TRASTUZUMAB (HERCEPTIN) SUBCUTANEOUS

1. For (neo-)adjuvant use in **early-stage** HER2-positive breast cancer, in patients also receiving chemotherapy

2. For HER2+ve **metastatic** breast cancer, administered in combination with paclitaxel or vinorelbine (i.e. only for patients not eligible for docetaxel, plus pertuzumab and trastuzumab)

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

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

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.

**Prescribing:**

**Early stage breast cancer:**
- Note: Patient only routinely needs to be seen in clinic for consent, and then before Doses 7 and 13, when trastuzumab 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)

**Metastatic breast cancer:**
- At each clinical review, all trastuzumab doses are to be prescribed and confirmed up until the next clinical review is due.

**Frequency:**

**Early stage breast cancer:**
- 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)
**Metastatic breast cancer:**
Every 3 weeks - administer until disease progression outside of the CNS

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)

**Anti-emetics:**
mildly emetogenic

<table>
<thead>
<tr>
<th>Early stage breast cancer</th>
<th>Metastatic breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC, U&amp;Es &amp; LFTs</td>
<td>baseline, then taken with Doses 6 and 12 ready for clinical review</td>
</tr>
<tr>
<td>Echo*/MUGA scan</td>
<td>baseline; then after Dose 6 and Dose 12, ready for clinical review before Dose 7 and Dose 13***</td>
</tr>
<tr>
<td>Blood pressure**</td>
<td>baseline, then at clinic review pre Dose 7 and Dose 13</td>
</tr>
</tbody>
</table>

* 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.

***Patients who develop asymptomatic cardiac dysfunction will require more frequent monitoring e.g. every 6–8 weeks.

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

Caution should be exercised in treating patients who present with a history of hypertension, or documented coronary artery disease.

The risk of developing heart failure is greatest when trastuzumab is used in combination with anthracyclines, and so they should not be used concurrently.

**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: **Early stage breast cancer:**

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:

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

\(^*\)Trastuzumab may be re-initiated if LVEF recovers to > 50%.

**Metastatic breast cancer:**

The above table may be followed, however if in doubt, discuss with Consultant; there may be occasions where the benefits for the individual patient of continuing with trastuzumab are deemed to outweigh the risks.

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  