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Topic: Adverse drug reactions, TEN

When Dermatological Therapy Goes Wrong: A Case Series of Unexpected Adverse Reactions to Systemic Treatments

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INTRODUCTION & OBJECTIVE

- Systemic therapies for inflammatory skin disease have transformed dermatological practice, offering effective control of **psoriasis** and **autoimmune blistering disorders** — yet adverse drug reactions (ADRs) remain a significant clinical challenge.
- **Bimekizumab**, a dual IL-17A/F inhibitor, is associated with serious hypersensitivity reactions at a rate of 0.1 per 100 patient-years.[1]
- **Guselkumab**, an IL-23 inhibitor, shows adverse events at 169 per 100 patient-years during long-term treatment.[2]
- **Azathioprine**-induced hepatotoxicity affects approximately 2.7% of patients, typically within the first months of therapy.[3,4]
- **Objective:** to present three cases illustrating diverse adverse reactions to commonly used systemic dermatological therapies, emphasising the importance of vigilant monitoring and early recognition.

REPORTED ADR RATES

0.1 / 100 PY
Bimekizumab — serious hypersensitivity reactions[1]

169 / 100 PY
Guselkumab — adverse events, long-term treatment[2]

≈ 2.7 %
Azathioprine — hepatotoxicity, mostly in the first 3 months[3,4]

CASE 1
Progressive hypersensitivity to bimekizumab

Patient: female, plaque psoriasis
Therapy: bimekizumab 320 mg subcutaneously

CLINICAL COURSE

- After the **first injection**: pruritus without visible cutaneous changes
- **Three days after the second injection**: generalised urticaria and angioedema requiring immediate intervention
- Bimekizumab permanently discontinued

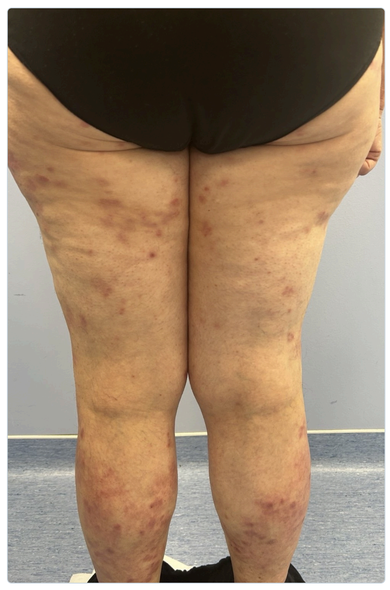


Fig. 1. Disseminated urticarial and excoriated papules on the lower extremities.

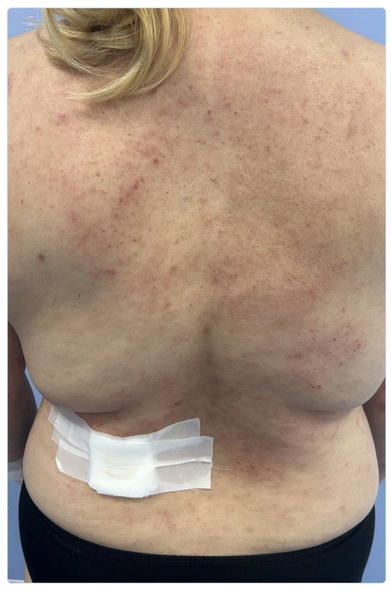


Fig. 2. Confluent urticarial erythema of the trunk and upper arms after the second dose.

Comment: escalation from isolated pruritus to urticaria with angioedema on the second exposure is compatible with drug-induced sensitisation rather than a first-dose infusion-type reaction.

Outcome: successfully switched to an alternative biologic agent, with subsequent tolerance and no further reactions.

CASE 2
Cutaneous adverse effects with guselkumab

Patient: male, plaque psoriasis
Therapy: guselkumab 100 mg, induction phase

CLINICAL COURSE

- Progressive **xerosis** and diffuse **non-scarring alopecia** starting after the first injection
- Progressive worsening after the second administration
- Work-up excluded thyroid dysfunction, nutritional deficiencies and other alternative aetiologies

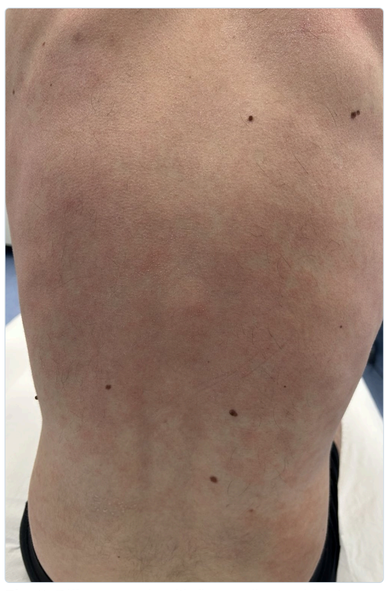


Fig. 3. Diffuse xerosis with fine scaling and faint erythema of the back.



Fig. 4. Xerotic, dull skin of the anterior trunk; no residual psoriatic plaques.

Comment: xerosis and diffuse telogen-type hair loss are rarely reported with IL-23 blockade; the temporal relationship with the induction doses and the exclusion of alternative causes support causality.

Outcome: findings attributed to guselkumab — an uncommon cutaneous adverse effect of IL-23 inhibition.

CASE 3
Azathioprine-induced hepatotoxicity in pemphigus

Patient: pemphigus vulgaris
Therapy: azathioprine 50 mg daily (steroid-sparing)

CLINICAL COURSE

- After **one month**, routine laboratory monitoring revealed **acute hepatitis**
- ALT and AST exceeding **5×**, GGT up to **25×** the upper limit of normal (ULN)
- Azathioprine immediately discontinued; no alternative cause of liver injury identified

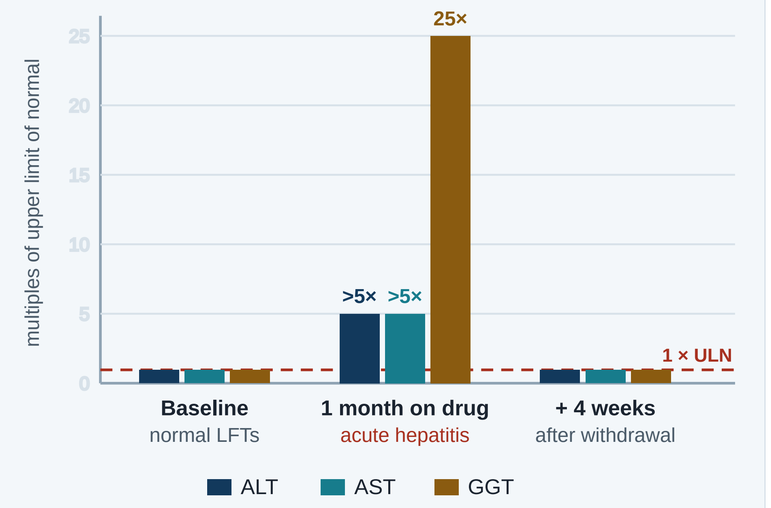


Fig. 5. Schematic course of liver enzymes (multiples of ULN) before, during and after azathioprine exposure.

Comment: the injury was detected while the patient was still asymptomatic — scheduled laboratory monitoring, not symptoms, made the diagnosis.

Outcome: liver function tests normalised within four weeks of withdrawal, confirming drug-induced hepatotoxicity; patient managed with an alternative immunosuppressant.

SUMMARY OF THE THREE CASES

#	Drug (class)	Indication	Time to onset	Clinical presentation	Management	Outcome
1	Bimekizumab (dual IL-17A/F inhibitor)	Plaque psoriasis	Pruritus after 1st dose; urticaria 3 days after 2nd dose	Generalised urticaria and angioedema	Immediate intervention; permanent discontinuation; switch to another biologic	Complete resolution; alternative biologic well tolerated
2	Guselkumab (IL-23 inhibitor)	Plaque psoriasis	After 1st dose, worsening after 2nd (induction)	Progressive xerosis; diffuse non-scarring alopecia	Full dermatological and laboratory work-up; alternative aetiologies excluded	Attributed to guselkumab; uncommon cutaneous ADR of IL-23 inhibition
3	Azathioprine (purine antimetabolite)	Pemphigus vulgaris	1 month after initiation	Acute hepatitis: ALT/AST >5× ULN, GGT up to 25× ULN	Immediate withdrawal; alternative immunosuppressive therapy	Liver function tests normalised within 4 weeks

PRACTICAL MONITORING POINTS DERIVED FROM THESE CASES

IL-17A/F inhibition — hypersensitivity

- Record any injection-related symptom, even isolated pruritus, before administering the next dose.
- Warn patients that reactions may appear **days** after injection, not only within minutes.
- On urticaria with angioedema: stop the drug permanently and treat as a systemic allergic reaction.

IL-23 inhibition — cutaneous effects

- Examine non-lesional skin and the scalp at every induction visit, not only PASI-relevant sites.
- Before attributing alopecia to the biologic, exclude thyroid disease, iron/zinc and protein deficiency, and telogen effluvium triggers.
- Document and report uncommon cutaneous events — real-world data complement trial safety pools.

Azathioprine — hepatic safety

- Baseline liver function tests and blood count before the first dose; consider TPMT/NUDT15 status.
- Repeat testing every 2–4 weeks for the first 3 months, then at least every 3 months.
- Transaminase elevation is usually asymptomatic and reversible if the drug is stopped promptly.

CONCLUSION

- Bimekizumab-associated hypersensitivity, though uncommon, can manifest with **progressive severity upon repeated exposure**, evolving from pruritus to urticaria and angioedema — a pattern suggesting sensitisation and underlining the need for patient education on delayed hypersensitivity symptoms.
- Cutaneous adverse effects such as **xerosis and alopecia under IL-23 inhibition** warrant systematic recognition and documentation in real-world practice, despite the overall favourable safety profile seen in large-scale studies.
- **Azathioprine hepatotoxicity** predominantly occurs within the first three months of therapy and is reversible upon prompt discontinuation, supporting baseline hepatic assessment and regular monitoring.

TAKE-HOME MESSAGES

1. Maintain a **high index of suspicion** for adverse drug reactions at every visit, including late in treatment.
2. Implement **structured surveillance protocols** — clinical review at each dose and scheduled laboratory monitoring.
3. Educate patients on **delayed hypersensitivity symptoms** and when to seek urgent care.
4. Early recognition and prompt drug withdrawal secure optimal patient safety and outcomes.

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DISCLOSURES & CONTACT

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Consent: written informed consent for publication of clinical photographs was obtained from all patients; images are de-identified.

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