CARBOplatin (AUC5-7.5) and PACLitaxel 175mg/m^2 Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Adjuvant treatment of high risk, stage I, epithelial ovarian cancer[i]	C56	00303a	N/A
Treatment of advanced ovarian cancer	C56	00303b	N/A
Treatment of primary peritoneal cancer	C48	00303c	N/A
Treatment of fallopian tube cancer	C57	00303d	N/A
Treatment of recurrent or advanced endometrial cancer (stage III or IV)[i]	C54	00303e	N/A
Treatment of advanced/recurrent non-small cell (NSC) cancer of the cervix[i]	C53	00303f	N/A
Treatment of carcinoma of unknown primary site[i]	C80	00303g	N/A

* This applies to post 2012 indications

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 patient's individual clinical circumstances.

CARBOplatin and PACLitaxel are administered once every **21 days** for 6 cycles or until disease progression or unacceptable toxicity develops, whichever occurs first.

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

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	PACLitaxel	175mg/m^2	IV infusion	500mL NaCl 0.9% over 3 hours	Every 21 days for 6 cycles
2	1	CARBOplatin	AUC (5-7.5)	IV infusion	500mL Glucose 5% over 30 minutes	Every 21 days for 6 cycles
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.						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

CARBOplatin dose:

The dose in mg of CARBOplatin to be administered is calculated as follows:

Dose (mg) = target AUC (mg/mL x minute) x (GFR mL/minute +25)

- **Measured GFR** (e.g., nuclear renogram) is preferred whenever feasible.
- **Estimation of GFR** may be performed using the Wright formula to estimate GFR or the Cockcroft and Gault formula to estimate creatinine clearance.
- The GFR used to calculate the AUC dosing should not exceed 125mL/min.

- For obese patients and those with a low serum creatinine, for example, due to low body weight or post-operative asthenia, estimation using formulae may not give accurate results; measured GFR is recommended.
    - where obesity (body mass index [BMI] ≥ 30 kg/m^2) or overweight (BMI 25-29.9) is likely to lead to an overestimate of GFR and isotope GFR is not available the use of the adjusted ideal body weight in the Cockcroft and Gault formula may be considered.
    - where serum creatinine is less than 63 micromol/L, the use of a creatinine value of 62micromol/L or a steady pre-operative creatinine value may be considered.
- These comments do not substitute for the clinical judgement of a physician experienced in prescription of CARBOplatin.

WRIGHT FORMULA

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1. *SCr measured using enzymatic assay*.

$$\text{GFR (mL/minute)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

2. *SCr measured using Jaffe assay*

$$\text{GFR (mL/minute)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

COCKCROFT-GAULT FORMULA

$$\text{GFR (mL/min)} = \frac{\text{S} \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

S= 1.04 for females and 1.23 for males

ELIGIBILITY:

- Indications as above
- ECOG status
    - 0-3 Advanced ovarian, primary peritoneal or fallopian tube cancer
    - 0-2 Adjuvant ovarian, advanced endometrial, advanced NSC cervical cancer

EXCLUSIONS:

- Hypersensitivity to CARBOplatin*, PACLitaxel or any of the excipients
- Disease progression while receiving platinum-based chemotherapy
- Pregnancy or breastfeeding
- Severe hepatic impairment (PACLitaxel)
- Baseline neutrophil count < 1.5 x 10^9 cells/L

*If it is felt that the patient may have a major clinical benefit from CARBOplatin, it may in exceptional circumstances be feasible to rechallenge a patient with a prior mild hypersensitivity reaction e.g. using a desensitisation protocol, but only with immunology advice, premedication as advised, and a desensitisation protocol under carefully controlled conditions with resuscitation facilities available and medical and/or ITU/ HDU supervision.

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Audiometry as clinically indicated
- Isotope GFR measurement (preferred) or GFR / CrCl estimation
- Assessment of peripheral neuropathy status as clinically indicated

Regular tests:

- FBC with differential, renal and liver profile prior to each cycle
- Assessment of peripheral neuropathy status as clinically indicated

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: Dose modifications for haematological toxicity

ANC (x 10^9/L) on Treatment Day	
0.5 to < 1.0	Delay treatment until recovery
< 0.5	Delay treatment until recovery and consider reducing PACLitaxel and CARBOplatin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing PACLitaxel and CARBOplatin by 25% for subsequent cycles
Platelets (x 10^9/L) at any stage in cycle	
50 to <100	Delay treatment until recovery
<50	Delay treatment until recovery and consider reducing PACLitaxel and CARBOplatin by 25% for subsequent cycles

For some patients, especially ECOG 2 or 3, treatment thresholds may be higher.

Table 2: Dose Modification of CARBOplatin and PACLitaxel in renal and hepatic impairment

Drug	**Renal Impairment**	**Hepatic Impairment**			
CARBOplatin[a]	See note below*	No need for dose adjustment is expected			
PACLitaxel[b]	No need for dose adjustment is expected Haemodialysis: no need for dose adjustment is expected	**ALT**		**Total bilirubin**	**Dose of PACLitaxel**
		< 10xULN	and	≤ 1.25xULN	No dose reduction
		< 10xULN	and	1.26-2xULN	75% of original dose
		< 10xULN	and	2.01-5xULN	50% of original dose
		≥10xULN	and/or	>5xULN	Contraindicated

[a] CARBOplatin (renal- See note below[c], hepatic - Giraud et al 2023)
[b] PACLitaxel (renal and hepatic – Giraud et al 2023)

***Renal dysfunction and CARBOplatin:**

- Patients with creatinine clearance (CrCl) values of <60mL/minute are at greater risk of developing myelosuppression.
- If GFR between 20 to ≤ 30mL/minute, CARBOplatin should be administered with extreme caution.
- In case of GFR ≤ 20mL/minute, CARBOplatin should not be administered at all.
- If Cockcroft & Gault or Wright formula are used, the dose should be calculated as required per cycle based on a serum creatinine obtained within 48 hours of drug administration.
- If isotope GFR is used, the dose should remain the same provided the serum creatinine is ≤110% of its value at the time of the isotope measurement. If the serum creatinine increases, consideration should be given to remeasuring the GFR or to recalculating using Cockcroft & Gault or Wright formulae.

Management of adverse events:

Table 3: Dose Modifications for Adverse Events

Adverse reactions	Recommended dose modification
Motor or sensory neuropathy Grade 2 Grade ≥ 3	 Reduce PACLitaxel by 25% If persists, reduce PACLitaxel by 50% Omit PACLitaxel
≥ Grade 3 reaction	Discontinue

Patients who cannot tolerate treatment after 2 dose reductions should be discussed with treating clinician regarding continuation of treatment.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

CARBOplatin: High **(Refer to local policy)**
PACLitaxel: Low **(Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- All patients must be premedicated with corticosteroids, antihistamines, and H_2 antagonists prior to the first dose of PACLitaxel treatment.
- The H_2 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 the use of alternative H_2 antagonists **(Refer to local policy).**

Table 4: Suggested premedications prior to treatment with PACLitaxel

Drug	Dose	Administration prior to PACLitaxel
dexAMETHasone	20mg oral or IV[a,b]	For oral administration: approximately 6 and 12 hours or for IV administration: 30 minutes
Chlorphenamine	10mg IV	30 minutes
Famotidine[c]	20mg IV	30 minutes
[a]Dose of dexAMETHasone may be reduced or omitted in the absence of hypersensitivity reaction according to consultant guidance.		
[b]If aprepitant is added to the anti-emetic regimen, consideration should be given to reducing the dose of dexAMETHasone to 12mg on the day of treatment.		
[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:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Ozols RF, Bundy BN, Greer BE, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol 2003; 21:3194-3200
2. Pignata S, Scambia G, Ferrandina G, et al. Carboplatin plus paclitaxel versus carboplatin plus pegylated liposomal doxorubicin as first-line treatment for patients with ovarian cancer: the MITO-2 randomized phase III trial. J Clin Oncol 2011; 29:3628-3635.
3. Miller D, Filiaci V & Fleming G. et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma. A gynecologic oncology group study. Gynecol Oncol 2012:125:771-773.
4. Pectasides, D., N. Xiros, G. Papaxoinis, et al. Carboplatin and paclitaxel in advanced or metastatic endometrial cancer. Gynecol Oncol 2008; 109(2):250-254.
5. Moore KN, Herzog TJ, Lewin S et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol 2007; 105:299-303.
6. Kitagawa R et al. Paclitaxel plus carboplatin versus paclitaxel plus cisplatin in metastatic or recurrent cervical cancer: the Open-Label Randomized Phase III Trial JCOG0505. J Clin Oncol 2015; 33:2129-2135.
7. NCCN Guidelines Version 3. 2017 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
8. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
9. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
10. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2012; 30 (13) 1553-1561.
11. Ekhart C, Rodenhuis S et al. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? Cancer Chemother Pharmacol 2009; 64:115-122.
12. NCCN CARBOplatin dosing in adults. Available at: https://www.nccn.org/docs/default-source/clinical/order-templates/appendix_b.pdf?sfvrsn=6286822e_6

13. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-459
14. Uptodate infusion reactions to systemic chemotherapy. Available at: https://www.uptodate.com/contents/infusion-reactions-to-systemic-chemotherapy#H37
15. CARBOplatin Summary of Product Characteristics. Last updated: 02/07/2024. Accessed March 2025. Available at: https://assets.hpra.ie/products/Human/28088/Licence_PA2059-032-001_02072024153224.pdf
16. PACLitaxel 6mg/mL. Summary of Product Characteristics. Last updated: 18/10/2023. Accessed March 2025. Available at: https://assets.hpra.ie/products/Human/27560/Licence_PA2315-115-001_18102023131024.pdf

Version	Date	Amendment	Approved By
1	08/04/2016		Prof Maccon Keane
2	18/04/2018	Updated with new NCCP regimen template. Treatment table updated for standardisation. Updated emetogenic status as per NCCN	Prof Maccon Keane
3	29/04/2020	Updated emetogenic potential Standardised table for suggested premedications prior to treatment Updated adverse event section.	Prof Maccon Keane
4	19/08/2020	Updated pre-medications table to include consideration of dexAMETHasone dosing where aprepitant is included as an anti-emetic	Prof Maccon Keane
5	29/08/2022	Updated CARBOplatin infusion time. Updated standard wording for CARBOplatin dosing and creatinine value. Updated dose modification of CARBOplatin in haematological toxicity. Updated PACLitaxel pre meds table.	Prof Maccon Keane
6	16/04/2025	Reviewed. Updated CARBOplatin dose wording, Tests (baseline and regular), renal and hepatic impairment dose modifications and CARBOplatin renal dysfunction wording. Amended emetogenic potential section, adverse effects, regimen specific complications and drug interactions as per NCCP regimen standardisation.	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.