The European Agency for the Evaluation of Medicinal Products
Post-Authorisation Evaluation of Medicines for Human Use

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EMEA PUBLIC STATEMENT ON TRASTUZUMAB (HERCEPTIN) - NEW PHARMACOKINETIC DATA -

The EMEA has been made aware of new information about the pharmacokinetics of Herceptin (trastuzumab) and would like to advise you that **the use of anthracyclines *after* stopping Herceptin *may* carry a higher risk of cardiac toxicity.**

Trastuzumab is is a humanised monoclonal antibody that binds to a transmembrane protein related to the epidermal growth factor receptor (HER2). It has been shown to inhibit the proliferation of human tumour cells that overexpress HER2. Within the European Union, a marketing authorisation was issued in August 2000 for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2. It is used either as monotherapy for the treatment of those patients who have received at least two chemotherapy regimens or in combination with paclitaxel for the treatment of those patients who have not received chemotherapy for their metastatic disease and for whom an anthracycline is not suitable. The Marketing Authorisation Holder for Herceptin is Roche Registration Ltd, UK.

It is already known that, when used in combination, Herceptin and anthracyclines are associated with an increased risk of cardiotoxicity, as mentioned in the Summary of Product Characteristics for Herceptin http://www.eudra.org/humandocs/humans/epar/herceptin/herceptin.htm (section 4.4 and 4.8). Recently, preliminary information has become available from an ongoing clinical study indicating that **the half-life[1] of Herceptin is longer than earlier studies first suggested.** The half-life is now estimated to be approximately 25 days, rather than 5-6 days. **Thus, Herceptin may persist in the circulation for up to 18 weeks (range 15-22 weeks) after stopping Herceptin treatment.**

- **Therefore, the use of anthracyclines *after* stopping Herceptin *may* carry a higher risk of cardiac toxicity.**
- **If possible, anthracycline based therapy should be avoided for up to 22 weeks after stopping Herceptin therapy.**
- **If anthracyclines need to be used, the patient's cardiac function should be monitored carefully.**

Physicians should continue to prescribe Herceptin at the dose and with the schedule recommended in the currently approved prescribing information (4mg/kg loading dose followed by 2mg/kg weekly) to ensure that patients receive adequate Herceptin.
The EMEA thought it necessary to provide this new information to the public. Furthermore, the MAH has brought it to the attention of prescribing physicians. Following the evaluation of the new data, the complete revised product information will be made available in the updated European Public Assessment Report of Herceptin published on the EMEA website.

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[1] The half- life is the time required for the elimination of 50% of a medicinal product from the blood plasma