Immunotherapy Cutaneous Toxicity Guidelines

RED FLAG SYMPTOMS:

URGENT DERMATOLOGY

REFERRAL

- Fever/hypothermia
- Pustules
- Blisters
- Skin shedding/peeling/ desquamation
- Mucosal involvement
- Target lesions
- Skin pain
- Purpura/bruising

Figure 3: Red Flag Symptoms

ASSESSMENT

HISTORY:

- Drug history timeline - list all drugs started in the last 8 weeks in chronological order
- Rash triggers e.g. Drugs (THINK antibiotics, over the counter medications/herbal remedies), infection

EXAMINATION: Fully undress!

- Rash subtype/distribution (see figure 1)
- Calculate BSA involvement of rash (see figure 2)
- Mucosal involvement? Eyes, mouth, genitalia
- Assess for lymphadenopathy
- Assess for RED FLAG symptoms (see figure 3)

INITIAL INVESTIGATIONS:

- Observations
- FBC, U&E, LFT, CRP, Glc, CK, wound swabs (bacterial + viral)
- Arrange medical photography

Calculate CTCAE grading (see figure 4)

Grade 1-2

Grade 3-4

ESSENTIAL SKIN CARE FOR ALL PATIENTS

TOPICAL STEROID *Potent for body* e.g. Betnovate ointment BD or Elocon ointment OD, *Moderately potent for head & neck* eg. Eumovate (clobetasone) ointment BD. All for 1-2 weeks. Widespread rash requires 30g applied daily Steroid application
Apply to red areas, wait 20 minutes, then apply…
EMOLLIENT e.g. Hydromol ointment QDS (not cream and warn patients about the fire risk (MHRA alert).
Epimax cream if too greasy/ointment poorly tolerated. **SOAP SUBSTITUTE** e.g. Dermol 500 lotion.
ANTIPRURITIC: Oral anti-histamine e.g. *Non-sedating*: Cetirizine 10mg OD or Fexofenadine 180mg OD or *Sedating:* Hydroxyzine 25mg nocte (useful at night if interfering with sleep, with or without daytime non-sedating antihistamine).
If itch persists, consider adding in **Topical** *(for dry skin with or without rash)* e.g. 1% menthol in aqueous cream.

Grade 1-2

ACTIONS:

- Aim to continue treatment as per 'Essential Skin Care'
- Regular monitoring/safety netting (May evolve rapidly)

ASSESS RESPONSE TO TREATMENT AFTER 1-2 WEEKS

- **IMPROVING -** Reduce topical steroid to alternate days for a week and then twice a week as required
- **NOT IMPROVING** increase potency of topical steroid e.g. Dermovate (Clobetasol) ointment to body. Maximum strength on face = potent (see above). Refer to oncall dermatologist for advice if still fails to respond
- **DETERIORATING or RED FLAG symptoms develop (at any time)** - See grade 3-4

Grade 3-4 *(Also any Red Flags)*

ACTIONS:

- Arrange URGENT dermatology review (within 24 hours. Contact oncall dermatology registrar via switchboard) & consider skin biopsy (H&E +/- IMF)
- Withhold immunotherapy & re-assess as above
- Oral prednisolone 0.5mg/kg/day (Maximum dose 60mg/day, see separate tapering guidance)
- If severe/life-threatening, instead consider 1-2mg/kg IV methylprednisolone for 3-5 days (ideally following dermatology review)
- Reconsider infection and/or other drug culprits
- If mucosal involvement (conjunctival or genital) arrange urgent Ophthalmology/Gynae review

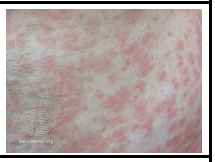
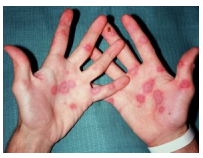
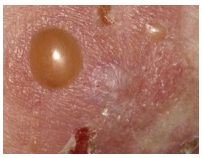
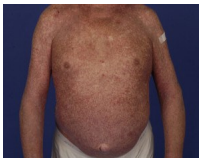
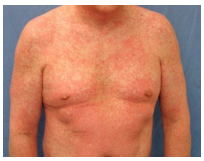
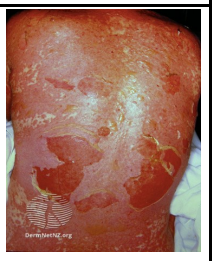
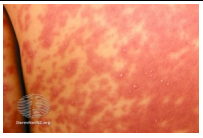
Rash	Description	Photo
Maculopapular/ Morbilliform	Generalised symmetrical red macules (flat patches) and papules (< 5mm lumps).	
Erythema Multiforme	Target lesions - sharp margin, regular round shape and three concentric colour zones: the centre is dusky or dark red with a blister or crust; the next ring is a paler pink and is raised due to oedema; the outermost ring is bright red. May be an early sign of SJS/TEN (see below).	
Blisters/Bullae	Fluid filled blisters >1cm. May be a sign of drug-induced bullous pemphigoid (may require oral tetracycline) or SJS/TEN (see below).	
Lichenoid/SLE-like eruption	Extensive slightly scaly purple papules and plaques distributed symmetrically over the trunk and limbs. May have a photosensitive distribution.	
Drug reaction with eosinophilia and systemic symptoms (DRESS)	Characterised by high fever, eosinophilia, lymphadenopathy and inflammation of one or more internal organs. The skin eruption can be varied but is most often a morbilliform eruption. Typically presents within 2-6 weeks of starting drug. Treat as at per Grade 3-4	
Stevens-Johnson syndrome (SJS) / Toxic Epidermal Necrolysis (TEN)	Tender/painful red skin rash with epidermal detachment (surface layer of skin peels away). Look for target lesions (see above) and mucosal membrane involvement (conjunctiva, oral and genital). Always Grade 3 or 4. Nikolsky sign - extension of a blister to adjacent un-blistered skin when pressure is put on the top of the blister. BAD guidelines on management	
Acute Generalised Exanthemous Pustulosis (AGEP)	Rapid appearance of areas of red skin studded with small sterile pustules.	

Figure 1: Rash subtypes

Rule of 9s: Only calculate involved skin eg. A confluent rash over all upper limb = 9%. If areas of sparing, then estimate involved skin surface area

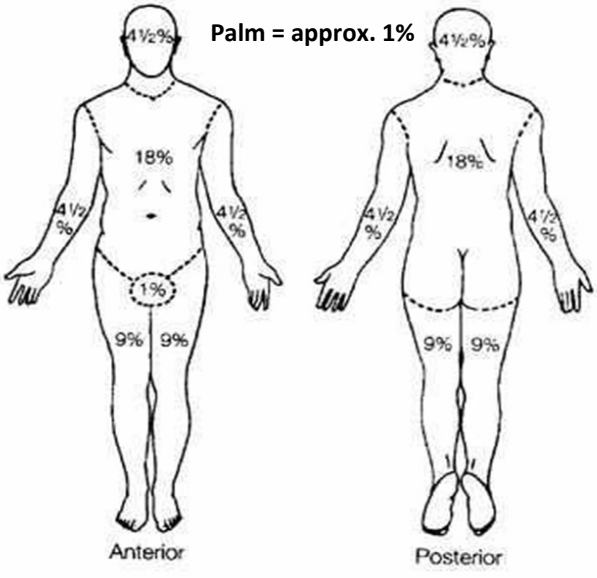


Figure 2: Body surface area calculator

CTCAE grade	Description
Grade 1	Skin rash, with or without symptoms, <10% BSA
Grade 2	Rash covers 10-30% BSA
Grade 3	Rash covers >30% BSA or Grade 2 with substantial symptoms
Grade 4	Skin sloughing >30% BSA with associated symptoms or life-threatening consequences.

Figure 4: Common Terminology Criteria for Adverse Events (CTCAE) grades