Indication	Cetuximab in combination with chemotherapy for the first line treatment of recurrent or metastatic squamous cell cancer of the head and neck (oral cavity only) or where the only systemic therapy for this recurrent/metastatic oral cavity tumour has been with pembrolizumab monotherapy.
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 cisplatin & fluorouracil & 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. • Consider **audiology** test for hearing impaired patients and monitor all patients for ototoxicity through-out treatment. • C+G or EDTA can be used to measure renal function at clinicians' discretion. Must be >/= 40ml/min. If CrCl 40-60ml/min consider dose reduction of cisplatin. • **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 </=1.5 and/or PLT </=100 d/w consultant. • **Hepatic Impairment:** • Cisplatin – no dose adjustment required. • 5FU - caution is advised, dose reduction may be required. • Cetuximab - no data available. • **Renal Impairment:** • Cisplatin – If CrCl is <30ml/min, discontinue platinum agent. • 5FU – caution is advised, dose reduction may be required in severe renal impairment. • Cetuximab – no data available. • **Dose modification:** ○ Consider 25%-50% dose reduction of cisplatin and 5FU if borderline performance status. ○ Consider dose reduction if grade 3 or 4 non-haematological toxicity OR repeat appearance of grade 2 (except N&V and alopecia) OR tinnitus. ○ 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/

	• **Infusion related reactions:** • **Cetuximab** can cause severe infusion related reactions, pre-meds must be given 1 hour prior to the 1st administration and then 30-60mins prior to subsequent administrations, 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. ○ **Tumour Lysis Syndrome:** Cases of tumour lysis syndrome associated with fluorouracil treatment have been reported. Patients at increased risk of tumour lysis syndrome (e.g. with renal impairment, hyperuricemia, high tumour burden, rapid progression) should be closely monitored. Preventive measures (e.g. hydration, correction of high uric acid levels) should be considered. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ Caution in patients receiving phenytoin, levels may be affected. ○ **Cisplatin:** Caution when used concurrently with other nephrotoxic or ototoxic drugs. ○ **5FU:** Caution with folinic acid or folic acid – potential for increased 5FU toxicity. If 5FU is 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-026 V3

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

Cycle 1 only: 21-day cycle

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	Dexamethasone	8mg	PO		Administer pre-medication 60 minutes prior to cetuximab infusion.
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**400mg/m^2 Loading dose**	IV	2hrs	To be given diluted or undiluted 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. **Start at the same time as 1000ml sodium chloride 0.9% below.**
	Sodium Chloride 0.9%	1000ml	IV	Over 2hrs	**To be started at the same time as cetuximab and run concurrently**
	Do not administer chemotherapy until at least 1 hour after the end of the cetuximab infusion				
	Sodium Chloride 0.9%	1000ml	IV	2 hrs	+ 20mmol KCL + 10mmol Mg2++
	Aprepitant	125mg	PO		Take ONE capsule 1 hour prior to chemo on Day 1.
	Mannitol 10%	200ml	IV	15 min	
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	CISPLATIN	**100mg/m^2**	IV	2hrs	In 1000ml Sodium Chloride 0.9%
	Furosemide	40mg	IV/PO		If urine output <100ml/hr or weight gain >2kg
	Sodium Chloride 0.9%	1000ml	IV	2hrs	+ 20mmol KCL + 10mmol Mg^2++
	*(Furosemide)	40mg	IV/PO	*** ONLY IF REQ'D**	If patient remains in a 2L positive balance
Days 1-4	**5-FLUOROURACIL**	**1000mg/m^2/day**	SC	96 hour pump	By continuous infusion pump
Day 8	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m^2**	IV	1 hour	To be given diluted or undiluted 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.

Cycle 1 Continued:

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 15	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m^2**	IV	1 hour	To be given diluted or undiluted 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 Cycle 1-6

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone tablets/liquid	6mg	PO	OM for 3 days starting on the day after cisplatin
	Metoclopramide tablets/liquid	10mg	PO	10mg TDS for 3 days and then 10mg TDS PRN. Do not take for more than 5 days continuously
	Aprepitant	80mg	PO	80mg OM on day 2 and day 3 only.
	Ondansetron tablets/liquid	8mg	PO	BD for 5 days (start evening of day 1)
	Filgrastim	300 micrograms or consider dose of 480mcg if patient > 80kg	SC	OD for 5 days starting on Day 2
	Doxycycline	100mg	PO	OD at the onset of rash, **prescribe if required.**

Cycles 2-6 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 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 diluted or undiluted 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. **Start at the same time as 1000ml sodium chloride 0.9% below**
	Sodium Chloride 0.9%	1000ml	IV	Over 2hrs	**To be started at the same time as cetuximab and run concurrently**
	Do not administer chemotherapy until at least 1 hour after the end of the cetuximab infusion				
	Sodium Chloride 0.9%	1000ml	IV	2 hrs	+ 20mmol KCL + 10mmol Mg2++
	Aprepitant	125mg	PO		Take ONE capsule 1 hour prior to chemo on Day 1.
	Mannitol 10%	200ml	IV	15 min	
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	CISPLATIN	**100mg/m²**	IV	2hrs	In 1000ml Sodium Chloride 0.9%
	Furosemide	40mg	IV/PO		If urine output <100ml/hr or weight gain >2kg
	Sodium Chloride 0.9%	1000ml	IV	2hrs	+ 20mmol KCL + 10mmol Mg^2++
	*(Furosemide)	40mg	IV/PO	*** ONLY IF REQ'D**	If patient remains in a 2L positive balance
Days 1-4	**5-FLUOROURACIL**	**1000mg/m²/day**	SC	96 hour pump	By continuous infusion pump
Day 8	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1 hour	To be given diluted or undiluted 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.

Cycle 2-6 continued

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 15	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**250mg/m²**	IV	1 hour	To be given diluted or undiluted 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.

Cycle 7 onwards Repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
1	Dexamethasone	8mg	PO		Administer pre-medication 30-60 minutes prior to cetuximab infusion
	Chlorphenamine	10mg	IV	bolus	
	CETUXIMAB	**500mg/m²**	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 diluted or undiluted 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/m²**	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 120minutes	To be given diluted or undiluted 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	
	Doxycycline	100mg	PO	OD at the onset of rash, **prescribe if required**	