

Paclitaxel – 3 weekly (gynae)

Indication

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

(NICE TA55 and TA91)

ICD-10 codes

Codes pre-fixed with C48, 56 and 57.

Regimen details

Day	Drug	Dose	Route
1	Paclitaxel	175mg/m ²	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:

Ranitidine 50mg IV slow bolus

Chlorphenamine 10mg IV slow bolus

Dexamethasone 16-20mg IV slow bolus

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

H₂ antagonist or PPI, 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	14 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	$\geq 1.0 \times 10^9/L$
Platelets	$\geq 100 \times 10^9/L$
Bilirubin	$< 1 \times \text{ULN}$
AST/ALT	$< 5 \times \text{ULN}$
Creatinine Clearance (CrCl)	$> 30 \text{ mL/min}$

Dose modifications

- Haematological toxicity

Neutrophils ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	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 $135\text{mg}/\text{m}^2$.

In the case of febrile neutropenia (neutrophils $< 0.5 \times 10^9/L$ and fever $> 38.5^\circ\text{C}$ requiring IV antibiotics) reduce to $135\text{mg}/\text{m}^2$ for all future doses.

- Renal impairment

No dose modifications required.

- Hepatic impairment

Bilirubin ($\times \text{ULN}$)		AST/ALT ($\times \text{ULN}$)	Paclitaxel dose
$< \text{ULN}$	and	< 5	100%
1-1.5	and	< 5	$135\text{mg}/\text{m}^2$
1.5-2.5	and		$75\text{mg}/\text{m}^2$
2.5-4	and		$50\text{mg}/\text{m}^2$
> 4	or		≥ 5

- **Other toxicities**

Toxicity	Definition	Paclitaxel dose
Fatigue	Grade 3	1st occurrence – 135mg/m ² , if persistent 90mg/m ² or discontinue
Neuropathy	Grade 2	1 st 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 with 135mg/m² dose. 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
 Infertility
 Teratogenicity
 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 2C8/9 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/m².

References

- Summary of Product Characteristics Paclitaxel (Hospira) accessed via www.medicines.org.uk (31 July 2014)
- National Institute for Clinical Excellence. Technology Appraisal Guidance 55. Accessed 6 August 2014 via www.nice.org.uk
- National Institute for Clinical Excellence. Technology Appraisal Guidance 91. Accessed 6 August 2014 via www.nice.org.uk

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