Kent and Medway Cancer Collaborative

Guidelines for Cetuximab or Panitumumab Induced Rashes

Network Guidance Document

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1.0 OVERVIEW

Skin reactions may develop in more than 80% of patients and mainly present as acne-like rash and/or, less frequently, as pruritus, dry skin, desquamation, hypertrichosis, or nail disorders (e.g. paronychia). Approximately 15% of the skin reactions are severe, including single cases of skin necrosis. The majority of acne-like skin reactions develop within the first three weeks of therapy. They generally resolve, without sequelae, over time following cessation of treatment if the recommended adjustments in dose regimen are followed.

Other side effects such as paronychia may not develop until after many months of treatment.

Skin lesions induced by cetuximab or panitumumab may predispose patients to superinfections (e.g. with S. aureus), which may lead to subsequent complications, e.g. cellulitis, erysipelas, or, potentially with fatal outcome, staphylococcal scalded skin syndrome or sepsis.

2.0 MANAGEMENT OF CETUXIMAB OR PANITUMUMAB INDUCED RASHES

2.1 General Measures

- Use of tepid water and bath/ shower oil instead of soap or detergent to ensure maximal hydration of the skin
- Use of an emollient cream (especially on the limbs) to prevent xerosis (dry skin). (e.g. aqueous cream, E45, Diprobase® - prescribe according to Trust formulary).
- A urea-containing emollient may be useful for dry, scaly conditions (e.g. Eucerin intensive®, Balneum®, Calmurid® - prescribe according to Trust formulary).
- Use sun protection to avoid hyperpigmentation and protect the skin.
- Wear shoes that are not too tight to avoid friction and pressure on the nail fold.
- Refer to the dermatologist when needed.

2.2 Acne-Like Rash (Papulopustular rash)

The rash associated with cetuximab or panitumumab therapy is found on the upper body, especially the face and scalp and may be associated with pain and itching. It tends to appear 8-10 days after the initiation of treatment, becomes progressively worse peaking at around 14 days and generally resolves without sequelae over time. Whilst the rash is acneiform in appearance it differs from acne vulgaris in its distribution, the absence of comedones and its response to medications.

2.2.1 Table 1: Cetuximab or panitumumab induced acneiform rash

Treatment Principles:

- All patients should use an emollient whilst on cetuximab or panitumumab
- Advise all patients to take appropriate precautions against prolonged sun exposure

At development of **GRADE 1 CTCAE V5:** **Rash acneiform**: Papules and/or pustules covering <10% BSA, which may or may not be associated with symptoms of pruritus or tenderness; psychosocial impact limiting instrumental ADLs	**Continue cetuximab at current dose** **Commence** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd ○ Ensure emollient use ○ Reinforce precautions against sun exposure ○ Consider antihistamine ○ Consider analgesia **Reassess** After 2 weeks
If reaction worsens or does not improve. **Up to GRADE 2 CTCAE V5:** **Rash acneiform:** Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; papules and/or pustules covering > 30% BSA with or without mild symptoms	**Continue cetuximab at current dose** **Continue** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd **Add** Topical low/ moderate steroid – hydrocortisone 2.5% ○ Ensure emollient use ○ Reinforce precautions against sun exposure ○ Consider antihistamine ○ Consider analgesia **Reassess** After 2 weeks
If deterioration to **GRADE 3 CTCAE V5 (or intolerable GRADE 2):** **Rash acneiform:** Papules and/or pustules covering >30%. BSA with moderate or severe symptom; limiting self-care ADL; associated with local superinfection	**Interrupt** cetuximab or panitumumab until resolution to grade 0-2 Consultant referral required SEE TABLE 2 for dose reductions on reintroduction of cetuximab. **Continue oral antibiotic for 6 weeks:** Doxycycline 100mg bd OR Minocycline 50mg bd OR Oxytetracycline 500mg bd **Consider** Topical low to topical moderate steroid **Add** Systemic corticosteroids (prednisolone 0.5-1mg/kg for 7 days) **Reassess**

	After 2 weeks If reaction worsens or does not improve for dose interruption or discontinuation Consider dermatology input for consideration of isoretinoin at low doses (20-30mg/day)
General Remarks:	○ All patients should use an emollient bd whilst on cetuximab preferably urea-containing (5-10%) ○ All patients should avoid excessive sun exposure and use sun protection products UVA/UVB>15 ○ Oral tetracyclines: treat for a prolonged period to benefit from their anti-inflammatory properties. Advise patients to take appropriate precautions against prolonged sun exposure

2.2.2 Table 2: Cetuximab or panitumumab dose modification following treatment interruption due to Grade 3 acneiform skin rash

Occurrence of skin symptom(s): ≥ grade 3	Management
1st occurrence	• Withhold 1 or 2 doses • Improved (< grade 3): continue at 100% of original dose • Not recovered: Discontinue
2nd occurrence	• Withhold 1 or 2 doses • Improved (< grade 3): continue at 80% of original dose • Not recovered: Discontinue
3rd occurrence	• Withhold 1 or 2 doses • Improved (< grade 3): continue at 60% of original dose • Not recovered: Discontinue
4th occurrence	**DISCONTINUE**

2.3 Xerosis

Dry skin can develop gradually over the course of cetuximab or panitumumab therapy. Patients may present with dry, scaly, itchy skin especially of the limbs and skin areas that were affected by acneiform eruption.

Xerosis (abnormal dryness)	
General measures	• Face, chest and back: stop using alcoholic lotions or gels. Switch to hydrating products e.g. creams • Limbs: Use zinc based emollients or ointment e.g.Sudocrem® or zinc and castor oil ointment.
Additional measures if eczema is present	• Use weak topical corticosteroids only on eczema for a short period (1-2 weeks) • Take a swab for supra-infection if eczema becomes wet and treat with antibiotics.
General remarks	• It is important to keep the correct balance in terms of hydration as occlusive ointments may facilitate the development of folliculitis lesions

2.4 Fissures

Fissures generally appear after 2 to 4 months of treatment. They cause pain and functional impairment which may impact on activities of daily living and quality of life. Fissures appear as painful cracks and vascular proliferation in the skin, particularly on the toes, heels and fingertips.

Fissures	
Treatment suggestions	• Treat with hydrocolloid dressing e.g. Comfeel • Urea- containing emollients (e.g. Eucerin Intensive® - prescribe according to Trust formulary). • Treat with propyleneglycol 50% solution under plastic occlusion • Treat with salicylic acid 10% ointment • Treat with flurandrenolone tape or liquid cryanocrylate glue • Treat with ferric subsulfate, silver nitrate, aluminium chloride solution or zinc oxide (20-30%) • Consider dermatologist referral

2.5 Paronychia

Paronychia associated with EGFR inhibition typically appears several months later than the rash. Patients may experience pain, inflammation, purulent discharge, swelling, fissuring, cracking or ridging of nails or pyogenic granuloma. The condition can take weeks to improve following cessation of the EGFR inhibitor.

Paronychia	
Treatment suggestions	• Prevention of infection with regular use of antiseptic or antibiotic soaks and/or creams • Drying paste containing an antiseptic and/or an antifungal can be applied to the affected area • A topical steroid may be added to this preparation in severe cases. Discuss with dermatologist • Treat with silver nitrate caustic pencil for pyogenic granuloma

3.0 REFERENCES

- Erbitux® Summary of Product Characteristics accessed online 10.09.21. Last updated 06.06.2019
- Correspondence from Merck Serono Medical Information dated 4th May 2011
- Common Terminology Criteria for Adverse Events (CTCAE) Version 4 May 2009
- Pinto C et al Management of skin toxicity associated with cetuximab treatment in combination with chemotherapy or radiotherapy. Oncologist 2011; 16: 228-238

4.0 GLOSSARY

Acronyms in common usage throughout KMCC documentation

BNF	British National Formulary
BOPA	British Oncology Pharmacist Association
CNB	Cancer Network Board
COSHH	Control of substances hazardous to health regulations.
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
DGT	Dartford and Gravesham NHS Trust
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
EPS	Electronic Prescribing System
FP10(HNC)	Prescriptions issued by hospital doctors for dispensing in the community
GP	General Practitioner
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
IV	Intravenous
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
KOMS	Kent Oncology Management System
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NHS	National Health Service
NMP	Non-medical prescriber
NPSA	National Patient Safety agency
NOG	Non Surgical Oncology Group *(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)*
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)

QoL	Quality of life
QSIS	Quality service information system
QST	Quality Surveillance Team
RAT	Research and Trial Group *(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)*
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
SACT	Systemic Anti-Cancer therapy
SACT regimen	Systemic Anti-cancer prescription on the electronic prescribing system
SACT protocol	Systemic Anti-cancer protocol on KMCC website
TTO	Treatment to take home
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

5.0 DOCUMENT ADMINISTRATION

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Principal author	Kate Miller
Co-author(s)	Colorectal NOG/Chemotherapy group
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The document is located http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/	
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November 2013	2	Colorectal NOG	Addition of “zinc- based” emollients and creams to section 2.3, general measures for xerosis
November 2014	2.1 – 2.2	C Waters / CRC NOG / N Rowell	Revised whole of document in discussion with clinicians.
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February 2021	V3	Reviewed at CRC NOG	Approved fit for use no changes required.

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October 2024	4.1	CRC NOG; Meeta Durve	Addition of panitumumab, inclusion of 2.2.1 Table 1: Cetuximab or panitumumab induced acneiform rash and 2.2.2 Table 2: Cetuximab or panitumumab dose modification following treatment interruption due to Grade 3 acneiform skin rash Section 2.3 removed
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