## ORIGINAL RESEARCH



# Canadian Consensus Guidelines for the Management of Atopic Dermatitis with Topical Therapies

Melinda J. Gooderham · H. Chih-ho Hong · Charles Lynde · Kim A. Papp ·

Jensen Yeung · Harvey Lui · Yvette Miller-Monthrope · Julien Ringuet · Irina Turchin ·

Vimal H. Prajapati

Received: January 21, 2025 / Accepted: March 11, 2025 / Published online: April 25, 2025 © The Author(s) 2025

# **ABSTRACT**

Introduction: Atopic dermatitis (AD) is a highly prevalent disease in Canada with significant patient burden. Treatment guidance for topical therapy (the mainstay of AD management), with particular consideration of emerging treatments, may further improve patient

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s13555-025-01386-2.

M. J. Gooderham (⊠)

SKiN Centre for Dermatology, 775 Monaghan Rd, Peterborough, ON K9J 5K2, Canada e-mail: mgooderham@centrefordermatology.com

M. J. Gooderham

Probity Medical Research, Peterborough, ON, Canada

M. I. Gooderham

Queen's University, Peterborough, ON, Canada

H. C. Hong · H. Lui

Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

H. C. Hong

Probity Medical Research, Surrey, BC, Canada

C. Lynde

Lynde Institute for Dermatology, Markham, ON, Canada

C. Lvnde

Probity Medical Research, Markham, ON, Canada

care. Here, we aim to provide healthcare professionals with AD treatment recommendations from the perspective of 10 Canadian dermatologists with expertise in managing AD.

**Methods:** The panel of dermatologists conducted a systematic literature review and leveraged their clinical experience to develop generally accepted principles, consensus statements, and a treatment algorithm using an iterative consensus process.

**Results:** The panel collectively developed six generally accepted principles, 10 consensus

K. A. Papp · I. Turchin

Probity Medical Research, Waterloo, ON, Canada

K. A. Papp  $\cdot$  J. Yeung  $\cdot$  Y. Miller-Monthrope Division of Dermatology, Temerty School of Medicine, University of Toronto, Toronto, ON, Canada

K. A. Papp

Alliance Clinical Research, Waterloo, ON, Canada

J. Yeung · Y. Miller-Monthrope

Women's College Hospital, Toronto, ON, Canada

J. Yeung

Probity Medical Research, Toronto, ON, Canada

H. Lui

Vancouver Coastal Health Research Institute, Vancouver, BC, Canada

J. Ringuet

Centre de Recherche Dermatologique du Québec Métropolitain, Quebec City, QC, Canada statements, and a treatment algorithm. The guidance notes that assessment of disease severity should encompass both physician-rated measures and patient-reported outcomes. Disease education, lifestyle-based strategies (e.g., trigger avoidance), and supportive measures (e.g., moisturizers) can help reduce signs and symptoms of AD. Choice of therapy should consider disease-, patient-, and treatment-related factors. Although topical corticosteroids (TCS) are often used as first-line treatment in AD, they should be limited to intermittent short-term use. Noncorticosteroid topical therapies (e.g., topical calcineurin inhibitors; topical phosphodiesterase-4

inhibitors; and topical Janus kinase inhibitors) can be used for widespread involvement of AD according to approved use. Once treatment goals are achieved, noncorticosteroid topical maintenance therapy should continue to prevent flares and reduce the need for TCS.

**Conclusion:** Guidance reflecting the benefits and limitations of topical AD treatments in conjunction with patient understanding of treatment goals supports robust shared decision-making in the management of AD.

J. Ringuet

McGill University, Montreal, QC, Canada

I Turchin

Brunswick Dermatology Center, Fredericton, NB, Canada

I. Turchin

Department of Medicine, Dalhousie University, Halifax, NS, Canada

V. H. Prajapati

Division of Dermatology, Department of Medicine, University of Calgary, Calgary, AB, Canada

V. H. Prajapati

Section of Community Pediatrics, Department of Pediatrics, University of Calgary, Calgary, AB, Canada V. H. Prajapati

Section of Pediatric Rheumatology, Department of Pediatrics, University of Calgary, Calgary, AB, Canada

V. H. Prajapati

Dermatology Research Institute, Calgary, AB, Canada

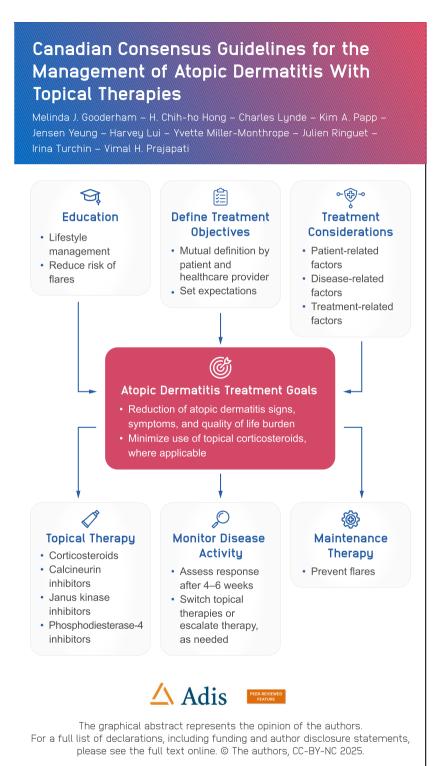
V. H. Prajapati

Skin Health and Wellness Centre, Calgary, AB, Canada

V. H. Prajapati

Probity Medical Research, Calgary, AB, Canada

# **Graphical Abstract:**



**Keywords:** Atopic dermatitis; Janus kinase inhibitor; Phosphodiesterase-4 inhibitor; Topical calcineurin inhibitor; Topical corticosteroid

# **Key Summary Points**

# Why carry out this study?

Atopic dermatitis is primarily treated with topical therapy, and guidance on the use of new and emerging treatments may further improve patient care.

The study asked how a panel of 10 Canadian dermatologists with expertise in managing atopic dermatitis would propose managing the disease.

## What was learned from the study?

The panel provided generally accepted principles, consensus recommendations, and a treatment algorithm for the management of atopic dermatitis that reflect the changing atopic dermatitis treatment landscape.

Healthcare providers will be better prepared to assess disease severity in patients with atopic dermatitis and use a recently expanded repertoire of topical treatments in conjunction with other supportive measures to optimize patient therapy.

# DIGITAL FEATURES

This article is published with digital features, including a graphical abstract to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.28573703.

# INTRODUCTION

Atopic dermatitis (AD) is a chronic and relapsing immune-mediated inflammatory disease of the skin characterized by intense pruritus and typical eczematous morphology, including

erythema, edema, excoriation, lichenification, oozing/crusting, and/or xerosis [1]. Signs and symptoms typically begin in infancy or childhood and may continue into or first appear in adulthood [2–4]. AD can negatively affect sleep, mental health, and quality of life (QoL) [5, 6]. In Canada, the prevalence of AD is approximately 15% for children and 4% for adults, with the majority of patients having mild-to-moderate disease severity [7, 8].

Optimal management of AD involves assessment of disease burden, education, and non-pharmacologic flare-mitigating measures that are most often accompanied by topical therapy and sometimes systemic therapy [9–11]. It has become necessary to revisit these topics given recent changes in the treatment landscape (e.g., approval of topical therapies that inhibit phosphodiesterase-4 [PDE-4i] [12] and Janus kinase [JAKi] [13]) to ensure adequate guidance.

Here, we provide generally accepted principles, consensus recommendations, and a practical treatment algorithm for the management of AD, as developed by a panel of 10 Canadian dermatologists with expertise in managing AD.

# **METHODS**

A panel of 10 Canadian dermatologists with substantial clinical and research experience in AD participated in an iterative consensus process for the development of generally accepted principles, consensus statements, and a treatment algorithm.

At a meeting in November 2022, the full panel convened to propose themes, clinical questions, and population, intervention, control, and outcomes (PICO) terms that would guide a subsequent literature review. A literature review was then conducted that aimed to address the question "What is the disease burden in patients with AD treated with topical therapies?", including the characterization of disease burden before topical therapies were used (Supplementary Material Table 1). It also aimed to address the question "How should treatment algorithms be modified to incorporate new topical therapies for AD?" with a focus on new treatments or

those for which fewer data were available during the development of the 2023 American Academy of Dermatology guidelines (Supplementary Material Table 2).

A subset of the full panel of dermatologists (MJG, HCH, CL, KAP, and JY) used data extracted from the literature search and expert opinion to draft, validate, and refine generally accepted clinical principles, consensus statements, and a treatment algorithm. This process occurred at a meeting in June 2023, with further refinement occurring asynchronously among the five subpanel members; a survey was used to categorize statements as generally accepted principles or consensus statements.

At an in-person meeting in September 2023 consisting of the full 10-member panel, generally accepted principles were discussed, and the final consensus statements and treatment algorithm were voted on using an iterative consensus process. Voting occurred according to a 5-point Likert scale (1, "strongly disagree"; 5, "strongly agree"), with  $\geq 75\%$  agreement (i.e., mean Likert score  $\geq 3.75$  out of 5) required to reach consensus.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

# **RESULTS AND DISCUSSION**

# **Literature Search and Expert Statements**

The first question ("What is the disease burden in patients with AD treated with topical therapies?") resulted in 33 sources for data extraction. Findings helped inform the practical assessment of disease severity based on clinical and patient-oriented characteristics. The second question ("How should treatment algorithms be modified to incorporate new topical therapies for AD?") resulted in 111 sources for data extraction. Findings informed clinical practice and treatment considerations, particularly for newer topical therapies, such as topical JAKi and topical PDE-4i. Following discussions and an iterative consensus process, six generally accepted principles

(Table 1) and 10 consensus statements (Table 2) were adopted. The final treatment algorithm (Fig. 1) had a level of agreement of 94%.

## Assessment of Disease Burden

Disease burden is a function of the clinical severity of AD in terms of visibly apparent skin pathology as well as patient-centric features, such as the frequency and severity of skin itch and pain, and the resulting effects on QoL (e.g., sleep; mental health burden; and school/work productivity) [5, 6]. Quantitative AD-validated assessment tools may help healthcare providers assess disease severity and engage in shared decision-making with the patient about treatment options. Body surface area (BSA) is a basic metric used for quantifying disease extent. The Eczema Area and Severity Index (EASI) (range, 0-72 [higher score indicates greater severity]), which has been validated in patients with AD, considers morphologic skin pathology (erythema; induration/edema/papulation; excoriations; and lichenification) and is weighted by BSA and body region [14]. The Investigator's Global Assessment (IGA) has a 5-point scale (range, 0-5 [higher score indicates greater severity]) based on the overall appearance of morphologic skin features (e.g., erythema; papulation; lichenification; and oozing/crusting) and has been validated in patients with AD [15].

Patient-reported outcomes validated in AD assess patient-centric perspectives on disease severity. The Dermatology Life Quality Index (DLQI) is a 10-question patient questionnaire about itch/pain, daily activities, and QoL impact (range, 0-30 [higher score indicates greater impairment]) [16]. The DLQI has been validated in patients with AD and other dermatologic diseases [16]. The Patient-Oriented Eczema Measure (POEM) is an AD-validated assessment tool with seven questions that consider itch, sleep disturbance, and characteristics of affected skin (range, 0-28 [higher score indicates greater severity]) [17]. Numerical rating scales (NRS) have been developed to assess itch [18] and sleep disturbance [19] in AD (range, 0 [no itch or no sleep loss due to AD] to 10 [worst itch or did not sleep at all]).

## Table 1 Generally accepted principles for AD

#### Statement

#### Disease burden

Clinical disease severity in patients with AD can be assessed by BSA, EASI, and IGA. In addition, the patient perspective can be assessed by DLQI, POEM, pruritus NRS, and sleep disturbance

#### Treatment considerations

Consider patient's preference, age, sensitive areas, disease extent, chronicity, severity, and patient-reported symptoms when evaluating treatment options for AD

It is important to involve the patient with AD in therapeutic decisions

Low AD disease activity may impact QoL

#### Maintenance therapy

Maintenance therapy is an essential part of the management of patient with AD

#### Safety

Noncorticosteroid topical therapies are generally not recommended for the treatment of AD in patients who are pregnant or breastfeeding

AD atopic dermatitis, BSA body surface area, DLQI Dermatology Life Quality Index, EASI Eczema Area and Severity Index, IGA Investigator's Global Assessment, NRS numerical rating scale, POEM Patient-Oriented Eczema Measure, QoL quality of life

Scoring Atopic Dermatitis (SCORAD) is an AD-validated assessment tool that incorporates both objective physician-rated signs (extent of BSA; intensity of erythema, edema/papulation, oozing/crusting, excoriation, lichenification, and dryness [scale of 0–3]) and patient-reported symptoms (pruritus and sleep loss [scale of 0–10]) of AD; the total score ranges from 0 to 103 [20].

Although patient-centric scores can be used to serially assess changes in disease severity over time and in response to treatment, open-ended questions may be a more practical alternative in the clinic [21]. Assessment of disease severity should encompass both physician-rated measures and patient-reported outcomes because of potential for significant QoL impact even in patients displaying milder apparent disease activity, especially among those with involvement of more visible or sensitive areas (e.g., scalp; face/neck; hands/feet; genitals) [21]. Although the above assessment tools are commonly used in clinical trials, BSA, IGA, and pruritus NRS are the most practical for assessing

disease severity in routine clinical practice [Consensus Statement 1 (Table 2)] [22].

## Nonpharmacologic Therapy

Education about the disease and lifestyle-based strategies, such as trigger avoidance, can help reduce signs and symptoms of AD [23]. Moisturizers have been recommended for daily use (often multiple times per day and especially after bathing) to support and restore the skin's barrier function and prevent flares [9, 10, 24]. Bathing practices, such as baths containing a dilute concentration of bleach, have been previously suggested as an adjunctive therapy for AD [9], but their benefits are not supported by strong evidence (Consensus Statement 2). Therefore, bleach baths are not routinely recommended.

Wet wraps involve the use of wet dressings to prevent excoriation, improve skin hydration, and enhance skin penetration of topical therapies (usually lower potency topical corticosteroids [TCS]) during exacerbations; they are

Table 2 Consensus statements for AD

Statement	Level of agreement,	Mean (SD) Likert score
Disease burden	,	,
1. For routine clinical practice, BSA, IGA, and pruritus assessment are the most practical disease severity measures in patients with AD	98	4.9 (0.3)
Bleach baths, wet wraps, and moisturizers		
2. Bleach baths have been used as an adjunctive therapy for AD, but their benefits are not supported by evidence. Therefore, bleach baths are not recommended	94	4.7 (0.6)
3. Although wet wraps may be helpful for extensive or recalcitrant AD, they are impractical for routine use	96	4.8 (0.4)
Topical therapies		
4. TCS in AD should ideally be limited to short-term use. If there is insufficient response after 4 weeks of treatment, consider alternative therapeutic options	90	4.5 (0.5)
5. Noncorticosteroid topical therapies can be used for widespread involvement of AD according to approved use	90	4.5 (0.5)
6. Topical JAKi do not have the same risk profile as TCS in AD and may be used continuously for extended periods on all sites, including sensitive areas	98	4.9 (0.3)
7. Treatment with TCS, TCI, topical PDE-4i, or topical JAKi is not advised in patients with AD who have an active skin infection unless they are receiving appropriate antimicrobial therapy	92	4.6 (0.5)
8. Off-label use of topical therapy in AD may be necessary to achieve the desired treatment outcomes	98	4.9 (0.3)
9. Topical JAKi can be used concomitantly with biologic therapies in the treatment of AD	80	4.0 (1.5)
10. The thresholds for considering phototherapy and systemic therapies for AD may shift as a wider disease spectrum may be amenable to treatment with novel noncorticosteroid topical therapies	92	4.6 (0.7)

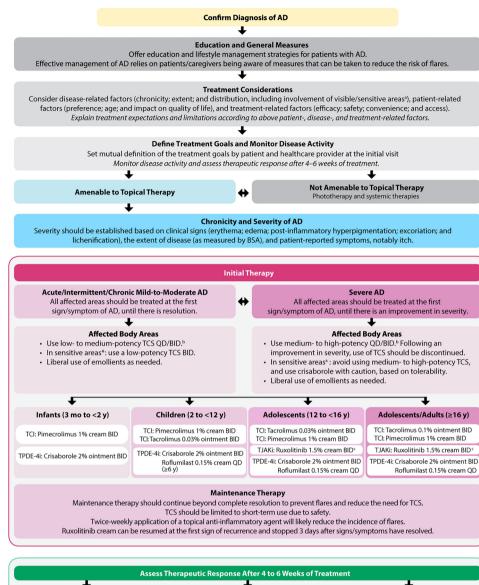
AD atopic dermatitis, BSA body surface area, IGA Investigator's Global Assessment, JAKi Janus kinase inhibitors, PDE-4i phosphodiesterase-4 inhibitors, TCI topical calcineurin inhibitors, TCS topical corticosteroids

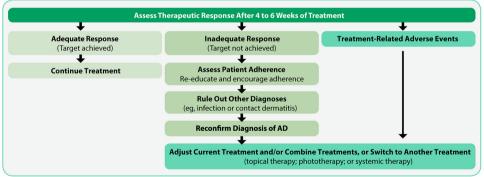
generally considered safe [25]. Although wet wraps may be helpful for extensive or recalcitrant AD [26], they are impractical for routine use (Consensus Statement 3) because substantial time and effort are required for implementation and patients and/or their caregivers must be carefully educated on their proper use [10].

# **Considerations for Pharmacologic Therapy**

If supportive measures do not control disease, pharmacologic interventions are advised [9, 10]. The choice of therapy should consider disease-related factors (severity; extent; distribution [e.g., involvement of visible and/

<sup>&</sup>lt;sup>a</sup>The Likert scale ranges from 1 to 5, with higher scores indicating more agreement





◆Fig. 1 Algorithm for the topical therapy of AD in children, adolescents, and adults. <sup>a</sup>Sensitive areas include the face (eyelids and perioral region), neck, axillary/inguinal region, and genital region. <sup>b</sup>Cochrane review has shown that QD application of TCS is as effective as BID application of TCS. <sup>c</sup>Ruxolitinib (1.5% cream) can be resumed at the first sign of recurrence and stopped 3 days after signs/symptoms have resolved. *AD* atopic dermatitis, *BID* twice daily, *BSA* body surface area, *QD* once daily, *TCI* topical calcineurin inhibitor, *TCS* topical corticosteroid, *TJAKi* topical Janus kinase inhibitor, *TPDE-4i* topical phosphodiesterase-4 inhibitor

or sensitive areas]; chronicity; symptoms), patient-related factors (age; impact on QoL; preference), and treatment-related factors (efficacy; safety; convenience; access; cost). Topical therapies are the mainstay of AD treatment, as they are generally considered safe and effective [10, 27].

It is important to involve the patient with AD in therapeutic decisions. A mutual definition of treatment goals should be decided by the patient and healthcare provider and periodically reevaluated.

# **Topical Therapies**

TCS have low-, medium-, high-, and very highpotency formulations. High- and very highpotency TCS are the most efficacious of the topical therapies, but carry a greater risk of adverse events (AEs) [10, 28, 29]. AEs may include local cutaneous AEs, such as atrophy, striae, and hypopigmentation (more commonly in patients with darker skin tones), as well as rare systemic AEs, such as adrenal insufficiency (due to hypothalamic-pituitary-adrenal axis suppression) if sufficient systemic absorption occurs [28]. Corticosteroid addiction/withdrawal is a possibility but is most often associated with extended use of high-potency formulations [30, 31]. Given these risks, TCS in AD should ideally be limited to intermittent short-term use (Consensus Statement 4) [10].

Noncorticosteroid topical therapies (Table 3) can be used for widespread involvement of AD (including on sensitive skin) according to approved use (Consensus Statement 5) and do

not carry the risk of causing the corticosteroidinduced AEs listed above [12, 32, 33]. Topical calcineurin inhibitors (TCI) are one such noncorticosteroid alternative and include tacrolimus (0.03% and 0.1% ointment) and pimecrolimus (1% cream), which are approved for second-line use for moderate-to-severe and mild-to-moderate disease, respectively [32, 33]. Tacrolimus 0.1% ointment has comparable efficacy to mediumpotency TCS, and tacrolimus 0.03% ointment and pimecrolimus 1% cream are comparable to low-potency TCS [29]. AEs may include local stinging and/or burning (approximately 20–58% of patients for tacrolimus, and 8–28% of patients for pimecrolimus in some studies) [34–36]. Although rare cases of skin cancer and lymphoma have also been reported with TCI, a causal relationship has not been established [32, 33], and this risk has not been substantiated by recent long-term analyses [37, 38]. A boxed warning about these malignancies has since been removed for tacrolimus ointment and pimecrolimus cream in Canada [32, 33].

Topical PDE-4i are another noncorticosteroid alternative. Crisaborole (2% ointment) is approved for mild-to-moderate AD [12]. Efficacy relative to vehicle was modest in phase 3 studies [36, 39]. Like TCI, AEs include stinging and/or burning (approximately 4% of patients in phase 3 studies [36, 40] and 14% and 32% of patients in real-world studies [41, 42]) at the application site. Roflumilast (0.15% cream) was approved in 2024 for mild-to-moderate AD in the USA [43] and approved in March 2025 in Canada [44]. It has demonstrated moderate antiinflammatory action relative to vehicle cream in phase 3 studies [45].

Ruxolitinib (1.5% cream), a topical JAKi, is another noncorticosteroid alternative for mild-to-moderate AD most recently approved in Canada [13]. Efficacy was improved compared with triamcinolone acetonide (0.1% cream), a medium-potency TCS in a phase 2 study [46, 47]. Treatment is well tolerated, with infrequent occurrences of application site reactions [46, 48–50]. The JAKi class carries a boxed warning (serious infections; malignancies; major adverse cardiovascular events [MACE]; and thrombosis [13]), which originated from data with orally administered tofacitinib when compared with

	ıes	
	l therap	
•	teroid	
	Noncorticosteroid topica	
•	3	
E	Iable	

Carried Carried	ביים ביים ביים ביים ביים ביים ביים ביים					
Name	Manufacturer	Formulation	Application Indication frequency	Indication	Health Canada approval date	Pivotal study
TCI						
Pimecrolimus	Bausch Health,	1% cream	BID	Second-line therapy for	Nov 3, 2011	Luger TA, et al. [64]
(Elidel <sup>*</sup> ) [33]	Canada			short-term and intermittent (aged ≥ 2 years)	$(aged \ge 2 years)$	Meurer M, et al. [65]
				long-term therapy of	Oct 17, 2019	Sigurgeirsson B, et al.
				mild-to-moderate AD in	$(aged \ge 3 months)$	(phase 3) [66]
				nonimmunocompromised		
				patients aged ≥ 3 months,		
				in whom the use of		
				alternative, conventional		
				therapies is deemed		
				inadvisable because of		
				potential risks, or in the		
				treatment of patients		
				who are not adequately		
				responsive to or intolerant		
				of alternative, conventional		
				therapies		

Table 3 continued						
Name	Manufacturer	Formulation	Application frequency	Indication	Health Canada approval date	Pivotal study
Tacrolimus (Protopic) [32]	LEO Pharma	0.03% and 0.1% ointment	CIB	Second-line therapy in adults (0.03% and 0.1% ointment) and children aged 2–15 years (0.03% ointment) for short- and long-term intermittent treatment of moderate-tosevere AD in nonimmuno-compromised patients, in whom the use of conventional therapies is deemed inadvisable because of potential risks, or in those who are not adequately responsive to or intolerant of conventional therapies. It is also indicated for maintenance therapy to prevent flares and prolong flare-free intervals in patients with moderate-to-severe AD experiencing a high frequency of flares (i.e., occurring ≥ 5 times per year) who have had an initial response (i.e., lesions cleared, almost cleared or mildly affected) with ≤ 6 weeks of treatment BID	Feb 17, 2011	Paller A, et al.  (phase 3) [67]  Hanifin JM, et al.  (phase 3) [68]  Soter N, et al.  (phase 3) [69]  Reitamo S, et al.  (phase 3) [70]  Reitamo S, et al.  (phase 3) [71]

Table 3   continued						
Name	Manufacturer	Formulation	Application frequency	Indication	Health Canada approval date	Pivotal study
Topical PDE-4i						
Crisaborole (Eucrisa") [12]	Pfizer Canada	2% ointment	BID	Topical treatment of mild- to-moderate AD in adults and pediatric patients aged ≥ 3 months	Nov 7, 2018 $(aged \ge 2 \text{ years})$ July 15, 2021 $(aged \ge 3 \text{ months})$	Paller AS, et al. (phase 3) [36]
Roflumilast [44]	Arcutis Canada	0.15% cream	G)	Topical treatment of mild- to-moderate AD in adults and pediatric patients aged ≥ 6 years	Mar 17, 2025	Simpson EL, et al. (phase 3) [45]
Topical JAKi Ruxolitinib (Opzelura) [13]	Incyte Biosciences Canada	1.5% cream	BID	Topical treatment of mild-to-moderate AD in patients aged ≥ 12 years, for whom AD not adequately controlled with conventional topical prescription therapies (TCI, TCS) or when those	Oct 11, 2024	Papp K, ct al. (phase 3) [48]

AD atopic dermatitis, BID twice daily, JAKi Janus kinase inhibitor, PDE-4i phosphodiesterase-4 inhibitor, QD once daily, TCI topical calcineurin inhibitor, TCS topical corticosteroid

therapies are not advisable

subcutaneously administered adalimumab in adults or etanercept in adults aged≥50 years with rheumatoid arthritis [51–53]. However, observed incidences of such events in phase 3 studies of ruxolitinib (0.75% and 1.5% cream) were not increased and were generally comparable to the overall AD population [48]; serious infections, MACE, or thromboses have not been found in the first year following its US approval [54]. Since topical JAKi do not have the same risk profile as TCS in AD, they may be suitable for continual use over extended periods on all sites including sensitive areas for this chronic disease (Consensus Statement 6).

Additional considerations are necessary when using topical therapies for the treatment of patients with AD who are pregnant or breast-feeding. Noncorticosteroid topical therapies are generally not recommended for the treatment of patients with AD who are pregnant or breast-feeding, largely because of lack of data regarding potential risks [12, 13, 32, 33]. However, their use may be justified in some cases [55].

Treatment with TCS [56], TCI [32, 33], topical PDE-4i [36], or topical JAKi [13] is not advised in patients with AD who have an active skin infection unless they are receiving appropriate concomitant antimicrobial therapy (Consensus Statement 7).

# **Initial Therapy**

Initial therapy of mild-to-moderate AD should begin with low- or medium-potency TCS once daily (QD) or twice daily (BID) on affected body areas until visible skin findings have resolved. In sensitive areas, a low-potency TCS should be used OD or BID.

First-line treatment of severe AD should begin with medium- or high-potency TCS until disease severity has improved or the recommended duration of treatment has been reached. In sensitive areas, medium- or high-potency TCS should be avoided. For TCS, QD may be equally as effective as BID dosing [57]. Liberal, as-needed use of emollients should accompany therapy [58]. Specific best practices for emollient use have been discussed previously [11]. Other treatments may be used when

TCS are not desired because of potential risks or when AD is not adequately controlled or patients are intolerant to TCS.

TCI are often second line with the specific drug and concentration depending on patient age, according to the label (Fig. 1). Tacrolimus has been approved in patients aged 2–15 years (0.03% ointment BID) and patients aged≥16 years (0.1% ointment BID) [32]. Pimecrolimus (1% cream BID) has been approved in patients aged ≥ 3 months [33]. After TCI, other therapies may be used. Crisaborole (2% ointment BID) is approved in patients aged  $\geq 3$  months [12], and ruxolitinib (1.5%) cream BID) is approved in Canada for use in patients aged ≥ 12 years [13]. These therapeutic options are recommended on the basis of their effectiveness and clinical experience and are in alignment with their indicated ages for use and line of use [12, 13, 32, 33].

Emergence of treatment-related AEs during management or the inability to achieve treatment goals by 6 weeks (or 4 weeks for TCS [Consensus Statement 4]) may necessitate adjusting current treatment or switching to or adding another treatment (topical therapy, phototherapy, or systemic therapy) or a combination of these. In cases of inadequate response, lack of adherence, environmental triggers, infection, and competing diagnoses should first be excluded as reasons for nonresponse [9].

When modifying treatment, off-label use of topical therapy in AD may be necessary to achieve the desired treatment outcomes (Consensus Statement 8). For instance, tacrolimus (0.1% ointment) may be needed to control disease in children aged 2–15 years [59]. Clinical experience suggests that topical JAKi can be used concomitantly with systemic biologics in the treatment of AD [60] (Consensus Statement 9), despite the combination being a limitation of use in the label [13].

Although treatments beyond topical therapies may be needed for refractory cases, the threshold for considering phototherapy and systemic therapies for AD may shift toward topical therapies as a wider disease spectrum may be amenable to treatment with novel noncorticosteroid topical therapies (Consensus Statement 10) [61].

# **Maintenance Therapy**

If the goal of initial therapy is achieved, maintenance therapy should continue beyond complete resolution to prevent flares and reduce the need for TCS. Maintenance therapy is an essential part of the management of patients with AD; twice-weekly application of a topical anti-inflammatory agent will likely reduce the incidence of flares [9, 10, 48, 62, 63]. BID TCS should be limited to intermittent short-term use due to safety [10]. Tacrolimus (0.03% and 0.1% ointment), applied QD twice per week, is indicated for maintenance therapy in patients with a high frequency of flares (e.g., at least five times per year) [32]. Ruxolitinib (1.5% cream) can be resumed at the first sign of recurrence and stopped 3 days after signs/symptoms have resolved. Proactive topical therapy specifically for patients with moderate-to-severe AD has been discussed previously [9, 11]. Patients with frequent recurrence despite maintenance therapy may be candidates for systemic therapy [21].

## Limitations

The broad applicability of these guidelines may be limited in some areas since opinions originated exclusively from experts practicing in Canada.

# **CONCLUSIONS**

The management of AD continues to evolve. Assessment of disease severity should consider both physician-rated measures and patient-reported outcomes. Emerging topical therapies focus on new targets underlying inflammation and the itch–scratch cycle. Improved clarity around the benefits, risks, and limitations of available therapies supports the development of robust treatment algorithms. Further, there is an understanding that maintenance therapy provides an opportunity to avoid disease flares and maintain patient QoL. It is important that treatment decisions for AD consider disease-,

patient-, and treatment-related factors and are based on a mutual understanding of therapeutic goals in conjunction with the patient.

Medical Writing/Editorial Assistance. Medical writing support was provided by Andrew Barszczyk, PhD, from The Curry Rockefeller Group, LLC, a Citrus Health Group, Inc., company (Chicago, IL), and was funded by Incyte Corporation. The authors thank Christine Jean, Kaitryn Campbell, and Jean-François Dicaire from Pinnacle Marketing & Education Inc (Hudson, QC, Canada) for their contributions to this initiative.

Author Contributions. Melinda J. Gooderham, H. Chih-ho Hong, Charles Lynde, Kim A. Papp, Jensen Yeung, Harvey Lui, Yvette Miller-Monthrope, Julien Ringuet, Irina Turchin, and Vimal H. Prajapati contributed to the discussions, research, and validation of the generally accepted principles and consensus statements reported in this manuscript. Melinda J. Gooderham, H. Chih-ho Hong, Charles Lynde, Kim A. Papp, Jensen Yeung, Harvey Lui, Yvette Miller-Monthrope, Julien Ringuet, Irina Turchin, and Vimal H. Prajapati critically reviewed and revised the draft manuscript for important intellectual content and approved the final version for submission.

**Funding.** This study and the Rapid Service Fee for this journal were funded by Incyte Corporation (Wilmington, DE, USA). Incyte had no editorial control or influence on the content of the manuscript or output from the expert panel.

**Data Availability.** Data sharing is not applicable to this article as no new datasets were generated or analyzed during the current study.

## Declarations

Conflict of Interest. Melinda J. Gooderham has served as a principal investigator for AbbVie, Alumis, Amgen, AnaptysBio, Apogee, Arcutis, Aristea, Aslan, Bausch Health, Boehringer Ingelheim International GmbH, Bristol Myers Squibb, Cara Therapeutics, Coherus

Biosciences, Dermira, Eli Lilly, Galderma SA, GlaxoSmithKline, Incyte Corporation, InMagene, JAMP, Janssen, LEO Pharma, MedImmune, Meiji, MoonLake, Nektar Therapeutics, Nimbus, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, Takeda Pharmaceutical Company, Tarsus, UCB, Ventyx, and Vyne; a consultant for AbbVie, Amgen, Apogee, Aslan, Bausch Health, Boehringer Ingelheim International GmbH, Eli Lilly, Janssen, Novartis Pharmaceuticals, Sanofi Genzyme, Sun Pharma, and UCB; an advisory board member for AbbVie, Amgen, Apogee, Arena Pharmaceuticals, Asana BioSciences, Aslan, Bausch Health, Boehringer Ingelheim International GmbH, Eli Lilly, Galderma SA, Incyte Corporation, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, and Union; and a paid speaker for AbbVie, Amgen, Bausch Health, Bristol Myers Squibb, Boehringer Ingelheim International GmbH, Eli Lilly, Galderma SA, Janssen, JAMP, LEO Pharma, L'Oréal, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB. H. Chih-ho Hong has served as a speaker, advisor, consultant, and/or investigator for AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cutanea, Dermira, Dermavant, DS Biopharma, Eli Lilly, Galderma, GlaxoSmith-Kline, Incyte Corporation, Janssen, LEO Pharma, Medimmune, Merck, Mirimar, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, Roche, and UCB. Charles Lynde has served as a speaker and/or consultant for AbbVie, Amgen, Aralez, Arcutis, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cipher, Dermavant, Eli Lilly, Fresnius Kabi, Galderma, GlaxoSmithKline, Incyte Corporation, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma, L'Oréal, Medexus, MedX, Merck, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, Sun Pharma, TEVA, Tribute, UCB, Valeant, Viatris, and Volo Health and has served as a principal investigator for AbbVie, Acelyrin, Akros, Altius, Amgen, Aralez, Arcutis, Avillion, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cipher, Concert, Dermavant, Devonian, Eli Lilly, Evelo, Galderma, GlaxoSmithKline,

Incyte Corporation, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma, L'Oréal, Medexus, MedX, Merck, MoonLake, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, Sun Pharma, TEVA, Tribute, UCB, Valeant, Viatris, and Volo Health. Kim A. Papp has received honoraria and/or grants as a consultant, speaker, investigator, or scientific officer from AbbVie, Acelyrin, Akros, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, Dermavant, Dermira, DICE Pharmaceuticals, DICE Therapeutics, Eli Lilly and Company, Evelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte Corporation, Janssen, Kymab, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Nimbus Therapeutics, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tarsus Pharmaceuticals, UCB Pharma, and Zai Lab. Jensen Yeung has served as a consultant, investigator, or speaker or received honoraria from AbbVie, Amgen, Arcutis, Apogee, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb. Celltrion. Fresenius Kabi. Galderma. Incyte Corporation, JAMP Pharma, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, Takeda, and UCB. Harvey Lui has served as an advisor, consultant, investigator, and/or speaker for AbbVie, Incyte Corporation, L'Oréal, Novartis, and Vita Imaging. Yvette Miller-Monthrope has served as an advisor, consultant, and/or speaker for AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Fresenius Kabi, Galderma, Incyte Corporation, Janssen, Sanofi, Sun Pharma, Novartis, and UCB. Julien Ringuet has served as an advisor, consultant, and/or speaker for AbbVie, Amgen, Apogee, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galderma, Incyte Corporation, Janssen, LEO Pharma, L'Oréal, NKS Health, Novartis, Organon, Pfizer, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB and served as an investigator for AbbVie, Alumis, Amgen, Aristea, Aslan, Bristol Myers Squibb, Celgene, Concert Pharmaceuticals, CorEvitas, DICE Therapeutics, Incyte Corporation, Innovaderm, Janssen, LEO Pharma, Merck, Pfizer, Sanofi-Genzyme,

Sun Pharma, and UCB. Irina Turchin has served as a speaker, advisor, consultant, or investigator for AbbVie. Amgen. Arcutis. Aristea. Bausch Health, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Galderma, Horizon Therapeutics, Incyte Corporation, Janssen, Kiniksa, LEO Pharma, Mallinckrodt, MoonLake, Novartis, Pfizer, Sanofi, Sun Pharma, UCB, and Ventyx Biosciences. Vimal H. Prajapati has served as an advisor, consultant, and/or speaker for AbbVie, Actelion, Amgen, Apogee Therapeutics, Aralez, Arcutis, Aspen, Bausch Health, BioScript Solutions, Boehringer Ingelheim, Bristol Myers Squibb, Canadian Psoriasis Network, Celgene, Celltrion, Cipher, Concert, CorEvitas, Eczema Society of Canada, Eli Lilly, Galderma, Glaxo-SmithKline, Homeocan, Incyte Corporation, JAMP Pharma, Janssen, Johnson & Johnson, LEO Pharma, Medexus, Novartis, Organon, Pediapharm, Pfizer, Sanofi Genzyme, Sun Pharma, Tribute, UCB, and Valeant; served as an investigator for AbbVie, AnaptysBio, Arcutis, Arena, Asana, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, CorEvitas, Dermavant, Dermira, Eli Lilly, Galderma, Incyte Corporation, Janssen, LEO Pharma, Meiji Pharma, Nektar Therapeutics, Nimbus Lakshmi, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Reistone, Sanofi Genzyme, Sun Pharma, Takeda, and UCB: and received grants from AbbVie. Bausch Health, Janssen, LEO Pharma, Novartis, and Sanofi Genzyme.

*Ethical Approval.* This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

*Open Access.* This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons

licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc/4.0/.

# REFERENCES

- Kirchhof MG, Landells I, Lynde CW, Gooderham MJ, Hong CH. Approach to the assessment and management of adult patients with atopic dermatitis: a consensus document. Section I: pathophysiology of atopic dermatitis and implications for systemic therapy. J Cutan Med Surg. 2018;22(1 suppl):6S-9S.
- 2. Garmhausen D, Hagemann T, Bieber T, et al. Characterization of different courses of atopic dermatitis in adolescent and adult patients. Allergy. 2013;68(4):498–506.
- 3. Kay J, Gawkrodger DJ, Mortimer MJ, Jaron AG. The prevalence of childhood atopic eczema in a general population. J Am Acad Dermatol. 1994;30(1):35–9.
- Lee HH, Patel KR, Singam V, Rastogi S, Silverberg JI. A systematic review and meta-analysis of the prevalence and phenotype of adult-onset atopic dermatitis. J Am Acad Dermatol. 2019;80(6):1526–32.
- 5. Silverberg JI, Gelfand JM, Margolis DJ, et al. Patient burden and quality of life in atopic dermatitis in US adults: a population-based cross-sectional study. Ann Allergy Asthma Immunol. 2018;121(3):340–7.
- Kwatra SG, Gruben D, Fung S, DiBonaventura M. Psychosocial comorbidities and health status among adults with moderate-to-severe atopic dermatitis: a 2017 US national health and wellness survey analysis. Adv Ther. 2021;38(3):1627–37.
- 7. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: results from an international survey. Allergy. 2018;73(6):1284–93.
- 8. Silverberg JI, Barbarot S, Gadkari A, et al. Atopic dermatitis in the pediatric population: a cross-sectional, international epidemiologic study. Ann Allergy Asthma Immunol. 2021;126(4):417–28.

- Chu DK, Schneider L, Asiniwasis RN, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/ American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations. Ann Allergy Asthma Immunol. 2023;132(2):274–312.
- 10. Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023;89(1):e1–20.
- 11. Wollenberg A, Kinberger M, Arents B, et al. European guideline (EuroGuiDerm) on atopic eczema part II: non-systemic treatments and treatment recommendations for special AE patient populations. J Eur Acad Dermatol Venereol. 2022;36(11):1904–26.
- 12. Pfizer Canada Inc. EUCRISA® (crisaborole). Product Monograph. Kirkland: 2021.
- Incyte Corporation and Innomar Strategies. Opzelura<sup>®</sup> (ruxolitinib cream). Product Monograph. Oakville: 2024.
- 14. Hanifin JM, Thurston M, Omoto M, et al. The Eczema Area and Severity Index (EASI): assessment of reliability in atopic dermatitis. Exp Dermatol. 2001;10(1):11–8.
- 15. Simpson EL, Bissonnette R, Paller AS, et al. The Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD): a clinical outcome measure for the severity of atopic dermatitis. Br J Dermatol. 2022;187(4):531–8.
- 16. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19(3):210–6.
- 17. Charman CR, Venn AJ, Williams HC. The Patient-Oriented Eczema Measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. Arch Dermatol. 2004;140(12):1513–9.
- 18. Yosipovitch G, Reaney M, Mastey V, et al. Peak Pruritus Numerical Rating Scale: psychometric validation and responder definition for assessing itch in moderate-to-severe atopic dermatitis. Br J Dermatol. 2019;181(4):761–9.
- 19. Puelles J, Fofana F, Rodriguez D, et al. Psychometric validation and responder definition of the sleep disturbance numerical rating scale in moderate-to-severe atopic dermatitis. Br J Dermatol. 2022;186(2):285–94.

- 20. Severity scoring of atopic dermatitis: the SCO-RAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology. 1993;186(1):23–31.
- 21. Simpson EL, Bruin-Weller M, Flohr C, et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. J Am Acad Dermatol. 2017;77(4):623–33.
- 22. Gooderham MJ, Bissonnette R, Grewal P, Lansang P, Papp KA, Hong CH. Approach to the assessment and management of adult patients with atopic dermatitis: a consensus document. Section II: tools for assessing the severity of atopic dermatitis. J Cutan Med Surg. 2018;22(1):10S-S16.
- 23. Heratizadeh A, Werfel T, Wollenberg A, et al. Effects of structured patient education in adults with atopic dermatitis: multicenter randomized controlled trial. J Allergy Clin Immunol. 2017;140(3):845–53.
- 24. van Zuuren EJ, Fedorowicz Z, Arents BWM. Emollients and moisturizers for eczema: abridged Cochrane systematic review including GRADE assessments. Br J Dermatol. 2017;177(5):1256–71.
- 25. Schoch JJ, Davis DMR. A practical guide to outpatient wet dressings for pediatric atopic dermatitis. Curr Derm Rep. 2013;2:212–5.
- 26. Dabade TS, Davis DM, Wetter DA, et al. Wet dressing therapy in conjunction with topical corticosteroids is effective for rapid control of severe pediatric atopic dermatitis: experience with 218 patients over 30 years at Mayo Clinic. J Am Acad Dermatol. 2012;67(1):100–6.
- 27. Yang YB, Gohari A, Lam J. Brief academic review and clinical practice guidelines for pediatric atopic dermatitis. Curr Pediatr Rev. 2021;17(3):229–37.
- 28. Broersen LH, Pereira AM, Jorgensen JO, Dekkers OM. Adrenal insufficiency in corticosteroids use: systematic review and meta-analysis. J Clin Endocrinol Metab. 2015;100(6):2171–80.
- 29. Chu DK, Chu AWL, Rayner DG, et al. Topical treatments for atopic dermatitis (eczema): systematic review and network meta-analysis of randomized trials. J Allergy Clin Immunol. 2023;152(6):1493–519.
- 30. Hajar T, Leshem YA, Hanifin JM, et al. A systematic review of topical corticosteroid withdrawal ("steroid addiction") in patients with atopic dermatitis and other dermatoses. J Am Acad Dermatol. 2015;72(3):541–9.

- 31. Hwang J, Lio PA. Topical corticosteroid withdrawal ('steroid addiction'): an update of a systematic review. J Dermatolog Treat. 2022;33(3):1293–8.
- 32. LEO Pharma Inc. PROTOPIC<sup>®</sup> (tacrolimus). Product Monograph. Toronto: 2022.
- 33. Bausch Health Canada Inc. ELIDEL® (pimecrolimus). Product Monograph. Laval: 2020.
- 34. Chen SL, Yan J, Wang FS. Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a meta-analysis of randomized clinical trials. J Dermatolog Treat. 2010;21(3):144–56.
- 35. Amiri D, Schwarz CW, Gether L, Skov L. Safety and efficacy of topical calcineurin inhibitors in the treatment of facial and genital psoriasis: a systematic review. Acta Derm Venereol. 2023;103;adv00890.
- 36. Paller AS, Tom WL, Lebwohl MG, et al. Efficacy and safety of crisaborole ointment, a novel, non-steroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. J Am Acad Dermatol. 2016;75(3):494–503.
- 37. Devasenapathy N, Chu A, Wong M, et al. Cancer risk with topical calcineurin inhibitors, pime-crolimus and tacrolimus, for atopic dermatitis: a systematic review and meta-analysis. Lancet Child Adolesc Health. 2023;7(1):13–25.
- 38. Asgari MM, Tsai AL, Avalos L, Sokil M, Quesenberry CP Jr. Association between topical calcineurin inhibitor use and keratinocyte carcinoma risk among adults with atopic dermatitis. JAMA Dermatol. 2020;156(10):1066–73.
- 39. Ahmed A, Solman L, Williams HC. Magnitude of benefit for topical crisaborole in the treatment of atopic dermatitis in children and adults does not look promising: a critical appraisal. Br J Dermatol. 2018;178(3):659–62.
- 40. Eichenfield LF, Call RS, Forsha DW, et al. Longterm safety of crisaborole ointment 2% in children and adults with mild to moderate atopic dermatitis. J Am Acad Dermatol. 2017;77(4):641–9.
- 41. Pao-Ling Lin C, Gordon S, Her MJ, Rosmarin D. A retrospective study: application site pain with the use of crisaborole, a topical phosphodiesterase 4 inhibitor. J Am Acad Dermatol. 2019;80(5):1451–3.
- 42. Ma C, Sun J, Liu Z, Zhang C. Real-world efficacy of 2% crisaborole ointment on chronic hyperplasia lesions in 49 patients with atopic dermatitis. Int J Dermatol. 2024;63(10):1375–82.

- 43. Arcutis Biotherapeutics. ZORYVE® (roflumilast). Full Prescribing Information. Westlake Village: 2024.
- 44. Arcutis Canada. ZORYVE® (roflumilast cream). Product Monograph. North York: 2025.
- 45. Simpson EL, Eichenfield LF, Alonso-Llamazares J, et al. Roflumilast cream, 0.15%, for atopic dermatitis in adults and children: INTEGUMENT-1 and INTEGUMENT-2 randomized clinical trials. JAMA Dermatol. 2024;160(11):1161–70.
- 46. Kim BS, Howell MD, Sun K, Papp K, Nasir A, Kuligowski ME. Treatment of atopic dermatitis with ruxolitinib cream (JAK1/JAK2 inhibitor) or triamcinolone cream. J Allergy Clin Immunol. 2020;145(2):572–82.
- 47. Kim BS, Sun K, Papp K, Venturanza M, Nasir A, Kuligowski ME. Effects of ruxolitinib cream on pruritus and quality of life in atopic dermatitis: results from a phase 2, randomized, dose-ranging, vehicle- and active-controlled study. J Am Acad Dermatol. 2020;82(6):1305–13.
- 48. Papp K, Szepietowski JC, Kircik L, et al. Long-term safety and disease control with ruxolitinib cream in atopic dermatitis: results from two phase 3 studies. J Am Acad Dermatol. 2023;88(5):1008–16.
- 49. Leung DYM, Paller AS, Zaenglein AL, et al. Safety, pharmacokinetics, and efficacy of rux-olitinib cream in children and adolescents with atopic dermatitis. Ann Allergy Asthma Immunol. 2023;130(4):500–7.
- 50. Eichenfield LF, Stein Gold LF, Simpson EL, et al. A phase 3 study of ruxolitinib cream in children aged 2–<12 years with atopic dermatitis (TRuE-AD3): 8-week analysis. In: Presented at 32nd European Academy of Dermatology and Venereology (EADV) Congress; 2023 October 11–14; Berlin
- 51. US Food and Drug Administration. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions. 2021. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-relat ed-events-cancer-blood-clots-and-death. Accessed Feb 2, 2024.
- 52. Charles-Schoeman C, Wicker P, Gonzalez-Gay MA, et al. Cardiovascular safety findings in patients with rheumatoid arthritis treated with tofacitinib, an oral Janus kinase inhibitor. Semin Arthritis Rheum. 2016;46(3):261–71.
- 53. Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and cancer risk with

- tofacitinib in rheumatoid arthritis. N Engl J Med. 2022;386(4):316–26.
- 54. Hu W, Thornton M, Livingston RA. Real-world use of ruxolitinib cream: safety analysis at 1 year. Am J Clin Dermatol. 2024;25(2):327–32.
- 55. Vestergaard C, Wollenberg A, Barbarot S, et al. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. J Eur Acad Dermatol Venereol. 2019;33(9):1644–59.
- Merck Canada Inc. DIPROSONE® (betamethasone dipropionate). Product Monograph. Kirkland: 2017.
- 57. Lax SJ, Harvey J, Axon E, et al. Strategies for using topical corticosteroids in children and adults with eczema. Cochrane Database Syst Rev. 2022;3(3):CD013356.
- 58. van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. Cochrane Database Syst Rev. 2017;2(2):CD012119.
- 59. Kang S, Lucky AW, Pariser D, Lawrence I, Hanifin JM. Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. J Am Acad Dermatol. 2001;44(1 Suppl):S58-64.
- 60. Stefanko NS, Quan VL, Chovatiya R. Efficacy, safety, and treatment patterns of ruxolitinib 1.5% cream in adult atopic dermatitis: a single center retrospective study. J Am Acad Dermatol. 2023;89(2):415–7.
- 61. Simpson EL, Kircik L, Blauvelt A, et al. Ruxolitinib cream in adolescents/adults with atopic dermatitis meeting severity thresholds for systemic therapy: exploratory analysis of pooled results from two phase 3 studies. Dermatol Ther (Heidelb). 2024;14(8):2139–51.
- 62. Schmitt J, von Kobyletzki L, Svensson A, Apfelbacher C. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and meta-analysis of randomized controlled trials. Br J Dermatol. 2011;164(2):415–28.

- 63. Glazenburg EJ, Wolkerstorfer A, Gerretsen AL, Mulder PG, Oranje AP. Efficacy and safety of fluticasone propionate 0.005% ointment in the long-term maintenance treatment of children with atopic dermatitis: differences between boys and girls? Pediatr Allergy Immunol. 2009;20(1):59–66.
- 64. Luger TA, Lahfa M, Folster-Holst R, et al. Long-term safety and tolerability of pimecrolimus cream 1% and topical corticosteroids in adults with moderate to severe atopic dermatitis. J Dermatolog Treat. 2004;15(3):169–78.
- 65. Meurer M, Fartasch M, Albrecht G, et al. Long-term efficacy and safety of pimecrolimus cream 1% in adults with moderate atopic dermatitis. Dermatology. 2004;208(4):365–72.
- 66. Sigurgeirsson B, Boznanski A, Todd G, et al. Safety and efficacy of pimecrolimus in atopic dermatitis: a 5-year randomized trial. Pediatrics. 2015;135(4):597–606.
- 67. Paller A, Eichenfield LF, Leung DY, Stewart D, Appell M. A 12-week study of tacrolimus ointment for the treatment of atopic dermatitis in pediatric patients. J Am Acad Dermatol. 2001;44(1 Suppl):S47-57.
- 68. Hanifin JM, Ling MR, Langley R, Breneman D, Rafal E. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: part I, efficacy. J Am Acad Dermatol. 2001;44(1 Suppl):S28-38.
- 69. Soter NA, Fleischer AB Jr, Webster GF, Monroe E, Lawrence I. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: part II, safety. J Am Acad Dermatol. 2001;44(1 Suppl):S39-46.
- 70. Reitamo S, Rustin M, Ruzicka T, et al. Efficacy and safety of tacrolimus ointment compared with that of hydrocortisone butyrate ointment in adult patients with atopic dermatitis. J Allergy Clin Immunol. 2002;109(3):547–55.
- 71. Reitamo S, Van Leent EJ, Ho V, et al. Efficacy and safety of tacrolimus ointment compared with that of hydrocortisone acetate ointment in children with atopic dermatitis. J Allergy Clin Immunol. 2002;109(3):539–46.