Trastuzumab IV for HER2 positive Breast Cancers

DRUG ADMINISTRATION SCHEDULE

Given as either as a weekly schedule:

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Trastuzumab (variable brand)</td>
<td>4 mg/kg</td>
<td>IV Infusion</td>
<td>250mls Normal Saline over 90 mins</td>
</tr>
<tr>
<td>Day 8,15 etc</td>
<td>Trastuzumab (variable brand)</td>
<td>2 mg/kg</td>
<td>IV Infusion</td>
<td>250mlsNormal Saline over 30 to 90 mins</td>
</tr>
</tbody>
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Or given as a three weekly schedule:

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Trastuzumab (variable brand)</td>
<td>8 mg/kg</td>
<td>IV Infusion</td>
<td>250mls Normal Saline over 90 mins</td>
</tr>
<tr>
<td>Day 22, etc</td>
<td>Trastuzumab (variable brand)</td>
<td>6 mg/kg</td>
<td>IV Infusion</td>
<td>250mls Normal Saline over 30 to 90 mins</td>
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</tbody>
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PRECAUTION: Trastuzumab prescribing
- In order to reduce the risk of medication errors it is recommended that all trastuzumab products are referred and prescribed as ‘trastuzumab (brand name)’.
- Trastuzumab is available as biosimilar brands which are clinically the same as the originator Herceptin Brand. The most cost effective product should be used.

NUMBER OF DAYS PER CYCLE
1. Every 21 days or 7 days per cycle for advanced until disease progression
2. 21 days per cycle, total 18 doses in adjuvant use, 1 x loading dose (8mg/kg) followed by 17 maintenance doses (6mg/kg).

APPROVED INDICATIONS
- Treatment of patients with metastatic breast cancer whose tumours over-express human epidermal growth factor receptor 2 (HER2).
- Note Can be used in combination with Docetaxel, Paclitaxel or Vinorelbine in metastatic disease, see individual chemo regimen protocols.
- Adjuvant treatment as monotherapy following chemotherapy

ELIGIBILITY CRITERIA
Must only be used in patients whose tumours have HER2 over-expression at a 3+ level as determined by immunohistochemistry (HER2 +++ by IHC or FISH)

Inclusion criteria for metastatic use of Trastuzumab
Monotherapy for patients who have received at least two chemotherapy regimens for their metastatic disease. Prior chemotherapy must have included at least an anthracycline and a taxane unless patients are unsuitable for these treatments. Hormone receptor positive patients must also have failed hormonal therapy, unless patients are unsuitable for these treatments

In combination with docetaxel, paclitaxel or vinorelbine * for the treatment of those patients who have not yet received chemotherapy for their metastatic disease and for whom an anthracycline is unsuitable.
Inclusion criteria for adjuvant use of Trastuzumab

- HER2+ breast cancer
  - 3+ on IHC or 2+ confirmed as having amplified gene copy number by FISH testing.
  - Patients with HER-2 0 or 1+ staining are regarded as HER-2 Negative and do not require FISH testing.
- At least T1c or lymph node positive tumour
- Must have received >= 4 cycles of an approved adjuvant/neo-adjuvant chemotherapy regimen
  - May receive concomitant radiotherapy and/or endocrine treatment as clinically indicated
- Normal base line cardiac function (determined by ECHO (greater than 55%) or normal MUGA scan)

EXCLUSION CRITERIA
Weekly Trastuzumab IV not recommended for adjuvant treatment.
Note Herceptin SC is predominantly used for adjuvant treatment.

PREMEDICATION
Only required when used in combination with chemotherapy, see chemo regimen.

RECOMMENDED TAKE HOME MEDICATION
None required

INVESTIGATIONS / MONITORING REQUIRED
Pre-treatment  HER2 test. Cardiac assessment incl. history and physical exam (esp. in those with prior AC exposure), ECG, Echocardiogram +/- MUGA
During infusion Observe for fevers and chills or other infusion-related symptoms for at least 6 hours after the start of the first infusion, and for 2 hours after the start of subsequent infusions
3 to 4 monthly  Cardiac function (ECHO/MUGA)

ASSESSMENT OF RESPONSE
Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW
On cycles where not seen by clinician.

ADMINISTRATION NOTES
- May not need to stop treatment for minor hypersensitivity e.g. reactions, flushing, localised rash. Must be stopped for major reactions, e.g. hypotension, dyspnoea, angioedema or generalised urticaria.
- Antihistamines, paracetamol and hydrocortisone can be used to treat reactions and should be available if required but must not be used prophylactically.
- If patient has hypersensitivity reaction follow manufacturers re-challenge guidelines before continuing with treatment.
- Units administering trastuzumab must have facilities available for the treatment of anaphylaxis and resuscitation.
EXTRAVASATION  See NCA / Local Policy

TOXICITIES
Trastuzumab is contraindicated in patients with severe dyspnoea at rest due to complications of advanced malignancy or requiring supplementary oxygen therapy.
- Risk of infusion reactions, hypersensitivity and anaphylaxis, particularly on first cycle. The majority of these events occur during or within 2.5 hours of the start of the first infusion.
- Pulmonary events, such as dyspnoea, bronchospasm, asthma and hypoxia. Adult Respiratory Distress Syndrome (ARDS) has been reported rarely with fatal outcome
- Cardiotoxicity - Do not give with anthracycline or give anthracycline within six months of patient receiving last dose of Trastuzumab.
- Chills and fevers common with first infusion
- Pain, Myalgia, arthralgia

DOSE MODIFICATION / TREATMENT DELAYS
Cardiac Toxicity
The NCA Breast Guidelines give detailed guidance on management and monitoring of cardiac function during trastuzumab therapy.

Navigation through the guidelines may be facilitated by the adoption of a traffic light system summarised below.

| Green | LVEF above the LLN, no signs or symptoms of CHF and any trastuzumab-related LVEF fall being < 0.10 (10%) |
| Amber | LVEF between the LLN and 0.40 (40%), with no signs or symptoms of CHF, or a trastuzumab-related LVEF reduction of 0.1 (10%) or more. |
| Red   | LVEF ≤ 0.40 (40%) or symptoms and signs of cardiac failure. |

<table>
<thead>
<tr>
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<th>Pre Chemo</th>
<th>Pre Trastuzumab</th>
<th>During Trastuzumab</th>
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</thead>
<tbody>
<tr>
<td>Green</td>
<td>-</td>
<td>Trastuzumab OK</td>
<td>Trastuzumab OK</td>
</tr>
<tr>
<td>Amber</td>
<td>Consider non-anthracycline chemo. Repeat ECHO before trastuzumab</td>
<td>Wait for green</td>
<td>Continue with ACE inhibitor. (Refer to cardiology if already on ACEi)</td>
</tr>
<tr>
<td>Red</td>
<td>Unlikely to be safe to give trastuzumab</td>
<td>Delay trastuzumab, start ACEi and refer to cardiology</td>
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LVEF Monitoring
At least 4 monthly for adjuvant patients, metastatic patients can be monitored less frequently (see breast guidelines for details)

TREATMENT LOCATION
Can be given at Cancer Centre or Cancer Unit
REFERENCES:

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