National Essential Medicine List Review Process
Component: Oncology

Medication names: Trastuzumab **Date of review:** 24 February 2016

Indication: Adjuvant treatment for early stage HER-2 positive breast cancer

Introduction:
Trastuzumab is a recombinant humanised IgG1 monoclonal antibody specifically targeting the extracellular domain of HER2.[1] As a result, trastuzumab has been shown to inhibit the proliferation of human tumour cells that over express HER2.

Efficacy and safety:
The evidence presented suggests that trastuzumab-containing regimens improves disease-free survival and overall survival in women with HER2-positive breast cancer, but increases risk of cardiac toxicities, such as LVEF decline and congestive cardiac failure. Although a treatment course over 6 months was shown to have less cardiac toxicity than a 12-month course, it is non-inferior with regards to efficacy.[2] Concurrent (rather than sequential) adjunctive therapy with trastuzumab also appears to be more efficacious.[3] The results confirm that 1 year of adjuvant trastuzumab remains the standard of care for HER2-positive early breast cancer patients. The significant improvement in disease free survival and overall survival persists over time and the incidence of cardiac endpoints remains low at a median follow-up of 8 years.[4, 5, 6]

Cost
The price option evaluated was:

R6622,69/vial

At the vial price of R6 622,69, the budget impact is the region of R31 million for the first year.

Dosing of trastuzumab for HER2-positive using the 3-weekly schedule: [7]

Initial loading dose:	8 mg/kg body weight	**Route:**	Intravenous infusion over approximately 90 minutes.
Maintenance dose:	6 mg/kg body weight		
Frequency:	3 weekly	**Duration:**	12 months (total of 18 doses)

Recommendation
Using the information from the National Essential Medicines List Committee (NEMLC) and the Pharmacoeconomic Evaluation Unit.
The National Health Council (April 2017) recommended that Trastuzumab be made available for the adjuvant management of early stage breast cancer administered 3-weekly for a period of 12 months.

[1] Garnock-Jones KP, et.al. Trastuzumab A Review of its Use as Adjuvant Treatment in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Early Breast Cancer. Drugs 2010;70(2);215-239.
[2] Pivot X, et.al. 6 months versus 12 months of adjuvant trastuzumab for patients with HER2-positive early breast cancer (PHARE): a randomised phase 3 trial. Lancet Oncology;2013:14:741-48.
[3] Perez EA, et.al. Sequential versus concurrent trastuzumab in adjuvant chemotherapy for breast cancer. Journal of Clinical Oncology;2011:29(34):4491-97.
[4] Goldhirsh A, et.al. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomized controlled trial. Lancet;2013:382:1021-28.
[5] Gianni L, et.al R. Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: a 4-year follow-up of a randomized controlled trial. Lancet Oncology;2011(12)236-44.
[6] Piccart-Gebhart, et. al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. NEJM 2005 10/20;353(16):1659-1672.
[7] Roche Products (Pty) Limited: HERCLON Range (460866/7 Regd). Approved Package Insert. 7 December 2012.