Trastuzumab (Breast)

Indication

Adjuvant treatment of patients with HER2-positive early stage breast cancer.
May be administered concurrently with taxanes for suitable patients receiving neo-adjuvant or adjuvant treatment.

(NICE CG101)

As monotherapy or in combination with chemotherapy for HER2-positive metastatic breast cancer.

(NICE CG81)

ICD-10 codes

Codes prefixed with C50

Regimen details

Intravenous

Day	Drug	Dose	Route
Loading dose – cycle 1	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

Sub-cutaneous

Day	Drug	Dose	Route
1	Trastuzumab	600mg	SC

No loading dose is required.

Cycle frequency

21 days

Number of cycles

Early stage breast cancer: 1 year of treatment (18 cycles) or for patients with lower risk (e.g.T1 N0 tumours), after discussion between consultant and patient, consider 6 months (9 cycles). Treatment should be discontinued if unacceptable toxicity or relapsed disease on adjuvant therapy.

Metastatic breast cancer: continue until unacceptable toxicity or 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 administration
Cycle 1:
Trastuzumab is administered in 250mL sodium chloride 0.9% over 90 minutes.
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. Patients should be observed for 6 hours after the first dose and up to 2 hours after subsequent doses for administration related reactions (or according to local policy).

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 (or according to local policy).

Subcutaneous administration
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 30 minutes after the first dose and for 15 minutes after subsequent doses for administration related reactions (or according to local policy).

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

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	3 monthly
U+E (including creatinine)	3 monthly
LFT	3 monthly
ECHOCARDIOGRAM	3 - 4 monthly or in metastatic patients every 6 months if stable (more frequently if patient developing asymptomatic cardiac dysfunction)

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%) and <10 point change from baseline (see below)

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: LVEF must be above LLN for treatment to go ahead. If LVEF percentage drops ≥10 points from baseline AND to below 50% (cardiotoxicity), treatment should be withheld, patients should be started on a beta-blocker (e.g. bisoprolol 1.25mg od) and an angiotensin-converting enzyme (ACE) inhibitor (e.g. ramipril 1.25mg od), referred to a cardiologist and a repeat LVEF assessment performed within 3 weeks.

Anti- HER2 therapy may be resumed if the LVEF has recovered to > 45%, or to 40-45% associated with a difference of < 10 points below pre-treatment values. If LVEF has not improved, or declined further, or symptomatic cardiac failure has developed, anti-HER2 should be discontinued, unless the benefits for the individual patient are deemed to outweigh the risks.

Other indications to refer to cardiology and repeat LVEF assessment within 3 weeks include LVEF percentage drop of <10% to below 50% (Possible subclinical cardiotoxicity) and if LVEF percentage drops ≥10 points from baseline but remains above 50% AND an accompanying relative decline in global longitudinal strain (GLS) >15% (probable subclinical cardiotoxicity). However, providing patients are not symptomatic they should continue on treatment.

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 normally 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.

Trastuzumab may persist in the circulation for up to 7 months after stopping treatment.

References

- National Institute for Health and Clinical Excellence. CG101. Accessed 16 February 2023 via www.nice.org.uk
- National Institute for Health and Clinical Excellence. CG81. Accessed 16 February 2022 via www.nice.org.uk
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- Lyon, AR. et al. 2022 ESC Guidelines on cardio-oncology. European Heart Journal 43(41):4229-4361

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