TRASTUZUMAB (HERCEPTIN) SUBCUTANEOUS
for early stage breast cancer

For neo-adjuvant or adjuvant use in early-stage HER2-positive breast cancer, following surgery and chemotherapy
Initiation with (neo-) adjuvant docetaxel-based chemotherapy has been agreed as standard practice

Drug/Dosage: Trastuzumab (Herceptin) 600mg s/c slow bolus every 3 weeks

N.B. Patient only routinely needs to be seen in clinic for consent, and then before Doses 7 and 13, when trastuzumab (Herceptin) s/c should be prescribed and confirmed as follows:

Pre Dose 1: Doses 1 – 6 (and arrange echo/MUGA for after dose 6)
Dose 7 visit: Doses 7 - 12 (and arrange echo/MUGA for after dose 12)
Dose 13 visit: Doses 13 – 18, and arrange follow-up for end of treatment plan

Administration: Paracetamol 1000mg po 30 minutes before the 1st dose only.
Administer trastuzumab as a 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 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard.

In combination with docetaxel:
If the first dose of s/c trastuzumab is being given with the 1st or 2nd dose of docetaxel, both drugs may be given on the same day: administer the s/c trastuzumab first, wait one hour, then initiate the docetaxel infusion.
For subsequent doses of s/c trastuzumab, there is no need for a specific time interval between the trastuzumab and starting docetaxel.

It has been agreed locally that patients starting a new course of s/c trastuzumab should be observed for signs or symptoms of administration-related reactions after each dose as follows:
- for 4 ½ hours after the first injection
- for 30 minutes after the second injection
- no observation period after subsequent doses

No observation period is necessary for patients switching mid-course from IV to s/c trastuzumab.

Patients should also be counselled about the possibility of delayed symptoms, and instructed to contact the hospital in the event of these occurring.

Frequency: Every 3 weeks for 12 months, to total 18 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)

If the patient misses a dose, administer the next 600 mg dose (i.e. the missed dose) as soon as possible. The interval between consecutive trastuzumab s/c doses should not be less than three weeks.

Main Toxicities: Administration-related symptoms: fever, chills, hypotension, wheeze, bronchospasm, tachycardia, reduced oxygen saturation, headache, nausea, rash (occur mainly with 1st dose)
Local reactions at injection site: erythema, pruritis, oedema, rash

cardiotoxicity (see Comments)

Reason for Update: LVEF cut-off reduced to > 50%	Approved by Consultant: Dr S Houston
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 20.5.15
Prepared by: S Taylor	Checked by: C Tucker

Anti-emetics: mildly emetogenic

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 s/c 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
BO22227 clinical trial (unpublished)

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