such as on the trunk or back.[22,23] However, in adolescents and adults, AD typically presents over flexural areas such as the antecubital and popliteal fossae. Flare-ups of AD can present as intensely pruritic, erythematous, weeping oedematous lesions sometimes associated with crusting. Erosions and excoriations are common, and lichenification or thickening of the skin is a sign of disease chronicity.[19,22,23]

Disease severity scales most relevant to healthcare practitioners in Australia are the Eczema Area and Severity Index (EASI) and Physician Global Assessment (PGA). A minimum rating on these two scales (a baseline EASI of at least 20 and PGA of 4) is required for a PBS subsidy if considering a patient for treatment with an advanced targeted therapy. Other scales have been validated and used in research settings including the Scoring Atopic Dermatitis (SCORAD) index and the Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score that aims to objectively describe the clinical features of AD. To measure the impact of AD on sleep, mood and quality of life, the Patient-Oriented Eczema Measure and Dermatology Quality of Life Index (DLQI) severity scale have been developed.[19] For prescribing new

targeted therapies in Australia, the DLQI score is required at baseline and is then repeated with each continuous prescription application.

Treatment

Physical therapies and antibiotics

AD is a relapsing disease. General management recommendations for patients with AD include avoiding irritants such as perfumed products and avoiding exposure to triggers (Box 1).[1,24] Moisturising at least twice daily is recommended to maintain the integrity of the skin barrier.[19,25] Daily bathing or luke warm showers are recommended to reduce bacterial skin load and are limited to a five-minute duration to avoid skin flares.[1,19,24,25] Wet dressings may reduce skin irritation and protect the skin from further trauma but can be cumbersome and time consuming to apply and cause irritation if left overnight.[1,25-27] Bleach baths may be recommended to avoid secondary skin infections.[1,23,25,26,28] Other physical therapies, such as controlled exposure to narrowband ultraviolet light therapy, are also considered for AD because of their immunosuppressive effects and ability to enhance the epidermal barrier.[24]

AD-affected skin can be colonised by *S. aureus*; therefore, a positive culture from a swab alone cannot differentiate between colonisation and active infection. The decision to treat with systemic antibiotics depends on the clinical relevance, ideally with antimicrobial sensitivities confirmed through culture.[1,29] Skin swabs (viral and bacterial) are recommended in circumstances where a secondary skin infection is suspected, to confirm the diagnosis and guide treatment choice.

Topical corticosteroids

The mainstay of treatment for AD is the use of topical corticosteroids to reduce inflammation (Box 2).[2] The recommended potency of topical corticosteroids depends on the severity and location of the AD. A mild-potency topical corticosteroid is recommended for the face and flexures (e.g. axilla, inframammary, inguinal, cubital or popliteal fossa, genitals) and high potency for thickened, lichenified areas and the palms and soles.[1] The potency of corticosteroids is well documented.[30] Topical corticosteroids can be applied directly onto skin, or in conjunction with emollients, which are generally applied over topical corticosteroids on inflamed skin.

Clobetasol 0.05% ointment and cream, the most ultrapotent topical corticosteroid, is now PBS listed from 1 May 2025, available in a 30g tube.

Long-term inappropriate use of corticosteroids can lead to skin atrophy, striae, rosacea, telangiectasias and purpura.[30] A standard unit used for topical corticosteroid application is the fingertip unit (FTU), which covers the area of two adult hands (i.e. 1 FTU = 0.5 g = 2 palms = 2% of an adult's body surface area).[31,32] The recommended FTUs for adequate effectiveness is well documented.[31,32] However, there is a plethora of misinformation about the safety of topical corticosteroids in the media leading to a suboptimal treatment response.[33] Reassurance and regular clinical reviews can help overcome treatment barriers.

It is important to select an appropriate base for the topical therapy. Creams are reserved for hair-bearing areas or patient comfort, whereas ointments will increase the topical steroid potency and minimise stinging (thus prescribed for severe flares with major excoriations).

Alternative topical therapies to corticosteroids

Alternative topical therapies to corticosteroids for AD available in Australia are calcineurin inhibitors and crisaborole.

Topical calcineurin inhibitors include tacrolimus ointment (0.03% and 0.1% strengths) and pimecrolimus cream (1% strength). These topical calcineurin inhibitors are naturally produced by *Streptomyces* bacteria and inhibit T-cell activation, reducing the inflammatory response in AD.[34] Topical pimecrolimus 1% is PBS listed for the treatment of AD and is safe to use in sensitive areas such as the eyelids and face in children over the age of 3 months.[35] To date, access to topical tacrolimus requires compounding in Australia but the 0.1% tacrolimus ointment is TGA approved for the treatment of moderate-to-severe AD, and is due for release soon.

Crisaborole 2% is a nonsteroidal topical ointment that inhibits the activity of phosphodiesterase-4 (PDE-4), the levels of which are elevated in patients with AD. The reported barriers are cost and tolerability.[36] It is approved by the TGA for the treatment of mild-to-moderate AD in patients 2 years of age and older; however, it is not currently

1. PHYSICAL THERAPIES FOR ATOPIC DERMATITIS

Trigger avoidance
- Avoiding hot showers and the use of cosmetics, fragrances and detergents

Cool compresses
- Short-term use for flares
- Generally two to three times per day for one week
- Left on for five to 10 minutes

Wet dressings
- Short-term use for flares
- Generally two to three times per day for one week
- Left on for one to two hours; remove when dry
- Wet dressings can be used over topical corticosteroid treatments to enhance absorption

Bleach baths
- 12 mL household bleach (4% sodium hypochlorite) per 10 L of water
- Five-minute soak daily during active flare (usually daily for one month, then three times a week for one month, then once a week for one month)
- Bath oil may be added
- Bath temperature: 28 to 30°C

Narrowband ultraviolet B (phototherapy)
- Controlled exposure to a narrow peak of ultraviolet light (311 nm), three times weekly, reassessed every six to 12 weeks
- Used in conjunction with topical or systemic treatments
- Accessed via referral to specialist dermatologist or major public health service

2. TOPICAL, ORAL AND SUBCUTANEOUS TREATMENTS FOR ATOPIC DERMATITIS

Topical*

Topical corticosteroids

***Mild*†**
- Hydrocortisone 0.5–1%
- Desonide 0.05%

Moderate
- Methylprednisolone aceponate 0.1%
- Triamcinolone acetonide 0.02%
- Betamethasone valerate cream 0.02%, 0.05%
- Clobetasone butyrate 0.05%

Potent
- Betamethasone dipropionate 0.05%
- Betamethasone valerate ointment 0.1%
- Mometasone furoate 0.1%

Ultrapotent
- Betamethasone dipropionate 0.05% in optimised vehicle
- Clobetasol propionate 0.05% (PBS listed from 1st May 2025)

Nonsteroidal topical treatments†
- Calcineurin inhibitors
  - Pimecrolimus 1% (PBS listed for AD)
  - Tacrolimus 0.1%, 0.03% (compounded); both considered safe in children from 3 months of age[35]
- PDE-4 inhibitor
  - Crisaborole 2% (TGA approved for mild-to-moderate AD in patients 2 years of age and older, but is not currently PBS listed)

Emerging therapies (not currently TGA approved)
- Delgocitinib 2% (pan JAK inhibitor)
- Tapinarof 1% (aryl hydrocarbon receptor agonist)

Emollients plus
- Emollients containing ceramides
- Emollients containing other nonprescription beneficial ingredients

Oral

Oral corticosteroid avoidance
- Prednisolone is rarely used and reserved only for emergency settings under very close supervision

Corticosteroid-sparing agents
- Ciclosporin‡
- Methotrexate
- Azathioprine
- Mycophenolate mofetil

JAK inhibitors
- Upadacitinib (selective JAK-1 inhibitor)
  - 15 mg to 30 mg once daily
  - PBS listed for patients over 12 years of age for chronic severe AD
- Abrocitinib (selective oral JAK-1 inhibitor)
  - 100 to 200 mg once daily
  - TGA approved for moderate-to-severe AD but not PBS listed

Subcutaneous

Novel targeted treatments
- Dupilumab (IL-4Rα monoclonal antibody that blocks IL-4/IL-13 signalling)
  - loading dose: 600 mg (week 0)
  - maintenance: 300 mg every 2 weeks
  - PBS listed for patients aged 12 years and older with chronic severe AD

Emerging treatment (TGA approved)
- Lebrikizumab (IL-13 monoclonal antibody)
  - loading dose: 500 mg (at weeks 0 and 2)
  - induction: 250 mg every 2 weeks (until week 16)
  - maintenance dose: 250 mg every 4 weeks
  - TGA approved for patients 12 years of age and older with moderate-to-severe AD but not currently PBS listed

Emerging treatments (not currently TGA approved)
- Tralokinumab (IL-13 monoclonal antibody)
- Nemolizimab (IL-31Rα antagonist)
- Rocatinlimab (OX40 monoclobal antibody)
- Amlitelimab (OX40 ligand monoclonal antibody)

Abbreviations: AD = atopic dermatitis; JAK = Janus kinase; PDE-4 = phosphodiesterase-4.

* Treatment times depend on the severity of disease. AD should be treated until inflammation is settled with supervision.
† Preferred for sensitive areas such as the face, axilla and groin.
‡ Ciclosporin is the only conventional systemic agent that is TGA approved and PBS listed for AD.

PBS listed (available for purchase in 60 g at a nonsubsidised private price).

Oral corticosteroids and conventional systemic agents

Oral corticosteroids are rarely required for management of severe AD. Patients with a severe flare can be managed with wet dressings and must be prescribed sufficient quantities of topical therapies. Moreover, these patients require a prompt review for initiation of a systemic therapy. Corticosteroid-sparing agents, such as methotrexate and ciclosporin, may be considered; however, with the increasing availability of targeted treatments, these systemic treatments are no longer the mainstay of treatment for severe AD because of their potential for severe life-threatening side effects (e.g. myelosuppression and hepatotoxicity with methotrexate; and hypertension and renal failure with ciclosporin).[37]

Novel targeted therapies approved and PBS subsidised for use in Australia

Patients with severe refractory cases of AD may be referred to a dermatologist to access novel systemic treatments. Practical considerations when referring patients to dermatologists for more advanced therapies are outlined in Box 3.

Dupilumab

Dupilumab is a human monoclonal antibody that binds IL-4Rα and inhibits signalling mediated by IL-4 and IL-13, key drivers of the inflammatory response of a variety of Th2-mediated diseases, including AD, asthma, rhinosinusitis, nasal polyposis and eosinophilic oesophagitis.[38] It is administered fortnightly as a subcutaneous injection (300 mg, after a loading dose of 600 mg). It is generally well tolerated. Commonly reported side effects include

conjunctivitis, injection-site reactions, nasopharyngitis, headache and oral herpes simplex virus reactivation.[39] Rarer adverse effects that have been reported include seronegative arthritis and enthesitis, de novo psoriasis, paradoxical head and neck dermatitis and worsening of alopecia areata.[40-42] Recent literature has raised the possibility of an increased risk of cutaneous T cell lymphoma, although further research is needed as reported data appear to be inconclusive.[43,44]

Dupilumab has been listed on the PBS since March 2021 for the treatment of chronic severe AD in patients aged 12 years and older who have failed to respond to optimally prescribed topical treatments. It is approved internationally for use in infants as young as 6 months of age, and real-world data already exist for children.[44] Skin areas before and after treatment with dupilumab are shown in Figures 2 to 5.

Upadacitinib

Upadacitinib is an oral small molecule that selectively inhibits the signalling of Janus kinase (JAK)-1, which is a key intracellular mediator of Th2 cytokine signalling integral to AD pathogenesis. Upadacitinib has been PBS listed since March 2022 for patients over 12 years of age with chronic severe AD and has been successfully used to control inflammation in a range of inflammatory conditions including rheumatoid arthritis, psoriatic arthritis and inflammatory bowel disease.[46] A head-to-head study comparing the efficacy of upadacitinib with dupilumab in adults with moderate-to-severe AD showed that upadacitinib was slightly superior to dupilumab. At week 16, 61.6% of patients treated with 30 mg upadacitinib achieved 90% improvement in the EASI (EASI90) versus 40.3% with 300 mg dupilumab.[47] Upadacitinib was more rapid at improving itch symptoms compared with dupilumab.[46]

Upadacitinib is a well-tolerated, convenient, once-daily oral treatment, but requires close monitoring because of its immunosuppressive effect. Side effects include acne, upper respiratory tract infections, headache, gastrointestinal disorders, urinary tract infections and opportunistic infections such as herpes zoster reactivation.[48] Haematological abnormalities such as anaemia, thrombocytosis, elevated transaminases and creatine kinase levels and changes in lipid profile have been noted in some patients following the initiation of treatment and require monitoring.

Major serious adverse effects have been described with general JAK inhibition and include cardiovascular events such as venous thromboembolism, stroke and increased risk of malignancy. The TGA has therefore recommended that JAK inhibitors should not be prescribed in patients who are aged over 65 years with a history of cardiovascular disease or at risk of cancer unless there are no alternative treatments. These recommendations are presented as a black box warning in the US , which were triggered by reported outcomes with tofacitinib (a small molecule with nonspecific JAK inhibition [JAK-1, JAK-2, JAK-3 and tyrosine kinase 2] prescribed in rheumatological patients).[49] Shingrix and pneumococcal vaccination should be administered to all patients considering treatment with JAK inhibitors.

Emerging topical therapies

Delgocitinib

Delgocitinib is a topical pan-JAK inhibitor for moderate-to-severe hand dermatitis.[50] Internationally, it is a 2% formulation, applied twice daily. To date, in Australia, compounding of this agent is unavailable. The medication is expecting TGA approval in late 2025. Pooled analysis of the DELTA 1 and 2 trials (phase 3) showed that 20% and 29% of patients treated with delgocitinib , respectively, achieved treatment success with improved hand eczema severity scores and DLQI scores after 16 weeks compared with 10% and 7% of patients who received the cream vehicle (placebo arm), respectively.[51]

Tapinarof

Tapinarof 1% is a novel nonsteroidal topical aryl hydrocarbon receptor (AhR) agonist applied once daily, which was originally approved by the US Food and Drug Administration for psoriasis. AhR is a cytoplasmic receptor that is ubiquitously expressed, and holds key roles in gene expression, cellular homeostasis and immune responses.[52] Its anti-inflammatory effect is mediated by the downregulation of Th2 cytokines, reducing oxidative stress and improving the skin barrier. The phase 3 ADORING trials demonstrated favourable

3. CONSIDERATIONS FOR REFERRAL TO A DERMATOLOGIST

Patient factors
- Compliance issues or concerns with topical therapies
- Psychosocial impact (missed school or work, impact on relationships)

Disease factors
- Impact on sleep and high itch scores (>4 on Visual Analogue Scale)
- Severe regional presentation (face, hand, feet), refractory to 4 weeks of daily topical corticosteroids or topical calcineurin inhibitors
- Severe generalised presenation, refractory to 4 weeks of daily topical corticosteroids or topical calcineurin inhibitors
- Diagnostic challenges (mimickers e.g. scabies, tinea, psoriasis, contact allergy)

Complications
- Eczema herpeticum (secondary herpes simplex infection)
- Impetiginised eczema (secondary staphylococcal infection)
- Erythroderma, dyspigmentation, lichenification

Key PBS criteria* for targeted therapies (dupilumab and upadacitinib)
- Physician Global Assessment baseline score of at least 4
- Eczema Area and Severity Index baseline score of at least 20
- DLQI baseline score of any value† but a score of 6 or more indicates the disease is having a moderate effect on the patient's life
- Chronic severe AD lesions present for at least 6 months (affecting either the whole body or the face and hands)

Abbreviation: DLQI = Dermatology Life Quality Index.

* These PBS criteria serve only as a guide, as many patients with refractory disease who do not meet all the criteria will still benefit from a specialist assessment. Variations of this scoring system are used overseas for the prescription of advanced targeted therapies.

† For continuing prescription in Australia, patients need to demonstrate an improvement in DLQI score of at least 4 points compared with baseline (thus logically the minimum baseline DLQI must be ≥4).

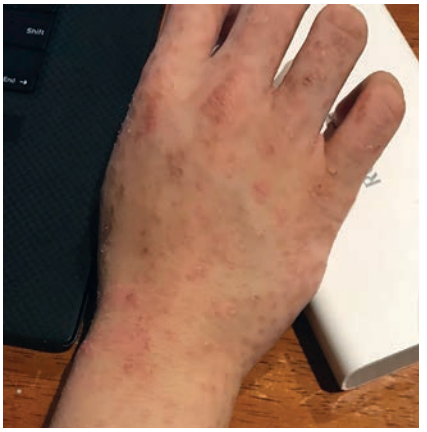

Figure 2a. Right hand of patient A before dupilumab treatment.
Image published with patient consent.

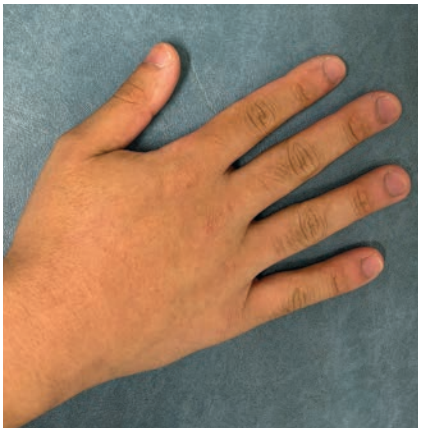

Figure 2b. Right hand of patient A after dupilumab treatment.
Image published with patient consent.

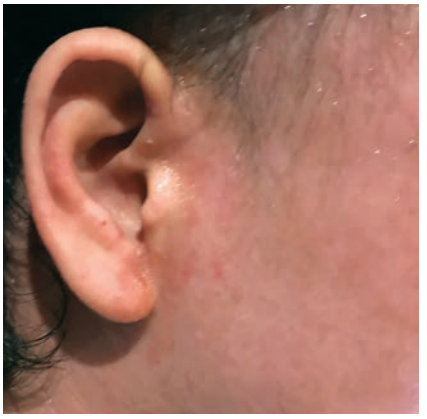

Figure 3a. Right lateral face of patient A before dupilumab treatment.
Image published with patient consent.

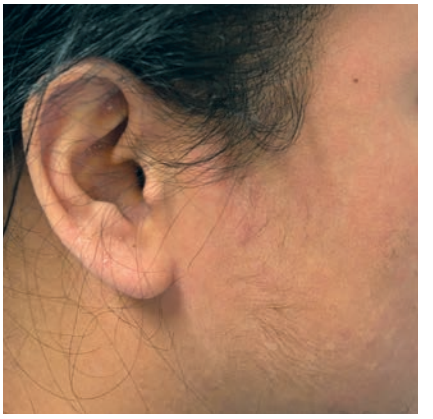

Figure 3b. Right lateral face of patient A after dupilumab treatment.
Image published with patient consent.

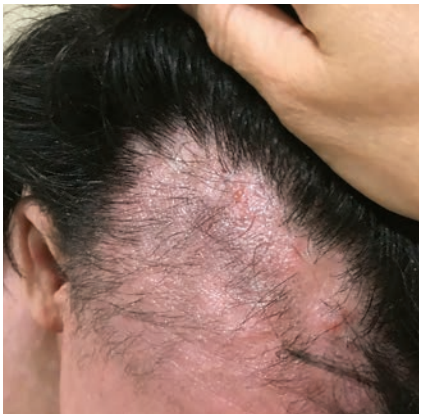

Figure 4a. Right frontal scalp of patient A before dupilumab treatment.
Image published with patient consent.

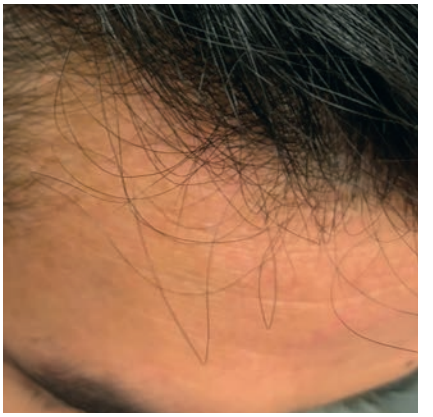

Figure 4b. Right frontal scalp of patient A after dupilumab treatment.
Image published with patient consent.

tolerability, safety and efficacy with the use of tapinarof in patients with AD from the age of 2 years. After eight weeks of therapy, an improvement of 75% in EASI (EASI75) was achieved in 56% of patients versus 23% for vehicle.[15,53] Common adverse events, although minimal, include folliculitis, headache and nasopharyngitis.

Emerging oral and subcutaneous therapies

Abrocitinib

Abrocitinib is a selective oral JAK 1 inhibitor used for the treatment of moderate-to-severe AD. It is TGA approved for moderate-to-severe AD and recently was recommended for a PBS listing (November 2024) for adult patients with chronic severe AD. In a phase 3, double-blind, clinical trial, abrocitinib at a dose of either 200 mg or 100 mg once daily resulted in a significantly improved EASI75 response for moderate-to-severe AD than placebo at weeks 12 and 16, comparable with dupilumab at the study end point.[54] However, the 200 mg dose of abrocitinib was superior to dupilumab with respect to itch response at week 2.[54] The most commonly reported side effects associated with this treatment included nausea, acne and herpes zoster infection.[54]

Lebrikizumab

Lebrikizumab is a selective anti IL-13 human monoclonal antibody that is effective for AD particularly because of its slow dissociation rate.[55] Lebrikizumab prevents the formation of the IL-13Rα/IL4Rα complex, thus blocking IL-13 signalling (via binding to only the IL-13 α1 chain), which is thought be the key driver of inflammation in AD. Two phase 3 clinical trials have shown that in adults and adolescents with moderate-to-severe AD, treatment with lebrikizumab monotherapy every two weeks improved skin clearance compared with placebo over a 16-week induction period.[56] An EASI75 response was seen in 58.8% of patients receiving lebrikizumab compared with 16.2% for placebo.[57] Most side effects were mild in severity, with conjunctivitis and

herpes zoster infections most commonly reported.[56,57] Lebrikizumab is TGA approved for the treatment of moderate-to-severe AD in patients 12 years of age and older, but the drug is currently not listed on the PBS (it received a recommendation for a PBS listing in March 2024).

Tralokinumab

Tralokinumab is also a selective anti IL-13 human monoclonal antibody, which is different to lebrikizumab in that it blocks the binding of IL-13 to both receptor chains. Phase 2 studies have shown that tralokinumab was superior to placebo at 16 weeks of treatment and was well tolerated, with most responders not requiring any rescue medication such as topical corticosteroids for the duration of the study.[58] Selective IL-13 agents appear to be better tolerated compared with IL-4/-13 inhibitors owing to fewer ocular adverse effects and fewer injection-site reactions.

Nemolizumab

Nemolizumab is an IL-31Rα antagonist that prevents binding of IL-31 to its receptor. IL-31 has been implicated in the pathophysiology of multiple Th2-mediated atopic disorders. Notably, IL-31 has been identified as one of the main drivers of pruritus that characterises AD, exacerbating skin barrier disruption.[59] Two replicate phase 3, double-blind, randomised clinical trials (ARCADIA 1 and ARCADIA 2) have demonstrated that nemolizumab 30 mg improved eczema assessment scores, itch and sleep at 16 weeks in adolescent and adult patients with moderate-to-severe AD.[60] Generally, the treatment was well tolerated with minimal adverse effects, although those commonly reported were nasopharyngitis and upper respiratory tract infections.[60] Moreover, there was no increased rates of conjunctivitis, herpes zoster infections or de novo cases of asthma reported.

Rocatinlimab and amlitelimab

The expression of OX40-positive T cells is increased in patients with AD compared with healthy controls. OX40 is present on sensitised T cells after antigen-specific activation, leading to the expression of OX40 on the surface of effector and memory cells, thereby promoting T cell survival and memory.[61] It is not expressed in naïve T cells. Moreover, OX40 expression is increased in pathogenic T cells. In skin biopsies of AD lesions, OX40 and OX40 ligand-positive cells were co-localised in the dermis, lending strong support for their role in AD pathogenesis.[61,62] The OX40 and OX40 ligand interaction has been reported to enhance cell mobility, promote an effector T cell phenotype, increase cytokine production and conversely, suppress the action of T regulatory cells.[63,64]

Rocatinlimab is an anti-OX40 monoclonal antibody that binds to OX40 present on an activated CD4-positive, CD8-positive T cell.[63] It reduces the number and inhibits the expression of OX40-expressing pathogenic T cells. A phase 2 clinical trial has shown that rocatinlimab treatment improved EASI scores by 60% compared with placebo (15%) over the duration of the study period. The most efficacious response was noted in the group that received 300 mg, fortnightly.[65] The most common adverse effects were pyrexia, chills, headache, aphthous ulcers and nausea.[65]

Amlitelimab is a OX40 ligand monoclonal antibody that binds to the OX40 ligand on antigen-presenting cells. In a phase 2a multicentre study, amlitelimab showed improvements in EASI scores of 80%, compared with 50% in the placebo arm.[66] Adverse effects noted with this treatment included headache, hyperhidrosis, pyrexia, iron-deficiency anaemia and elevated aspartate aminotransferase levels.[66]

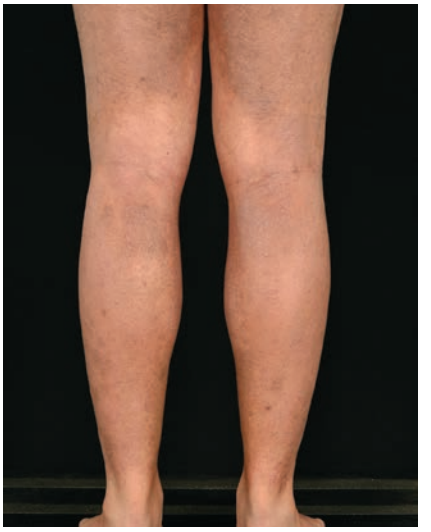

Figure 5a. Posterior legs of patient B, skin type 3, before dupilumab treatment.

Figure 5b. Posterior legs of patient B, skin type 3, after dupilumab treatment.

Conclusion

AD is a complex, multifactorial disease with a relapsing and remitting course. An improved understanding of the pathogenesis of AD has contributed to an array of novel therapeutics.[67] In the era of precision medicine, specific targeted treatments for AD offer promise to patients who have not responded to conventional management. Although some agents are not yet PBS listed in Australia, many are in fact already in use overseas for patients with chronic severe AD with 'real world' experience being compiled. This will certainly shed light on the safety and efficacy of these novel therapeutics over years to come. MT

References

A list of references is included in the online version of this article (https://medicinetoday.com.au/mt/2025/june/supplements/dermatology-collection-vol-9-no-1).

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Atopic dermatitis
New and emerging treatments

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