Positive Quality Intervention: Managing EGFR Inhibitor Induced Rash

**Purpose:** Rash occurs in approximately 90% of patients treated with epidermal growth factor receptor (EGFR) inhibitors\(^1\) with 10-20% developing severe eruption.\(^1\) Studies have shown that the presence of this rash is indicative of response to treatment.\(^1\) Therefore, it is important to prevent and manage this side effect appropriately in an effort to avoid holding or decreasing the dose of EGFR inhibitors.

**Background:** EGFR inhibitors are in integral part of treatment for advanced lung, pancreatic, colorectal, and head and neck cancers. These include monoclonal antibodies (amivantamab, cetuximab, panitumumab, necitumumab) and small-molecule tyrosine kinase inhibitors (afatinib, dacomitinib, erlotinib, gefitinib, osimertinib, mobocertinib, lapatinib). A common side effect of these agents is a papulopustular or “acneiform” rash. EGFR inhibitor induced rash can decrease the quality of life for patients and result in dose interruptions or discontinuation by patients. The rash affects areas rich in sebaceous glands, such as the scalp, face, nose, cheeks, nasolabial folds, and perioral region. In addition, the rash can extend to the upper trunk and the “V” region of the neck and chest. Patients commonly report itching, pain, irritation, and stinging. Symptoms can begin as early as the first week of therapy, commonly with an abnormal sensation with redness and edema. As therapy progresses through the first 3 weeks, papules and pustules begin to develop. By the end of the first month of therapy, crusting from the purulent material forms and there is persistent redness and dryness. These initial pustules are sterile; however, a secondary infection can occur with bacteria, fungus, or viruses. These symptoms wax and wane despite continued EGFR inhibitor therapy.\(^1\) There are a few risk factors for developing severe form of the rash. Patients with pale skin that do not tan are at an increased risk of a grade 3/4 rash.\(^1\) Incidence of grade 3 rash was higher in patients treated with combination therapy that included an EGFR inhibitor versus single agent.\(^1\) Patients with non-small cell lung cancer on erlotinib who also smoked had a lower incidence of skin eruption, possibly due to enhanced clearance of the drug.\(^1\)

**PQI Process:**
- Identify patients starting EGFR inhibitor therapy
- Initiate patients on oral antibiotics with or without topical low/moderate strength steroids to face and chest twice daily for first 6 weeks\(^2\)
- After patients start therapy, monitor symptoms of rash on a biweekly basis
  - Consider adding call back reminder in chart
- Grade rash as symptoms develop according to NCCN CTCAE Criteria and impact on quality of life

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Continue EGFRi at current dose</th>
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<tbody>
<tr>
<td>&lt;10% body surface area (BSA) papules and/or pustules; With or without symptoms of pruritus or tenderness</td>
<td>Topical steroid moderate strength*</td>
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<tr>
<td></td>
<td>Topical antibiotic* bid</td>
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<tr>
<td>Grade 2</td>
<td>Continue EGFRi at current dose</td>
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<tr>
<td>10 - 30% BSA papules and/or pustules; With or without symptoms of pruritus or tenderness; Psychosocial impact; Limiting instrumental activities of daily living (ADL)</td>
<td>Oral antibiotic for 6 weeks (doxycycline 100 mg bid; minocycline 100 mg bid)</td>
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<td></td>
<td>Stop topical antibiotic if being used</td>
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<tr>
<td></td>
<td>Topical steroid moderate strength*</td>
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<tr>
<td></td>
<td>Reassess after 2 weeks-if reactions worsens or does not improve proceed to next step</td>
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<tr>
<td>Grade ≥3</td>
<td>Interrupt EGFRi and monitor</td>
</tr>
<tr>
<td>&gt;30% BSA papules and/or pustules;</td>
<td>Oral antibiotic for 6 weeks (doxycycline 100 mg bid; minocycline 100 mg bid)</td>
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**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual’s sole responsibility to seek guidance from a qualified healthcare professional. Updated 5.22.24
With or without symptoms of pruritus or tenderness; Limiting self-care ADL; Associated with local superinfection with oral antibiotics indicated

If infection suspected (yellow crusts, purulent discharge, painful skin/nares):
Switch oral antibiotic to broad spectrum/gram negative coverage
Consider skin swab for bacterial culture
Systemic steroid (prednisone 0.5-1 mg/kg x 7 days)
Topical steroid moderate strength*
Reassess after 2 weeks if reactions worsens or does not improve dose interruption or discontinuation may be needed

* Example topical steroids and antibiotics

<table>
<thead>
<tr>
<th>Topical steroids moderate strength</th>
<th>Triamcinolone acetonide 0.025%; Desonide 0.05%; Fluticasone propionate 0.05%; Aclometasone 0.05%; Hydrocortisone 2.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical antibiotics</td>
<td>Clindamycin 1 - 2%; Erythromycin 1% -2%; Metronidazole 1%</td>
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Patient-Centered Activities:

- Monitor skin and call provider if rash worsens
- Counsel on the importance of preventative measures to decrease severity of rash
  - Patients should limit sun exposure and use sunscreen (SPF 30 or higher; reapply multiple times a day)
  - Mild cleansers and shampoos and avoid fragrant soaps and detergents
  - Use lukewarm water for bathing
  - Use thick, alcohol-free emollients twice daily
    - Caution for fall risk if used on the feet; recommend non-slip socks, slippers, shoes
  - When starting therapy, an oral antibiotic for a minimum of 6 weeks of therapy is indicated
  - Patients should be counseled on not treating acneiform rash with any products for acne, such as benzoyl peroxide, salicylic acid, and other exfoliating scrubs (may worsen rash)
  - Apply topical steroid cream on commonly affected areas once a day (avoid eyes)
    - Prolonged use may cause steroid-induced rash (especially on face and scalp)
    - Referral to dermatology warranted if a steroid-induced rash suspected

References: