Cetuximab (head and neck)

Indication

In combination with radiotherapy for patients with locally advanced squamous cell cancer of the head and neck whose Karnofsky performance-status score is 90% or greater (WHO performance status 0 or 1) and for whom all forms of platinum-based chemo-radiotherapy treatment are contraindicated.

(NICE TA145)

ICD-10 codes

Codes prefixed with C00-C13

Regimen details

Day	Drug	Dose	Route
Loading dose	Cetuximab	400mg/m^2	IV infusion
Maintenance dose	Cetuximab	250mg/m^2	IV infusion

Cetuximab is administered concurrently with radiotherapy. The loading dose should be one week before the start of radiation therapy with subsequent doses administered concomitantly until completion of radiotherapy.

Cycle frequency

Weekly

Number of cycles

Up to 8 weeks

Administration

Loading dose: Cetuximab is administered as an intravenous infusion over 120 minutes (maximum infusion rate must not exceed 5mg/min).
Maintenance dose: Cetuximab is administered as an intravenous infusion over 60 minutes (maximum infusion rate must not exceed 10mg/min).

Cetuximab is supplied undiluted at a concentration of 5mg/mL in an empty infusion bag.

Patients should be observed for fever and chills and other symptoms of infusion-related reaction during and for at least 1 hour after the completion of the infusion (heart rate, blood pressure, temperature, respiration rate should be taken prior to commencing infusion, at 30 minutes and post infusion). Interruption and slowing down the infusion rate may help control such symptoms.

If a mild or moderate infusion-related reaction occurs, the infusion may be resumed once the symptoms abate. It is recommended to maintain the lower infusion rate for subsequent infusions.

Severe infusion-related reactions have been documented and require immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment. Resuscitation equipment must be available during administration.

Pre-medication

The following should be administered 30 minutes prior to each dose of cetuximab:

- Chlorphenamine 10mg IV
- Ranitidine 150mg PO/PEG
- Dexamethasone 8mg IV
- Paracetamol 1g PO

Ensure regular use of moisturiser. Additional medication may be required for skin toxicities, as per guidelines below.

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Loperamide if required.
See below for guidelines for management of cetuximab induced skin toxicities.

Extravasation

Cetuximab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
Magnesium	14 days
Calcium	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFT	7 days
Magnesium	7 days
Calcium	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥1.0 x 10^9/L
Creatinine Clearance (CrCl)	≥ 30ml/min
Bilirubin	≤ 1.5 x ULN
AST/ALT	≤ 3.0 x ULN

Dose modifications

- **Haematological toxicity**

Cetuximab has not been studied in patients with pre-existing haematological disorders. Generally cetuximab is not myelosuppressive and treatment may continue during periods of mild myelosuppression.
Discuss with consultant if concerned.

As per radiotherapy protocol for squamous cell cancer of the head and neck, patients should receive a blood transfusion if haemoglobin is <11.5 g/dL.

- **Renal impairment**

There is little experience of administering cetuximab in patients with renal impairment.
Discuss with consultant if CrCl <30mL/min.

- **Hepatic impairment**

Bilirubin		AST/ALT	Cetuximab dose
≤1.5 x ULN	and	≤3 x ULN	100%
> 1.5 x ULN	and/or	>3 x ULN	Discuss with consultant

There are no studies to date of patients with impaired hepatic function.

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Severe skin reaction	≥ grade 3 acneiform rash	Stop treatment until reaction resolved to ≤ grade 2 (see information below)
Electrolyte disturbance	Hypomagnesaemia, hypokalaemia (due to diarrhoea), hypocalcaemia	Replace electrolytes as appropriate; hypomagnesaemia is reversible following cetuximab discontinuation
Dyspnoea	May occur as result of infusion related reaction but may occur several weeks into treatment	Discontinue cetuximab treatment if interstitial lung disease is diagnosed.

Skin reactions

For any grade of skin reaction follow the guidelines below:
- Ensure regular use of moisturiser
- Start doxycycline 100mg OD to continue throughout treatment (increase to BD if ≥ grade 3 and if no response consider switching to erythromycin 500mg QDS)
- Oral antihistamine for pruritis

Interrupt cetuximab in severe skin reactions (≥ grade 3 acneiform rash). Treatment may only be resumed if the reaction has resolved to grade 2, according to the dosing table below:

≥ Grade 3 acneiform rash	Cetuximab dose after resolution to ≤ grade 2
1st occurrence	100% previous dose
2nd occurrence	Reduce from 250 mg/m^2 to 200 mg/m^2
3rd occurrence	Reduce from 200 mg/m^2 to 150 mg/m^2
4th occurrence	Discontinue permanently

If the skin reaction does not resolve to ≤ grade 2, treatment should be discontinued.

Cetuximab related acne-like rash in patients on concurrent radiotherapy typically appears within irradiated fields approximately 3 to 5 weeks after commencing treatment.

The management for radiation dermatitis guidelines should be used for the management of ≥ grade 2 acneiform rash co-existing with radiation dermatitis within irradiated fields.

Beneficial treatment approaches for cetuximab related skin reactions (also outside irradiated fields) include topical anti-inflammatory or antibiotic medication and oral antihistamines for pruritus.

Patients may be predisposed to super-infection with *S.aureus* and therefore appropriate additional antibiotic

treatment may be required.

The long-term use of corticosteroids should be avoided due to the potential to induce or exacerbate acne and other skin conditions and to interfere with the antibody-dependent cell-mediated cytotoxicity reactions thought to contribute to the anti-tumour effects of cetuximab.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

S.aureus super-infection
Infusion related toxicity

- **Frequently occurring side effects**

Skin reactions
Nausea and vomiting
Diarrhoea
Headache
Mucositis
Dyspnoea
Conjunctivitis
Electrolyte imbalances particularly hypomagnesaemia

- **Other side effects**

Nil

Significant drug interactions – for full details consult product literature/ reference texts

No documented significant reactions.

Additional comments

Cetuximab use is contraindicated in patients with known severe (grade 3 or 4) hypersensitivity reaction.

Contraindications to radiation therapy must be considered prior to initiation of treatment with cetuximab.

Cetuximab should be used with caution in patients with active peripheral, cerebral or coronary vascular disease or severe myelosuppression.

Patients with medical contraindications to receiving platinum therapy (pre-existing thrombocytopaenia, impaired renal function, impaired hearing or peripheral neuropathy) should be treated with care and the requirement for a WHO performance status of ≥ 1 must be adhered to when initiating therapy.

It is recommended to warn patients of the possibility of late onset infusion reactions and instruct them to contact their doctor/nurse team if symptoms of an infusion-related reaction occur. If severe, a reaction requires immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment.

Cetuximab causes sun-sensitivity that may exacerbate skin reactions. Protect from sun.

References

- Bonner JA, Harari PM, Giralt J, Azarnia N, Shin DM, Cohen RB et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2009:354:567-78
- National Institute for Health and Clinical Excellence. Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. TA145. Accessed 23 Apr 2014 via www.nice.org.uk
- Baxter K, editor. Stockley's Drug Interactions accessed 23 Apr 2014 via

https://www.medicinescomplete.com/mc/

- Summary of Product Characteristics - Cetuximab (Merck Serono) accessed 23 Apr 2014 via www.medicines.org.uk

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