Trastuzumab

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)

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 – 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

Day	Drug	Dose	Route
1	Trastuzumab	600mg	SC

No loading dose is required.

Cycle frequency

21 days

Number of cycles

Early breast cancer: 1 year of treatment (usually 17 or 18 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 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.

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.

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 up to 2 hours 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
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 monthly (more frequently if patient developing asymptomatic cardiac dysfunction)^
Weight*	3 monthly

*IV dosing only
^ This is the recommended frequency for patients receiving adjuvant therapy. For patients with metastatic disease who are established on trastuzumab the frequency can be reduced to 6 monthly or according to consultant decision.

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: LVEF must be above LLN for treatment to go ahead. If LVEF percentage drops ≥10 points from baseline AND to below 50%, treatment should be withheld and a repeat LVEF assessment performed within approximately 3 weeks. If LVEF has not improved, or declined further, or symptomatic cardiac failure has developed, trastuzumab should be discontinued, unless the benefits for the individual patient are deemed to outweigh the risks. All such patients should be referred for assessment by a cardiologist and followed up.

If symptomatic cardiac failure develops during trastuzumab therapy, it should be treated with standard medicinal products for CHF such as an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) and a beta-blocker. Trastuzumab may be continued at the discretion of the consultant.

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.

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. CG80. Accessed 29 August 2018 via www.nice.org.uk
- National Institute for Health and Clinical Excellence. CG81. Accessed 29 August 2018 via www.nice.org.uk
- Summary of Product Characteristics. Trastuzumab IV injection (Roche) accessed 29 August 2018 via www.emc.medicines.org.uk
- Summary of Product Characteristics. Trastuzumab SC injection (Roche) accessed 29 August 2018 via www.emc.medicines.org.uk

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