**Systemic Anti-Cancer Treatment Protocol**

# CETUXIMAB
# Single agent with radiotherapy

# PROCEDURE REF: MPHACETUX
# (Version No: 1.1)

## Approved for use in:

Locally advanced squamous cell cancer of the head and neck whose Karnofsky performance-status score is 90% or greater and for whom all forms of platinum-based chemo-radiotherapy treatment are contraindicated.

## Dosage:

| Drug | Dose | Route | Frequency |
|---|---|---|---|
| **Cetuximab** | **400mg/m$^2$** | IV | Loading dose administered one week prior to radiotherapy followed by maintenance treatment |
| **Cetuximab** | **250mg/m$^2$** | IV | Weeks 1 to 7 of radiotherapy |

Cetuximab is administered weekly for up to eight weeks with radiotherapy

### Supportive Treatments:

Domperidone 10mg three times when required
Pliazon cream

## Extravasation risk:

Non-vesicant minimal risk

## Administration:

### Loading dose – to be given one week prior to radiotherapy (day -7)

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | Ranitidine | 50mg | IV | 30 minutes prior to cetuximab |
| 1 | Chlorphenamine | 10mg | IV | 30 minutes prior to cetuximab |
| 1 | Dexamethasone | 8mg | PO | 30 minutes prior to cetuximab |
| 1 | Paracetamol | 1000mg | PO | 30 minutes prior to cetuximab |
| 1 | **Cetuximab** | **400mg/m$^2$** | **IV** | Administered undiluted as an infusion over 120 minutes |

### Maintenance dose – weeks 1 to 7 of radiotherapy

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | Ranitidine | 50mg | IV | 30 minutes prior to cetuximab |
| 1 | Chlorphenamine | 10mg | IV | 30 minutes prior to cetuximab |
| 1 | Dexamethasone | 8mg | PO | 30 minutes prior to cetuximab |
| 1 | Paracetamol | 1000mg | PO | 30 minutes prior to cetuximab |
| 1 | **Cetuximab** | **250mg/m$^2$** | **IV** | Administered undiluted as an infusion over 60 minutes (maximum infusion rate must not exceed 10mg/mL) |

## Main Toxicities:

**Dermatological:** The majority of skin reactions develop within the first three weeks of therapy. Skin reactions mainly present as acne-like rash and/or, less frequently, as pruritus, dry skin, desquamation, hypertrichosis, or nail disorders

The risk for secondary infections (mainly bacterial) is increased and cases of staphylococcal scalded skin syndrome, necrotising fasciitis and sepsis, in some cases with fatal outcome, have been reported

Cetuximab causes sun-sensitivity that may exacerbate skin reactions. Patients should be counselled to protect themselves from sunlight.

**Hypersensitivity reactions** including anaphylaxis (infusion-related reactions occur with mild to moderate symptoms in more than 10% of patients and with severe symptoms in more than 1% of patients)

Gastrointestinal – diarrhea, nausea, vomiting, mucositis and anorexia
occasionally increases in liver enzymes, hypomagnesaemia, and hypocalcaemia.

Keratitis - acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist (see toxicity management section)

## Investigations and Treatment Plan:

Routine FBC is not required during treatment with cetuximab.

| | Pre | Week 1 | Week 2 | Week 3 | Ongoing |
|---|---|---|---|---|---|
| Medical Assessment | X | | | X | At end of treatment |
| Nursing Assessment | | X | X | X | Every cycle |
| FBC | X | | | | Only if clinically indicated |
| U+E & LFT & Mg | X | | | | Only if clinically indicated |
| CT scan | X | | | | As clinically relevant |
| Informed Consent | X | | | | |
| PS recorded | X | X | X | X | |
| Toxicities documented | X | X | X | X | |
| Weight recorded | X | X | X | X | Every week |

## Dose Modifications and Toxicity Management:

**Dermatological**

Skin reactions are very common and treatment interruption or discontinuation may be required. Prophylactic use of oral tetracyclines (6 - 8 weeks) and topical application of 1% hydrocortisone cream with moisturiser should be considered.

If a patient experiences an intolerable or severe skin reaction (≥ grade 3) cetuximab therapy must be interrupted. Treatment may only be resumed if the reaction has resolved to grade 2.

Recommended dose modifications for management of severe skin reactions:

| | |
|---|---|
| ≥ grade 3 skin reaction | Cetuximab dose after resolution to ≤ grade 2 |

<table>
<tr><td></td><td>
<table>
<tr><td>1st occurrence</td><td>Resume at full dose</td></tr>
<tr><td>2nd occurrence</td><td>200mg/m$^2$</td></tr>
<tr><td>3rd occurrence</td><td>150mg/m$^2$</td></tr>
<tr><td>4th occurrence</td><td>Discontinue treatment</td></tr>
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</td></tr>
<tr><td>Ocular</td><td>Patients presenting with signs and symptoms suggestive of keratitis such as acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist.<br><br>If a diagnosis of ulcerative keratitis is confirmed, treatment with cetuximab should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered.</td></tr>
<tr><td>Hypersensitivity reactions including anaphylaxis</td><td>Mild or moderate infusion-related reactions are very common: comprising symptoms such as fever, chills, dizziness or dyspnoea that predominately occur when patients receive their first cetuximab infusion.<br><br>If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions.<br><br>Close monitoring of patients, particularly during the first administration, is required. Special attention is recommended for patients with reduced performance status and pre-existing cardio-pulmonary disease.<br><br>If an infusion-related reaction develops later during the infusion or at a subsequent infusion further management will depend on its severity:
<table>
<tr><td>Infusion related reaction (NCI CTC version 4)</td><td>Management</td></tr>
<tr><td>Grade 1</td><td>Slow the rate of infusion to a previously tolerated rate, decrease the infusion rate by 50% and the patient keep under close supervision.</td></tr>
<tr><td>Grade 2</td><td>Decease the infusion rate by 50% and immediately administer treatment for symptoms, and the patient keep under close</td></tr>
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| | |
|---|---|
| | supervision. |
| Grade 3 and 4 | Stop infusion immediately, treat symptoms. The patient should receive no further treatment with cetuximab |

A cytokine release syndrome (CRS) typically occurs within one hour on the infusion and is less commonly associated with bronchospasm and urticaria. CRS is normally most severe in relation to the first infusion.

| **Cetuximab** | |
|---|---|
| Hepatic impairment | There is little experience of administering cetuximab in patients with hepatic impairment. Deteriorating organ function may be a sign of disease progression. Discuss with consultant if baseline transaminases ≥ 5 times the upper limit of normal and/or bilirubin ≥1.5 times the upper limit of normal. |
| Renal impairment | There is little experience of administering cetuximab in patients with renal impairment. Deteriorating organ function may be a sign of disease progression. Discuss with consultant if baseline CrCl <30mL/min. |

## References:

J. Bonner, P. Harari, J. Giralt, N. Azarnia, M. Dong, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. N Eng J MED 354;6. 2006

Erbitux 5mg/ml solution for infusion,Summary of Product Characteristics. Merck Serono, Middlesex 29/06/2004. Available from www.medicines.org.uk/emc/medicine.
Last updated 04/08/2014.

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - (Version 3 - updated January 2009)

Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage (Version 3 - updated January 2009)

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