

## Cetuximab Therapy-14 days<sup>i</sup>

### INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing RAS wild-type metastatic colorectal cancer (mCRC) in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan	C18	00732a	N/A

\*This is for post 2012 indications only

### TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Cetuximab is administered once every 14 days, treatment continued until disease progression or unacceptable toxicity.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Cetuximab	500mg/m <sup>2</sup>	IV infusion Observe post infusion <sup>a</sup>	See footnote <sup>b</sup> below	Repeat every 14 days
<sup>a</sup> Obtain vital signs pre-infusion, at 1 hour and post-infusion. 1 hour observation period following end of 1 <sup>st</sup> and 2 <sup>nd</sup> cetuximab infusions. If no infusion reactions occur for 2 consecutive doses, then may discontinue observation period and vital signs.					
<sup>b</sup> The initial dose should be given slowly and speed of infusion must not exceed 5 mg/min. For subsequent doses, the maximum infusion rate must not exceed 10 mg/min if no adverse reaction to first infusion. May be administered diluted in 0.9% NaCl or undiluted. Flush the line with 0.9% NaCl at the end of the cetuximab infusion.					

### ELIGIBILITY:

- Indications as above
- Wild type RAS tumours verified by a validated test method
- ECOG 0-3
- Adequate marrow reserve
- Adequate renal and liver function

### EXCLUSIONS:

- Hypersensitivity to cetuximab or to any of the excipients
- Patients with mutant RAS mCRC or unknown RAS mCRC status

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**PRESCRIPTIVE AUTHORITY:**

The treatment plan must be initiated by a Consultant Medical Oncologist.

**TESTS:**

**Baseline tests:**

- FBC, renal and liver profile
- Complete medical history specifically asking about any previous infusion related reactions (IRR) to another antibody, allergy to red meat or tick bites, or any results of tests for IgE antibodies against cetuximab

**Regular tests:**

- FBC, renal and liver profile
- Post treatment: monthly electrolytes, magnesium, calcium for 2 months after last cetuximab treatment

**Disease monitoring:**

Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

**DOSE MODIFICATIONS:**

- Any dose modification should be discussed with a Consultant.

**Renal and Hepatic Impairment:**

**Table 1: Dose modification of cetuximab in renal and hepatic impairment**

Renal Impairment	Hepatic Impairment
No need for dose adjustment is expected	No need for dose adjustment is expected
Haemodialysis: no need for dose adjustment is expected	
Dose modifications from Giraud et al 2023	

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**Management of adverse events:**

**Table 2: Dose Modification of cetuximab for Adverse Events**

Adverse reactions	Recommended dose modification
<b>Infusion Reaction</b>	
Grade 1	Continue slow infusion under close supervision.
Grade 2	Continue slow infusion and immediately administer treatment for symptoms.
Grade 3 and 4	Stop infusion immediately, treat symptoms vigorously and contraindicate further use of cetuximab.
<b>Interstitial lung disease</b>	Discontinue treatment
<b>Skin reaction grade 1 or 2</b>	No dosage adjustment required. See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions.
<b>Severe skin reaction ≥ grade 3*</b>	
First occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at <b>500mg/m<sup>2</sup></b> .
Second occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at <b>400mg/m<sup>2</sup></b> .
Third occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at <b>300mg/m<sup>2</sup></b> .
Fourth occurrence	Discontinue

**SUPPORTIVE CARE:**

**EMETOGENIC POTENTIAL:** Low (Refer to local policy)

**PREMEDICATIONS:**

Patients must receive premedication with an antihistamine and a corticosteroid before receiving cetuximab infusion. This premedication is recommended at least one hour prior to all subsequent infusions. Patient should be educated about the possibility of delayed infusion-related symptoms.

**Table 3: Suggested pre-medications prior to cetuximab infusion:**

Drugs	Dose	Route
Chlorphenamine	10mg	IV bolus 60 minutes prior to cetuximab infusion
dexAMETHasone	8mg	IV bolus 60 minutes prior to cetuximab infusion

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**OTHER SUPPORTIVE CARE:**

See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions.

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:**

*The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.*

- **Infusion-related reactions (IRR):**
  - The first dose should be administered slowly and the speed must not exceed 5 mg/min whilst all vital signs are closely monitored for at least two hours. If during the first infusion, an infusion-related reaction occurs within the first 15 minutes, the infusion should be stopped. A careful benefit/risk assessment should be undertaken including consideration whether the patient may have preformed IgE antibodies before a subsequent infusion is given.
  - If an IRR develops later during the infusion or at a subsequent infusion further management will depend on its severity (Ref Table 2).
  - In cases of mild or moderate infusion-related reaction, the infusion rate may be decreased and maintained at the lower rate in all subsequent infusions.
  - Severe infusion-related reactions may occur with symptoms usually occurring during the first infusion and up to 1 hour after the end of the infusion. They may occur several hours after or with subsequent infusions. Patients should be warned of the possibility of such a late onset and instructed to contact their physician if symptoms occur.
  - Occurrence of a severe infusion-related reaction requires immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment.
  - Special attention is recommended for patients with reduced performance status and pre-existing cardio-pulmonary disease.
- **Respiratory disorders:** Interstitial lung disease has been observed with EGFR inhibitors. Treatment should be withheld in the event of onset or worsening respiratory symptoms. If pneumonitis or lung infiltrates are confirmed, treatment should be discontinued.
- **Cardiovascular:** An increased frequency of severe and sometimes fatal cardiovascular events and treatment emergent deaths has been observed. When prescribing cetuximab, the cardiovascular and performance status of the patients and concomitant administration of cardiotoxic compounds such as fluoropyrimidines should be taken into account.
- **Skin reactions:** This is the main adverse reaction of cetuximab. Refer to local policy for skin care regime and to Table 2 under Dose Modifications for management of treatment if patient experiences skin reactions.
- **Electrolyte disturbances:** Hypomagnesaemia, hypokalaemia or hypocalcaemia may occur. Electrolyte repletion is recommended, as appropriate.

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## DRUG INTERACTIONS:

- When cetuximab is used in combination with platinum based chemotherapy, it may result in increased frequency of severe leukopenia or severe neutropenia.
- When cetuximab is used in combination with fluoropyrimidines, the frequency of palmar-plantar erythrodysesthesia and of cardiac ischaemia including myocardial infarction and congestive heart failure were increased.
- When cetuximab is used in combination with capecitabine and oxaliplatin, the frequency of severe diarrhoea may be increased.
- Current drug interaction databases should be consulted for more information.

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Version	Date	Amendment	Approved By
1	08/09/2022		Prof Maccon Keane
2	08/02/2024	Reviewed. Updated treatment table as per NCCP standardisation. Updated renal and hepatic information in line with Giraud recommendations, 2023. Added Table 3: Suggested pre-medications prior to cetuximab infusion.	Prof Maccon Keane

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Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

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<sup>i</sup> This is an unlicensed posology for the use of cetuximab in Ireland. Patient's should be informed of this and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be fully aware of their responsibility in communicating any relevant information to the patient and also ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.'

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