Kent & Medway Cancer Collaborative NHS

Network Guidance Document

Guidelines for Cetuximab induced rashes

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Contents

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 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 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 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.

Do not use CTCAE grading to assess cetuximab induced rash.

The rash is classified as follows:
Moderate: requires 1st line treatment on development of rash
Severe: failed 1st line treatment

Acne-like rash Treatment Principles		
Severity of rash.	**Moderate: on development of rash requires 1st line treatment**	**Severe: requires 2nd line treatment**
Systemic antibiotics	YES Doxycycline 100mg od or alternatively Minocycline 100mg od	YES Doxycycline 100mg od or alternatively Minocycline 100mg od
Delay Cetuximab	NO	YES Consultant referral required
General remarks	• All patients should use an emollient whilst on cetuximab • Oral tetracyclines: treat for a prolonged period to benefit from their anti-inflammatory properties. Advise patients to take appropriate precautions against prolonged sun exposure • Consider oral anti histamine for symptomatic relief	

2.3 Cetuximab treatment interruption and re-introduction in response to skin toxicity

Occurrence of grade ≥3 skin toxicity	**Adjustment to cetuximab treatment**	
	SEVERE (failed 1st line treatment)	On resolution to MODERATE
First time	Interrupt treatment	Treatment may be resumed at previous dose
Second time	Interrupt treatment	Treatment may be resumed but at reduced dose (20% DOSE REDUCTION)
Third time	Interrupt treatment	Treatment may be resumed but at reduced dose (40% DOSE REDUCTION)
Fourth time	Discontinue treatment	

2.4 Xerosis

Dry skin can develop gradually over the course of cetuximab 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

2.5 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

2.6 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

References

Erbitux® Summary of Product Characteristics accessed online 24th May 2011. Last updated 09/05/2011

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 assoiciated with cetuximab treatment in combination with chemotherapy or radiotherapy. Oncologist 2011; 16: 228-238

Document Administration

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Document Location

The document is located in the Kent and Medway Cancer Collaborative office, in hardcopy and electronic format.
Also mention here if it can be found on any of the Network websites

DATE OF NEXT REVIEW

This item is next to be reviewed in 2017 by Colorectal NOG & Head & Neck NOG

Revision History

Date	Version	Status	Author	Summary of Changes
July 2011 Oct 2011	0.1 1	Draft Final	K Miller / Colorectal NOG K Miller/ Colorectal NOG	New document PUBLISHED
November 2013	2	Final	Colorectal NOG	Addition of “zinc- based” emollients and creams to section 2.3 , general measures for xerosis
November 2014	2.1-2.2	Draft	C Waters / CRC NOG/ N Rowell	Revised whole of document in discussion with clinicians.
February 2015	3	Final	C Waters / CRC NOG/ N Rowell	PUBLISHED

MEASURES ADDRESSED BY THIS EVIDENCE ITEM

This item of evidence is submitted against the following measures:

ORIGINATORS OF THIS EVIDENCE ITEM

K Miller July 2011