LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Paclitaxel weekly in Early Breast Cancer

Indication:	Neoadjuvant or adjuvant alternative therapy to docetaxel, for high risk patients unable to tolerate docetaxel or where there is a contraindication for high dose steroids			
Regimen details:	Paclitaxel	80 - 90mg/m^2	IV	Day 1
Administration:	Paclitaxel in 250ml Sodium Chloride 0.9% or Glucose 5% over 60 minutes Paclitaxel to be given via non-PVC infusion bag, with a 0.22 micron in-line filter. Paclitaxel must be diluted to a concentration of 0.3-1.2mg/ml to maintain stability in clinical practice			
Frequency:	Day 1, every 7 days, for 12 cycles			
Premedication:	Dexamethasone	*8mg	IV	30 – 60 minutes prior to paclitaxel administration
	Chlorphenamine	10mg	IV	30 – 60 minutes prior to paclitaxel administration over at least 1 minute
	Ranitidine	50mg	IV	30 – 60 minutes prior to paclitaxel administration over at least 2 minutes

*To minimise steroid side effects, the dose of dexamethasone may be reduced to 4mg if there has been no evidence of hypersensitivity.

Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.

Reason for Update: LCA Protocol Development	Approved by LCA Consultant: Mark Harries
Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016

Anti- emetics:	Low emetogenicity Follow local anti-emetic policy
Supportive medication:	Not routinely required
Extravasation:	Vesicant Paclitaxel should be administered with appropriate precautions to prevent extravasation. If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation
Regular investigations:	Prior to Cycle 1: FBC Day 1 (within 14 days) LFTs Day 1 (within 14 days) U&Es Day 1 (within 14 days) Prior to Day 1 (all cycles): FBC Day 1 (within 48 hours) Prior to Day 1, Cycles 4, 7, 10, 13, 16 LFTs Day 1 (within 48 hours) U&Es Day 1 (within 48 hours)
Toxicities:	Anaemia, neutropenia, thrombocytopenia, fatigue, nausea, vomiting, mucositis, diarrhoea, dysgeusia, hypersensitivity reactions (mainly flushing, rash and hypotension); infection; peripheral neuropathy, arthralgia, myalgia, alopecia

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		**Platelets (x 10^9/L)**	**Dose**
≥ 1.0	&	≥ 100	100% dose
≥ 1.0	&	75 - 99	Discuss with Consultant – treatment can be considered on medical advice. Or consider treatment delay for 1 week. Repeat FBC, if platelets recover to ≥ 100 x 10^9/L, resume treatment at 100% dose.

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< 1.0	or	< 75	Delay for 1 week. Repeat FBC, if recovered to above these levels, resume treatment with 75% dose for all subsequent cycles.

In neoadjuvant/adjuvant treatment, dose reduction and delays can compromise outcome.

- GCSF should be considered if more than one delay and/or before dose reduction. If in doubt, seek Consultant advice.
- If during the preceding cycle, the patient has experienced neutrophils < 0.5 x 10^9/L or has febrile neutropenia diagnosed, GCSF should be considered.
- If despite GCSF treatment, febrile neutropenia occurs or a dose delay is required - seek Consultant advice and consider dose reduction by 25%
- If platelets persistently < 100 x 10^9/L on Day 1 despite dose delay - seek Consultant advice and consider dose reduction by 25%

Non-haematological Toxicities

Renal Impairment

No dose adjustment required. Assess renal function when clinically indicated

Hepatic Impairment

Bilirubin (µmol/L)	Paclitaxel Dose
22 - 26	Give 75 – 80% dose
27 – 51	Give 40 – 45% dose
> 51	Give 30% dose

Dose modifications for other toxicities

PERIPHERAL NEUROPATHY

NCI CTCAE Grade	Sensory Neuropathy	Dose
1	Paraesthesia (including tingling), but not interfering with function	100% dose
2	Paraesthesia interfering with function, but not interfering with activities of daily living	75% dose
3	Paraesthesia interfering with activities of daily living	Omit paclitaxel
4	Disabling	Discontinue paclitaxel permanently

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ARTHRALGIA / MYALGIA

NCI CTCAE Grade	Arthralgia/Myalgia	Action
1	Joint and muscle pain, not interfering with function	Consider use of NSAIDs
2	Joint and muscle pain, interfering with function, but not interfering with activities of daily living	Consider use of NSAIDs

Location of regimen delivery: Outpatient setting
Availability of resuscitation equipment must be ensured as a standard precaution.

Comments:

Drug interactions: Concomitant administration of inducers or inhibitors of cytochrome P450 Isoenzymes (CYP2C8 and 3A4) emay alter the pharmacokinetics of Paclitaxel, presenting a theoretical interaction
Clozapine: avoid concomitant use, increased risk of agranulocytosis

References:

Accord Healthcare Ltd. Summary of product characteristics – paclitaxel. 07/11/2012. Available at www.medicines.org.uk
Seidman, AD et al, Dose-Dense Therapy With Weekly 1-Hour Paclitaxel Infusions in the Treatment of Metastatic Breast Cancer. JCO 1998; 16:3353 – 3361
Perez, EA et al, Proc ASCO 2000; 18: Abstract 480
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013

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