Systemic Anti Cancer Treatment Protocol

Paclitaxel Weekly
Advanced Breast Cancer

PROTOCOL REF: MPHAPAWEBR
(Version No: 1.0)

Approved for use in:

Locally advanced breast cancer

Metastatic breast cancer

Dosage

Drug	Dose	Route	Frequency
Paclitaxel	**80mg/m^2**	IV Infusion	Every 7 days

Treatment is repeated weekly for 12 weeks followed by review. Treatment can continue 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

Supportive Treatments:

Domperidone 10mg tablets, three times a day when required

Interactions

Antiepileptics (CYP 3A4 inducers)

Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages. Phenytoin, carbamezapine 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.

Extravasation risk:

Paclitaxel - vesicant.

Administration

Days	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	IV bolus	30 minutes before chemotherapy
1	Ranitidine	50mg	IV bolus	30 minutes before chemotherapy
1	Chlorphenamine	10mg	IV bolus	30 minutes before chemotherapy
1	**Paclitaxel**	**80mg/m^2**	**IV Infusion**	**250mL sodium chloride 0.9% over 60 minutes**

- 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
- Premedication treatment of chlorphenamine, dexamethasone and ranitidine is 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.

Hypersensitivity

As with all paclitaxel based chemotherapy, patients may experience allergic reaction during administration. The infusion should be stopped and the following should be administered.

- Hydrocortisone 100 to 200mg IV
- Chlorphenamine 10 mg IV

Refer to the Trusts Hypersensitivity Guidelines for further information.

It should be strongly noted that patients who have severe reactions should not be re-challenged

Main Toxicities

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

	Pre	Week 1	Week 2	Week 3	Week 4	Ongoing
Medical Assessment	X				X	At week 12
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X		X	X	X	Every cycle
U&E & LFT	X		X	X	X	Every cycle
CT scan	X					At week 12
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological Toxicity

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non-haematological Toxicity

Grading and Management of Toxicity

Toxicity should be grading 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
1st appearance	Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade 0/1, then continue at 80% of original dose	Discontinue treatment
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 80% of original dose	Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

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 ≥grade 3 omit further paclitaxel.

Hepatic Impairment

Paclitaxel

Bilirubin /µmol/l	Dose in mg/m^2
< 26	80
27-51	65
>51	withhold

Patients with severe hepatic impairment must not be treated with paclitaxel.

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 are available for patients with severe baseline cholestasis.
Patients should be monitored closely for the development of profound myelosuppression.

If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at 100%

Renal Impairment

No dose reductions necessary.

References

Verrill M et al ASCO Abstract LBA1005 2011

Kellokumpu-Lehtinen P et al, Anticancer Res 2013 33(6):2623-7

Miller K et al NEJM 2007 357:2666-2676

Dosage Adjustment for Cytotoxics in Hepatic and Renal Impairment. January 2009

UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

Stockley's drug interactions. Ninth edition. Edited K. Baxter. Pharmaceutical press. London. 2010