

PACLitaxel Monotherapy 80mg/m²

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
Second line chemotherapy for advanced or recurrent gastric cancer ⁱ	C16	00226c	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 the chemotherapy 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.
- Life expectancy > 3 months.

EXCLUSIONS:

- Hypersensitivity to PACLitaxel or to any of the excipients.
- Breast feeding
- Baseline neutrophil count < 1.5x10⁹ cells/L
- Severe hepatic impairment

NCCP Protocol: PACLitaxel 80mg/m ²	Published: 29/04/2015 Review: 16/03/2020	Version number: 4
Tumour Group: Breast/Gastrointestinal/Genitourinary/Gynaecology/Lung NCCP Protocol Code: 00226	ISMO Contributor: Prof Maccon Keane	Page 1 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoprotocols</i></p>		

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 ($\times 10^9/L$)		Platelets	Dose	Dose after neutropenic sepsis
≥ 1.5	and	> 90	$80\text{mg}/\text{m}^2$	$65\text{mg}/\text{m}^2$
*1-1.49	or	70-90	$65\text{mg}/\text{m}^2$	$50\text{mg}/\text{m}^2$
< 1	or	< 70	Delay and reduce next dose to $65\text{mg}/\text{m}^2$ 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 $80\text{mg}/\text{m}^2$ 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			Dose
	ALT		Total Bilirubin	
No recommended dose modifications in renal impairment	$< 10 \times \text{ULN}$	and	$\leq 1.25 \times \text{ULN}$	$80\text{mg}/\text{m}^2$
	$< 10 \times \text{ULN}$	and	1.26-2 x ULN	$60\text{mg}/\text{m}^2$
	$< 10 \times \text{ULN}$	and	2.01-5 x ULN	$40\text{mg}/\text{m}^2$
	$\geq 10 \times \text{ULN}$	and /or	$> 5 \times \text{ULN}$	Not recommended

NCCP Protocol: PACLitaxel $80\text{mg}/\text{m}^2$	Published: 29/04/2015 Review: 16/03/2020	Version number: 4
Tumour Group: Breast/Gastrointestinal/Genitourinary/Gynaecology/Lung NCCP Protocol Code: 00226	ISMO Contributor: Prof Maccon Keane	Page 2 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoprotocols</i></p>		

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 H₂ antagonists prior to PACLitaxel treatment. Table 4 outlines suggested premedications prior to treatment with PACLitaxel.

Table 4: Suggested premedications prior to treatment with PACLitaxel

Drug	Dose	Administration prior to PACLitaxel
Dexamethasone	10mg IV ^a	30 minutes
Diphenhydramine ^b	50mg IV	30 minutes
Cimetidine or ranitidine	300mg IV 50mg IV	30 minutes
^a Dose of dexamethasone may be reduced or omitted in the absence of hypersensitivity reaction according to consultant guidance.		
^b or an equivalent antihistamine e.g. chlorphenamine		

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

NCCP Protocol: PACLitaxel 80mg/m ²	Published: 29/04/2015 Review: 16/03/2020	Version number: 4
Tumour Group: Breast/Gastrointestinal/Genitourinary/Gynaecology/Lung NCCP Protocol Code: 00226	ISMO Contributor: Prof Maccon Keane	Page 3 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoprotocols

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.

ATC CODE:

PACLitaxel L01CD01

REFERENCES:

1. Seidman AD, Hudis CA, Albanell J, Tong W, Tepler I, Currie V, et al. Dose-dense therapy with weekly 1-hour paclitaxel infusions in the treatment of metastatic breast cancer. *J Clin Oncol.* 1998;16:3353-61.
2. Perez EA, Vogel CL, Irwin DH, et al. Multicenter phase II trial of weekly paclitaxel in women with metastatic breast cancer. *J Clin Oncol* 2001;19(22):4216-23.
3. Markman M, Blessing J et al. Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2006;101(3):436-40
4. Sparano JA, Wang M, et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. *N Engl J Med.* 2008; 358(16):1663-71
5. Hironaka S Zenda S et al. Weekly paclitaxel as second-line chemotherapy for advanced or recurrent gastric cancer *Gastric Cancer* 2006;9: 14–18
6. Kodera Y, Ito S et al. A Phase II Study of Weekly Paclitaxel as Second-line Chemotherapy for Advanced Gastric Cancer (CCOG0302 Study). *Anticancer Research* 2007;27: 2667-2672.
7. Yamamoto N et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. *Anticancer Res.* 2006 Jan-Feb;26(1B):777-81.
8. Sideris S et al. Efficacy of weekly paclitaxel treatment as a single agent chemotherapy following first-line cisplatin treatment in urothelial bladder cancer. *Mol Clin Oncol.* 2016 Jun; 4(6): 1063–1067
9. PACLitaxel. Summary of Product Characteristics. Accessed September 2019. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA1963-010-001_18022019145902.pdf

NCCP Protocol: PACLitaxel 80mg/m ²	Published: 29/04/2015 Review: 16/03/2020	Version number: 4
Tumour Group: Breast/Gastrointestinal/Genitourinary/Gynaecology/Lung NCCP Protocol Code: 00226	ISMO Contributor: Prof Maccon Keane	Page 4 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoprotocols

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

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.

NCCP Protocol: PACLitaxel 80mg/m ²	Published: 29/04/2015 Review: 16/03/2020	Version number: 4
Tumour Group: Breast/Gastrointestinal/Genitourinary/Gynaecology/Lung NCCP Protocol Code: 00226	ISMO Contributor: Prof Maccon Keane	Page 5 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoprotocols</i></p>		