Trastuzumab - Herceptin® (upper GI)

Indication

HER2-positive (IHC3+ or IHC2+ with confirmatory FISH) metastatic adenocarcinoma of the stomach or gastro-oesophageal junction in patients who have not received prior treatment for their metastatic disease.
To be administered in combination with platinum and either capecitabine or 5FU chemotherapy.

(NICE TA208)

ICD-10 codes

Codes prefixed with C16

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.

Cycle frequency

21 days

Number of cycles

Until disease progression.

Administration

Trastuzumab and the cisplatin-based chemotherapy may be given on the same day.

Facilities for the treatment of hypotension and bronchospasm must be available.

Cycle 1:
Trastuzumab should be given prior to starting the cisplatin pre-hydration.
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 reaction (e.g. fever, chills).

Cycle 2 onwards, (providing trastuzumab well tolerated):
Trastuzumab can be given after the cisplatin pre-hydration but before the mannitol. Trastuzumab is administered in 250mL sodium chloride 0.9% and may be given over 30 minutes. The patient should be observed for 2 hours after the start of the infusion.

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.

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** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
Echocardiogram	Baseline
Weight	Baseline

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	Only if clinically indicated
U+E (including creatinine)	Only if clinically indicated
LFT	Only if clinically indicated
Echocardiogram	3 – 4 monthly reducing to 6 monthly if stable (more frequently if patient developing asymptomatic cardiac dysfunction)
Weight	3 monthly

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**

Full blood counts should be monitored during chemotherapy however patients may continue trastuzumab therapy during periods of reversible, 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

- Bang YJ, Van Cutsem E, Feyereislova A, Chung HC, Shen L, Sawaki A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010; 376 (9742): 687 – 697.
- National Institute for Health and Clinical Excellence. TA208. Accessed 25 June 2014 via www.nice.org.uk
- Summary of Product Characteristics. Trastuzumab (Roche) accessed 25 June 2014 via www.emc.medicines.org.uk/

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