Indication	Untreated metastatic (NOT locally advanced) pancreatic adenocarcinoma cancer only if other combination chemotherapies are unsuitable for the patient and they would otherwise have gemcitabine monotherapy (i.e. patient is not considered to be a suitable for oxaliplatin and irinotecan-based combination chemotherapy). The following criteria apply: • No previous systemic chemotherapy for pancreatic cancer unless given as a radiosensitiser in the neo-adjuvant or adjuvant setting and completed at least 6 months previously. • Patient has a performance status of 0 or 1 • No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).
Treatment Intent	Palliative treatment
Frequency and number of cycles	Every 28 days Continue until progressive disease or unacceptable toxicity.
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. • Monitor U&Es and LFTs at each cycle. • Monitor FBC at baseline, then day 1, 8 and 15 of each cycle. • **Day 1**, if neutrophils <1.5 and / or PLT <100 delay all treatment until recovery. • Omit **day 8 or day 15** doses if neuts <1.0 and/or platelets < 75. • **Hepatic Impairment:** o **Paclitaxel albumin bound:** For patients with mild **hepatic impairment** (total bilirubin > 1 to </= 1.5 x ULN and AST </= 10 x ULN), no dose adjustments are required. Insufficient data in moderate to severe hepatic impairment, d/w consultant. o **Gemcitabine:** If total bilirubin <27µmol/L: no dose adjustment is needed. o 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 **Paclitaxel albumin bound:** No dose adjustments of are required in mild to moderate renal impairment (CrCl ≥30 to <90 ml/min). Insufficient data in severe renal impairment (CrCl <30ml/min). o **Gemcitabine:** If CrCl >/= 30ml/min no dose adjustment required. Use with caution in renal impairment – d/w consultant. • **Management of adverse reactions and Dose Modification:** • When a **dose reduction** is required the first reduction should be to paclitaxel albumin bound 100mg/m^2 & gemcitabine 800mg/m^2, and the second reduction to paclitaxel albumin bound 75mg/m^2 & gemcitabine 600mg/m^2. If this is not tolerated treatment should be discontinued. • **Grade 3 or 4 febrile neutropenia,** withhold treatment until afebrile and neuts >/=1.5 and resume at next lower dose level of both drugs.

	• **Grade 3 or 4 peripheral neuropathy,** withhold dose until </=grade 1 and then resume at next lower dose level of paclitaxel albumin bound (no dose reduction of gemcitabine). • **Grade 2 or 3 cutaneous toxicity,** reduce to next lower dose level of both drugs. If cutaneous toxicity persists, discontinue treatment. • **Grade 3 mucositis or diarrhoea,** withhold doses until </= grade 1, then resume at next lower dose level of both drugs. • Dose reduction should be considered if any other 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. • **Cautions**: o Patients should be monitored for signs and symptoms of pneumonitis. After ruling out infectious etiology, permanently discontinue treatment with paclitaxel albumin bound and gemcitabine when a diagnosis of pneumonitis is made and initiate appropriate treatment. 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. • **Driving and operating machinery:** Patients should be advised not to drive and use machines if they feel tired or dizzy. • **Drug interactions (for comprehensive list refer to BNF/SPC)**: Use paclitaxel albumin bound with caution in patients receiving concomitant inhibitors (e.g. ketoconazole, erythromycin, fluoxetine, cimetidine) or inducers (e.g. rifampicin, carbamazepine, phenytoin) of CYP2C8 or CYP3A4.
Reference(s)	KMCC protocol UGI-047 V6 CDF list accessed online 30.05.2024

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

Repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
1	Metoclopramide	20mg	IV	Bolus	
	Dexamethasone	8mg	po		
	PACLITAXEL ALBUMIN BOUND (Abraxane ®/ Pazenir®)	**125mg/m²**	IV	30 mins	To be administered undiluted in a sterile PVC or non-PVC type intravenous bag. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer infusions.
	GEMCITABINE	**1000mg/m²**	IV	30 mins	In sodium chloride 0.9% to a final concentration of 0.1mg/ml – 10mg/ml If final volume >500ml consider extending infusion duration
8	Metoclopramide	20mg	IV	Bolus	
	Dexamethasone	8mg	po		
	PACLITAXEL ALBUMIN BOUND (Abraxane ®/ Pazenir®)	**125mg/m²**	IV	30 mins	To be administered undiluted in a sterile PVC or non-PVC type intravenous bag. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer infusions.
	GEMCITABINE	**1000mg/m²**	IV	30 mins	In sodium chloride 0.9% to a final concentration of 0.1mg/ml – 10mg/ml If final volume >500ml consider extending infusion duration
15	Metoclopramide	20mg	IV	Bolus	
	Dexamethasone	8mg	po		
	PACLITAXEL ALBUMIN BOUND (Abraxane ®/ Pazenir®)	**125mg/m²**	IV	30 mins	To be administered undiluted in a sterile PVC or non-PVC type intravenous bag. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer infusions.
	GEMCITABINE	**1000mg/m²**	IV	30 mins	In sodium chloride 0.9% to a final concentration of 0.1mg/ml – 10mg/ml If final volume >500ml consider extending infusion duration

TTO	Drug	Dose	Route	Directions
Day 1	Metoclopramide	10mg	PO	10mg three times a day for 3 days after Day 1, Day 8 and Day 15, then 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously.
	Dexamethasone	4mg	PO	OM for 2 /7 after day 1, 8 & 15