



**Clinical Guideline for the  
Management of Skin Toxicity associated with  
Systemic Anti-Cancer Therapy (SACT) in Adult  
Patients**

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## **1. Outline of Procedure**

This document covers the prevention and treatment of skin toxicity associated with systemic anti-cancer therapy in adult patients. Please refer to other appropriate guidelines for paediatric patients or skin toxicity related to other causes for example radiotherapy. Management of skin toxicity due to immunotherapy treatments is detailed in the North Guideline for Management of Immunotherapy Toxicity and is not covered in this document.

## **2. Area of Application**

This guideline applies to all adult SACT services across the North region, except for the administrative areas of Argyll and Bute in NHS Highland which is linked to the WOSCAN CEL (2012) 30 governance framework.

## **3. Introduction**

This document gives advice on the management of common skin toxicities related to SACT. SACT may cause other dermatological conditions (skin toxicities) which are not covered in this document and where necessary advice should be sought from a dermatologist. Dermatological conditions may occur due to the underlying cancer, other medical conditions and medications and therefore alternative causes should always be considered.

## **4. General Skin Care Advice**

Patients prescribed SACT should have regular review for toxicities as outlined in the relevant tumour specific Clinical Management Guidelines (available on the NCA website) or within relevant local SACT protocols.

The general advice detailed below in Table 1 is applicable to any patient prescribed SACT. Advise patients to contact their doctor / treatment nurse or the Cancer Treatment Helpline number if there are any significant changes to their skin that they are concerned about during treatment. Encourage them that early reporting should enable timely intervention.

**Table 1: General Skin Care Advice**

BODY
<ul style="list-style-type: none"><li>• Recommend good fluid intake.</li><li>• Avoid wearing tight clothes.</li><li>• Use lukewarm water to bathe and avoid long periods in the bath or shower</li><li>• Avoid soap, use perfume free soap substitute products e.g.BP emulsifying ointment or Zerobase® cream.</li><li>• Use regular emollients ideally 2 -3 times per day, apply in the direction of hair growth to reduce the risk of folliculitis.</li><li>• Avoid alcohol based or irritant antibacterial skin products, use oils rather than gels.</li><li>• Dry skin gently with a soft towel by patting the skin.</li><li>• Use hypoallergenic make up products.</li><li>• Consider using non-biological washing detergents.</li><li>• If shaving is required, use an electric razor.</li><li>• Do not scratch itchy skin.</li><li>• Avoid sun exposure and cover sun exposed areas with light clothing. If sun exposure cannot be avoided, then a sunscreen of at least SPF30 with protection against UVA and UVB must be applied 30 minutes pre-exposure.</li></ul>
HAIR
<ul style="list-style-type: none"><li>• Use mild shampoo for washing hair e.g. baby shampoo.</li><li>• Avoid using hairdryers, straighteners or hot rollers.</li><li>• Avoid permanent colouring or perming.</li></ul>
HANDS AND FEET
<ul style="list-style-type: none"><li>• Keep nails clean and trimmed.</li><li>• Avoid pushing back cuticles or tearing the skin around the nail.</li><li>• Ensure to dry between the toes after bathing.</li><li>• Wear loose fitting shoes to avoid pressure on the nail.</li><li>• Avoid Shellac® or gel nail polish.</li><li>• Wear gloves when washing dishes or using chemical agents.</li><li>• Vaseline® around the nail beds can act as a barrier.</li></ul>

## 5.1 Initial Assessment

All patients presenting with rash should be reviewed face to face as skin toxicities are difficult to assess over the phone. It is important to make a diagnosis of, and treat appropriately, skin rash unrelated to SACT for example shingles, cellulitis, exacerbation of underlying skin condition.

**Patients receiving SACT are at risk of neutropenic sepsis, check temperature if neutropenic sepsis suspected and manage as per local guidelines.**

- Ascertain which SACT regimen the patient is on and the date of last treatment. If the patient has received treatment with which skin rash is commonly associated e.g. EGFR inhibitor, capecitabine, then refer to the specific section of this document.
- Check if the patient has had recent radiotherapy, or stem cell or bone marrow transplant.
- Check if the patient has recently started any medication and assess if a drug reaction is likely.
- Check if there is a history of skin complaints.
- Assess the rash. Document the site, appearance, whether it is localised or widespread, flat or raised and the presence or absence of any pustules, ulcers, peeling, fluid filled vesicles or bleeding.
- Check if the rash is itchy. Consider liver/kidney problems, dry skin or allergy.
- Check the general health of the patient and if there are any signs of infection.
- Ask if the patient has been in recent contact with shingles or chicken pox.

## 5.2 General Management of Patients admitted with skin rash thought to be due to SACT

Ensure general care measures as per Table 1.

### Initial Management

- Assessment of fluid balance status, establish IV access if any signs of dehydration or sepsis
- Intravenous fluids according to fluid balance status and renal function
- Swab any open areas for infection and send to microbiology
- Treat any infected lesions as appropriate and adjust antibiotics according to clinical condition, myelosuppression, swab results and local antibiotic guidelines.
- Check platelet count as rash may be secondary to thrombocytopenia
- Interrupt SACT treatment and discuss with medical team

### Ongoing Management

- Reassess daily (close monitoring of routine observations as at risk of infection)
- Observe for development of neutropenic sepsis, neutropenia or other SACT toxicities
- Fluid balance and/or daily weights
- Dermatology review if concerns / uncertainty of diagnosis

## Consider Prescribing

- Topical creams (alcohol free, hypoallergenic) – apply regularly to all affected areas
- Antihistamines if rash causes itch
- Analgesia if painful (caution with paracetamol if risk of neutropenic sepsis)

Inform specialist team for further advice and to ensure next treatment is adjusted if necessary.

## 6. General Skin Rash Toxicity Grading

Note scale different for EGFR inhibitors - please see Table 4.

This table describes the grading and management of skin rash. Drug rashes are usually mild, widespread red rashes with no other symptoms.

**Table 2: Skin rash toxicity grading as per UKONS Acute Oncology Guidelines 2015**

Grade 1 (Green)	Grade 2 (Amber)	Grade 3 (Red)	Grade 4 (Red)
Scattered macular or papular eruption or erythema that is asymptomatic	Scattered macular or papular eruption or erythema that is asymptomatic or other associated symptoms	Generalised symptomatic macular, papular or vesicular eruption	Exfoliative or ulcerating dermatitis
<b>Action</b> General skin care advice as per Table 1 Consider analgesia/antihistamines	<b>Action</b> General skin care advice as per Table 1 Consider analgesia/antihistamines	<b>Action</b> advice as for grades 1 and 2	<b>Action</b> advice as for grades 1 and 2
Continue treatment	Continue treatment	Interrupt SACT treatment Modify next dose	Stop SACT treatment Dermatology review

## 7. Palmar-plantar erythrodysesthesia (PPE) or hand-foot syndrome (HFS)

- Palmar-plantar erythrodysesthesia is also known as hand-foot syndrome. It is characterised by scaling surrounded by erythema commonly present on pressure bearing areas of the hands and feet. Although less common it can occur on other areas of the skin, such as the knees and the elbows.
- Drugs known to cause PPE include capecitabine, 5-FU, liposomal doxorubicin, idarubicin, docetaxel, paclitaxel, lapatinib, cytarabine, etoposide, axitinib, sunitinib, sorafenib, pazopanib, vemurafenib, regorafenib.
- With SACT agents, signs and symptoms usually appear after 2-3 months. However targeted therapy symptoms are usually worse within the first 6 weeks.
- Signs and symptoms include tingling, burning, redness, flaking, dryness, swelling, small blisters, sores, usually on palms and or soles of feet.
- For Preventative Measures, see advice as detailed in Table 1. In addition, patients could be advised to apply emollients to hands and feet prior to bed and covering with cotton socks and gloves. Also advise to keep affected areas cool except if developed while on a combination regimen such as oxaliplatin (could exacerbate cold induced neuropathy).

**Table 3: PPE Toxicity Grading as per CTCAE v5.0**

Grade 1 (Green)	Grade 2 (Amber)	Grade 3 (Red)	Grade 4 (Red)
Minimal skin changes or dermatitis (e.g. erythema, oedema, or hyperkeratosis) without pain	Skin changes (e.g. peeling, blisters, bleeding, fissures, oedema or hyperkeratosis) with pain, limiting instrumental ADL*	Severe skin changes (e.g. peeling, blisters, bleeding, fissures, oedema, or hyperkeratosis) with pain; limiting self care ADL	No CTC grading
<p><b>Action</b></p> <p>Moisturise frequently with an emollient according to local formulary</p> <p>Advise patient to phone/report if symptoms worsen</p>	<p><b>Action</b></p> <p>Moisturise frequently with an emollient according to local formulary</p> <p>Advise patient to phone/report if symptoms worsen</p>	<p><b>Action</b></p> <p>Close assessment of patient to identify presence of ulcers, broken areas or evidence of infection.</p> <p>Review to exclude infection and consider antibiotics</p> <p>Admit if not settling or any additional SACT toxicities.</p>	N/A
Continue treatment	<p><b>Consider Interrupting treatment</b></p> <p>Review patient within 48 hours</p> <p>Restart when improved, or resolved to grade 1.</p> <p>Consider dose reduction</p>	<p><b>Stop treatment</b></p> <p>Consider restarting when improved/resolves to grade 0-1. Consider dose reduction for further cycles or discontinuation of drug.</p>	N/A

## 8. Epidermal Growth Factor Receptor Inhibitors

- The most common EGFRi-related adverse events are dermatological due to the concurrent inhibition of physiological EGFR signalling in the skin; to date, this is a class-effect of all EGFRis. Most patients experience mild to moderate symptoms, although the associated physical and psychosocial discomfort can be significant. Consequently, such dermatological toxicities in addition to patient compliance may lead to suboptimal dose-intensity delivery.
- EGFR tyrosine kinase inhibitors (TKIs) such as erlotinib, afatinib and intravenous monoclonal antibody EGFR inhibitors such as cetuximab, panitumumab are known to cause EGFRi related skin toxicity. Commonly experienced dermatological side effects include papulopustular (acneiform) rash, hair changes, radiation dermatitis enhancement, pruritus, mucositis, xerosis/ fissures, and paronychia.

### 8.1 Acneiform rash

- Acneiform rash is the most common side effect of epidermal growth factor receptor (EGFR) inhibitors and it occurs in 50-100% of patients. It is dose dependant and usually develops within the first 1-2 weeks, peaks at 3-4 weeks on therapy. Intensity decreases after 2 weeks but can often persist over several months. The lesions typically look like acne but comedones which are a distinguishing feature of acne are never present.
- Signs and symptoms include a follicular papulopustular (acneiform) eruption on the face, scalp, chest, and upper back.

### Preventative Measures and Advice

Give general advice as detailed in Table 1, in addition to the following:

- Emollients from day 1 for example Zerobase® cream or equivalent, recommend to moisturise 3-4 x day
- Soap substitute to be used as required
- Prophylactic doxycycline 100mg once daily to start on day 1 of treatment.
  - Continue for duration of treatment and for 2 weeks after
  - Increase dose to 100mg twice if grade 1 rash develops (see Table 4)
  - Avoid if tetracycline allergy, discuss with pharmacist regarding suitable alternatives.

#### DOXYCYCLINE – Prescribing notes

- Take with plenty of water in a sitting/ standing position to prevent gastric ulceration / irritation
- Do not take prior to bed
- Can be taken with food and drink to minimise irritation
- Can cause photosensitivity – ensure patient using sun protection
- Alcohol may increase half life
- Caution in hepatic impairment
- Absorption may be impaired by antacids or drugs containing aluminium, calcium, magnesium, iron or bismuth.
- May prolong prothrombin time in patients taking warfarin



In addition for patients prescribed **cetuximab or panitumumab**:-

- Hydrocortisone 1% cream at night
- Pliazon® cream should be supplied
  - Can commence up to 1-2 weeks prior to treatment
  - Avoid application on the eyes, mucous membranes and wounds
  - Apply at least once a day, more frequently if necessary.

**Table 4: Acneiform rash Toxicity Grading as per CTCAE v5.0**

Grade 1 (Green)	Grade 2 (Amber)	Grade 3 (Red)	Grade 4 (Red)
<p>Papules+/- pustules covering &lt;10% BSA which may or may not be associated with symptoms of pruritis or tenderness</p>	<p>Papules+/- pustules covering 10 -30% BSA which may or may not be associated with symptoms of pruritis or tenderness associated with psychological impact; limiting instrumental ADL; papules and/or pustules covering &gt;30% BSA with or without mild symptoms</p>	<p>Papules and/or pustules covering &gt;30% BSA with moderate or severe symptoms; limiting self-care ADL; associated with local superinfection with oral antibiotics indicate</p>	<p>Life threatening consequences; papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritis or tenderness and are associated with extensive superinfection with IV antibiotics indicated</p>
<p>Continue EGFRi</p> <p>Review skin care advice and consider <b>TOPICAL STEROID</b> 1<sup>st</sup> Line 2.5% hydrocortisone cream twice daily (1% for face) 2<sup>nd</sup> Line Betamethasone valerate 0.1% cream BD</p> <p>Add metronidazole gel 0.75% 1-2/day or clindamycin 1% lotion to areas with pustules</p> <p>Increase doxycycline to 100mg BD for 2 weeks if not already on BD dosing</p> <p>If scalp affected consider betamethasone 1% scalp application +/- Capasal<sup>®</sup> shampoo</p>	<p>Continue EGFRi</p> <p>Check FBC/U&amp;Es/LFTs</p> <p>Review skin care advice and consider <b>TOPICAL STEROID</b> as per grade 1 and metronidazole gel 0.75% 1-2/day to affected area</p> <p>Consider switching doxycycline to oxytetracycline 500mg BD for 2 weeks</p> <p>Chlorphenamine 4mg PRN/QDS for itch</p>	<p>Stop EGFRi or dose reduce in line with SACT protocol and in discussion with consultant Check bloods Swab affected areas Review skin care advice and consider</p> <ul style="list-style-type: none"> <li>• Betamethasone valerate 0.1% BD</li> <li>• Metronidazole 0.75% gel 2-5/day</li> <li>• Fusidic acid 2% cream 3-4/day if concern about gram +ve infections</li> <li>• 10-20 mg prednisolone for 7-14 days</li> <li>• Oxytetracycline 500mg BD for 14 days then review</li> <li>• Other oral / IV antibiotics as indicated by swabs or signs and symptoms</li> <li>• Analgesia</li> <li>• Chlorphenamine</li> </ul>	<p>Stop EGFRi</p> <p>Check bloods Swab affected areas Review skin care advice and consider</p> <ul style="list-style-type: none"> <li>• Betamethasone valerate 0.1% BD</li> <li>• Metronidazole 0.75% gel 2-5/day</li> <li>• Fusidic acid 2% cream 3-4/day if concern about gram +ve infections</li> <li>• 10-20 mg prednisolone for 7-14 days</li> <li>• Oxytetracycline 500mg BD for 14 days then review</li> <li>• Other oral / IV antibiotics as indicated by swabs or signs and symptoms</li> <li>• Analgesia</li> <li>• Chlorphenamine</li> </ul>
<p><u>Continue topical therapy</u> Until resolution of rash Review in 2 weeks</p>	<p><u>Continue topical therapy</u> Until resolution of rash Consider medical review if very symptomatic Review in 2 weeks</p>	<p><u>Continue topical therapy</u> Until resolved to grade 0-1, patient reassessed and decision is made regarding EGFRi further treatment</p> <p>Review in 2 weeks or sooner if clinically indicated</p>	<p><u>Continue topical therapy</u> Until resolved to grade 0-1, patient reassessed and decision is made regarding further EGFRi treatment</p> <p>Review in 2 weeks or sooner if clinically indicated Consider requesting dermatology review</p>

## 8.2 Hair Changes

### **Trichomegaly** (elongation and curling of the eyelashes)

Appears after first 1-2 months of treatment and symptoms tend to persist for duration of therapy. Can be associated with patient discomfort and the abnormal eyelash growth can lead to corneal abrasions and further ocular complications. Recommend lash clipping every 2-4 weeks. Refer to an ophthalmologist if irritation or persistent discomfort.

### **Hypertrichosis** (excessive hair growth, often presenting as facial hirsutism)

Appears after first 1-2 months of treatment and symptoms tend to persist for duration of therapy. Can be treated with temporary or permanent hair removal.

### **Scalp hair changes**

Can range from brittleness and slowed growth to alopecia. For patients with scarring alopecia follow the acneiform rash recommendations in Table 4.

Alopecia generally resolves after discontinuation of therapy.

## 8.3 Pruritus

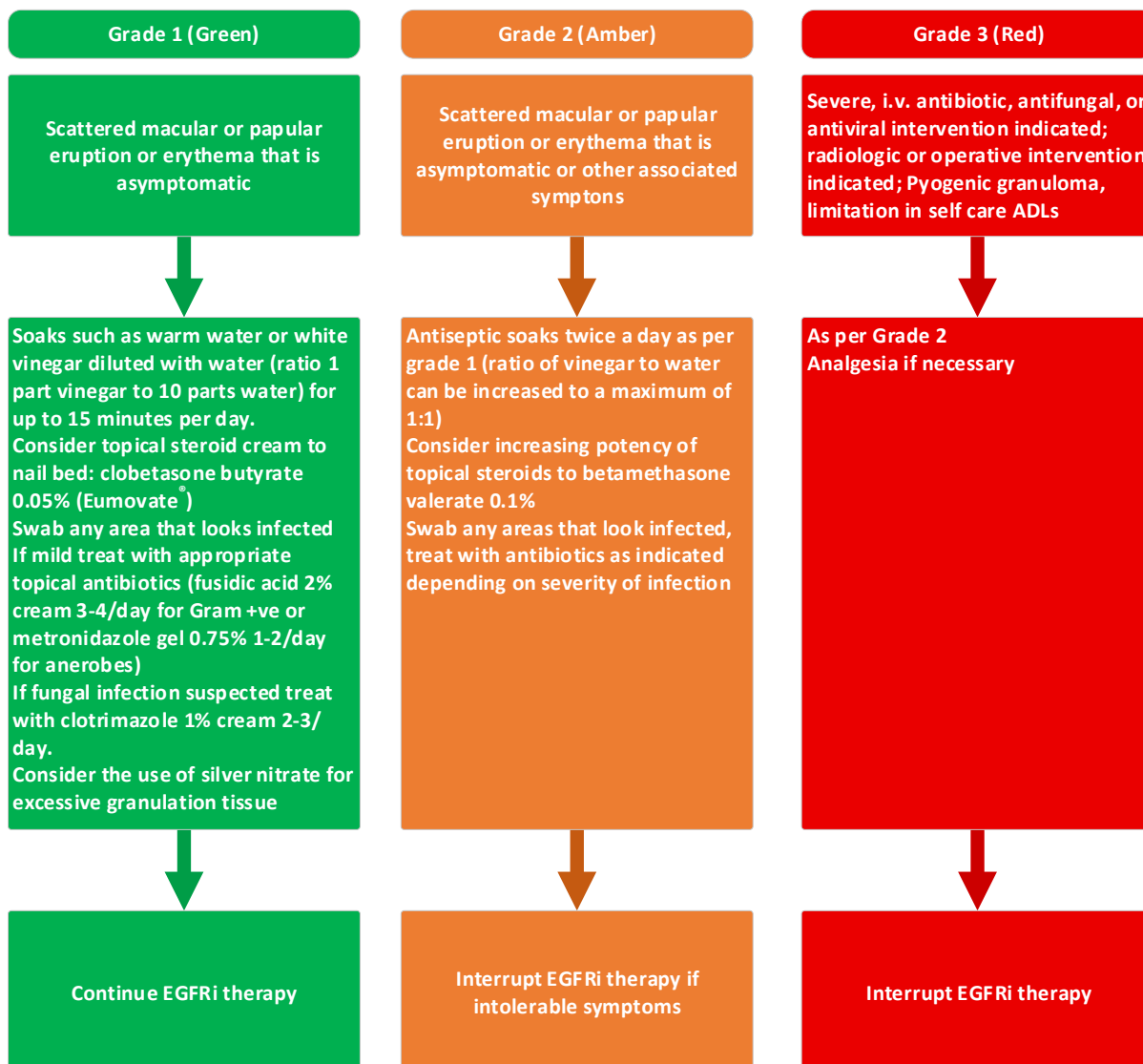
Pruritus occurs in approximately half of all EGFR-treated patients, and although it rarely requires dose modifications or discontinuation of drug therapy, it can impact upon the patient's quality of life. Pruritus often accompanies papulopustular (acneiform) rash at onset, therefore the treatment of underlying rash also can alleviate the pruritic symptoms. Because itching can also occur as a consequence of dry skin, it is important to ensure adequate measures are provided to prevent dryness, see Table 1 general skin care advice. Non-sedating antihistamines are recommended to alleviate day time symptoms for example loratadine. If pruritus is interfering with sleep then a sedating antihistamine, to be used at night, can be considered, for example chlorphenamine. Menthol cream applied 1-2 times daily for its cooling effect can also be considered. Gabapentin or pregabalin can be considered as second line treatment but only if antihistamines fail.

## 8.4 Nail Changes – Paronychia

Paronychia is an often tender inflammation of the nail fold (mainly of the big toe, although other toes and fingers may be involved). In severe cases it can mimic an ingrown toenail and Pyogenic granuloma of the nail fold can develop. Secondary infection with *Staphylococcus aureus* is not uncommon. Due to local pain, limitation of activities of daily living may occur rapidly.

Nail changes are seen in 10-15% of patients and are a late event, starting usually not earlier than 4-8 weeks into treatment.

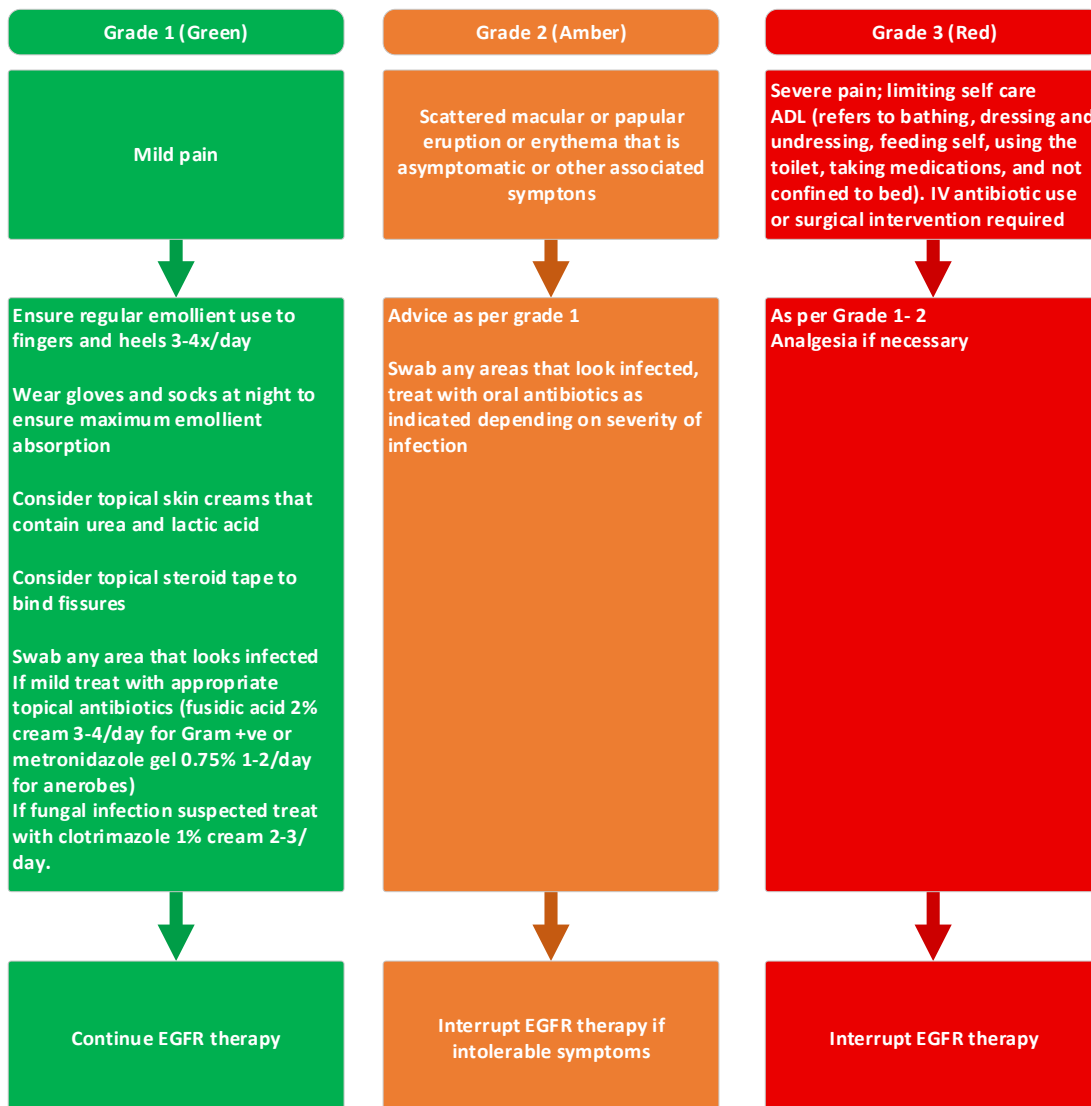
**Table 5: Paronychia Toxicity Grading as per ESMO Oncology in Practice Guidelines**



## 8.5 Finger and Heel Fissures

Fissures are skin cracks caused by xerosis in skin areas where the epidermis is thick (tops of fingers or toes, knuckles and nail folds). Pain associated with fissures may be graded.

**Table 6: Finger and Heel Fissures Toxicity Grading as per ESMO Oncology in Practice Guidelines**



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<b>Purpose/description:</b>	Sets out the guidelines to be followed for the prevention and management of skin toxicity associated with SACT
<b>Policy statement:</b>	It is the responsibility of all staff to ensure that they are working to the most up to date and relevant clinical process documents.
<b>Responsibilities for implementation within Local NHS Boards:</b>	<p><b>Organisational:</b> <i>Operational Management Team and Chief Executive</i></p> <p><b>Sector:</b> <i>General Managers, Medical Leads and Nursing Leads</i></p> <p><b>Departmental:</b> <i>Clinical Leads</i></p> <p><b>Area:</b> <i>Line Manager</i></p>
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\* Changes marked should detail the section(s) of the document that have been amended i.e. page number and section heading.(If there is no previous document please insert N/A into the boxes in the top row of the table below)