27 March 2017

HERCEPTIN® (trastuzumab): Reminder of importance of cardiac monitoring guidance during trastuzumab therapy to reduce the frequency and severity of left ventricular dysfunction and congestive heart failure (CHF).

Dear Healthcare Provider,

Roche Products Ltd. in agreement with the European Medicines Agency (EMA) and the Maltese Medicines Authority would like to highlight the importance of the information available in the Herceptin (trastuzumab) EU Summary of Product Characteristics (SmPC) with respect to cardiac monitoring.

Summary
The objective of this DHPC is to highlight the importance of the trastuzumab cardiac monitoring information and treatment algorithm as stated in the Herceptin (trastuzumab) EU SmPC, in order to ensure appropriate management of left ventricular dysfunction and congestive heart failure (CHF).

Key messages for prescribing oncologists are highlighted below:

- Cardiac assessments, as performed at baseline, should be repeated every 3 months during trastuzumab treatment.
- Please adhere to the stopping rules as detailed in the Herceptin (trastuzumab) EU SmPC Section 4.2: Posology and method of administration, including cases when LVEF percentage drops ≥ 10 percent points from baseline AND to below 50%, trastuzumab treatment should be suspended and a repeat left ventricular ejection fraction (LVEF) assessment performed within approximately 3 weeks.
- Trastuzumab and anthracyclines should not be given concurrently in combination in the metastatic breast cancer (MBC) setting and in the adjuvant breast cancer treatment setting. Refer to Herceptin EU SmPC Section 4.4: Special warnings and precautions for use.
- Continue monitoring every 6 months following discontinuation of trastuzumab treatment until 24 months from the last administration of trastuzumab. In patients who receive anthracycline-

containing chemotherapy, further monitoring is recommended, and should occur yearly up to 5 years from the last administration of trastuzumab, or longer if a continuous decrease of LVEF is observed.

- If symptomatic cardiac failure develops during trastuzumab therapy, it should be treated with standard medicinal products for CHF. Most patients who developed CHF or asymptomatic cardiac dysfunction in pivotal trials improved with standard CHF treatment consisting of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) and a beta-blocker.
- LVEF measurement continues to be the required method to monitor cardiac function; biomarkers may be a supportive tool for patients specifically at risk to experience CHF but cannot replace LVEF assessment by echocardiogram (ECHO) or multiple gated acquisition (MUGA) scan.
- Prescribing physicians should highlight to other physicians responsible for the follow-up of a trastuzumab treatment patient that it is important to continue regular cardiac monitoring as per the Herceptin (trastuzumab) EU SmPC.

Background for this Cardiac Monitoring Reminder

Although there are no new cardiac safety risk signals with trastuzumab therapy, results from surveys have shown that adherence to cardiac monitoring could be improved to reduce the frequency and severity of left ventricular dysfunction and CHF in patients treated with trastuzumab therapy.
Cardiac risk of trastuzumab therapy has been shown to be reversible in some patients upon discontinuation of trastuzumab treatment, underscoring the importance of monitoring LVEF function of patients during trastuzumab treatment and after trastuzumab treatment discontinuation.

Therapeutic Indications

As per the currently approved Herceptin (trastuzumab) EU SmPC, Herceptin should only be used in patients with metastatic or early breast cancer and metastatic gastric cancer whose tumours have either human epidermal growth factor receptor-2 (HER2) overexpression or HER2 gene amplification as determined by an accurate and validated assay.

Reporting adverse events

Roche Product Ltd. would like to remind physicians about the importance of reporting suspected adverse reactions following the use of Herceptin (trastuzumab), in order to facilitate continuous monitoring of the benefit/risk balance of the product. Healthcare professionals are asked to report any suspected adverse reactions via the national spontaneous reporting system

Reporting forms and information can be found at www.medicinesauthority.gov.mt/adrportal and sent to postlicensing.medicinesauthority@gov.mt or sent to Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000, Malta.

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Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44 (0)1707 367554.

Further Information

Should you have any questions regarding the use of Herceptin (trastuzumab), or if you would like to request a copy of the SmPC, please feel free to contact Roche Medical Information **(Tel: +44(0)800 328 1629 or email: medinfo.uk@roche.com)**.

The SmPC for Herceptin is available at www.medicines.org.uk.

Yours faithfully,

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