Paclitaxel – 3 weekly (gynae)

Indication
Palliative therapy for relapsed ovarian, fallopian tube or primary peritoneal cancer.

(NICE TA389)

ICD-10 codes
Codes pre-fixed with C48, 56 and 57.

Regimen details

Day	Drug	Dose	Route
1	Paclitaxel	175mg/m²	IV infusion

Cycle frequency
21 days

Number of cycles
6 cycles

Administration
Paclitaxel is administered in a 500mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter over 3 hours.
Blood pressure and pulse should be monitored regularly (e.g. every 30 minutes) during paclitaxel infusion.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of paclitaxel. Facilities for the treatment of hypotension and bronchospasm **must** be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of paclitaxel and appropriate therapy should be initiated.

Pre-medication
30 minutes prior to each infusion:

Chlorphenamine 10mg IV slow bolus
Dexamethasone 16-20mg IV slow bolus

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Proton Pump Inhibitor, if required, as per local policy
Mouthwashes as per local policy

Extravasation

Paclitaxel – vesicant (Group5)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days
CA125	28 days

Investigations – pre subsequent cycles

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

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	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Bilirubin	< 1 x ULN
AST/ALT	< 5 x ULN
Creatinine Clearance (CrCl)	> 30 mL/min

Dose modifications

Paclitaxel

Dose level	Paclitaxel dose
Full dose	175mg/m^2
First dose reduction	135mg/m^2
Second dose reduction	90mg/m^2
Third dose reduction	Discontinue

Haematological toxicity

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Paclitaxel dose**
≥ 1.0	and	≥ 100	100%
< 1.0	or	< 100	Delay 1 week (or until recovery) resume at full dose.
< 1.0	and	< 100	Delay until recovery then resume at next dose reduction level.

In the case of febrile neutropenia (neutrophils < 0.5 × 10^9/L and fever > 38.5°C requiring IV antibiotics) reduce to next dose reduction level for all future doses.

- **Renal impairment**

No dose modifications required.

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Paclitaxel dose**
≤1.25	and	<10	100%
1.25-2	and		135mg/m^2
2-5	and		90mg/m^2
> 5	or	≥10	Not recommended (consultant decision)

- **Other toxicities**

Toxicity	**Definition**	**Paclitaxel dose**
Fatigue	Grade 3	1st occurrence – 135mg/m^2, if persistent 90mg/m^2 or discontinue
Neuropathy	Grade 2	1st occurrence – 135mg/m^2 for all future cycles, if persistent 90mg/m^2 or discontinue
	Grade ≥ 3	Withhold until ≤ grade 1, restart at 90mg/m^2.
Arthralgia/Myalgia	Grade ≥ 2	Consider diclofenac +/- cocodamol or prednisolone 10mg BD for 5 days starting 24 hours post paclitaxel. If persists reduce dose to 135mg/m^2

For all other grade 3 toxicities (except alopecia and nausea and vomiting) withhold until grade ≤ 1 and continue at next dose reduction level. If further toxicity, consider additional dose reduction, discuss with consultant.

For any grade 4 toxicity (except alopecia and nausea and vomiting) withhold and discuss with consultant.

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

- **Rare or serious side effects**

Myelosuppression
Hypersensitivity reactions
Pulmonary fibrosis
Electrolyte disturbances
Arrhythmias
Cardiac failure

- **Frequently occurring side effects**

Nausea and vomiting
Mucositis, stomatitis
Myelosuppression
Diarrhoea, constipation
Peripheral neuropathy
Oedema
Phlebitis
Myalgia, arthralgia
Alopecia
Fatigue

- **Other side effects**

Taste changes
Headache
Abdominal pain

Elderly patients may have a higher incidence of severe neuropathy, severe myelosuppression, or cardiovascular events compared to younger patients.

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.

Clozapine: increased risk of agranulocytosis

Paclitaxel is a CYP 2C8 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

Additional comments

In patients with significant frailty or co-morbidity where chemotherapy is nevertheless deemed appropriate, consider strategies to minimise toxicity such as reducing the paclitaxel dose to 135mg/m^2.

References

- Summary of Product Characteristics Paclitaxel (Accord) accessed 12 August 2021 via www.medicines.org.uk
- National Institute for Clinical Excellence. Technology Appraisal Guidance 389. Accessed 12 August 2021 via www.nice.org.uk
- Cantu MG, Buda A, Parma G et al. Randomized controlled trial of single-agent paclitaxel versus cyclophosphamide, doxorubicin and cisplatin in patients with recurrent ovarian cancer who respond to first-line platinum-based regimens. *J Clin Oncol* 2002 20(5) 1232-1237.
- Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment – supplementary appendix. *Lancet Oncol* 2019; **20:** e201–08.

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