**Tebentafusp-tebn Care Step Pathway - Skin Toxicities**

**Assessment**

**Look:**
- Does the patient appear uncomfortable?
- Does the patient appear unwell?
- Does the patient look sunburned?
- Is the patient scratching during the visit?
- Is skin integrity intact?
- Are there skin changes?
- Xerosis (dry skin)
- Changes in skin pigment or color
- Is there oral involvement of the rash?
- Does the patient look swollen?

**Listen:**
- Does the patient have pruritus with or without rash?
- Is there rash with or without associated symptoms?
- Does the patient report swelling?
- Are symptoms interfering with ADLs?
- Are symptoms worsening?
- Does the patient report a burning sensation?

**Recognize:**
- Is there a history of dermatitis, pre-existing skin issues (psoriasis, eczema, warts, prior irradiation to region, etc.)?
- Laboratory abnormalities consistent with other etiologies (e.g., eosinophilia on complete blood count, 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)
- Advise strict sun protection
- Advise vigilant skin care

**Grade 2 (Moderate)**
- Macules/papules covering 10-30% BSA with or without symptoms (e.g., pruritus, burning, tightness); having psychological affect and limiting instrumental ADLs; rash covering >0% 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

**PRURITUS**

**Definition:** A disorder characterized by an intense itching sensation

**Grade 1 (Mild)**
- Mild or localized; topical intervention indicated

**Grade 2 (Moderate)**
- Widespread and intermittent; skin changes from scratching
  - (e.g., edema, papulation, excoriation, lichenification)
  -厚皮，皮膚組織增生
  - limited instrumental ADLs; oral intervention indicated

**Grade 3 (Severe)**
- Widespread and constant; limiting self-care ADLs or sleep
  - Systemic corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
  - Immunosuppressive therapy indicated

**Management**

**Overall Strategy**
- Encourage use of moisturizers and non-irritating cleansers before patients start tebentafusp-tebn
- Assess for other etiology of rash: Ask patient about new medications, herbs, supplements, alternative/complementary therapies, lotions, etc.
- Educate patients that skin toxicity frequency and severity should drop drastically after the week 3 or week 4 dosages.
- Anticipate development of rash around 1 day after the first 3 dosages
- Advise patients that skin toxicity is very manageable. Very few people have to come off therapy because of this toxicity
- The likelihood of progression of skin toxicities to Grade 4 is very low (no cases reported in trials), but it’s good to be aware of what more severe cases could look like

**Grade 1 (Mild)**
- Tebentafusp-tebn therapy to continue
- Oral antihistamines to be given for symptomatic patients (e.g., diphenhydramine HCL 25 mg PO q 6 hrs PRN)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, or ibuprofen 400 mg q 6 hrs PRN, tramadol 50 mg q 6 hrs PRN)
- Moderate potency topical corticosteroids may be used in some patients
  - Advise vigilant skin care
  - Twice daily applications of non-steroidal moisturizers or emollients applied to moist skin
  - Moisturizers with ceramides and lipids are advised; however, if cost is an issue, petroleum jelly is also effective
  - Soothing methods
- Cool cloth applications
- Topicals with cooling agents such as menthol or camphor
- Refrigerating products prior to application
  - Avoid hot water; bathe or shower
  - Cool temperature for sleep
  - Soothing methods
- Avoid strict sun protection

**Grade 2 (Moderate)**
- Without tebentafusp-tebn until skin toxicity is Grade 1 or below (resume tebentafusp at same dosage level)
- High-potency topical corticosteroids to be used; if unresponsive to topical, consider low-dose oral corticosteroids (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Oral antihistaminosomal anti-pruritics can be used (moderate to high-potency topical corticosteroids can be considered for rash alone)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, ibuprofen 400 mg q 6 hrs PRN, tramadol 50 mg q 6 hrs PRN, or narcotics as needed)
- Advise vigilant skin care
  - Gentle skin care
  - Topical baths, oatmeal baths
  - Avoid strict sun protection

**Grade 3 (Severe)**
- Without tebentafusp-tebn until skin toxicity is Grade 1 or below (resume tebentafusp at same dosage level)
- Do not escalate dosage if Grade 3 skin reactions occur during initial dose escalation; resue escalation once dosage is tolerated
- High-potency topical corticosteroids to be used; if unresponsive to topical, consider low-dose oral corticosteroids (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, ibuprofen 400 mg q 6 hrs PRN, tramadol 50 mg q 6 hrs PRN, or narcotics as needed, could escalate to hydroxyurea or doxepin if itching has progressed)
- Oral antihistaminosomal anti-pruritics can be used
- Consider dermatology consult
  - Avoid strict sun protection

**Grade 4 (Potentially Life-Threatening)**
- Permanently discontinue tebentafusp-tebn for potentially life-threatening skin disease or any cases of SJS and TEN
- High-potency topical corticosteroids to be used (up to 2 mg/kg/day of prednisolone)
- If unresponsive to topical, consider low-dose oral corticosteroids (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Urgent dermatology consult +/- biopsy

**Administration of Corticosteroids:**
- Corticosteroid taper instructional calendar as a guide but not absolute
  - Taper should consider patient’s current symptom profile
  - Close follow-up in person or by phone, based on individual need & symptomatology
  - Corticosteroids may cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on corticosteroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
  - Review corticosteroid 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)

**RED FLAGS:**
- Extensive rash (>50% BSA), or rapidly progressive
- Anal, genitourinary, vaginal, or any mucous membrane involvement
- Concern for supranefrectomy

*ADLs = activities of daily living; BSA = body surface area; PO = by mouth; ICI = immune checkpoint inhibitor; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis

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