LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Subcutaneous Trastuzumab in Advanced Breast Cancer

Indication:	First-line treatment in HER2 positive advanced breast cancer (3+ by IHC or CISH/FISH+) As monotherapy in patients who have received at least two chemotherapy regimens for metastatic disease. Prior chemotherapy will generally have included at least an anthracycline and a taxane unless patients are unsuitable for these treatments. In combination with docetaxel or paclitaxel in patients who have not received chemotherapy for their metastatic disease and for whom an anthracycline is not suitable. Patients receiving intravenous trastuzumab may be offered a switch to the subcutaneous injection. Refer to LCA Breast Cancer Clinical Guidelines.
Regimen details:	Trastuzumab 600mg subcutaneous Day 1
Administration:	Trastuzumab subcutaneous injection over 2 – 5 minutes. The injection site should be alternated between the left and right thigh. New injections should be given at least 2.5cm from the old site. Administration-related reactions/hypersensitivity reactions such as chills and/or fever, dyspnoea, hypotension, wheezing, bronchospasm, tachycardia, reduced oxygen saturation, respiratory distress, rash, nausea, vomiting, headache are known to occur with trastuzumab. Local reactions include erythema, pruritis, oedema and rash at the site of the injection. Patients should be observed for at least 6 hours after the first injection, and for up to 2 hours after subsequent injections for signs and symptoms of administration-related reactions. Availability of resuscitation equipment must be ensured as a standard precaution.

Version: 2.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014
Reason for Update: cardiac monitoring	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

Frequency:	Day 1, every 21 days, until disease progression or unacceptable toxicity	
Pre-medication:	Not routinely required	
Anti- emetics:	Low emetogenicity Follow Local Anti-emetic Policy	
Supportive medication:	Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever	
Extravasation:	Non-vesicant	
Regular investigations:	FBC	Baseline, at 4 and 8 months, then 4 to 6 monthly thereafter
	LFTs	Baseline, at 4 and 8 months, then 4 to 6 monthly thereafter
	U&Es	Baseline, at 4 and 8 months, then 4 to 6 monthly thereafter
	LVEF (MUGA/ ECHO)	Baseline, at 4 and 8 months, then 4 to 6 monthly thereafter (see cardiac monitoring)
	Blood Pressure	Prior to each cycle*
	* Treat blood pressure of >140/85mmHg with an ACE inhibitor licensed for the treatment of heart failure.	
Toxicities:	Administration-related reactions (see above), cardiotoxicity, pulmonary events, diarrhoea, rash, hepatotoxicity (rare)	

DOSE MODIFICATIONS

Haematological Toxicity

Dose reductions are not recommended.

Perform full blood count at the same time as the cardiac monitoring.

Patients may continue trastuzumab therapy during periods of reversible, chemotherapy-induced myelosuppression but monitor closely for complications of neutropenia.

Non-haematological Toxicities

Renal Impairment

Dedicated pharmacokinetic studies have not been carried out. Perform renal function tests at the same time as cardiac monitoring.

Hepatic Impairment

Dedicated pharmacokinetic studies have not been carried out. Perform liver function tests at the same time as cardiac monitoring.

Dose modifications for other toxicities as appropriate

Cardiac contra-indications

History of documented congestive heart failure, coronary artery disease with previous Q-wave myocardial infarction or evidence of transmural infarction on ECG, angina pectoris requiring medication, poorly controlled hypertension, clinically significant valvular disease, or high risk of uncontrolled arrhythmias.

Cardiac monitoring

A left ventricular ejection fraction (LVEF) above the lower limit of normal (> 50%) is required for the treatment to go ahead (measured on echocardiography (ECHO) or multigated acquisition (MUGA).

Cardiac monitoring is carried out at baseline, at 4 and 8 months. Beyond this, LVEF should be monitored every 4 to 6 months as clinically indicated. A further end of treatment assessment is recommended in patients requiring cardiovascular intervention during trastuzumab treatment.

Refer to LCA Breast Cancer Clinical Guidelines for cardiac monitoring and discuss with the consultant.

Pulmonary events

Severe pulmonary adverse events have been reported with the use of the intravenous formulation. Fatal events have been reported and may occur as part of an infusion-related reaction or with delayed onset. In addition, cases of interstitial lung disease including lung infiltrates, acute respiratory distress syndrome, pneumonia, pneumonitis, pleural effusion, respiratory distress, acute pulmonary oedema and respiratory insufficiency have been reported with the intravenous preparation.

Patients experiencing dyspnoea at rest due to advanced malignancy or requiring supplementary oxygen therapy may be at increased risk of a fatal administration-related reaction and should only be treated with trastuzumab with extreme caution.

Location of regimen delivery:	Outpatient setting. Availability of resuscitation equipment must be ensured as a standard precaution.
Comments:	None
Drug interactions:	No formal drug interaction studies have been performed.

References:

Roche Products Limited, 2013. Summary of product characteristics: Herceptin 600mg/5ml solution for injection. Available at http://www.medicines.org.uk [accessed 4/10/2013]

LCA Breast Cancer Clinical Guidelines October 2013

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