**Indication**
Adjuvant treatment of patients with HER2 + early stage breast cancer.

May be administered concurrently with taxanes for suitable patients receiving neo-adjuvant or adjuvant treatment.

(NICE CG80)

**ICD-10 codes**
Codes prefixed with C50

**Regimen details**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading dose – cycle 1</td>
<td>Trastuzumab</td>
<td>8mg/kg</td>
<td>IV infusion</td>
</tr>
<tr>
<td>Cycle 2 onwards</td>
<td>Trastuzumab</td>
<td>6mg/kg*</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

*if treatment is delayed by >7 days patients should have a further loading dose of 8mg/kg.

OR

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Trastuzumab</td>
<td>600mg</td>
<td>SC</td>
</tr>
</tbody>
</table>

No loading dose is required.

**Cycle frequency**
21 days

**Number of cycles**
Treat for 1 year or until disease progression (whichever occurs first).

**Administration**
Facilities for the treatment of hypotension and bronchospasm must be available.

It is important to check the product labels to ensure that the correct formulation (intravenous or subcutaneous) is being administered to the patient. The two formulations are NOT interchangeable.

**Intravenous dosing**
Cycle 1:
Trastuzumab is administered in 250mL sodium chloride 0.9% over 90 minutes. The patient should be observed for 6 hours after the start of the infusion for symptoms of infusion related reactions (e.g. fever, chills).

Cycle 2 onwards, (providing trastuzumab well tolerated):
Trastuzumab is administered in 250mL sodium chloride 0.9% and may be given over 30 minutes.

It may not be necessary to stop treatment for minor hypersensitivity reactions e.g. flushing, localised rash but infusions must be stopped for major reactions, e.g. hypotension, dyspnoea, angioedema or generalised urticaria.
Maintenance intravenous dose of 6mg/kg may be dose banded according to the following table:

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Trastuzumab dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-44.9</td>
<td>250</td>
</tr>
<tr>
<td>45-53.9</td>
<td>300</td>
</tr>
<tr>
<td>54-61.9</td>
<td>350</td>
</tr>
<tr>
<td>62-69.9</td>
<td>390</td>
</tr>
<tr>
<td>70-80.9</td>
<td>450</td>
</tr>
<tr>
<td>81-91.9</td>
<td>515</td>
</tr>
<tr>
<td>92-105.9</td>
<td>600</td>
</tr>
<tr>
<td>106-117.9</td>
<td>670</td>
</tr>
<tr>
<td>118-132.9</td>
<td>750</td>
</tr>
</tbody>
</table>

If treatment is delayed by > 7 days patients should have a further loading dose of 8mg/kg. If this is within 12 weeks of their previous dose then only 2 hours observation from start of infusion is required. If greater than 12 weeks then observe for 6 hours.

**Subcutaneous dosing**

Trastuzumab is administered as a flat dose of 600mg in a volume of 5mL by subcutaneous injection over 2-5 minutes. The injection site should be alternated between left and right thigh, with new injections at least 2.5cm from the old site. Avoid administration into sites that are bruised, inflamed, tender or hard. Other medicinal products for subcutaneous administration should preferably be injected at different sites.

Patients should be observed for 6 hours after the first dose and 2 hours after subsequent doses for administration related reactions.

**Pre-medication**

Antihistamines, paracetamol and hydrocortisone can be used to treat reactions and should be available if required but should not be used as primary prophylaxis before the first dose.

**Emetogenicity**

This regimen has no significant emetogenic potential.

**Additional supportive medication**

Nil

**Extravasation**

Trastuzumab is neutral (Group 1)

**Investigations – pre first cycle**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>14 days</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFT</td>
<td>14 days</td>
</tr>
<tr>
<td>ECHOCARDIOGRAM</td>
<td>Baseline</td>
</tr>
<tr>
<td>Weight*</td>
<td>Baseline</td>
</tr>
</tbody>
</table>

*IV dosing only
Investigations - pre subsequent cycles

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>Only if clinically indicated</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>Only if clinically indicated</td>
</tr>
<tr>
<td>LFT</td>
<td>Only if clinically indicated</td>
</tr>
<tr>
<td>ECHOCARDIOGRAM</td>
<td>3 monthly (more frequently if patient developing asymptomatic cardiac dysfunction)</td>
</tr>
<tr>
<td>Weight*</td>
<td>3 monthly</td>
</tr>
</tbody>
</table>

*IV dosing only

Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/consultant.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECHOCARDIOGRAM – ejection fraction</td>
<td>≥ LLN for institution (usually 50%)</td>
</tr>
</tbody>
</table>

Dose modifications
- Haematological toxicity
  No dose modifications required. Patients may continue on trastuzumab during periods of chemotherapy induced myelosuppression.

- Renal impairment
  No dose modifications required.

- Hepatic impairment
  No dose modifications required.

- Other toxicities
  Cardiac toxicity
  It is recommended that cardiac monitoring of patients receiving trastuzumab follows UK guidelines.

Trastuzumab may be initiated in patients with left ventricular ejection fraction (LVEF) above the lower limit of normal (LLN) for the institution.

Symptomatic patients: Patients who develop symptomatic cardiac dysfunction should have trastuzumab discontinued, be commenced on ACE inhibitor therapy and be referred to a cardiologist. Further treatment should be discussed with consultant.

Asymptomatic patients: LVEF of 0.4 (40%) or less represents biologically significant left ventricular systolic dysfunction (LVSD). If the LVEF decreases to 0.40 or less, trastuzumab should be interrupted. An ACE inhibitor should be started by the oncologist, and the patient should be referred to a cardiologist. Investigation and treatment is recommended in accordance with national and international guidelines on the management of congestive heart failure in adults. The LVEF measurement should be repeated after 6–8 weeks. Trastuzumab may be re-initiated if the LVEF is restored to a level above the lower limit of normal (LLN).

If the LVEF decreases to below the LLN but >0.40, trastuzumab may be continued, but an ACE inhibitor should be initiated. If this decrease occurs despite pre-existing ACE inhibitor therapy, the patient should be referred to a cardiologist.

If the LVEF decreases by 0.10 points or more and remains above the LLN, trastuzumab may be continued, but an ACE inhibitor should be initiated. Monitoring should be repeated after 6–8 weeks. A decrease of 0.10 or more may suggest an increased risk of heart failure, and intervention with an ACE inhibitor is recommended to reduce this risk.
**Adverse effects** - for full details consult product literature/ reference texts

- **Serious side effects**
  Hypersensitivity reactions, including bronchospasm, tachycardia, angioedema, anaphylaxis
  Hepatotoxicity
  Left ventricular cardiac dysfunction
  ARDS, pneumonitis, pleural effusion, dyspnoea

- **Frequently occurring side effects**
  Nausea and vomiting
  Diarrhoea
  Headache
  Hypertension
  Conjunctivitis

- **Other side effects**
  Myalgia
  Arthralgia
  Fatigue
  Asthenia

**Significant drug interactions** – for full details consult product literature/ reference texts
No documented significant reactions.

**Additional comments**
Trastuzumab should NOT be given in combination with anthracyclines. Particular care should be taken when prescribing trastuzumab to patients heavily pre-treated with anthracyclines.

Trastuzumab is contra-indicated in patients with severe dyspnoea at rest due to complications of advanced malignancy or co-morbidities.

Because the half-life of trastuzumab is approximately 4-5 weeks, it may persist in the circulation for up to 20-25 weeks after stopping trastuzumab treatment.

**References**
- Summary of Product Characteristics. Trastuzumab IV injection (Roche) accessed 29 October 2014 via [www.emc.medicines.org.uk](http://www.emc.medicines.org.uk)