Guideline for Healthcare Professionals on the Management of Symptomatic Toxicity from EGFR inhibitor therapy (monoclonal antibodies and TKIs)

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BACKGROUND

Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) such as **erlotinib, afatinib, dacomitinib, gefitinib, lapatinib, osimertinib, neratinib** and **vandetanib** commonly cause gastrointestinal (diarrhoea and stomatitis/mucositis) and cutaneous (rash, dry skin and paronychia) adverse events (AEs). Many of these are used in the treatment of lung cancer*.

Intravenous monoclonal antibody EGFR antagonists such as **cetuximab, panitumumab** and **necitumumab** commonly cause AEs of acneiform rash over face, head and chest, paronychia, low magnesium and gastrointestinal upset (diarrhoea).

Patients on any form of EGFRi therapy above will require regular review for toxicities and imaging to assess response to treatment – as outlined in the relevant tumour Clinical Management Guidelines on the Lothian Intranet.

Before/on commencing EGFRi therapy, all patients should be given skin advice as below and supplied with a pre-prepared prescription (found on OOQS) of prophylactic skin therapy, which have been shown to reduce the intensity of skin reactions (see Section 1).

If skin toxicity develops, increasing supportive treatment and/or interrupting/ adjusting EGFRi doses may be indicated (see Section 2 and Figure 1).

1. PREVENTATIVE MEASURES AND ADVICE

PRE-PREPARED PRESCRIPTIONS AVAILABLE FOR BOTH TKIS AND MABS:

- 100mg OD doxycycline to start before/on day 1 of treatment (see prescribing notes for doxycycline**)
  - Prophylactic
  - Minimum of 4 weeks
  - Continue for duration of treatment and for 2 weeks post treatment
  - Increase to 100mg BD if pustular skin rash worsens
  - Avoid if tetracycline allergy (if pustular/inflamed could consider clarithromycin)
- Zerobase Cream , 1 application, 3-4 x/day (as emollient) –moisturise from day 1- and as soap substitute, 1 application, PRN
- **For cetuximab** – Pliazon cream*** emollient and Hydrocortisone 1% cream at night
- In addition to skin care, also provide loperamide 2mg to take with each loose stool (4mg first dose)

GENERAL SKIN CARE ADVICE:

- Regular emollient – apply to face, hands, feet, neck, back and chest ideally 3-4x/day
- Zerobase Cream (LJF first line). Oilatum Cream or Zerodouble Gel (LJF second line)
- Apply the preferred emollient in the direction of hair growth to reduce risk of folliculitis
- Avoid soap – use perfume-free soap substitutes e.g. Zerobase Cream or emulsifying ointment or Hydromol Ointment
- Avoid alcohol-based lotions/gels (e.g aqueous cream)
- Advise hypoallergenic make-up products and for shaving use an electric razor
- Advise general good skin care e.g:
  - Dry skin gently with a soft towel by patting the skin dry after bathing
  - Use lukewarm water to bathe/avoid long periods in the bath or shower
  - Encourage good fluid intake

  - Avoid wearing tight clothes and underwear
  - Ensure to dry between the toes
- Avoid scratching itchy skin – an antihistamine may be required (chlorphenamine 4mg PRN)
- Consider using non-biological washing detergents

SUNSHINE:
- 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 & UVB should be applied 30mins pre-exposure.
- Warn that using sunscreens on affected areas can cause skin irritation
- Photosensitivity can be exaggerated with doxycycline

HANDS/FEET/NAILS (INCLUDING PARONYCHIA):
- Use regular emollients ideally 3-4x/day – as outlined above
  - Applying emollients to hands and feet prior to bed and covering with cotton socks and gloves to retain moisture can be helpful
  - Vaseline around nail beds can help as a barrier
- Keep nails clean & trimmed
  - Avoid pushing back cuticles or tearing the skin around the nail
- Wear loose fitting shoes to avoid pressure on the nail
- Wear cotton socks/natural fibres to avoid skin irritation
- Wear gloves when washing dishes or using chemical agents

HAIR:
- Use a mild shampoo such as a baby shampoo or 'Head&Shoulders'
- As a second line, Oilatum shampoo can be prescribed
- Prescribe wig if required for hair thinning
- If scalp is dry then advise generous use of Oilatum cream to scalp overnight

***For lung patients it is important to inform the CNS of patients commencing TKIs**
- A CNS will contact the patient 7-14 days after starting TKI to check for side effects
- Encourage early reporting to doctor or nurse of any changes to skin during treatment
- Avoid concomitant anti-acid therapy if possible – if unavoidable, take H2 blockers/ PPIs/ antacids 2hours after TKIs

****Prescribing notes for Doxycycline 100mg**
Avoid if tetracycline allergy. Take with plenty of water in a sitting/standing position to prevent gastric ulceration/irritation. Do not take prior to bedtime. Can be taken with food and drink. Photosensitivity: exaggerated sunburn reaction can occur- use 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. Dosages should be maximally separated. May prolong prothrombin time in patients taking concurrent warfarin.

*****Pliazon Cream**
- Cream is supplied to patients via their hospital pharmacy department (Merck supplies free of charge to patients on EGFRi). Can commence 1-2 weeks prior to starting EGFRi treatment.
- Avoid application on the eyes, mucous membranes & wounds.

2. TREATMENT OF EGFRI TOXICITIES

MANAGEMENT OF EGFRI SKIN TOXICITY

See Figure 1 for treatment of EGFR skin toxicity and adjustments to EGFRi doses

MANAGEMENT OF PARONYCHIA

- Use Dermol 500 lotion
- Soaks such as warm water or white vinegar diluted with water (ratio of 1 vinegar:10 water increasing as severity/grade increases to max of 1:1) for 15 minutes/day
- Consider topical steroid cream to nail beds: clobetasone butyrate 0.05% (Eumovate®) increasing to betamethasone valerate 0.1% (potent steroid) as severity/grade increases
- Swab any areas that look infected
- If mild treat with appropriate topical antibiotics (fusidic acid 2% cream 3-4/day for Gram +ve or metronidazole gel 0.75% 1-2/day for anaerobes)
- If more severe treat with oral / IV antibiotics as indicated, depending on severity of infection
- If suspicion of fungal infection treat with clotrimazole 1% cream 2-3/day

Interrupt EGFRi therapy if intolerable grade 2 (oral antimicrobial use, nail fold oedema/pain, limitation in instrumental ADLs) or grade 3 (as grade 2 plus self-care ADL limitation, IV antibiotic use or surgical intervention)

MANAGEMENT OF FINGER AND HEEL FISSURES/HACKS:

- Ensure regular emollient use to fingers and heels 3-4x/day (e.g Zerobase Cream)
- Wear gloves and socks at night to ensure maximum emollient absorption
- Consider topical skin creams that contain urea and lactic acid
- Consider steroid tape to bind fissures (if available)
- Swab and treat infections as per paronychia above

Interrupt EGFRi therapy if intolerable grade 2 (oral antimicrobial use, pain, limitation in instrumental ADLs) or grade 3 (as grade 2 plus self-care ADL limitation, IV antibiotic use or surgical intervention)

MANAGEMENT OF DIARRHOEA:

- First episode generally occurs within 14 days
- Keep anti diarrhoeal medication close and use at first sign of diarrhoea/change in bowel habit
- If grade 3 or 4: Stop EGFRi, do stool culture. Start loperamide unless high suspicion of infective cause. Consider other causes, ensure hydrated, consider octreotide (100-200 micrograms daily SC) if symptoms do not resolve after a few days of discontinuation of EGFRi or if becoming dehydrated and seek advice from gastroenterology
- Check serum K and Mg levels and replace as needed

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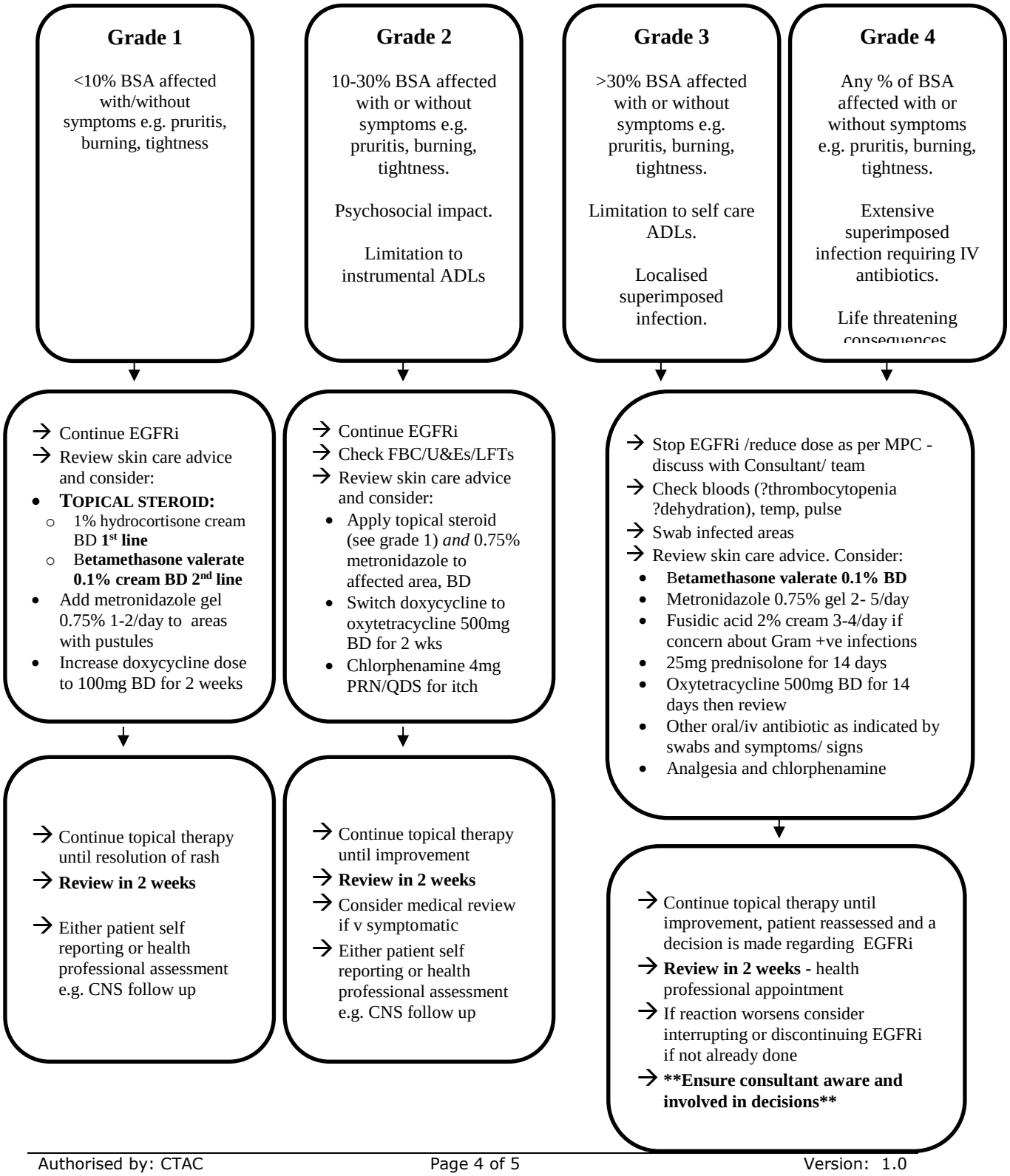
Figure 1

Examine skin, swab wounds, consider FBC/U&Es/LFTs/CRP +/- blood cultures depending on severity/grade. **Inform consultant/SpR *if admitted* and review daily.** Ensure well hydrated. De-lineate and record affected area. Prescribe creams, analgesia, antihistamines, antibiotics +/- steroids if needed



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