Cetuximab Therapy-7 day

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	00207a	N/A
Treatment of patients with squamous cell cancer of the head and neck: In combination with radiation therapy for locally advanced disease.	C76	00207b	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 a week. The initial dose is 400 mg/m^2. All subsequent weekly doses are 250 mg cetuximab/m^2.

Colorectal cancer: Treatment continued until disease progression or unacceptable toxicity.

Locally advanced squamous cell cancer of the head and neck: Used concomitantly with radiation therapy.

It is recommended to start cetuximab therapy one week before radiation therapy and to continue cetuximab therapy until the end of the radiation therapy period.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Cetuximab	400mg/m^2	IV Infusion. Observe post infusion[a]	Over 2 hours[b]	1
1	Cetuximab	250mg/m^2	IV Infusion. Observe post infusion[a]	Over 60 minutes	2 and further cycles
[a]Obtain vital signs pre-infusion, at 1 hour and post-infusion. 1 hour observation period following end of 1st and 2nd cetuximab infusions. If no infusion reactions occur for 2 consecutive doses, then may discontinue observation period and vital signs.					
[b]The initial dose should be given slowly and speed of infusion must not exceed 5 mg/minute. The recommended infusion period is 120 minutes. For the subsequent weekly doses, the recommended infusion period is 60 minutes. The maximum infusion rate must not exceed 10 mg/minute 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.					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

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

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 Haemodialysis: No need for dose adjustment is expected	No need for dose adjustment is expected
Renal and hepatic – Giraud et al 2023	

Management of adverse events:

Table 2: Dose Modification of cetuximab for Adverse Events

Adverse reactions	Recommended dose modification
Infusion Reaction 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
Interstitial lung disease	Discontinue treatment
Skin reaction grade 1 or 2	No dosage adjustment required. See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions.
Severe skin reaction ≥ grade 3* First occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at **250**mg/m^2
Second occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at **200**mg/m^2
Third occurrence	Hold cetuximab treatment for a maximum of 2 weeks. Reinitiate therapy only if reaction has resolved to grade 2 at **150**mg/m^2
Fourth occurrence	Discontinue

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic Anti Cancer Therapy (SACT) Induced Nausea and Vomiting- Available on the NCCP website

Cetuximab: Low **(Refer to local policy).**

For information:

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

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

OTHER SUPPORTIVE CARE:

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

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Cunningham D, et al: Cetuximab Monotherapy and Cetuximab plus Irinotecan in Irinotecan-Refractory Metastatic Colorectal Cancer. NEJM 2004; 351:337 – 345.
2. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous cell carcinoma of the head and neck. N Engl J Med 2006;354:567-78

3. Vermorken JB, Ricard MD, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. N Engl J Med 2008; 359:1116-27.
4. Irish Medicines Board :Drug Safety Newsletter April 2014 – Issue Number 60 Available at: https://www.hpra.ie/docs/default-source/publications-forms/newsletters/drug-safety-newsletter-issue-no-60-april-2014.pdf?sfvrsn=12
5. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
6. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
7. Cetuximab 5mg/mL (Erbitux®) Summary of Product Characteristics. Last updated: 16/08/2024. Accessed November 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/erbitux-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	10/02/2014		Dr Maccon Keane
2	10/02/2016	Expanded information on management of infusion reactions. Clarified infusion rate of first infusion	Prof Maccon Keane
3	07/02/2018	Clarified indications and updated with new NCCP regimen template	Prof Maccon Keane
4	12/02/2020	Regimen review. Standardisation of renal and hepatic impairment	Prof Maccon Keane
5	27/01/2025	Regimen reviewed. Update to renal and hepatic dose modifications table to align with Giraud et al. Addition of text and Table 3 for pre medications. Regimen updated in line with NCCP standardisation (emetogenic potential, adverse effects, regimen specific complications and drug interactions).	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.