nab-PACLitaxel and Gemcitabine Therapy– 28 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
nab-PACLitaxel in combination with gemcitabine is indicated for the first-line treatment of adult patients with metastatic adenocarcinoma of the pancreas.	C25	00256a	nab-PACLitaxel : ODMS Gemcitabine: N/A

*For post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

nab-PACLitaxel is administered on days 1, 8 and 15 of each 28-day cycle until disease progression or unacceptable toxicity. Gemcitabine is administered immediately after completion of nab-PACLitaxel administration on Days 1, 8 and 15 of each 28-day cycle.

Facilities to treat anaphylaxis MUST be present when the systemic anti-cancer therapy (SACT) is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1, 8 and 15	nab-PACLitaxel	125mg/m^2	IV infusion	over 30 minutes	Repeat every 28 days
2	1, 8 and 15	Gemcitabine	1000 mg/m^2	IV infusion	250 mL 0.9% NaCl over 30 minutes	Repeat every 28 days

The use of medical devices containing silicone oil as a lubricant (i.e. syringes and IV bags) to reconstitute and administer nab-PACLitaxel may result in the formation of proteinaceous strands.

Administer nab-PACLItaxel using an infusion set incorporating a 15 µm filter to avoid administration of these strands. Use of a 15 µm filter removes strands and does not change the physical or chemical properties of the reconstituted product. If strands are present and a filter is not available, the product must be discarded.

nab-PAClitaxel is an albumin-bound nanoparticle formulation of PACLitaxel, which may have substantially different pharmacological properties compared to other formulations of PACLitaxel. It should not be substituted for or with other PACLitaxel formulations.

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indications as above
- Histologic/Cytologic proof of pancreatic adenocarcinoma
- ECOG status 0-2
- Adequate haematological, hepatic and renal function (ANC ≥ 1.5 x10^9/Land bilirubin levels ≤ ULN)

CAUTIONS:

Use with caution in patients with

- Biliary stents: increased risk of biliary sepsis
- CNS metastases-safety not established
- Grade ≥ 2 sensory or motor neuropathy

EXCLUSIONS:

- Hypersensitivity to nab-PACLitaxel, albumin, gemcitabine or to any of the excipients
- Severe hepatic impairment
- Baseline Neutrophil Counts < 1.5 x 10^9/L
- Pregnancy
- Breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Glucose
- Assessment of cardiac function, e.g. ECG, ECHO/MUGA scan if significant cardiac history

Regular tests:

- FBC and renal profile prior to treatment
- Liver profile prior to each cycle.
- Cardiac function if clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Table 1: Dose level reductions for patients with pancreatic adenocarcinoma

Dose Level	nab-PACLitaxel Dose (mg/m^2)	Gemcitabine Dose (mg/m^2)
Full Dose	125	1000
1st Dose Level Reduction	100 (20%)	800 (20%)
2nd Dose Level Reduction	75 (40%)	600 (40%)
If additional dose reduction required	Discontinue treatment	Discontinue treatment

Haematological:

Table 2: Dose modifications for neutropenia and/or thrombocytopenia at the start of a cycle or within a cycle for patients with pancreatic adenocarcinoma.

Cycle	ANC (x10^9/L)		Platelets (x10^9/L)	nab-PACLitaxel	Gemcitabine
Day 1	< 1.5	OR	<100	Delay doses until recovery	
Day 8	≥ 0.5 but < 1	OR	≥ 50 but < 75	Reduce doses by 1 dose level	
Day 8	< 0.5	OR	< 50	Withhold doses	
Day 15: If Day 8 doses were given without modifications:					
Day 15	≥ 0.5 but < 1	OR	≥ 50 but < 75	Treat with Day 8 dose level and add G-CSF **OR** Reduce doses by 1 dose level from Day 8 doses	
	< 0.5	OR	< 50	Withhold doses	
Day 15: If Day 8 doses were reduced:					
Day 15	≥ 1	AND	≥ 75	Return to the Day 1 dose levels and add G-CSF **OR** Treat with same doses as Day 8	
	≥ 0.5 but < 1	OR	≥ 50 but <75	Treat with Day 8 dose level and add G-CSF **OR** Reduce doses by 1 dose level from Day 8 doses	
	< 0.5	OR	<50	Withhold doses	
Day 15: If Day 8 doses were withheld:					
Day 15	≥ 1	AND	≥ 75	Return to Day 1 dose levels and add G-SCF **OR** Reduce doses by 1 dose level from Day 1 doses	
	≥ 0.5 but < 1	OR	≥ 50 but < 75	Reduce 1 dose level and add G-CSF **OR** Reduce doses by 2 dose levels from Day 1 doses	
	< 0.5	OR	<50	Withhold doses	

Renal and Hepatic Impairment:

Table 3: Dose modification of nab-PACLitaxel and gemcitabine in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
nab-PACLitaxel[a]	**CrCl (mL/min)**	**Dose**	Mild: no dose adjustment is needed Moderate and severe: contraindicated. Bilirubin > 5 x ULN or AST > 10 x ULN: contraindicated	
	≥ 30	No dose adjustment is needed		
	<30	No need for dose adjustment is expected		
	Haemodialysis	No need for dose adjustment is expected		
Gemcitabine[b]	≥30	No dose adjustment is needed	**Bilirubin (micromol/L)**	**Dose**
			< 27	No dose adjustment is needed
	<30	No need for dose adjustment is expected	≥ 27	Either start at 80% of the original dose and increase the dose if tolerated or start with full dose with active monitoring
	Haemodialysis	No need for dose adjustment is expected. Start haemodialysis 6-12 hours after administration		

[a]nab-PACLitaxel (renal and hepatic - Giraud et al 2023);
[b]Gemcitabine (renal and hepatic -Giraud et al 2023)

Management of adverse events:

Table 4: Dose Modifications for Adverse Events

Adverse reactions	Recommended dose modification	
	nab-PACLitaxel Dose	Gemcitabine Dose
Grade ≥3 Febrile neutropenia	Withhold doses until fever resolves and ANC ≥ 1.5; resume at next lower dose level[a]	
Grade ≥3 Peripheral neuropathy	Withhold dose until improves to ≤ Grade 1; Resume at next lower dose level[a].	Treat with same dose.
Grade 2 or 3 Cutaneous toxicity	Reduce to next lower dose level[a]; discontinue treatment if adverse reaction persists.	
Grade 3 Mucositis or diarrhoea	Withhold doses until improves to ≤ Grade 1; resume at next lower dose level[a].	
Pneumonitis	Discontinue treatment	
Haemolytic Uremic Syndrome (HUS)	Discontinue treatment	

[a] See Table 1 for dose level reductions

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on NCCP website

nab-PACLitaxel: Low **(Refer to local policy)**

Gemcitabine: Low **(Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology) - Available on NCCP website
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - Available on NCCP website

PREMEDICATIONS: None usually required.

OTHER SUPPORTIVE CARE:

- G-CSF support may be required to mitigate the risk of haematological toxicities. **(Refer to local policy)**
- Myalgias and arthralgias may occur with nab-PACLitaxel. Analgesic cover should be considered.

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS:

- **Pulmonary Toxicity:** Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
- **Cardiovascular:** Due to the risk of cardiac and/or vascular disorders with gemcitabine, particular caution must be exercised with patients presenting a history of cardiovascular events.
- **Renal Toxicity:** Irreversible renal failure associated with haemolytic uraemic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal impairment.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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3. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2017; 35(28):3240-61.
4. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
6. nab-PACLitaxel (Abraxane®) Summary of Product Characteristics. Last updated: 30/01/2019. Accessed March 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/abraxane-epar-product-information_en.pdf
7. nab-PACLitaxel (Pazenir®) Summary of Product Characteristics.Last updated 30/08/2024. Accessed March 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/pazenir-epar-product-information_en.pdf
8. Gemcitabine 40mg/mL Summary of Product Characteristics. Last updated 07/02/2025. Accessed March 2025. Available at: https://www.hpra.ie/find-a-medicine/for-human-use/authorised-medicines/details/27418

Version	Date	Amendment	Approved By
1	15/02/2016		Dr Derek Power, Prof Maccon Keane
2	10/02/2018	Updated with new NCCP regimen template. Updated emetogenic status and dosing in renal and hepatic impairment.	Prof Maccon Keane
3	26/02/2020	Reviewed.	Prof Maccon Keane
4	24/02/2022	Brand name Abraxane® removed.	Prof Maccon Keane

		ATC codes removed. Updated reference section.	
5	14/03/2024	Updated renal and hepatic recommendations in line with Giraud et al, 2023. Updated adverse effects for gemcitabine as per NCCP standardisation.	Prof Maccon Keane
6	16/04/2025	Regimen reviewed. Updated eligibility section. Updated exclusions and cautions section. Supportive care, adverse effects and regimen specific complications updated in line with NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.