Trastuzumab (IV) Monotherapy - 7 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of patients with HER2 positive metastatic breast cancer (MBC)	C50	00201a	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

MBC: Treatment administered every 7 days unless unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when trastuzumab is administered.

Cycle 1 For **NEW** patients **ONLY**.
Omit for patients continuing single-agent trastuzumab following a trastuzumab containing chemotherapy regimen

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Trastuzumab	4mg/kg	IV infusion Observe post infusion*	250ml 0.9% sodium chloride** over 90min	1

Cycle 2 and subsequent cycles or for patients who have just completed a trastuzumab containing chemotherapy regimen

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Trastuzumab	2mg/kg	IV infusion Observe post infusion*	250ml 0.9% sodium chloride over 30min	2 and further cycles

*****Recommended Observation period: Patients should be observed for at least six hours after the start of the first infusion and for two hours after the start of the subsequent infusions for symptoms like fever and chills or other infusion-related symptoms. Any deviation should be noted in local policies.

** Trastuzumab is incompatible with glucose solution

ELIGIBILTY:

- Indications as above
- HER2 overexpression or HER2 gene amplification as determined by an accurate and validated assay
- ECOG status 0-3

EXCLUSIONS:

- Clinically significant cardiac disease (history of symptomatic ventricular arrhythmias, congestive heart failure or myocardial infarction within previous 12 months).

- Hypersensitivity to trastuzumab or any of the excipients.
- Patients experiencing dyspnoea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of a fatal infusion reaction.

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC
- Cardiac function (LVEF using ECHO or MUGA scan)

Regular tests:

- FBC every 6 weeks.
- Cardiac function, liver profile, creatinine every 12 weeks. Where there are signs of cardiac impairment four to eight weekly checks may be more appropriate

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- None usually recommended. Discontinue if unacceptable toxicity occurs
- Weight monitored at each visit and dose adjusted accordingly
- If the patient misses a dose of trastuzumab by one week or less, then the usual maintenance dose of 2 mg/kg should be given as soon as possible. Do not wait until the next planned cycle. Subsequent maintenance doses should then be given according to the previous schedule.
- If the patient misses a dose of trastuzumab by more than one week, a re-loading dose of trastuzumab (4 mg/kg) should be given over approximately 90 minutes, at the discretion of the clinician. Subsequent trastuzumab maintenance doses (2 mg/kg) should then be given weekly from that point.

Renal and Hepatic Impairment:

Table 1: Dose modification of trastuzumab in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No dedicated studies of trastuzumab in patients with renal impairment have been conducted. Based on a population pharmacokinetic (PK) analysis renal impairment was not shown to affect trastuzumab disposition.	No dedicated studies of trastuzumab in patients with hepatic impairment have been conducted. Probably no dose reduction necessary.

Management of adverse events:

Table 2: Dose Modification of trastuzumab for Adverse Events

Adverse reactions	Recommended dose modification
LVEF drops 10 ejection fraction points from baseline and to below 50%	Withhold treatment. Repeat LVEF after 3 weeks. No improvement or further decline, consider discontinuation. Discuss with consultant and refer to cardiologist.
Symptomatic heart failure	Discontinue
NCI-CTCAE Grade 4 hypersensitivity reactions	Discontinue
Haematological	Treatment may continue during periods of reversible, chemotherapy-induced myelosuppression. Monitor carefully for any complications of neutropenia.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal **(Refer to local policy).**

PREMEDICATIONS:
Not usually required unless the patient has had a previous hypersensitivity.
Paracetamol and antihistamine cover should be considered.
Patient should be educated about the possibility of delayed infusion-related symptoms

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Cardiac toxicity**:
  - Trastuzumab has been associated with moderate to severe cardiac failure. Baseline and 3 monthly cardiac function tests are required during treatment especially for those with prior anthracycline exposure.
  - If LVEF drops by greater than or equal to 10 ejection fraction (EF) points from baseline AND to below 50 %, treatment should be withheld and a repeat LVEF assessment carried out within approximately 3 weeks. If LVEF has not improved, or declined further, discontinuation of trastuzumab should be strongly considered, 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.
  - Trastuzumab and anthracyclines should not be given concurrently in combination due to cardiotoxicity risk.
  - The half-life of trastuzumab is approximately 4-5 weeks.
- **Trastuzumab infusion-associated symptoms**, usually chills and fever may occur. Stop infusion and consider antihistamine cover. When symptoms have resolved the infusion may be recommenced. For serious reactions, discontinue the trastuzumab infusion and provide supportive therapy such as oxygen, beta-agonists and corticosteroids.
- **Pulmonary events:** Severe pulmonary adverse reactions occur in association with the use of trastuzumab and have been associated with a fatal outcome. These events may occur as part of an infusion-related reaction or with a delayed onset. Caution should be exercised for pneumonitis, especially in patients being treated concomitantly with taxanes.

DRUG INTERACTIONS:

- A possible interaction with warfarin has been reported. An increased INR and bleeding may occur in patients previously stabilized on warfarin. The interaction was noted in two patients after 8-10 doses of trastuzumab. An INR prior to starting the trastuzumab is recommended, then every 2 weeks for the first 3 months and then monthly if stable. Inform patient to watch for any bleeding. Modification of the warfarin dose may be needed (1).
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Trastuzumab - L01XC03

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3. Lee, R., D. Incekot, P. Ng.. Rapid 30 minute infusion of trastuzumab 6mg/kg every 3 weeks: cost effective and safe. J Oncol Pharmacy Practice 2006 ; 12(1):22
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6. Perez, E. A., V. J. Suman, N. E. Davidson, et al.. Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial. J Clin Oncol 2008; 26:1231-1238.
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8. Trastuzumab (Herceptin®) Summary of Product Characteristics. Last updated: 14/10/2019. Accessed January

2020 Available at: https://www.ema.europa.eu/en/documents/product-information/herceptin-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	10/02/2014		Dr Maccon Keane
2	10/02/2016	Added Disease Monitoring	Dr Maccon Keane
3	07/02/2018	Updated infusion time recommendations and emetogenic potential. Clarification of dosing in renal and hepatic impairment. Formatting in new NCCP Regimen Template	Prof Maccon Keane
4	15/01/2020	Reviewed	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.