# Herceptin SC (Subcutaneous Trastuzumab)

NHS Northern Cancer Alliance

## DRUG ADMINISTRATION SCHEDULE

| Day | Drug | Dose | Route | Rate |
|---|---|---|---|---|
| 1 | Herceptin SC (trastuzumab) | 600mg | S/C | 2 to 5 mins |

*PRECAUTION: In order to reduce the risk of medication errors it is recommended that all trastuzumab products are referred to by brand name, i.e **Herceptin SC**

### DOSE FORM
Supplied as 600mg in 5ml vials in solution ready for subcutaneous injection

### CYCLE LENGTH AND NUMBER OF DAYS
Every 21 days (3 weeks) for 18 cycles (1 year) for adjuvant disease.

Every 21 days (3 weeks) until disease progression for metastatic disease. Can be given in combination with paclitaxel, docetaxel or vinorelbine (see specific protocols).

### APPROVED INDICATIONS
NHS England has approved all licenced indications for the treatment of patients with metastatic breast cancer whose tumours over-express human epidermal growth factor receptor 2 (HER2). See eligibility criteria below and Summary of Product Characteristics (SPC) available at http://www.medicines.org.uk/emc/default.aspx

### ELIGIABILITY 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 Herceptin**

- 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.
- In combination with an aromatase inhibitor

**Inclusion criteria for adjuvant use of Herceptin**

- HER2 + breast cancer
  - 3+ on IHC or 2+ confirmed as having amplified gene copy number by FISH.
  - 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)
- Neo-adjuvant – surgery should be planned for after administration of 8 cycles of Herceptin SC with no interruption in Herceptin SC treatment.

## EXCLUSION CRITERIA

- Cumulative dose of > 720mg/m$^2$ epirubucin or > 360 mg/m$^2$ doxorubicin
- History of documented congestive cardiac failure, previous Q-wave myocardial infarction, coronary artery disease, angina requiring medication, unstable arrhythmia, poorly controlled hypotension.
- Clinically significant valvular heart disease
- Patients requiring continuous oxygen therapy
- Patients with no indication for cytotoxic chemotherapy
- More than six months since completion of adjuvant chemotherapy

## PREMEDICATION

Only required when used in combination with chemotherapy

## RECOMMENDED TAKE HOME MEDICATION

None required

## INVESTIGATIONS / MONITORING REQUIRED

| | |
|---|---|
| Pre-treatment | HER2 test, FBC, biochemistry, history, physical exam, height, weight, LVEF by ECHO or MUGA (to be within normal limits of Trust), performance status, vital signs (blood pressure, heart rate and temperature – seated patient), pregnancy test. |
| During infusion | Observe for fevers and chills or other injection-related symptoms for at, undertake post dose observation time as per SPC. |
| 3 monthly | LVEF by ECHO or MUGA every 4 cycles (3-monthly), physical exam and performance status, FBC, biochemistry, weight. |

## REVIEW BY CLINICIAN

To be reviewed by either a Nurse or Clinician before every cycle.

## NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

## STORAGE AT WARD LEVEL

Herceptin SC should be supplied as an unopened vial in the original packaging, only dispensed against an individual prescription, and not prepared aseptically in pharmacy. Vials of Herceptin SC should be stored in the refrigerator until 1 hour prior to administration to the patient is required. Max 6 hours out of the fridge.

## SUBCUTANEOUS ADMINISTRATION NOTES

- Existing patients on IV Herceptin may be switched to SC Herceptin at any point in their treatment pathway
- Herceptin SC 600 mg, assisted administration into the thigh over a period of approximately 2 to 5 minutes, using handheld syringes with hypodermic needles (25 or 27 gauge)
- Patients can be advised in advance to wear comfortable, loose-fitting clothing allowing easy access to the thigh for administration of Herceptin SC. If necessary, clothing can be removed to expose the injection. The manufacturers Roche can provide information on administration techniques.
- The injection site should be alternated between the left and right thigh. New injections should be given at least 2.5cm from the old site and never into areas where the skin is red, bruised, tender or hard.

1. A fold of skin should be gently pinched with the thumb and forefinger
2. The needle should then be inserted at a 300 angle, as per clinical trials with Herceptin SC, to achieve uniform placement in the subcutaneous space
3. The injection solution should be administered by pushing carefully and slowly on the plunger at a rate that is comfortable for the patient
4. Administration should take between 2-5 minutes
5. When the injection has been completed, the needle should be held in place briefly before withdrawal, to help prevent backtracking

**POST DOSE OBSERVATION**

Based on standard practice at various hospitals and the clinical evidence, as well as several years of clinical experience, trusts may wish to consider adapting the specified post-administration observation period associated with trastuzumab for the benefit and convenience of their patients. Local clinical audit of reduced observation time, including no observation from cycle 3 onwards has shown no significant risks in omitting the observation time recommended in the SPC.

The Alliance Chemotherapy Group consensus is for zero observation time with at least 30 minutes after first dose which would encompass normal care

Any provider which does opt to deviate from the SPC specified observation period is requested to record any reported adverse effects and the time at which the effects were first noted in relation to the conclusion of dose administration.
The observation period recommended for 'signs or symptoms of administration-related reactions' in the summary of product characteristics for all trastuzumab (Herceptin®) formulations is 6 hours after the first dose and 2 hours after each subsequent dose

**Disclaimer**

The NCA cannot accept responsibility for any adverse drug events resulting from use of the administration schedule described above. For full information on the dosage, administration and possible adverse effects of Subcutaneous Herceptin consulted the most up-to date manufacturer's data sheets (SPC). **The administration schedule recommend by the Alliance Chemotherapy Group is outside of the product license and users follow the advice of this protocol at their own risk.**

**INTERACTION WITH OTHER MEDICATION:** None noted.

**EXTRAVASATION** N/A

**TREATMENT LOCATION:** Can be given at Cancer Centre, Cancer Unit or Community

**TOXICITIES**

Any injection-related symptoms must have resolved before the patient is discharged. Patients who experience injection-related symptoms may be pre-medicated with paracetamol and antihistamines for subsequent injections.

- Hypersensitivity, hypotension, tachycardia, cough, and dyspnoea.
- Local reactions included erythema, pruritus, oedema and rash at the site of the injection.
- Cardiotoxicity
- Myalgia, arthralgia

## DOSE MODIFICATION / TREATMENT DELAYS

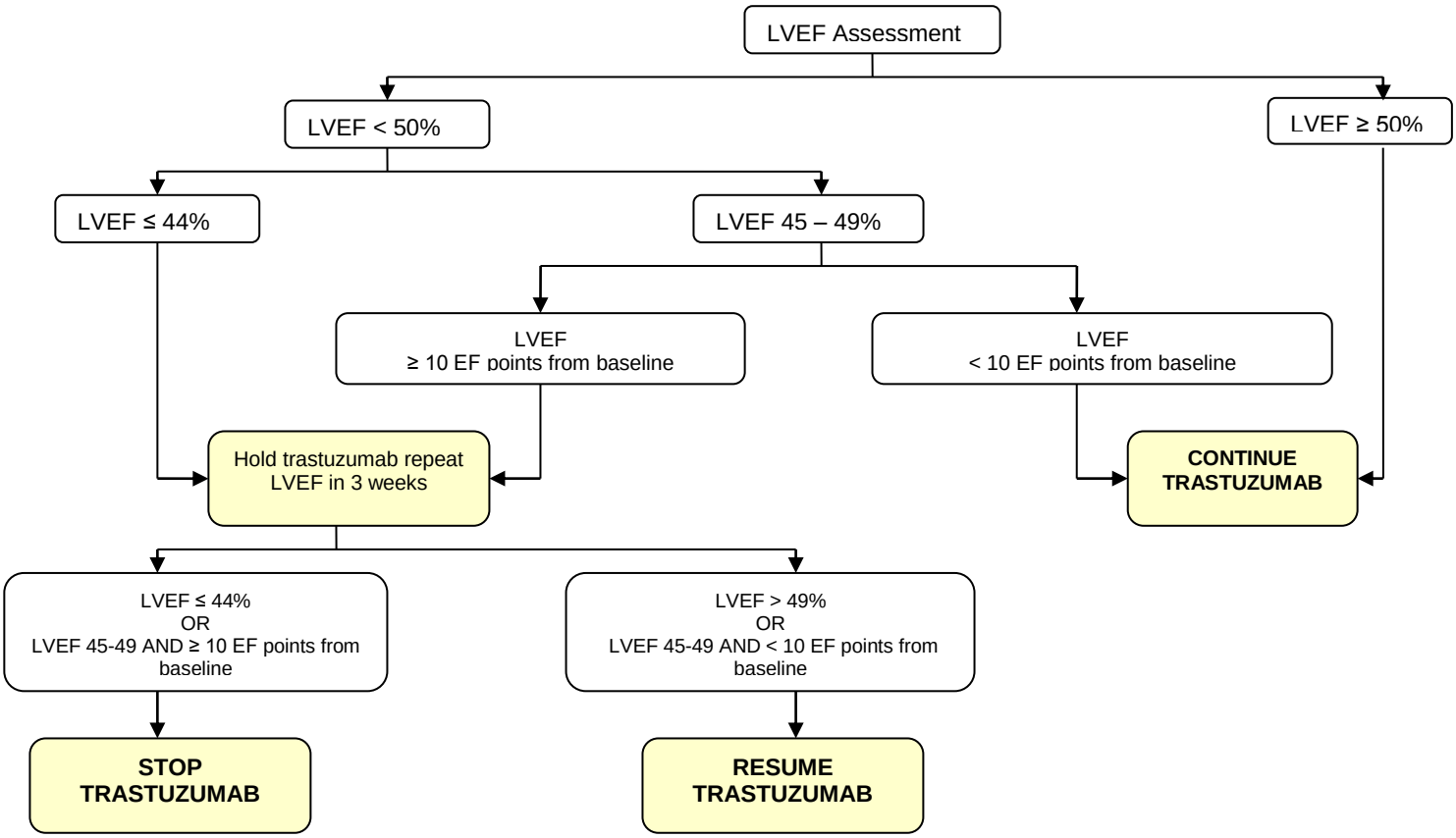
For toxicities related to concurrently administered chemotherapy, follow the relevant SPC/Network protocol. In the case of chemotherapy-related haematological or non-haematological toxicity, the following action should be applied:

- Grade 1 or 2, continue Herceptin SC treatment
- Grade 3 or 4, hold Herceptin SC treatment until recovery to ≤ Grade 2

If the patient misses a dose of Herceptin SC, then the usual dose should be given as soon as possible, with subsequent doses given every 3 weeks.
No dose adjustment is needed in case of delayed administration or toxicity.

| Toxicity related to Herceptin SC | Action |
|---|---|
| **Haematological & Non-haematological toxicity (excluding cardiac)** | |
| 1. Grade 1 or 2 | Continue Herceptin SC therapy (all medication in cycle) |
| 2. Grade 3 or 4 | Hold Herceptin SC therapy (all medication in the cycle) until recovery to grade ≤2.<br>Toxicity resolved to grade ≤2 within a max of 5 weeks from last administration – resume treatment<br>Toxicity not resolved to grade ≤2 within a max of 5 weeks from last administration – permanently discontinue treatment (continue other treatments as deemed appropriate by prescriber) |
| 3. Recurrence of non-haematological grade 3 or 4 toxicity upon re-challenge | Discontinue Herceptin SC permanently. Continue other treatments as deemed appropriate by prescriber |
| **Cardiac toxicity** | |
| 4. Significant asymptomatic drop in LVEF (≥10% points from baseline and to a LVEF <50%) | Hold treatment (all medication in cycle), continue/resume as per algorithm below |
| 5. Symptomatic congestive heart failure | Discontinue Herceptin SC permanently |
| 6. Other cardiac toxicity (other than significant asymptomatic LVEF drop of CHF) | Follow actions 1-3 for non-haematological toxicities |

### Cardiac Toxicity Algorithm




## REFERENCES:

1. NICE Clinical Guidelines CG80 Breast cancer (early & locally advanced) Issued: February 2009 Available at http://www.nice.org.uk/cg80
2. NICE Clinical Guidelines CG81 Breast cancer (advanced) Issued: February 2009 Available at http://www.nice.org.uk/cg81
3. Baselga J, Cortés J, Kim S,B, et al for the CLEOPATRA Study Group* Pertuzumab plus Trastuzumab plus Docetaxel for Metastatic Breast Cancer N Engl J Med 2012;366:109-19.
4. Trastuzumab (Herceptin®) Summary of Product Characteristics Available at
5. SafeHer protocol V2.0 Dated 19th November 2012

## Document Control

| | | | |
|---|---|---|---|
| **Document Title:** | 4 | | |
| **Document No:** | CRP B13001 | **Current Version:** | 1.5 |
| **Reviewers:** | Chris Beck Chemotherapy Pharmacist Northern Cancer Alliance | **Date Approved:** | 28.02.18 |
| **Approved by:** | Steve Williamson Consultant Pharmacist Northern Cancer Alliance | **Due for Review** | 01.03.21 |
| **Summary of Changes** | 1.0 | Updated and combined CDDFT trial protocol and NECN IV protocol | |
| | 1.1 | Numbering updated, safety warning regarding using brand name added | |
| | 1.2 | Updated post dose observation recommendations | |
| | 1.3 | Observation time reduced to Zero, disclaimer added | |
| | 1.5 | Review & tidy up | |