Indication	For the treatment of locally advanced inoperable cholangiocarcinoma.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days Maximum 8 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. • EDTA/DTPA should be used to measure GFR prior to cycle 1. C+G may be used to estimate CrCl if there is a delay in obtaining EDTA result, CrCl must be >/=30ml/min. Repeat EDTA if Creatinine clearance drops by 25%. • Monitor U+Es, FBC and LFTs prior to each cycle and FBC only on day 8. • If WBC >3 and neuts 1.0-1.5 and PLT >100 proceed with chemo OR If neuts >1.5 and PLT >100 proceed with chemo. • If blood parameters not met defer day 1 chemo for 1 week, or omit day 8. Consider dose reduction. • **Hepatic impairment:** o Carboplatin: No dose adjustment required. o Gemcitabine: There is limited information about use of gemcitabine in hepatic o 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 Carboplatin: stop if CrCl<30ml/min. o Gemcitabine: CrCl >/= 30ml/min no dose adjustment. • **Infusion-related reactions:** o Patients developing hypersensitivity reactions to 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. • **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 o 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.

	○ **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>:** ○ **Carboplatin:** Caution with other nephrotoxic drugs. ○ **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	SPC accessed online 11.07.2023 KMCC proforma UGI-055 V2

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

<u>Repeat every 21 days</u>

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 minutes	Sodium chloride 0.9% 50ml
	Dexamethasone	8mg	PO		
	CARBOPLATIN	**AUC 5** **Maximum dose 700mg** **Dose = AUC X (GFR +25)**	IV	30 minutes	In Glucose 5% 500ml
	GEMCITABINE	**1000mg/m^2**	IV	30 minutes	Diluted in 0.9% sodium chloride to a final concentration of 0.1mg/ml – 10mg/ml. Consider extending infusion duration if final volume >500ml
8	Metoclopramide	10mg	PO		
	GEMCITABINE	**1000mg/m^2**	IV	30 minutes	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 after Day 1	
	Metoclopramide	10mg	PO	10mg three times a day for 3 days after day 1 and Day 8, then 10mg up to 3 times a day as required (max. 30mg per day including 10mg pre-chemo dose on day 8). Do not take for more than 5 days continuously.	