Indication	First line treatment of recurrent or metastatic squamous cell cancers of the head and neck (oral cavity only) in selected patients who have not received previous treatment with cetuximab or where the only systemic therapy for this recurrent/metastatic oral cavity tumour has been with pembrolizumab monotherapy. This group may include younger patients with WHO PS 0-1 with well or moderately differentiated primary tumours.
Treatment Intent	Palliative
Frequency and number of cycles	Cycles 1 -6 repeat every 21 days Cycle 7 onwards repeat every 28 days. Maximum of 6 cycles of Carboplatin, 5-Fluorouracil and Cetuximab, followed by maintenance cetuximab to continue until disease progression, unacceptable toxicity or patient choice.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **DPD testing:** DPD testing must be undertaken in all patients before starting treatment; the result must be checked before treatment is started. • **Cardiotoxicity:** • ECG baseline and during treatment as clinically indicated. • Caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris. • C and G or EDTA can be used at clinicians' discretion to calculate the dose of carboplatin. • **Blood Parameters and monitoring:** • Monitor LFTs and FBC at each cycle. • Monitor U+Es prior to treatment and every week thereafter during cycles 1-6 in particular Mg2+, K+ and Ca2+. 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. • **Hepatic Impairment:** • Carboplatin – no dose adjustment required. • 5FU – caution is advised, dose reduction may be required. • Cetuximab – no data available. • **Renal Impairment:** • Carboplatin - discontinue if Crcl <30ml/min. • 5FU - caution is advised, dose reduction may be required in severe renal impairment. • Cetuximab – no data available. • **Dose Modification:** o Consider 25%-50% dose reduction of carboplatin and 5FU if borderline performance status. o 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. o See Guidance on Treatment of Acne- like Skin Rash and the interruption and

	re-introduction of cetuximab in response to skin toxicity. **www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/** • **Infusion related reactions:** ○ **Carboplatin:** Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate. If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be rechallenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment. Severe (grade 3): Do not restart infusion. Consider alternative treatment. Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. ○ **Cetuximab** can cause severe infusion related reactions, pre-meds must be given 1 hour before 1st administration and then 30-60mins prior to subsequent administrations and patients must be monitored every 30 minutes during the infusion and for a 1-hour period after. If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions. For severe reactions discontinue treatment. • **Adverse reactions** ○ **Skin reactions:** Skin reactions are very common with cetuximab and treatment interruption or discontinuation may be required. For full guidance on cetuximab induced rashes see KMCC document "Guidelines for Cetuximab or Panitumumab Induced Rashes" **www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/** ○ **Interstitial lung disease (ILD):** Patients should report any new or worsening respiratory symptoms. Cetuximab should be permanently discontinued in patients with confirmed ILD. ○ **Ocular toxicities:** Cetuximab should be used with caution in patients with a history of keratitis ulcerative keratitis or severe dry eye. If a diagnosis of ulcerative keratitis is confirmed, treatment with cetuximab should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Carboplatin:** Caution when used concurrently with other nephrotoxic or ototoxic drugs. ○ **5-FU:** Concomitant use with phenytoin may increase phenytoin levels, monitor for toxicity. If used concomitantly with warfarin monitor INR and prothrombin time closely. Brivudine, sorivudine or their analogues irreversibly inhibit DPD, which may lead to increased fluoropyrimidine-related toxicities with potentially fatal outcome.
References	KMCC protocol HNT-025 v3 CDF list accessed online V1.336

NB For funding information, refer to CDF and NICE Drugs Funding List

Cycle 1 only: loading dose 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	8mg	PO		Administer pre-medication 60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**400mg/m²**	IV	2hrs	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given 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 Max 700mg**	IV	30 min	Glucose 5% 500ml
1-4	**5-FLUOROURACIL**	**1000mg/m²/day**	IV	96 hour pump	By continuous infusion pump
8	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1hr	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion.
15	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1hr	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given 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	10mg TDS for 3 days and then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	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 2-6: Maintenance dose repeat every 21 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1hr	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given 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 Max 700mg**	IV	30 min	Glucose 5% 500ml
1-4	**5-FLUOROURACIL**	**1000mg/m²/day**	IV	96 hour pump	By continuous infusion pump
8	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1hr	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion.
15	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1hr	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given 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	OD for 3 days
	Metoclopramide tablets/liquid	10mg	PO	10mg TDS for 3 days and then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	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
1	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**500mg/m^2**	IV	Give the first dose of 500mg/m^2 over **120 minutes.** If the 1st dose is tolerated, all subsequent doses may be given over 90 minutes (or 60 mins if tolerated)	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion.
15	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**500mg/m^2**	IV	If the 1st dose was tolerated, all subsequent doses may be given over **90 minutes** (or 60 mins if tolerated) If previous dose not tolerated give over **120 minutes**	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml or 500ml. To be given at a max rate of 10mg/min. Flush line with sodium chloride 0.9% IV post cetuximab infusion.

TTO	Drug	Dose	Route	Directions
1	Doxycycline	100mg	PO	OD at the onset of rash, **prescribe if required.**