Gemcitabine and Paclitaxel Albumin (Abraxane ®)

Indication
First-line palliative therapy for locally advanced, metastatic or relapsed pancreatic cancer.

Funding must be agreed prior to commencing treatment.

ICD-10 codes
Codes pre-fixed with C25

Regimen details

Day	Drug	Dose	Route
1, 8, 15	Paclitaxel albumin	125 mg/m²	IV infusion
1, 8, 15	Gemcitabine	1000 mg/m²	IV infusion

Cycle frequency
28 days

Number of cycles
Usual maximum of 6 cycles or until disease progression.

Administration
Paclitaxel albumin should be administered first. It is administered as a 5mg/mL infusion over 30 minutes.
It should be administered using an infusion set incorporating a 15µm filter.

Gemcitabine is administered in 250-500mL sodium chloride 0.9% over 30 minutes.

Pre-medication
Nil routinely required.

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Mouthwashes as per local policy
Antiemetics as per local policy
H_2 antagonist or PPI, if required, as per local policy

Extravasation
Paclitaxel albumin – vesicant (Group 5)
Gemcitabine – neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Baseline echocardiogram and ECG if significant cardiac history or previous anthracycline exposure. Monitor as clinically indicated.

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours*
U+E (including creatinine)	7 days
LFTs	7 days

* FBC is also required within 48 hours of days 8 and 15.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.5 x 10^9/L
Platelets	≥ 100 x 10^9/L
AST/ALT	< 2 x ULN
Bilirubin	≤ 1.5 x ULN
Creatinine Clearance (CrCl)	≥ 30 mL/min

Dose modifications

Dose level	**Paclitaxel albumin dose**	**Gemcitabine dose**
Full dose	125mg/m^2	1000mg/m^2
1st dose reduction	100mg/m^2	800mg/m^2
2nd dose reduction	75mg/m^2	600mg/m^2
Additional dose reductions	Discontinue	Discontinue

- **Haematological toxicity**

Day 1

If neutrophils < 1.5 x 10^9/L or platelets < 100 x 10^9/L delay treatment until recovery.

Day 8 and 15

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Gemcitabine and Paclitaxel albumin dose**
≥ 1.0	and	> 100	Full doses
0.5 – 1.0	or	50-100	Reduce by one dose level
< 0.5	or	< 50	Withhold doses

If febrile neutropenia, withhold doses until recovery and resume with one dose level reduction.

- **Renal impairment**

If CrCl < 30mL/min consider dose reduction of both agents (consultant decision).

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Paclitaxel albumin dose**
< 1.5	and	< 2	100%
1.5 – 5	or	2 - 10	Reduce by one dose level
> 5	or	> 10	Discontinue

Lack of information available on the use of gemcitabine in patients with hepatic impairment, therefore, used with caution. If bilirubin > 1.5 x ULN, consider reducing dose by one dose level (consultant decision).

- **Other toxicities**

Toxicity	Definition	Paclitaxel albumin dose	Gemcitabine dose
Neuropathy	Grade 1-2	No dose reduction usually required.	Dose reduction not usually required.
	Grade 3	Withhold until recovery to ≤ grade 1, resume with one dose level reduction. If 2nd occurrence: Withhold until recovery to ≤ grade 1, resume with another dose level reduction.	
	Grade 4	Discontinue or continue with dose reduction as above – consultant decision.	
Any other toxicity (except alopecia)	Grade 1	No dose reduction usually required.	
	Grade 2-3	Withhold until recovery to ≤ grade 1, resume with one dose level reduction.	
	Grade 4	Discontinue or discuss with consultant.	

Paclitaxel albumin
Post-marketing experience has identified rare reports of reduced visual acuity due to cystoid macular oedema. Treatment should be discontinued.

Rare reports of congestive heart failure and left ventricular dysfunction have been observed in patients with underlying cardiac history or previous exposure to cardiotoxic products such as anthracyclines. Patients should be monitored for the occurrence of cardiac events.

If hypersensitivity reaction occurs, treatment should be discontinued immediately and symptomatic treatment should be initiated. The patient should not be re-challenged.

Adverse effects - for full details consult product literature/ reference texts

- **Rare or serious side effects**

Myelosuppression
Infertility
Haemolytic uraemic anaemia*
Interstitial pneumonitis, ARDS
Cardiotoxicity
Hepatotoxicity
Hypersensitivity

Gemcitabine should be discontinued at the first sign of microangiopathic haemolytic anaemia (such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevated bilbirubin, creatinine, blood urea nitrogen or LDH. Renal failure may not be reversible with discontinuation of therapy, dialysis may be required.

- **Frequently occurring side effects**

Nausea and vomiting
Myelosuppression
Mucositis, stomatitis
Diarrhoea, constipation
Peripheral neuropathy
Oedema
Haematuria
Myalgia, arthralgia
Influenza like symptoms
Rash
Peripheral neuropathy

- **Other side effects**

Raised transaminases
Headache
Alopecia
Fatigue
Insomnia
Depression
Eye problems
Skin reactions

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Gemcitabine is a radiosensitiser.

Paclitaxel albumin
Clozapine: increased risk of agranulocytosis.

The metabolism of paclitaxel is catalysed, in part, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. Caution should be exercised when administering paclitaxel concomitantly with medicines known to:
inhibit (e.g. ketoconazole and other imidazole antifungals, erythromycin, fluoxetine, gemfibrozil, cimetidine, ritonavir, saquinavir, indinavir, and nelfinavir)
or
induce (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) either CYP2C8 or CYP3A4.

Additional comments

When reconstituted, paclitaxel albumin (Abraxane ®) contains approximately 425 mg sodium per dose. This should be considered if a patient is on a controlled sodium diet.

References

- Summary of Product Characteristics Gemcitabine (Lilly) accessed 24 May 2017 via www.medicines.org.uk
- Summary of Product Characteristics Abraxane (Celgene) accessed 24 May 2017 via www.medicines.org.uk
- Von Hoff DD et al. Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine N Engl J Med 2013;369:1691-703

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