Trastuzumab (Herceptin®) (metastatic breast cancer)

Indication

As monotherapy or in combination with chemotherapy for HER2-positive (IHC3+ or IHC2+ with FISH ratio ≥ 2.0) metastatic breast cancer.

(NICE CG81)

ICD-10 codes

Codes prefixed with C50

Regimen details

Day	Drug	Dose	Route
Loading dose	Trastuzumab	8mg/kg	IV infusion
Cycle 2 onwards	Trastuzumab	6mg/kg*	IV infusion

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

OR

Day	Drug	Dose	Route
1	Trastuzumab	600mg	SC

Cycle frequency

21 days

Number of cycles

Until disease progression.

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. Patients should be observed for 2 hours after the start of the infusion for symptoms of infusion related reactions.

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 dose of 6mg/kg may be dose banded according to the following table:

Weight (kg)	**Trastuzumab dose** (mg)
40-44.9	250
45-53.9	300
54-61.9	350
62-69.9	390
70-80.9	450
81-91.9	515
92-105.9	600
106-117.9	670
118-132.9	750

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 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

Investigation	**Validity period**
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
ECHOCARDIOGRAM	Baseline
Weight*	Baseline

*IV dosing only

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Only if clinically indicated
U+E (including creatinine)	Only if clinically indicated
LFT	Only if clinically indicated
ECHOCARDIOGRAM	3 months after commencing treatment then 6 monthly (more frequently if patient developing asymptomatic cardiac dysfunction)
Weight*	3 monthly

*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.

Investigation	Limit
ECHOCARDIOGRAM – ejection fraction	≥ LLN for institution (usually 50%)

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 epirubicin. 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

- National Institute for Health and Clinical Excellence. CG81. Accessed 29 October 2014 via www.nice.org.uk
- Summary of Product Characteristics. Trastuzumab IV injection (Roche) accessed 29 October 2014 via www.emc.medicines.org.uk
- Summary of Product Characteristics. Trastuzumab SC injection (Roche) accessed 29 October 2014 via www.emc.medicines.org.uk

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