Cetuximab

Indication
First line treatment of RAS wild type, metastatic colorectal cancer in combination with FOLFOX or FOLFIRI chemotherapy.

Regimen details

Drug	Dose	Route
Cetuximab	500 mg/m^2	IV infusion

RAS status must be confirmed prior to commencing treatment

Cycle frequency
14 days

Number of cycles
Continued until disease progression or unacceptable toxicity

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

Cetuximab is supplied in 500ml 0.9% sodium chloride.

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. If given in combination with chemotherapy, cetuximab is given first, followed by a 1 hour gap before commencing the chemotherapy (or at the consultants' discretion)

Pre-medication
The following should be administered 30 minutes prior to each dose of cetuximab:
- Chlorphenamine 10mg IV
- Dexamethasone 8mg IV

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Patients should be prescribed skin reaction prophylaxis from cycle 1 as per the skin management pathway: https://northwest-nhs.iqemo.com/authenticated/documents/e47e30fa-c29b-42a0-9b72-a43e87c0e5dd.pdf

Emollient	Light emollient cream (e.g. Cetraben) and Dermol 500 lotion (soap substitute)
Topical Steroid	Hydrocortisone cream 1% (prn/QDS)
Sunscreen	SPF 50 (can be requested from GP as not on trust formulary)
Oral antibiotics	Doxycycline 100mg OD

Extravasation

Cetuximab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period**
FBC	14 days
U+E (including creatinine)	14 days
LFTs (including AST)	14 days
Bone profile	14 days
Calcium	14 days
Magnesium	14 days
CEA	14 days
Hepatitis B serology (HBsAG, HBcAb)	none
HbA1c	3 months
Random glucose	14 days

Investigations - pre-subsequent cycles

FBC, U&Es, LFT (including AST), calculated creatinine clearance, calcium, magnesium, random glucose, CEA (4 weekly)

Standard limits for administration to go ahead

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

Note: Refer to parameters in relevant chemotherapy protocol in addition to below.

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Bilirubin	< 1.5 x ULN
Creatinine Clearance (CrCl)	≥ 30 mL/min

Electrolyte disturbances should be corrected prior to treatment

Dose modifications

- **Haematological toxicity**

Refer to relevant chemotherapy protocol for advice. If chemotherapy is delayed, cetuximab should also be delayed.

- **Renal impairment**

The safety and efficacy of cetuximab has not been studied in patients with renal impairment. Discuss with consultant if CrCl <30ml/min

- **Hepatic impairment**

The safety and efficacy of cetuximab has not been studied in patients with impaired hepatic function.

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

- **Other toxicities**

Refer to appropriate chemotherapy protocol for advice regarding chemotherapy toxicity.

Toxicity	**Definition**	**Dose adjustment**
Severe skin reaction	≥ grade 3	See guidance below
Electrolyte disturbance	Hypomagnesaemia, hypokalaemia, hypocalcaemia	Replace electrolyte as appropriate
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.
Any other toxicity	≥ grade 3	Withold until resolved to < grade 2

Interstitial lung disease ILD, which may be acute in onset, has been observed and some cases have been fatal. If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, cetuximab should be interrupted and the patient should be promptly investigated. If ILD is confirmed, cetuximab should be discontinued and the patient treated appropriately.
Cetuximab is contra-indicated in patients with interstitial pneumonitis or pulmonary fibrosis.

Skin reactions

Management of patients with mild, moderate and severe skin reactions should be as per the below guidance:

https://northwest-nhs.iqemo.com/authenticated/documents/e47e30fa-c29b-42a0-9b72-a43e87c0e5dd.pdf

Occurrence of ≥ grade 3 skin reaction	**Management**
1st occurrence	Withhold 1-2 doses If improved to < grade 3 continue 100% If no recovery: discontinue
2nd occurrence	Withhold 1-2 doses If improved to < grade 3 continue 80% If no recovery: discontinue
3rd occurrence	Withhold 1-2 doses If improved to < grade 3 continue 60% If no recovery: discontinue

4th occurrence	Discontinue

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

- **Serious side effects**

Infusion related toxicity
Interstitial lung disease
Acute renal failure
Severe skin reactions and risk of secondary bacterial infection, including necrotising fasciitis

- **Frequently occurring side effects**

Skin reactions
Nausea and vomiting
Abdominal pain
Diarrhoea, constipation
Headache
Mucositis
Dyspnoea, cough
Electrolyte imbalances particularly hypomagnesaemia, hypokalaemia, hypocalcaemia.
Ocular disorders, keratitis

- **Other side effects**

Cardiovascular disorders
Eye disorders- ulcerative keratitis

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

Cetuximab should not be administered in combination with bevacizumab containing chemotherapy.

Additional comments

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

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.

Fertility/Contraception

Patients should use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breastfeeding should be discontinued during treatment. Women using hormonal contraceptive must also use a barrier contraceptive method.

References

- Colorectal NICE guideline NG151 (updated 15 Dec 2021) accessed 9 May 2025
- National Institute for Health and Clinical Excellence. TA439. (Updated 25 September 2017) Accessed 9 May 2025 via www.nice.org.uk
- Summary of Product Characteristics - Cetuximab accessed 9 May 2025 via www.medicines.org.uk/

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON DESIGNATED LEAD CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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