TRASTUZUMAB (HERCEPTIN) IV
for early stage breast cancer

For use in early-stage HER2-positive breast cancer, following surgery and chemotherapy (neo-adjuvant or adjuvant)
NICE approved August 2006
Initiation with (neo-) adjuvant docetaxel-based chemotherapy has been agreed as standard practice
N.B. The subcutaneous route is now preferred; this protocol should be followed only for patients not tolerating the SC formulation

Drug/Dosage/Administration:

Loading dose:	Paracetamol	1000mg pre-med 30 minutes before treatment starts
	Trastuzumab (Herceptin)	8 mg/kg in 250ml sodium chloride 0.9% IV infusion over 90 minutes
Maintenance Doses:	*starting 3 weeks after loading dose*	
		Pre-medication not routinely needed.
	Trastuzumab (Herceptin)	6 mg/kg in 250ml sodium chloride 0.9% IV inf over 30 minutes, if loading dose tolerated

N.B. Patient only routinely needs to be seen in clinic for consent, and then before Doses 7 and 13, when trastuzumab (Herceptin) should be prescribed and confirmed as follows:
Pre Dose 1: Doses 1 – 6 (and arrange echo / MUGA for after cycle 6)
Dose 7 visit: Doses 7 - 12 (and arrange echo / MUGA for after cycle 12)
Dose 13 visit: Doses 13 – 18 (and arrange follow-up)

If the patient misses a dose by more than one week, a re-loading dose of trastuzumab is usually required. However, if the delay was due to cardiac toxicity, the doctor may choose not to re-load the patient.

Patients should be observed for 6 hours after start of first infusion (i.e. 4½ hours post-infusion), and for 30 minutes post-infusion for subsequent doses.
If a decision is made to allow the patient to leave in advance of these times, they must be counselled about the possibility of delayed infusion-related symptoms and instructed to contact the hospital in the event of these occurring.

NB. Infusion-related and pulmonary symptoms may also rarely occur more than 6 hours after the start of a trastuzumab infusion. Patients should be warned about this and instructed to contact the hospital if any such symptoms occur.

Frequency: Every 3 weeks for 12 months: loading dose, followed by 17 maintenance doses.
To be initiated no earlier than 3 weeks after the last dose of anthracycline-based chemotherapy.
Clinical review pre Doses 7 and 13 (once corresponding LVEF result available)

Main Toxicities: Infusion-related symptoms (mild to moderate in severity): fever; chills; headache; nausea; rash; arthralgia; myalgia (occur mainly with 1st dose)
Infusion-related symptoms (serious but rare): dyspnoea; hypotension; bronchospasm; tachycardia; angioedema; anaphylaxis (occur mainly with 1st dose)

cardiotoxicity (see Comments)

Reason for Update: LVEF cut-off reduced to > 50%	Approved by Consultant: Dr S Houston
Version: 9	Approved by Lead Chemotherapy Nurse: V Mumford
Supersedes: Version 8	Date: 20.5.15
Prepared by: S Taylor	Checked by: C Tucker

Anti-emetics: mildly emetogenic

Extravasation: non-vesicant

Regular Investigations:	FBC	baseline, then taken with Doses 6 and 12 ready for clinical review
	U&Es and LFTs	baseline, then taken with Doses 6 and 12 ready for clinical review
	Echo*/MUGA scan	baseline; then after Dose 6 and Dose 12 ready for clinical review pre Dose 7 and Dose 13; then after Dose 18 only if requested by Consultant
	Blood pressure**	baseline, then at clinic review pre Dose 7 and Dose 13

* An echocardiogram is the preferred test, but whichever test is used initially for an individual, should ideally be used throughout

** If blood pressure ≥ 140/90 mmHg, a diagnosis of hypertension needs to be confirmed by asking patient to visit GP for ambulatory or home blood pressure monitoring.
Patients with a confirmed diagnosis of hypertension should be treated with an ACE inhibitor which is also licensed for the treatment of heart failure e.g. ramipril.

Comments: A baseline LVEF > 50% is required for treatment to go ahead.

Prophylactic ACE inhibitor therapy should be initiated for any patient who experiences a significant decrease in LVEF as specified in the table below.

Dose Modifications: No reductions in the dose of trastuzumab were made during clinical trials. Patients may continue trastuzumab therapy during periods of chemotherapy-induced myelosuppression.

Dose Interruptions: In line with national guidance[1], see table below for indications for interruption of trastuzumab treatment, initiation of ACE inhibitor therapy, referral to cardiologist and increased monitoring:

LVEF	Signs or symptoms	Trastuzumab	Start ACE inhibitor	Cardiology referral	Additional monitoring
LVEF ≥ 50% **and** < 10 EF points decrease from baseline	None	Continue	No	No	No
LVEF 41 – 49% **or** ≥ 10 EF points decrease from baseline (even if still > 50%)	None	Continue	Yes*	*Refer if already on ACEI	After 6-8 weeks
LVEF ≤ 40%	Any	Stop	Yes	Refer	Within 6-8 weeks**
Any	Yes	Stop	Yes	Refer	Within 6-8 weeks**

**Trastuzumab may be re-initiated if LVEF recovers to > 50%.

References:
Romond, EH et al; NEJM (2005); 353: 1673 – 1684
Piccart-Gebhart, MJ et al; NEJM (2005); 353: 1659 – 1672
[1]Jones, AL et al; Br J Cancer 2009; 100: 684 - 692

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