Carboplatin, 5-Fluorouracil and Cetuximab for Head and Neck Cancer

Indication	Palliative treatment for squamous cell cancers of the head and neck in selected patients who have not received previous treatment with cetuximab. This group may include younger patients with WHO PS 0-1 with well or moderately differentiated primary tumours. To be prescribed in line with commissioning criteria.
Treatment Intent	Palliative
Frequency and number of cycles	Cycles 1-6: repeat every 21 days Cycle 7 onwards: repeat every 28 days Up to 6 cycles of carboplatin & fluorouracil & cetuximab Cetuximab then continues until disease progression
Monitoring parameters and management of adverse events & dose reductions	• For reasons of practicality the Head and Neck NOG recommends a C+G is used to calculate the dose of Carboplatin. • Consider 25% dose reduction of carboplatin and 5FU if borderline performance status. • If CrCl is ≤30ml/min, discontinue platinum agent • Monitor LFTs and FBC at each cycle. • Monitor U+Es prior to treatment and every week thereafter during cycles 1-6 in particular Mg^{2+}, K^{+} and Ca^{2+}. From cycle 7 monitor every 2 weeks. • If neuts 1.0-1.5 and PLT ≥100 d/w consultant. • If neuts <1.0 or PLT <100 delay carboplatin and 5FU. • Dose reduction should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to ≤ grade 1 • See Guidance on Treatment of Acne- like Skin Rash and the interruption and re-introduction of cetuximab in response to skin toxicity http://www.kentmedwaycancerguide.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/ • Do not administer chemotherapy until at least 1 hour after the end of the cetuximab infusion • If the patient experiences a mild or moderate infusion-related reaction, the infusion rate of cetuximab may be decreased. Maintain this lower infusion rate in all subsequent infusions
Reference(s)	HNT-004 Carboplatin and 5Fluorouracil without radiotherapy v3 and HNT-017 Cetuximab weekly v3 KMCC proformas NCDF list v1.47 accessed online 25.10.17

NB For funding information, refer to the SACT funding spreadsheet

Cycles 1-6
Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Dexamethasone	8mg	po		Administer pre-medication one hour prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB **400mg/m² loading dose - Day 1, Cycle 1 only** **250mg/m² maintenance dose – Day 1, cycle 2 onwards**		IV	**1st dose, Cycle 1 only- 2hrs** **Cycle 2 onwards over 1 hr**	**To be given undiluted at a max rate of 10mg/min.** **Flush line with sodium chloride 0.9% IV post cetuximab infusion**
	Do not administer chemotherapy until at least 1 hour after the end of the cetuximab infusion				
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	CARBOPLATIN (AUC 5) **Dose = (GFR + 25) x 5**		IV	30 min	Glucose 5% 500ml
Days 1-4	**5-FLUOROURACIL (1000mg/m²/day)** (prescribe for total of 4 days)		IV	96 hour pump	By continuous infusion pump
Day 8	Dexamethasone	8mg	po		Administer pre-medication one hour prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB (**250mg/m² maintenance dose**)		IV	1 hour	**To be given undiluted at a max rate of 10mg/min.** **Flush line with sodium chloride 0.9% IV post cetuximab infusion**
Day 15	Dexamethasone	8mg	po		Administer pre-medication one hour prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB (**250mg/m² maintenance dose**)		IV	1 hour	**To be given undiluted at a max rate of 10mg/min.** **Flush line with sodium chloride 0.9% IV post cetuximab infusion**

TTO	Drug	Dose	Route	Directions
1	Dexamethasone tablets/liquid*	6mg	po	om for 3 days
	Metoclopramide tablets/liquid*	10mg	po	up to 3 times a day for 3 days then 10mg up to 3 times a day as required
	Filgrastim 300 micrograms **or consider dose of 480 micrograms if patient > 80kg**		sc	od starting on day 2 for 5 days
	Doxycycline	100mg	po	od at the onset of rash, **prescribe if required**

Cycle 7 onwards
Repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Dexamethasone	8mg	po		Administer pre-medication one hour prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB (500mg/m² maintenance dose)		IV	2 hours	**To be given undiluted at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion**
Day 15	Dexamethasone	8mg	po		Administer pre-medication one hour prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB (500mg/m² maintenance dose)		IV	2 hours	**To be given undiluted at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion**
TTO	Drug	Dose	Route	Directions	
	Doxycycline	100mg	po	od at the onset of rash, **prescribe if required**	

Guidance on Treatment of Acne- like Skin Rash
Do not use CTCAE grading to assess cetuximab induced rash.

The rash is classified as follows:
Moderate: requires 1st line treatment on development of rash
Severe: failed 1st line treatment

Acne-like rash Treatment Principles

Severity of rash.	**Moderate: on development of rash requires 1st line treatment**	**Severe: requires 2nd line treatment**
Systemic antibiotics	YES Doxycycline 100mg od or alternatively Minocycline 100mg od	YES Doxycycline 100mg od or alternatively Minocycline 100mg od
Delay Cetuximab	NO	YES Consultant referral required
General remarks	• All patients should use an emollient whilst on cetuximab • Oral tetracyclines: treat for a prolonged period to benefit from their anti-inflammatory properties. Advise patients to take appropriate precautions against prolonged sun exposure • Consider oral anti histamine for symptomatic relief	

Cetuximab treatment interruption and re-introduction in response to skin toxicity

Occurrence of grade ≥3 skin toxicity	**Adjustment to cetuximab treatment**	
	SEVERE (failed 1st line treatment)	On resolution to MODERATE
First time	Interrupt treatment	Treatment may be resumed at previous dose
Second time	Interrupt treatment	Treatment may be resumed but at reduced dose (20% DOSE REDUCTION)
Third time	Interrupt treatment	Treatment may be resumed but at reduced dose (40% DOSE REDUCTION)
Fourth time	Discontinue treatment	