### Grade 1 (Mild)
- **Macules/papules** covering less than 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)
- Wide spread and intermittent; rash covering >30% BSA with or without symptoms and associated with severe to life-threatening toxicity

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### MACULOPAPULAR RASH (aka morbilliform rash)

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

### 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:**
  - Avoid soap. Instead, use non-soap cleansers that are fragrance- and dye-free (use mild soap on the axilla, genitalia, and feet)
  - Daily applications of non-stereoidal moisturizers or emollients containing humectants (urea, glycerin)
  - Apply moisturizers and emollients in the direction of hair growth to minimize development of folliculitis
  - Avoid hot water baths or showers
  - Assess patient & family understanding of prevention strategies and rationale
  - Identify barriers to adherence

### Grading Toxicity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>ADLs</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Mild)</td>
<td>Macules/papules covering less than 10% BSA with or without symptoms (e.g., pruritus, burning, tightness)</td>
<td>Moderate to high-potency topical corticosteroids</td>
<td>Patient education: Assess patient &amp; family understanding of skin care recommendations and rationale; identify barriers to adherence</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>Macules/papules covering 10-30% BSA with or without symptoms (e.g., pruritus, burning, tightness), having psychological effect and limiting instrumental ADLs; rash covering &gt;30% BSA with or without mild symptoms</td>
<td>Moderate to high-potency topical corticosteroids to be used (up to 2 mg/kg/day of prednisone); if unresponsive to topical, consider low-dose corticosteroids (0.5 mg/kg to start)</td>
<td>Consider holding ICI therapy and resuming after symptoms have resolved to Grade 1 (skin condition is mild/localized with only topical intervention indicated)</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>Macules/papules covering &gt;30% BSA with or without associated symptoms, limiting self-care ADLs; skin sloughing covering &lt;10% BSA</td>
<td>Low-potency topical corticosteroids to be used; if unresponsive to topical, consider moderate topical corticosteroids (0.5 mg/kg to start)</td>
<td>Consider discontinuation of ICI therapy to continue treatment discontinuation</td>
</tr>
<tr>
<td>Grade 4 (Potentially Life-Threatening)</td>
<td>Papules/pustules covering any % BSA with or without symptoms and associated with superinfection requiring IV antibiotics; skin sloughing covering 10-30% BSA</td>
<td>High-potency topical corticosteroids to be used (up to 2 mg/kg/day of prednisone); anticipate hospitalization</td>
<td>Permanent discontinuation of ICI therapy in the setting of severe life-threatening toxicities (Grade 3-4) including all cases of SJS and TEN</td>
</tr>
<tr>
<td>Grade 5 (Death)</td>
<td>Wide spread and intermittent; rash covering &gt;30% BSA with or without symptoms and associated with severe to life-threatening toxicity</td>
<td>Taper</td>
<td>Adjuvant corticosteroids to be used (up to 2 mg/kg/day of prednisone); anticipate hospitalization</td>
</tr>
</tbody>
</table>

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### Administering Corticosteroids:

- **Steroid taper**:
  - Steroid taper recommendations/calendars 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
  - Anticholinergic therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage >20 mg/day)
  - Review steroid medication side effects: mood changes (angry, reactive, hyperactive, 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 anticholinergic prophylaxis (atropine/trimethoprim double dose MW/F; single dose if used daily) or alternative if sulfia-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional anticholinergic and antibacterial coverage
- Avoid atorvastatin or other hepatoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

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### RED FLAGS:

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

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### 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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