LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Docetaxel in Advanced Breast Cancer

Indication:	First-line palliative treatment, with or without trastuzumab, for advanced breast cancer in patients for whom an anthracycline is not suitable.
Regimen details:	Docetaxel 75* - 100mg/m^2 IV Day 1 *75mg/m^2 may be considered depending on patient factors * use 75mg/m^2 when administered with pertuzumab & trastuzumab
Administration:	Docetaxel in 250ml or 500ml Sodium Chloride 0.9% depending on final concentration IV over 1 hour Hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills, usually during the first and second infusions and within a few minutes following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution. When used in combination with trastuzumab: In pivotal trials, docetaxel was administered the day following the first dose of trastuzumab, and immediately after the subsequent doses of trastuzumab if the preceding dose was well tolerated. *However, there is increasing worldwide experience that both trastuzumab and taxanes can be given on the same day: Trastuzumab may be administered first, followed by docetaxel on Day 1.*

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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

For details of doses, administration, monitoring and on-going treatment with trastuzumab (IV or SC), or pertuzumab and trastuzumab, see separate protocols in advanced breast cancer.

Frequency: Day 1, every 21 days, for 6 cycles

Pre-medication: Oral dexamethasone 8mg BD for 3 days, starting the day before docetaxel administration to reduce the incidence and severity of fluid retention and hypersensitivity reactions.
If the patient has not taken the oral pre-medication, clinicians may prescribe dexamethasone IV 20mg, chlorphenamine IV 10mg and ranitidine IV 50mg to be administered 1 hour prior to chemotherapy.
(note: there is no data available to support the use of IV steroids in this setting, responsibility remains with the prescribing clinician).

Paracetamol / 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
Docetaxel 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 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
CT scan	Every 3 cycles

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Toxicities: Neutropenia (reversible), anaemia, nausea, vomiting, diarrhoea, stomatitis, asthenia, peripheral neuropathy, hypersensitivity reactions, fluid retention, cutaneous reactions, alopecia, nail disorder, cystoid macular oedema, ovarian failure, infertility.

DOSE MODIFICATIONS

Haematological Toxicity

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

- Dose reduction and / or delay is more appropriate in the advanced setting
- 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 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.

Hepatic Impairment

ALP		AST / ALT		Bilirubin	Docetaxel Dose
≤ 2.5 X ULN	&	≤ 1.5 x ULN			100% dose
2.5 – 6 x ULN	&	1.6 – 3.5 x ULN			75% dose
> 6 ULN	&	> 3.5 x ULN	& / or	> 22µmol/L	Not recommended. Docetaxel should be administered with Consultant approval

Dose modifications for other toxicities as appropriate

NCI CTCAE Grade	Cutaneous Reactions	Dose
1	Erythema without associated symptoms	100% dose
2	Localised erythema of the palms of the hands and soles of the feet with oedema followed by	Consider dose reduction to 75% dose

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	desquamation	
3	Severe, generalised eruptions followed by desquamation	Delay until recovery to ≤ Grade 2, reduce to 75% dose For 2nd occurrence, discontinue docetaxel
4	Generalised exfoliative, ulcerative or bullous dermatitis	Discontinue docetaxel permanently

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	Consider dose reduction to 75% dose
3	Paraesthesia interfering with activities of daily living	Delay until recovery to ≤ Grade 2, reduce to 75% dose For 2nd occurrence, discontinue docetaxel
4	Disabling	Discontinue docetaxel permanently

Location of regimen delivery:	Outpatient setting Availability of resuscitation equipment must be ensured as a standard precaution.
Comments:	None
Drug interactions:	Concomitant administration of substrates, inducers or inhibitors of cytochrome P450-3A e.g. ciclosporin, terfenadine, ketoconazole, erythromycin etc may alter the pharmacokinetics of docetaxel presenting a potential interaction.

References:

Sanofi. 2013. Summary of product characteristics: Taxotere (docetaxel). Available at www.medicines.org.uk [accessed 07/11/2013]

Bullock K, Blackwell K. Clinical Efficacy of Taxane–Trastuzumab Combination Regimens for HER-2–Positive Metastatic Breast Cancer. *The Oncologist* 2008; 13:515-525.

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Nabholtz et al. Prospective Randomized Trial of Docetaxel Versus Mitomycin Plus Vinblastine in Patients With Metastatic Breast Cancer Progressing Despite Previous Anthracycline-Containing Chemotherapy. *J Clin Oncol* 1999; 17:1413-1424.

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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