

# Care Step Pathway - Skin Toxicities

## Assessment

### Look:

- Does the patient appear uncomfortable?
- Does the patient appear unwell?
- Is there an obvious rash?
- Is the patient scratching during the visit?
- Is skin integrity intact?
- Are there skin changes?
  - o Xerosis (dry skin)
  - o Changes in skin pigment or color
- Is there oral involvement of the rash?
- Does the rash involve the genital-vaginal region? The scalp?

### Listen:

- Does the patient have pruritus with or without rash?
- Is there a rash with or without pruritus?
- Are symptoms interfering with ADLs?
- With sleep?
- Have symptoms worsened?

### Recognize:

- Is there a history of dermatitis, pre-existing skin issues (psoriasis, eczema, wounds, prior radiation to region, etc.)?
- Laboratory abnormalities consistent with other etiologies (e.g., eosinophils on FBC, liver function abnormalities)

## Grading Toxicity

### MACULOPAPULAR RASH (aka morbilliform rash)

Definition: A disorder characterized by the presence of macules (flat) and papules (elevated); frequently affecting the upper trunk, spreading towards the center and associated with pruritus

#### Grade 1 (Mild)

Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)

#### Grade 2 (Moderate)

Macules/papules covering 10-30% BSA with or without symptoms (e.g., pruritus, burning, tightness); having psychological effect and limiting instrumental ADLs; rash covering >30% BSA with or without mild symptoms

#### Grade 3 (Severe)

Macules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADLs; skin sloughing covering <10% BSA

#### Grade 4 (Potentially Life-Threatening)

Papules/pustules covering any % BSA with or without symptoms and associated with superinfection requiring IV antibiotics; skin sloughing covering 10-30% BSA

#### Grade 5 (Death)

### PRURITUS

Definition: A disorder characterized by an intense itching sensation

#### Grade 1 (Mild)

Mild or localized; topical intervention indicated with steroid cream/ointments

#### Grade 2 (Moderate)

Widespread and intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification [thick, leathery skin], oozing/crusts); limiting instrumental ADLs; oral intervention indicated

#### Grade 3 (Severe)

Widespread and constant; limiting self-care ADLs or sleep; systemic corticosteroid or immunosuppressive therapy indicated

#### Grade 4 (Potentially Life-Threatening)

## Management

### Overall Strategy

- Assess for other etiology of rash: ask patient about new medications, herbals, supplements, alternative/complementary therapies, lotions, etc.

### Intervention in at-risk patients

- Advise gentle skin care:
  - o Avoid soap. Instead, use non-soap cleansers that are fragrance- and dye-free (use mild soap on the axillae, genitalia, and feet)
  - o Daily applications of non-steroidal moisturizers or emollients containing humectants (urea, glycerin)
  - o Apply moisturizers and emollients in the direction of hair growth to minimize development of folliculitis
- Advise sun-protective measures
- Assess patient & family understanding of prevention strategies and rationale
  - o Identify barriers to adherence

### Grade 1 (Mild)

- Immunotherapy to continue
- Oral antihistamines will be used in some patients
- Moderate potency topical corticosteroids may be used in some patients
- Advise vigilant skin care
  - o Increase to twice daily applications of non-steroidal moisturizers or emollients applied to moist skin
  - o Moisturizers with ceramides and lipids are advised; however, if cost is an issue, petroleum jelly is also effective
  - o Soothing methods
    - Cool cloth applications
    - Topicals with cooling agents such as menthol or camphor
    - Refrigerating products prior to application
  - o Avoid hot water; bathe or shower with tepid water
  - o Keep fingernails short
  - o Cool temperature for sleep
- Advise strict sun protection
- Monitor vigilantly. Instruct patient & family to call clinic with any sign of worsening rash/symptoms. Anticipate office visit for evaluation
- Assess patient & family understanding of skin care recommendations and rationale
  - o Identify barriers to adherence

### Grade 2 (Moderate)

- Consider holding pembrolizumab or nivolumab and monitor for improvement weekly. If no improvement, begin treatment with prednisone 1 mg/kg tapering over 4 weeks
- Ipilimumab will be withheld for any Grade 2 event
- High-potency topical corticosteroids to be used
- Oral corticosteroids\* (0.5 mg/kg–1.0 mg/kg) and oral antihistamines/oral antipruritics can be used (high-potency topical corticosteroids can be considered for rash alone)
- Consider dermatology referral
- Patient education:
  - o Proper administration of oral corticosteroids
    - Take with food
    - Take early in day
    - Concomitant medications may be prescribed
      - H2 blocker
      - Antibiotic prophylaxis
- Advise vigilant skin care
  - o Gentle skin care
  - o Tepid baths; oatmeal baths
- Advise strict sun protection
- Assess patient & family understanding of toxicity and rationale for treatment hold
  - o Identify barriers to adherence

### Grades 3/4 (Severe or Life-Threatening)

- Nivolumab or pembrolizumab to be withheld for any Grade 3 (severe) and discontinued for Grade 4 (life-threatening) skin conditions or confirmed SJS or TEN; Ipilimumab to be permanently discontinued for any Grade 3/4 event
- High-potency topical corticosteroids to be used; anticipate hospitalization and initiation of IV corticosteroids\* (0.1-1 mg/kg/day)
- Urgent dermatology consult +/- biopsy
- Provide anticipatory guidance:
  - o Rationale for hospitalization and treatment discontinuation
  - o Rationale for prolonged steroid taper
  - o Side effects of high-dose steroids
  - o Risk of opportunistic infection and need for antibiotic prophylaxis
  - o Effects on blood sugars, muscle atrophy, etc.
- For Grade 3/4 pruritus
  - o Corticosteroid\* dose 0.5-1.0 mg/kg/day;
  - o Consider GABA agonist, aprepitant, or omalizumab
- Assess patient & family understanding of toxicity and rationale for treatment discontinuation
  - o Identify barriers to adherence, specifically adherence with steroids when transitioned to oral corticosteroids

### \*Administering Corticosteroids:

#### Steroid taper instructions/calendar as a guide but not an absolute

- Taper should consider patient's current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review steroid medication side effects: mood changes (angry, reactive, hyperaware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

#### Long-term high-dose steroids:

- Consider antimicrobial prophylaxis (sulfamethoxazole/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulfa-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid alcohol/acetaminophen or other hepatotoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

### RED FLAGS:

- Extensive rash (>50% BSA), or rapidly progressive
- Anal, genitourinary, vaginal, or any mucous membrane involvement
- Concern for superimposed infection

