CETUXIMAB (Erbitux) CISPLATIN FLUOROURACIL

INDICATION (ICD10) C49

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (CET3)

1.Cetuximab in combination with chemotherapy for the first cytotoxic containing treatment of recurrent / metastatic squamous cell cancer of the head and neck only originating in the oral cavity with palliative intent. PS 0 or 1. (TA473)

REGIMEN

Day 1 Premedication 60 minutes prior to treatment:
Chlorphenamine 10mg IV bolus
Dexamethasone 8mg IV bolus
CETUXIMAB 500mg/m^2 in #ml sodium chloride 0.9% IV infusion
Prehydration
CISPLATIN 100mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
Posthydration
FLUOROURACIL 4000mg/m^2 over 96 hours via an infusor

diluent volume for dose prescribed as per national standardised product specification

NB Cetuximab first dose give over 120 minutes. If tolerated the second dose and subsequent doses may be given at a rate that does not exceed the maximum rate of 10mg/min.
Close monitoring is required during the cetuximab infusion and for at least 1 hour after the end of the infusion

CYCLE FREQUENCY AND NUMBER OF CYCLES

Cisplatin Fluorouracil every 21 days for 6 cycles
Cetuximab every 14 days for duration of 6 cycles cisplatin and fluorouracil
then prescribe cetuximab 2 weekly regimen as maintenance until disease progression

ANTI-EMETICS

Highly emetogenic day 1
Low emetogenic risk days 2, 3 and 4 and days of cetuximab monotherapy

CONCURRENT MEDICATION REQUIRED

Cetuximab	Ensure premedication chlorphenamine and dexamethasone given 60 minutes prior to treatment
Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cetuximab - neutral
Cisplatin – exfoliant
Fluorouracil - inflammitant

Filter not required
Central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E, Mg^{++} and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cetuximab	Dyspnoea - as part of a hypersensitivity reaction, or after several weeks of therapy. Older, poor PS or underlying pulmonary disorders may be at increased risk. May be severe and/or long-standing. Hypersensitivity - mild or moderate reaction infusion rate may be decreased. Maintain lower infusion rate for subsequent infusions. Severe - usually during the initial infusion and up to 1 hour after the end of infusion, but may occur after several hours. Requires immediate and permanent discontinuation of cetuximab and may necessitate emergency treatment. Infusion related reactions – If during the 1st infusion, an infusion-related reaction occurs within the first 15 minutes, the infusion should be stopped, risk assessment undertaken. If an infusion-related reaction develops later during the infusion or at a subsequent infusion further management will depend on its severity: 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. Skin reactions - severe skin reaction cetuximab must be interrupted. Treatment may only be resumed, if the reaction has resolved. With the 2nd occurrence of a severe reaction, treatment may be resumed at 75% after interruption. With the 3rd occurrence of a severe reaction, treatment may be resumed at 50% after interruption. If severe skin reactions occur a 4th time or do not resolve during treatment interruption, stop treatment permanently.
Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Fluorouracil	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. Special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Stomatitis

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.
Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin

DOSE MODIFICATIONS
Haematological
If neutrophils <1.5x10^9/L and/or the platelet count <100x10^9/L delay the second course by one week, recheck blood count.
If satisfactory (>1.5x10^9/L and >100x10^9/L) give 75% dose cisplatin and fluorouracil
If not satisfactory delay by a further week and recheck blood count, if satisfactory (>1.5x10^9/L and >100x10^9/L) then give 75% dose cisplatin and fluorouracil with GCSF or at Clinician's give 50% dose cisplatin and fluorouracil.
If still unsatisfactory after 2 week delay chemotherapy should usually be discontinued.

Non-haematological
Cisplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Hepatic impairment
Cetuximab
No dose adjustment required.

Fluorouracil

Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment. Always discuss deteriorating liver function with consultant.	
If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected in mild and moderate (without renal impairment).	
Bilirubin >85micromol/L	not recommended

Renal impairment
Cetuximab
No dose adjustment required.

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <45ml/min	not recommended

REFERENCES
1. EXTREME trial