LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Paclitaxel weekly in Advanced Breast Cancer

Indication:	Advanced breast cancer, where initial chemotherapy (including an anthracycline) has failed or is inappropriate The weekly regimen can be considered as an alternative in frail patients or for patients with bone marrow involvement or impaired liver function
Regimen details:	Paclitaxel *70 - 90mg/m^2 IV Day 1 * Consultant to decide dose basis, depending on patient status If given with trastuzumab, for cycle 1 only, give trastuzumab on Day 1 and paclitaxel on day 2. For subsequent cycles, administer the trastuzumab followed by the paclitaxel. For details of doses, monitoring and on-going treatment with trastuzumab, see separate protocol for trastuzumab in the advanced setting.
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 18 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

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

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

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

Anti- emetics: Low emetogenicity
Follow local anti-emetic policy

Supportive medication: Mouthcare as per Local policy

Extravasation: Vesicant
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 to reduce the risk of permanent tissue damage

Regular investigation:

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)

CT scan	Every 9 to 12 weeks

Toxicities: Anaemia, neutropenia, thrombocytopenia, fatigue, nausea, vomiting, mucositis, diarrhoea, dysgeusia, hypersensitivity reactions (mainly flushing, rash and hypotension), infection, peripheral neuropathy, arthralgia, myalgia, alopecia

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DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Paclitaxel Dose
≥ 1.5	&	≥ 50	100%
< 1.5	& / or	< 50	Delay for 1 week. Repeat FBC - if recovered to above these levels resume treatment with 100% dose

If neutrophils < 0.5 x 10^9/L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 25x 10^9/L,
Paclitaxel dose should be permanently reduced to 80% for subsequent cycles.

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	80% dose
3	Paraesthesia interfering with activities of daily living	Omit paclitaxel
4	Disabling	Discontinue paclitaxel permanently

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ARTHRALGIA / MYALGIA

Paclitaxel may cause Grade 1 or 2 Arthralgia or 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:	Out-patient setting Availability of resuscitation equipment must be ensured as a standard precaution
Comments:	None
Drug interactions:	Concomitant administration of inducers or inhibitors of cytochrome P450 Isoenzymes (CYP2C8 and 3A4) may 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 UCLH-Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH-Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 Seidman AD *et al* JCO (2008); 26 (10): 1642-1649 Miller K *et al* (2007) NEJM; 357: 2666-2676 LCA Breast Cancer Clinical Guidelines October 2013

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