

Quick Reference Guide: DECODING TYPE 2 INFLAMMATORY SKIN DISEASES

INTRODUCTION

Although atopic dermatitis (AD), chronic spontaneous urticaria (CSU), prurigo nodularis (PN), and bullous pemphigoid (BP) are clinically distinct diseases, type 2 inflammation and itch underlie and contribute to the pathophysiology of each. Therapies targeting key type 2 inflammatory mediators are approved for one or more of these conditions. Read on to learn more about recognition, differentiation, and treatment of these dermatoses.



PHASE 1: RECOGNIZE AND DIFFERENTIATE

Clinical Comparison at a Glance: Type 2 Inflammatory Skin Diseases

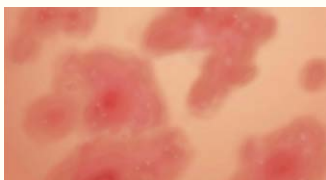
Feature	AD	CSU	PN	BP
Presentation	Chronic or relapsing pruritic eczematous dermatitis with xerosis, erythema, scale, excoriation, or lichenification.	Recurrent pruritic wheals with or without angioedema, occurring spontaneously for more than 6 weeks without an identifiable cause.	Intensely pruritic, firm papules or nodules sustained by repeated scratching or rubbing.	Pruritic urticarial plaques that frequently progress to tense vesicles or bullae.
Lesion Behavior	Persists days to weeks; recurrent or chronic.	Episodes of wheals usually resolve within 24 hours without residual change. Angioedema may last up to 72 hours.	Nodules persist for weeks to months.	Blisters and urticarial lesions persist; these are not transient.
Distribution	Flexures often involved in children and adults; face, hand, or extensor involvement more common in infants.	Any site; lesions are evanescent and change location.	Often symmetric on extensor arms, legs, and trunk; favors areas reachable by scratching.	Trunk and flexural extremities are common; may be widespread.
Patient Clues	Personal or family atopy; asthma, allergic rhinitis, or food allergy may coexist.	Episodic hives or angioedema without an identifiable external trigger.	Chronic itch-scratch cycle; may coexist with AD or systemic drivers of itch.	Usually an older adult; a nonbullous pruritic or urticarial phase may precede blisters.
Diagnostic Principle	Clinical diagnosis based on morphology, distribution, pruritus, and chronic or relapsing course.	Clinical diagnosis: spontaneous wheals or angioedema recurring for more than 6 weeks.	Triad: chronic pruritus, repeated scratching, and multiple pruriginous nodular lesions.	Clinical findings plus immunopathologic and serologic confirmation; can be drug-induced.
Useful Tests	Usually none unless the presentation is atypical or an alternative diagnosis is suspected.	Limited routine workup; target testing to history and examination. Urticaria index can be useful.	Targeted evaluation for dermatologic or systemic contributors to chronic pruritus.	Lesional edge for H&E; perilesional skin for DIF. BP180 or BP230 serology can support diagnosis.
Defining Clues	Eczematous or lichenified dermatitis with xerosis.	Transient, migratory wheals: ask whether each lesion disappears within 24 hours.	Persistent excoriated or hyperkeratotic nodules with relentless itch.	Tense bullae with linear basement membrane zone immunoreactivity.

DIF = direct immunofluorescence; H&E = hematoxylin and eosin.

Pattern Recognition Prompts

AD

- Look for persistent eczematous plaques with xerosis, scale, excoriation, or lichenification.
- Age-related distribution and a personal or family history of atopy strengthen the pattern.



CSU

- Look for smooth, edematous wheals that change shape or location.
- Ask whether each lesion clears within 24 hours without scale, bruising, or scarring; angioedema may coexist.



PN

- Look for fixed, firm, excoriated or hyperkeratotic papules and nodules, often symmetric on extensor or scratch-reachable sites.
- The chronic itch-scratch cycle is central.



BP

- In an older adult, severe itch or urticarial plaques may precede tense, intact bullae.
- Suspect nonbullous BP when persistent pruritic plaques do not behave like CSU, and confirm with biopsy, DIF, and BP180/230 ELISA.



RED FLAGS

- Wheals lasting more than 24 hours with bruising, pain, or burning suggest an alternative diagnosis, such as urticarial vasculitis.
- Predominant mucosal blistering or scarring suggests another autoimmune blistering disorder.

PHASE 2: CONFIRM

What Is Needed to Confirm the Diagnosis



Disease	Confirmation and Assessment
AD	Clinical pattern and course. If atypical, reconsider contact dermatitis, psoriasis, scabies, CTCL, or immunodeficiency. Track BSA, EASI or IGA, itch, sleep, and patient-reported burden as appropriate.
CSU	Confirm spontaneous wheals with or without angioedema for more than 6 weeks. Ask how long each wheal lasts. Use a limited, targeted workup. UAS7, UCT, and AAS can quantify activity or control.
PN	Confirm itch for at least 6 weeks, repeated scratching or rubbing, and multiple pruriginous nodules. Evaluate for contributing causes when indicated. Track itch NRS, IGA-PN, lesion burden, sleep, and quality of life.
BP	Biopsy a lesional blister or edge for H&E and perilesional skin for DIF. Consider BP180 or BP230 ELISA and IIF. Typical findings include a subepidermal blister and linear basement membrane zone immunoreactant deposition.

AAS = Angioedema Activity Score; BSA = body surface area; CTCL = cutaneous T-cell lymphoma; EASI = Eczema Area and Severity Index; ELISA = enzyme-linked immunosorbent assay; IGA = Investigator's Global Assessment; IGA-PN = Investigator's Global Assessment for Prurigo Nodularis; IIF = indirect immunofluorescence; NRS = Numeric Rating Scale; UAS7 = Urticaria Activity Score over 7 days; UCT = urticaria control test.

PHASE 3: TREAT

Foundational Treatment at a Glance

AD

Barrier care and emollients; topical agents (corticosteroids, JAK inhibitor, or calcineurin inhibitor); phototherapy; targeted systemic therapy for moderate-to-severe disease.

CSU

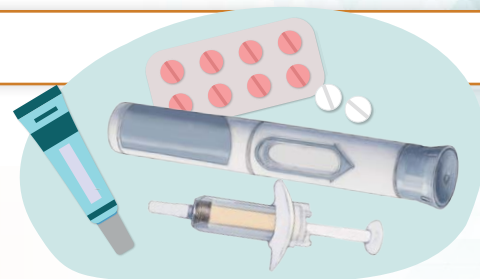
Second-generation H1 antihistamine, followed by guideline-directed dose optimization, add-on targeted therapy when control remains inadequate.

PN

Topical anti-inflammatory treatment and measures to interrupt the itch-scratch cycle; a low threshold for biologic therapy when warranted.

BP

Potent topical and/or systemic corticosteroids remain important; consider steroid-sparing approaches according to severity and comorbidity. Biologic therapy now FDA-approved.



Quick Reference: Current FDA-Approved Targeted Topical and Systemic Therapies

Indications and ages below are a quick reference, not a dosing or prescribing guide. Verify the current US Prescribing Information before treatment.

Therapy	Target	AD ^a	Antihistamine-refractory CSU	PN	BP
Dupilumab	IL-4Rα (anti-IL-4/-13)	≥6 months	≥2 years ^b	Adults	Adults
Nemolizumab	Anti-IL-31Rα	≥12 years ^c	—	Adults	—
Tralokinumab	Anti-IL-13	≥12 years	—	—	—
Lebrikizumab	Anti-IL-13	≥12 years, ≥40 kg	—	—	—
Omalizumab	Anti-IgE	—	≥12 years	—	—
Remibrutinib	BTK inhibitor	—	Adults ^b	—	—
Upadacitinib	JAK inhibitor	≥12 years ^d	—	—	—
Abrocitinib	JAK inhibitor	≥12 years ^d	—	—	—
Ruxolitinib, 1.5%	Topical JAK inhibitor	≥2 years	—	—	—

^a All applicable agents are indicated for moderate-to-severe AD, with the exception of topical ruxolitinib, which is indicated for mild-to-moderate AD. ^b For patients who remain symptomatic despite H1-antihistamine treatment. ^c In combination with topical therapy, when inadequately controlled with topical monotherapy. ^d Eligibility, weight criteria, boxed warnings, and monitoring apply; consult current labeling.

References:

1. Davis DMR, et al. *Am Acad Dermatol*. 2025;93(3):745.e1-745.e7; 2. Davis DMR, et al. *J Am Acad Dermatol*. 2026;95(1):121.e1-121.e26; 3. Zuberbier T, et al. *Allergy*. 2026;81(8):2582-2632; 4. Elmariah S, et al. *J Am Acad Dermatol*. 2021;84:747-760; 5. Werth VP, et al. *J Eur Acad Dermatol Venereol*. 2025;39(2):290-300; 6. Schmidt E, et al. *Am J Clin Dermatol*. 2026;27(5):859-877; 7. Khalil N, et al. *Front Immunol*. 2026;17:1917593; 8. Yosipovitch G, et al. *Dermatol Ther (Heidelb)*. 2026;16(4):1983-1995; 9. Warp PV, et al. *J Am Acad Dermatol*. Published online January 9, 2026. doi:10.1016/j.jaad.2025.12.106; 10. Chovatiya R, et al. *Int J Dermatol*. 2025;64(6):978-991; 11. Current US Prescribing Information: dupilumab, nemolizumab, lebrikizumab, tralokinumab, omalizumab, remibrutinib, upadacitinib, abrocitinib, and topical ruxolitinib.