Indication	Induction chemotherapy before concurrent chemo-radiation for loco-regionally advanced nasopharyngeal carcinoma. Recurrent or metastatic nasopharyngeal carcinoma – first line treatment.
Treatment Intent	Neo-adjuvant Palliative
Frequency and number of cycles	Neo-adjuvant: Repeat every 21 days for 3 cycles. Palliative: Repeat every 21 days for maximum of 6 cycles.
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. • Consider **audiology** test for hearing impaired patients and monitor all patients for ototoxicity through-out treatment. • Monitor FBC day 1 and day 8 of each cycle. C+G or EDTA can be used to measure renal function at clinicians' discretion. If CrCl <60ml/min d/w consultant (see below). • LFTs and U&Es day 1 of each cycle. • **Haematological toxicity:** o **Day 1**: If neuts >/=1.5 and PLT >/=100 proceed with treatment. If neuts 1.0 - <1.5 and / or PLT 75-99 d/w consultant. If neuts <1.0 and / or PLT <75 omit. o **Day 8**: If neuts >/=1.0 and PLT >/=100 proceed with treatment. If neuts >/=1.0 and PLT 75-99 d/w consultant. If neuts <1.0 and / or PLT <75 omit. • **Hepatic impairment:** o **Cisplatin:** no dose reduction required. o **Gemcitabine:** There is limited information about use of gemcitabine in hepatic impairment, therefore use with caution. If total bilirubin < 27µmol/L: no dose adjustment is needed. Total bilirubin >/= 27µmol/L: either start at 80% of the original dose and increase the dose if tolerated or start with full dose with active monitoring. • **Renal impairment:** o C+G should be used to measure CrCl prior to cycle 1. o If CrCl 45-59ml/min administer 75% dose of cisplatin or switch to carboplatin. o If CrCl <45ml/min consider carboplatin. o **Gemcitabine:** CrCl >/= 30ml/min no dose adjustment. • **Management of adverse reactions and dose adjustments:** 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 **Posterior Reversible Encephalopathy Syndrome (PRES)** has been rarely reported with gemcitabine. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of gemcitabine. o **Haemolytic uraemic syndrome.** Gemcitabine should be discontinued at the first signs of any evidence of microangiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH. o **Capillary leak syndrome.** Gemcitabine should be discontinued and supportive measures implemented if capillary leak syndrome develops during therapy. Capillary leak syndrome can occur in later cycles and has been associated in the literature with adult respiratory distress syndrome.

	• **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** o **Cisplatin:** Caution when used concurrently with other nephrotoxic or ototoxic drugs. o Caution in patients receiving phenytoin, levels may be affected. o **Gemcitabine:** No specific interaction studies have been performed. • **Driving**: gemcitabine may cause drowsiness, patients should be advised to avoid driving or operating machinery until they establish if they are affected.
References	KMCC proforma URO-006 V4 Clatterbridge protocol MPHACISGEM V1.2

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

Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Sodium chloride 0.9%	1000ml	IV	2 hrs	+ 20mmol KCL + 10mmol Mg^{2+}
	Sodium chloride 0.9%	1000ml	IV	2 hrs	+ 20mmol KCL
	Aprepitant	125mg	PO		Take one 125mg capsule **one hour prior to chemo** on Day 1
	Mannitol 10%	200mls	IV	15 min	
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium Chloride 0.9% 50ml
	Dexamethasone	8mg	PO		
	GEMCITABINE	**1000mg/m^2**	IV	30 min	Diluted in 0.9% sodium chloride to a final concentration of 0.1mg/ml – 10mg/ml. Consider extending infusion duration if final volume >500ml.
	CISPLATIN	**80mg/m^2**	IV	2 hours	In 1000ml Sodium chloride 0.9%
	Furosemide	40mg	PO/IV		Only if urine output <100ml/hour or weight gain >2kg
	Sodium Chloride 0.9%	1000ml	IV	2hrs	+ 20mmol KCL + 10mmol Mg^{2+}
	*(Furosemide)	40mg	IV/PO	***ONLY IF REQUIRED** If patient remains in a 2L positive balance	
8	Metoclopramide	10mg	IV		
	GEMCITABINE	**1000mg/m^2**	IV	30 min	Diluted in 0.9% sodium chloride to a final concentration of 0.1mg/ml – 10mg/ml. Consider extending infusion duration if final volume >500ml.
TTO	Drug	Dose	Route	Directions	
Day 1	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg TDS for 3 days and then 10mg up to TDS PRN. Do not take for more than 5 consecutive days	
	Aprepitant	80mg	PO	Take one 80mg capsule each morning on day 2 and day 3 only	