

Managing Skin Toxicities Related to Immune Checkpoint Inhibitor Therapy

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Principles

- Skin is the most common site of ICI toxicities; many patients already have underlying dermatoses (e.g. eczema, psoriasis) that will flare
- ICI skin AEs can happen anytime during or after therapy, up to 2 years
- Many ICI skin AEs can be managed with topical therapy and do not require stopping ICIs
- Systemic steroids can decrease efficacy of immunotherapy; reserve for life-threatening or very severe reactions (e.g. Stevens-Johnson syndrome/toxic epidermal necrolysis [SJS/TEN]-like, erythroderma, severe bullous disease)

Best practices checklist

- Document baseline skin history and current topical/systemic treatments
- **Educate on treatment-related skin toxicities**
- **Encourage preventative skin care** consisting of:
 - Gentle cleanser, thick moisturizer twice daily, broad-spectrum sunscreen (face, hands; caution about UVA through windows)
- **At each visit, ask about skin side effects**
- **Look for danger signs → urgent referral to dermatology/ER**
 - Fever, skin pain, blisters
 - Significant lab abnormalities
 - Rapidly spreading painful rash, target lesions, mucosal erosions
 - Widespread blisters, skin detachment, or erythroderma
- **Topical steroid treatment**
 - Use liberally: apply BID for 1–2 weeks, then decrease to QD 1–2 weeks
 - Betamethasone valerate 0.1% for body (100–450 g)
 - Desonide for face/folds (60 g)
 - Creams > ointments > solutions

Urgent care/urgent referral

- **Any rash with fever**
- **Any new bullae, skin detachment or skin pain**
- Any mucosal involvement: oral, ocular or genital
- **Any rash with significant abnormal labs (e.g. LFTs, eosinophilia)**

Refer to dermatology early for:

- Facial/genital involvement, bullous eruptions, lichenoid or psoriasiform disease not controlled with topicals; itch not controlled with antihistamines
- Exacerbation of pre-existing condition
- Need for systemic therapy or phototherapy
- Diagnostic uncertainty

Quick guidelines for managing skin toxicities

| Reaction | 1 st Line | 2 nd Line |
|--|--|---|
| Dermato-Cosmetic Regimen: Cleanse + Moisturize + Sun Protect | | |
| Pruritus | Topical steroids + antihistamines | Dupilumab or nemolizumab* |
| Eczematous | Topical steroids | Dupilumab |
| Lichenoid | Topical steroids | Acitretin 25–50 mg daily |
| Psoriasiform | Topical combinations (Vit D + CS or tazarotene + CS) or topical PDE4 | Phototherapy, acitretin or IL23 inhibitor |
| Exanthematous | Topical steroids + antihistamines | Systemic CS (10–20 mg/day) |
| Bullous Reactions | Topical steroids + tetracycline + nicotinamide | Dupilumab +/- systemic CS |
| Progressive Immunotherapy Induced Mucocutaneous Eruption | High-dose systemic corticosteroids (1.5 mg/kg min) | Etanercept, CsA or IVIG |

Topical steroids - body = betamethasone valerate 0.1%; Topical steroids – Face/Folds = desonide; *nemolizumab – not yet approved in Canada.

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AEs, adverse events; BID, twice per day; CS, corticosteroids; CsA, cyclosporin A; ER, emergency room; ICI, immune checkpoint inhibitor; IL, interleukin; IVIG, intravenous immunoglobulin; LFT, liver function tests; PDE4, phosphodiesterase 4; SJS/TEN, Stevens-Johnson syndrome/toxic epidermal necrolysis; QD, once per day; UVA, ultraviolet A. 1. Akdis CA et al. *Allergy*. 2006;61(8):969–987. 2. Eggermont AMM et al. *JAMA Oncol*. 2020;6(4):519–527. 3. Faje AT et al. *Cancer*. 2018;124(18):3706–3714. 4. Fournier C, Butler MO, Sauder MB. *SAGE Open Med Case Rep*. 2023 Jun 16;11:2050313X231181035. 5. Horvat TZ et al. *J Clin Oncol*. 2015;33(28):3193–8. 6. Khattab S et al. medRxiv preprint. 2025 Jan 8:2025.01.07.25320156. 7. Lebwohl M, Heymann W, Berth-Jones J, Coulson I. *Treatment of Skin Disease*. 4th ed. Saunders; 2013. 8. Lovegrove FE et al. *J Cutan Med Surg*. 2025 Jul 15. 9. Muntyanu A, Netchiporouk E, Gerstein W et al. *J Cutan Med Surg*. 2021 Jan-Feb;25(1):59–76. 10. Papp KA et al. *J Eur Acad Dermatol Venereol*. 2025;39(11):1881–94. 11. Sauder MB, Andriessen A, Claveau J, Hijal T, Lynde CW. Canadian Skin Management in Oncology (CaSMO) Algorithm for Patients with Oncology Treatment-Related Skin Toxicities. *Skin Therapy Lett*. STL Supplement. 15 Mar 2021. 12. Sauder MB et al. CaSMO management of cutaneous toxicities associated with immune checkpoint inhibitors: A practical primer. *Skin Therapy Lett*. 2022 Sept. 13. Ständer S, Pereira MP, Berger T et al. IFSI-guideline on chronic prurigo including prurigo nodularis. *Itch*. 2020;5(4):e42. 14. Thompson JA, Schneider BJ, Brahmer et al. NCCN Guidelines Insights: Management of Immunotherapy-Related Toxicities, Version 2.2024. *J Natl Compr Canc Netw*. 2024 Nov;22(9):582–592. 15. Vivar KL et al. *J Cutan Pathol*. 2017 Apr;44(4):381–384. 16. Voudouri D, Nikolaou V, Laschos K et al. *Curr Probl Cancer*. 2017 Nov–Dec;41(6):407–412.