

**Dose Dense DOXOrubicin, cycloPHOSphamide (AC 60/600) 14 day followed by weekly PACLitaxel (80) and weekly Trastuzumab Therapy (DD AC-TH)**

**Note: There is an option for Dose Dense DOXOrubicin, cycloPHOSphamide – PACLitaxel (14 days) and trastuzumab therapy described in regimen NCCP- 00316.**

**INDICATIONS FOR USE:**

INDICATION	ICD10	Regimen Code	Reimbursement Status
Adjuvant Treatment of HER2 positive, High Risk Node Negative or Node Positive Breast Cancer.	C50	00433a	Hospital
Neoadjuvant Treatment of HER2 positive, High Risk Node Negative or Node Positive Breast Cancer.	C50	00433b	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.*

DOXOrubicin and cycloPHOSphamide are administered once every 14 days for four cycles (one cycle = 14 days) followed by PACLitaxel and trastuzumab once every 7 days for 12 weeks.

Following completion of the 12 weeks, trastuzumab 6mg/kg (ref NCCP regimen 00200 Trastuzumab monotherapy-21days) every 21 days to complete one year of trastuzumab therapy may be given.

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

**G-CSF support (using standard or pegylated form) is required with all cycles of dose dense chemotherapy.**

**4 Cycles of DOXOrubicin/cycloPHOSphamide (Cycles 1-4 of treatment)**

Order of Admin.	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	DOXOrubicin	60mg/ m <sup>2</sup>	IV push	Slow IV push over 15minutes	Every 14 days for 4 cycles
2	1	cycloPHOSphamide	600mg/m <sup>2</sup>	IV infusion*	250ml 0.9% sodium chloride over 30minutes	Every 14 days for 4 cycles
* cycloPHOSphamide may also be administered as an IV bolus over 5-10mins						
Lifetime cumulative dose of DOXOrubicin is 450mg/m <sup>2</sup> <b>In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below<sup>i</sup> and to the age of the patient.</b>						

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## 4 Cycles of PACLitaxel/Trastuzumab (Cycles 5-8 of treatment)

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15	<sup>a,b</sup> PACLitaxel	80mg/m <sup>2</sup>	IV infusion	250 ml 0.9% sodium chloride over 1hr	Repeat every 21 days for cycle 5-8
1	<sup>c,d</sup> Trastuzumab	4mg/kg	IV infusion Observe post infusion	250ml 0.9% sodium chloride over 90minutes	Cycle 5, day 1 <b>only</b>
8, 15	<sup>c,d</sup> Trastuzumab	2mg/kg	IV infusion Observe post infusion	If no adverse reactions use 250ml 0.9% sodium chloride over 30minutes	Cycle 5, day 8 and day 15 only
1, 8, 15	<sup>c,d</sup> Trastuzumab	2mg/kg	IV infusion Observe post infusion	If no adverse reactions use 250ml 0.9% sodium chloride over 30minutes	Repeat every 21 days for cycle 6-8
<sup>a</sup> 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.					
<sup>b</sup> PACLitaxel should be diluted to a concentration of 0.3-1.2mg/ml.					
<sup>c</sup> Recommended observation period: Patients should be observed for at least six hours after the start of the first infusion and for two hours after the start of the subsequent infusions for symptoms like fever and chills or other infusion-related symptoms. Any deviation should be noted in local policies.					
<sup>d</sup> Trastuzumab is incompatible with glucose solution					

Following completion of the 12 weeks of PACLitaxel/trastuzumab treatment, trastuzumab 6mg/kg (Reference NCCP regimen 00200 Trastuzumab monotherapy-21 days) every 21 days to complete one year of trastuzumab therapy should be given.

### ELIGIBILITY:

- Indications as above
- HER2 overexpression or HER2 gene amplification as determined by an accurate and validated assay
- ECOG status 0-2

### EXCLUSIONS:

- Hypersensitivity to DOXOrubicin, cycloPHOSphamide, PACLitaxel, trastuzumab or any of the excipients
- Congestive heart failure (LVEF < 50%) or other or other clinically significant cardiac disease (history of symptomatic ventricular arrhythmias, congestive heart failure or myocardial infarction within previous 12 months)
- Baseline neutrophil count < 1.5 x 10<sup>9</sup>/L
- Severe hepatic impairment
- Breast feeding

### PRESCRIPTIVE AUTHORITY:

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

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## TESTS:

### Baseline tests:

- FBC, liver and renal profile
- ECG
- MUGA or ECHO (LVEF > 50% to administer DOXOrubicin) if >65 years or if clinically indicated

### Regular tests:

- FBC, liver and renal profile
- Cardiac function (MUGA or ECHO) every 12 weeks. Where there are signs of cardiac impairment four to eight weekly checks may be more appropriate.

### 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
- If the patient misses a dose of trastuzumab by one week or less, then the usual maintenance dose of 2mg/kg should be given as soon as possible. Do not wait until the next planned cycle. Subsequent maintenance doses should then be given according to the previous schedule.
- If the patient misses a dose of trastuzumab by more than one week, a re-loading dose of trastuzumab (4 mg/kg) should be given over approximately 90 minutes, at the discretion of the clinician. Subsequent trastuzumab maintenance doses (2 mg/kg) should then be given weekly from that point.

### Haematological:

**Table 1: Dose modifications for cycles of DOXOrubicin and cycloPHOSphamide only**

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose (Both Drugs)
≥ 1.0	and	≥ 100	100%
< 1.0	and	≥ 100	Delay for 1 week (or longer if needed), then give 100% dose if ANC > 1.0 and platelets ≥ 100.
≥ 1.0	and	< 100	Delay for 1 week (or longer if needed), then give 100% dose if ANC > 1.0 and platelets ≥ 100. Dose reduce to 75% after a second delay.

### Febrile neutropenia:

75% of dose for current and subsequent cycles

**Table 2: For cycles of PACLitaxel only**

ANC (x10 <sup>9</sup> /L)		Platelets	Dose	Dose after neutropenic sepsis
≥ 1.5	and	> 90	80mg/m <sup>2</sup>	65mg/m <sup>2</sup>
*1-1.49	or	70-90	65mg/m <sup>2</sup>	50mg/m <sup>2</sup>
< 1	or	< 70	Delay and reduce next dose to 65mg/m <sup>2</sup> or add G-CSF	Delay

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

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## Renal and Hepatic Impairment:

**Table 3: Dose modification of DOXOrubicin, cycloPHOSphamide and PACLitaxel in renal and hepatic impairment**

Drug	Renal Impairment		Hepatic Impairment	
	CrCl (ml/min)	Dose	Serum Bilirubin (micromol/L)	Dose
DOXOrubicin	>10	No dose adjustment is needed	20-50	50%
	<10	No need for dose adjustment is expected	51-86	25%
	Haemodialysis	75% of the original dose may be considered	>86 or Child-Pugh C	Not recommended
cycloPHOSphamide	CrCl (mL/min)	Dose	<b>Mild/moderate:</b> No need for dose adjustment is expected  <b>Severe:</b> Not recommended, due to risk of reduced efficacy	
	≥30	No dose adjustment is needed		
	10-29	Consider 75% of original dose		
	<10	Not recommended, if unavoidable consider 50% of original dose		
	Haemodialysis	Not recommended, if unavoidable consider 50% of original dose		
PACLitaxel	No need for dose adjustment is expected  Haemodialysis: no need for dose adjustment is expected		See Table 4 below	
Trastuzumab	CrCl (ml/min)	Dose	No need for dose adjustment is expected	
	≥30	No dose adjustment is needed		
	<30	No need for dose adjustment expected		
	Haemodialysis	No need for dose adjustment expected		

**Table 4: Dose modification of PACLitaxel in hepatic Impairment**

ALT		Total bilirubin	Dose of PACLitaxel
< 10xULN	and	≤ 1.25xULN	80mg/m <sup>2</sup>
< 10xULN	and	1.26-2xULN	60mg/m <sup>2</sup>
< 10xULN	and	2.01-5xULN	40mg/m <sup>2</sup>
≥10xULN	and/or	>5xULN	Not recommended

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## Non-Haematological Toxicity:

**Table 5: Dose modification schedule for PAclitaxel based on adverse events**

Adverse reactions	Discontinue	Recommended dose modification
Grade 2 motor or sensory neuropathy		Decrease dose by 10mg/m <sup>2</sup> .
All other grade 2 non-haematological toxicity		Hold treatment until toxicity resolves to ≤ grade 1. Decrease subsequent doses by 10mg/m <sup>2</sup> .
≥ Grade 3 reaction	Discontinue	

**Table 6: Trastuzumab dose modification schedule based on adverse events**

Adverse reactions	Discontinue	Recommended dose modification
LVEF drops 10 ejection fraction points from baseline and to below 50%		Withhold treatment. Repeat LVEF after 3 weeks. No improvement or further decline, consider discontinuation. Discuss with consultant and refer to cardiologist.
Symptomatic heart failure		Consider discontinuation – refer to cardiology for review. Clinical decision.
NCI-CTCAE Grade 4 hypersensitivity reactions	Discontinue	
Haematological		Treatment may continue during periods of reversible, chemotherapy-induced myelosuppression. Monitor carefully for any complications of neutropenia.

## SUPPORTIVE CARE:

### EMETOGENIC POTENTIAL:

DOXOrubicin cycloPHOSphamide (AC) cycles: High (**Refer to local policy**)

PAclitaxel and trastuzumab (TH): Low (**Refer to local policy**)

### PREMEDICATIONS:

DOXOrubicin cycloPHOSphamide (AC) cycles: None usually required

PAclitaxel:

- All patients must be premedicated with corticosteroids, antihistamines, and H<sub>2</sub> antagonists prior to first dose of PAclitaxel treatment.
- The H<sub>2</sub> 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<sub>2</sub> antagonists (**Refer to local policy**).

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**Table 7: Suggested premedications prior to treatment with PACLitaxel**

Day of treatment	Drug	Dose	Administration prior to PACLitaxel
Day 1	dexAMETHasone <sup>a</sup>	8mg IV	30 minutes
Day 1	Chlorphenamine	10mg IV	30 minutes
Day 1	Famotidine	20mg IV	30 minutes
Day 8 <sup>b</sup> and thereafter	dexAMETHasone <sup>a</sup>	None	
Day 8 and thereafter	Chlorphenamine	10mg IV	30 minutes
Day 8 and thereafter	Famotidine <sup>c</sup>	20mg IV	30 minutes
<sup>a</sup> 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.			
<sup>b</sup> Dose of dexAMETHasone may be added from day 8 if increased risk or previous hypersensitivity reaction according to consultant guidance.			
<sup>c</sup> Dose of famotidine may be omitted in the absence of hypersensitivity reaction according to consultant guidance.			

## OTHER SUPPORTIVE CARE:

Patients should have an increased fluid intake of 2-3 litres on day 1 to prevent haemorrhagic cystitis associated with cycloPHOSphamide.

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.

Please refer to:

- NCCP Regimen 00252 for information on the adverse effects associated with DOXOrubicin cycloPHOSphamide therapy.
- NCCP Regimen 00226 for information on the adverse effects associated with weekly PACLitaxel therapy.
- NCCP Regimen 00201 for information on the adverse effects associated with trastuzumab therapy.

## DRUG INTERACTIONS:

- CYP3A inhibitors decrease the conversion of cycloPHOSphamide to both its active and inactive metabolites. Patients should also be counseled with regard to consumption of grapefruit juice.
- CYP3A inducers may also increase the conversion of cycloPHOSphamide to both its active and inactive metabolites.
- Concurrent administration of calcium channel blockers with DOXOrubicin should be avoided as they may decrease the clearance of DOXOrubicin.
- Risk of drug interactions with CYP3A inhibitors may cause increased concentrations of PACLitaxel. Patients should also be counseled with regard to consumption of grapefruit juice.
- Risk of drug interactions with CYP3A inducers may cause decreased concentrations of PACLitaxel.
- Current drug interaction databases should be consulted for more information.

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## REFERENCES:

1. Perez E, Romond EH et al. Four-Year Follow-Up of Trastuzumab Plus Adjuvant Chemotherapy for Operable Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer: Joint Analysis of Data From NCCTG N9831 and NSABP B-31. *J Clin Oncol* 2011;29 (25): 3366-3373.
2. Romond EH, Perez E et al Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005;353(16):1673-1684.
3. Dang et al: The safety of dose dense DOXOrubicin and cyclophosphamide followed by PACLitaxel with trastuzumab in the HER-2/neu over-expressed/ amplified breast cancer. *J Clin Oncol* 2008; 26 (8): 1216-22.
4. Citron ML, Berry DA, Cirincione C. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *J Clin Oncol* 2003; 21 (8): 1431-1439
5. Quock J et al. Premedication strategy for weekly paclitaxel. *Cancer investigation*. Volume 20, 2002 issue 5-6
6. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Onco*/2019; 20:e201-08. [https://doi.org/10.1016/S1470-2045\(19\)30145-7](https://doi.org/10.1016/S1470-2045(19)30145-7)
7. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. 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>
8. Uptodate infusion reactions to systemic chemotherapy available at <https://www.uptodate.com/contents/infusion-reactions-to-systemic-chemotherapy#H37>
9. DOXOrubicin HCl 50mg Powder for Solution for Injection. Summary of Product Characteristics. Accessed Nov 2022. Available at: [http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC\\_PA0437-026-002\\_03032016152104.pdf](http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0437-026-002_03032016152104.pdf)
10. cycloPHOSphamide (Endoxana®) Injection 500mg Powder for Solution for Injection. Summary of Product Characteristics. Accessed Nov 2022. Available at: [https://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2299-027-002\\_21122018112109.pdf](https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2299-027-002_21122018112109.pdf)
11. Trastuzumab (Herceptin®) Summary of Product Characteristics. Accessed Nov 2022. Available at: [https://www.ema.europa.eu/en/documents/product-information/herceptin-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/herceptin-epar-product-information_en.pdf)
12. PACLitaxel. Summary of Product Characteristics. Accessed November 2022. Available at: [https://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2059-050-001\\_21092022103217.pdf](https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-050-001_21092022103217.pdf)

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Version	Date	Amendment	Approved By
1	23/10/2017		Prof Maccon Keane
2	16/03/2018	Treatment table updated for standardisation. Clarified dosing of PACLitaxel in haematological toxicity	Prof Maccon Keane
3	22/04/2020	Standardisation of cycloPHOSphamide infusion volume and recommendations in hepatic impairment. Updated recommended pre-medications pre PACLitaxel administration. Update of recommended dose modifications for symptomatic heart failure.	Prof Maccon Keane
4	17/04/2023	Updated pre medications table and section for PACLitaxel.	Prof Maccon Keane
5	18/10/2023	Updated G-CSF advice. Updated renal and hepatic dose modifications as per paper by Krens et al 2019.	Prof Maccon Keane

Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

<sup>i</sup>Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.

Risk factors for developing anthracycline-induced cardiotoxicity include:

- high cumulative dose, previous therapy with other anthracyclines or anthracenediones
- prior or concomitant radiotherapy to the mediastinal/pericardial area
- pre-existing heart disease
- concomitant use of other potentially cardiotoxic drugs

In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors above and to the age of the patient

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