

Systemic Anti Cancer Therapy Protocol

Paclitaxel Weekly Advanced Breast Cancer

PROTOCOL REF: MPHAPAWEBR
(Version No.: 1.3)

Approved for use in:

- Locally advanced breast cancer
- Metastatic breast cancer

Dosage:

Drug	Dose	Route	Frequency	Duration
Paclitaxel	80mg/m ²	IV infusion	Every 7 days	12 weeks followed by review. Beyond 12 weeks if clinical benefit and acceptable toxicity

Frequency can be adjusted to take account of neutropenia, for example administering 3 weeks out of 4 for individual patients

Administration:

Consider IV access, PICC line insertion is recommended for this regimen

- Paclitaxel must be administered using a non-PVC giving set with a 0.22 micron filter.
- Paclitaxel in solution may show haziness which is attributed to the formulation of paclitaxel.
- Excessive shaking, agitation, or vibration of paclitaxel may induce precipitation and should be avoided
- As treatment may continue beyond 12 weeks consider intravenous access, PICC line or port recommended

Issue Date: August 2023 Review Date: August 2026	Page 1 of 7	Protocol reference: MPHAPAWEBR
Author: Gabriella Langton	Authorised by: Drugs & Therapeutics Committee	Version No: 1.3

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

Metoclopramide 10mg tablets, three times a day when required

Add loperamide 4mg stat and then 2mg after each loose stool if diarrhoea occurs

Ondansetron 8mg orally pre-chemotherapy can also be considered if nausea is problematic

Extravasation risk:

Paclitaxel – vesicant

Refer to the CCC policy for the ‘Prevention and Management of Extravasation Injuries’

Dosing in renal and hepatic impairment:

Renal	No dose adjustments necessary
--------------	-------------------------------

Hepatic	Bilirubin and Transaminases	Percentage dose
	Transaminases <10 x ULN and bilirubin ≤1.25 x ULN	Dose at 100%
	Transaminases <10 x ULN and bilirubin >1.25 – 2 x ULN	80%
	Transaminases <10 x ULN and bilirubin 2-5 x ULN	50%
	Transaminase ≥10 x ULN or bilirubin >5 x ULN	Not recommended

Patients with hepatic impairment may be at increased risk of toxicity, particularly grade III-IV myelosuppression. There is no evidence that the toxicity of paclitaxel is increased when given as a 3-hour infusion to patients with mildly abnormal liver function. No data is available for patients with severe baseline cholestasis.

Patients should be monitored closely for the development of profound myelosuppression.

Interactions:

Antiepileptics (CYP 3A4 inducers)

Phenytoin, carbamazepine and phenobarbital increase the clearance of paclitaxel and increase its maximum tolerated dose.

Ciclosporin

Levels of paclitaxel increased after oral administration of ciclosporin.

Fluconazole/Ketoconazole (CYP3A4 inhibitors)

Paclitaxel levels may be increased

Quinine and Verpamil

Paclitaxel levels possibly increased.

For more detailed interactions please refer to the SPC

<https://www.medicines.org.uk/emc/product/3891/smpc#gref>

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
	Dexamethasone	6.6mg	IV	30 mins before chemotherapy Reduced to 3.3mg from cycle 2
	Chlorphenamine	10mg	IV	30 mins before chemotherapy
	PACLITAXEL	80mg/m²	IV infusion	Sodium Chloride 0.9% 250mL over 60 minutes

- Infusion volume may change dependent on dose
- Premedication treatment of chlorphenamine and dexamethasone are given prior to paclitaxel to reduce the risk of hypersensitivity. Paclitaxel reactions commonly occur within the first few minutes of starting the infusion most likely with the first two cycles. See hypersensitivity policy for more information

Main toxicities:

Paclitaxel	
Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	Risk of bradycardia and hypotension is common
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Musculoskeletal	Arthralgia, myalgia
Nervous system	Paclitaxel: peripheral neuropathy is very common
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Alopecia Allergic skin rash frequently associated with pruritus
General disorders and administration site conditions	Malaise, fever, chills, urticaria, flu-like syndrome, rash, pruritus. Injection site reactions (including localised oedema, pain, erythema, induration, on occasion extravasation can result in cellulitis, skin fibrosis and skin necrosis)

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment All patients on SACT should have at least one F2F review during treatment.	X				At week 12 or earlier if clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
FBC	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	Every Cycle
CT scan	X				At week 12 and when clinically indicated
ECG					If clinically indicated
Respiratory Rate					If clinically indicated
Weight recorded	X	X	X	X	Every cycle
Height recorded	X				

Issue Date: August 2023 Review Date: August 2026	Page 5 of 7	Protocol reference: MPHAPAWEBR
Author: Gabriella Langton	Authorised by: Drugs & Therapeutics Committee	Version No: 1.3

Dose Modifications and Toxicity Management: Haematological toxicity

Proceed on day 1 if:

ANC $\geq 1.0 \times 10^9/L$	Platelets $\geq 100 \times 10^9/L$ **
------------------------------	---------------------------------------

**** If platelets are between 80 -100 x 10⁹/L discuss with named consultant if can proceed**

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity

Peripheral Neuropathy

Paclitaxel
CTCAE grade 2 peripheral neuropathy: withhold paclitaxel until the neuropathy recovers to grade 1 then dose reduce to 75% of the original dose. Where the peripheral neuropathy is \geq grade 3 omit further paclitaxel.

Grading and Management of Toxicity

Toxicities should be graded according to the CTCAE v4.0 criteria. Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1 st appearance	Interrupt treatment until resolved to grade ≤ 1 , then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade ≤ 1 , then continue at 80% of original dose	Discontinue treatment

2nd appearance	Interrupt treatment until resolved to grade ≤ 1 , then continue at 80% of original dose	Interrupt treatment until resolved to grade ≤ 1 , then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade ≤ 1 , then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

References:

1. <https://www.medicines.org.uk/emc>
2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. BNF available via: <https://bnf.nice.org.uk/>

Circulation/Dissemination

Date added into Q-Pulse	9 th November 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
	1.1	Gabriella Langton	New format, added line regarding lower platelets, switched supportive medication from domperidone to metoclopramide
	1.3	Gabriella Langton	Removal of famotidine as per DTC approval, addition of F2F review reminder, update to wording of hepatic impairment

Issue Date: August 2023 Review Date: August 2026	Page 7 of 7	Protocol reference: MPHAPAWEBR
Author: Gabriella Langton	Authorised by: Drugs & Therapeutics Committee	Version No: 1.3