PACLitaxel Monotherapy 80mg/m^2 Day 1, 8, 15 and 22 – 28 Day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of metastatic breast carcinoma (mBC) in patients who have either failed or are not candidates for standard, anthracycline-containing therapy[i]	C50	00226a	Hospital
Second-line chemotherapy for metastatic ovarian cancer after failure of standard, platinum-containing therapy[i]	C56	00226b	Hospital
Relapsed or refractory small cell lung cancer[i]	C34	00226d	Hospital
Second line chemotherapy for metastatic bladder cancer[i]	C67	00226e	Hospital

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 patients individual clinical circumstances.

PACLitaxel is administered on day 1,8,15 and 22 of a 28 day treatment cycle until disease progression or unacceptable toxicity develops.
PACLitaxel may be administered on day 1, 8 and 15 of a 28 day treatment cycle at the discretion of the prescribing consultant.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1,8,15,22	PACLitaxel	80mg/m^2	IV infusion	250ml 0.9% sodium chloride over 1hr	Every 28 days
PACLitaxel must be supplied in non-PVC containers and administered using non-PVC giving sets and through an in-line 0.22 µm filter with a microporous membrane.					
PACLitaxel should be diluted to a concentration of 0.3-1.2mg/ml.					

ELIGIBILITY:

- Indications as above
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to PACLitaxel or to any of the excipients.
- Breast feeding
- Baseline neutrophil count < 1.5x10^9 cells/L
- Severe hepatic impairment

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- FBC, renal and liver profile prior to each treatment
- Day 8: FBC

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

Haematological:

Table 1: Recommended dose modifications for PACLitaxel for haematological toxicity

ANC ($x10^9$/L)		Platelets	Dose	Dose after neutropenic sepsis
≥ 1.5	and	> 90	80mg/m^2	65mg/m^2
*1-1.49	or	70-90	65mg/m^2	50mg/m^2
< 1	or	< 70	Delay and reduce next dose to 65mg/m^2 or add G-CSF	Delay
Patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment.				

*** If ANC 1 to less than 1.5 and patient fit and well can consider full dose of 80 mg/m^2 at discretion of prescribing Consultant**

Renal and Hepatic Impairment:

Table 2: Recommended dose modification for PACLitaxel in renal and hepatic impairment

Renal Impairment	Hepatic Impairment			
No recommended dose modifications in renal impairment	**ALT**		**Total Bilirubin**	**Dose**
	< 10 x ULN	and	≤ 1.25 x ULN	80mg/m^2
	< 10 x ULN	and	1.26-2 x ULN	60mg/m^2
	< 10 x ULN	and	2.01-5 x ULN	40mg/m^2
	≥10 x ULN	and /or	>5 x ULN	Not recommended

Management of adverse events:

Table 3: Recommended dose modification of PACLitaxel for adverse events

Adverse reactions	Dose
Grade 2 motor or sensory neuropathy	Decrease dose by 10mg/m^2
All other grade 2 non-haematological toxicity	Hold treatment until toxicity resolves to ≤ grade 1. Decrease subsequent doses by 10mg/m$^{2.}$
≥ Grade 3 reaction	Discontinue
Patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low **(Refer to local policy).**

PREMEDICATIONS:

- All patients must be premedicated with corticosteroids, antihistamines, and H_2 antagonists prior to first dose of PACLitaxel treatment.
- The H2 antagonist, famotidine , can potentially be omitted from the pre-medication requirements for PACLitaxel but the risk of hypersensitivity with this approach is unknown.
- Caution is advised particularly for patients receiving PACLitaxel every 3 weeks. It is recommended that if famotidine is omitted that patients are monitored closely for any signs of hypersensitivity. Any hypersensitivity should be managed as per local policy.
- Where a patient experiences hypersensitivity, consider use of alternative H2 antagonists **(refer to local policy)**

Table 4 outlines suggested premedications prior to treatment with PACLitaxel.

Table 4: Suggested premedications prior to treatment with PACLitaxel

Day of treatment	Drug	Dose	Administration prior to PACLitaxel
Day 1	dexAMETHasone[a]	8mg IV	30 minutes
Day 1	Chlorphenamine	10mg IV	30 minutes
Day 1	Famotidine	20mg IV	30 minutes
Day 8[b] and thereafter	dexAMETHasone[a]	None	
Day 8 and thereafter	Chlorphenamine	10mg IV	30 minutes
Day 8 and thereafter	Famotidine[c]	20mg IV	30 minutes
[a]Dose of dexAMETHasone may be altered, in the event of hypersensitivity reaction, to 20 mg of dexAMETHasone orally 12 hr and 6 hr prior to re-challenge with PACLitaxel according to consultant guidance.			
[b]Dose of dexAMETHasone may be added from day 8 if increased risk or previous hypersensitivity reaction according to consultant guidance.			
[c]Dose of famotidine may be omitted in the absence of hypersensitivity reaction according to consultant guidance.			

OTHER SUPPORTIVE CARE:

- Myalgias and arthralgias may occur with PACLitaxel. Analgesic cover should be considered.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Hypersensitivity:** Severe hypersensitivity reactions characterised by dyspnoea and hypotension requiring treatment, angioedema and generalised urticaria have occurred in <1% of patients receiving PACLitaxel after adequate premedication. In the case of severe hypersensitivity reactions, PACLitaxel infusion should be discontinued immediately, symptomatic therapy should be initiated and the patient should not be re-challenged with the drug**.**
- **Extravasation:** PACLitaxel causes pain and tissue necrosis if extravasated. **(Refer to local policy).**
- **Neutropenia:** This is the dose limiting toxicity. Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Peripheral neuropathy:** Occurs frequently but the development of severe symptoms is rare.
- **Arthralgia/myalgia:** May be severe in some patients; however, there is no consistent correlation between cumulative dose and infusion duration of PACLitaxel and frequency or severity of the arthralgia/myalgia. Symptoms are usually transient, occurring within 2 or 3 days after PACLitaxel administration, and resolving within days.
- **Cardiac conduction abnormalities:** If patients develop significant conduction abnormalities during PACLitaxel administration, appropriate therapy should be administered and continuous cardiac monitoring should be performed during subsequent therapy with PACLitaxel. Hypotension, hypertension, and bradycardia have been observed during PACLitaxel administration; patients are usually asymptomatic and generally do not require treatment. Frequent vital sign monitoring, particularly during the first hour of PACLitaxel infusion, is recommended.
- **Hepatic Dysfunction:** Patients with hepatic impairment may be at increased risk of toxicity, particularly grade 3-4 myelosuppression.

DRUG INTERACTIONS:

- Risk of drug interactions causing increased concentrations of PACLitaxel with CYP3A inhibitors. Patients should also be counselled with regard to consumption of grapefruit juice.
- Risk of drug interactions causing decreased concentrations of PACLitaxel with CYP3A inducers.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

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Version	Date	Amendment	Approved By
1	29/04/2015		Dr Maccon Keane
2	14/06/2017	Additions of indications for Small Cell Lung Cancer and for metastatic bladder Cancer. Clarified dosing in haematological toxicity	Prof Maccon Keane
3	16/03/2018	Updated diluents recommendations and dosing in haematological toxicity	Prof Maccon Keane
4	24/09/2019	Amended regimen name Clarified treatment cycle details Standardisation of administration times for pre-medications for PACLitaxel	Prof Maccon Keane
5	12/02/2020	Standardised table for suggested premedications prior to treatment	Prof Maccon Keane
6	30/11/2020	Removal of gastric cancer indication due to new regimen 621 - Paclitaxel 80mg/m^2 Monotherapy Day 1, 8, 15 – 28 Day. Updated premedication recommendations.	Prof Maccon Keane
7	22/09/2023	Updated premedications recommendations	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This regimen is outside its licensed indication in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.