17 May 2019

Lapatinib (Tyverb): important update to Summary of Product Characteristics

Dear Healthcare Professional,

On behalf of Novartis Pharma Services AG please find below official communication:

Novartis Europharm Ltd. in agreement with the European Medicines Agency would like to inform you of the following:

Summary

- The therapeutic indication (section 4.1 lapatinib Summary of Product Characteristics) has been amended to reinstate the information that **there is no data on the efficacy of lapatinib relative to trastuzumab, both used in combination with an aromatase inhibitor, in postmenopausal women with hormone receptor positive metastatic disease previously treated with trastuzumab or an aromatase inhibitor.**

- Corresponding information that relates to the results of Study EGF114299, has been deleted from section 5.1 of the SmPC.

- These changes are due to the detection of errors in the efficacy results of Study EGF114299. This study evaluated the efficacy and safety of lapatinib in combination with an aromatase inhibitor in postmenopausal women who had HR+/HER2+ metastatic breast cancer which had progressed after prior trastuzumab-containing chemotherapy regimen and endocrine therapies.

- **For patients who are currently receiving lapatinib in combination with an aromatase inhibitor, who have previously progressed on trastuzumab containing therapy, a decision on continuation of therapy should be made on a case-by-case basis.**

Background

Currently, lapatinib (Tyverb) is indicated for the treatment of adult patients with breast cancer, whose tumours overexpress HER2 (ErbB2):

- in combination with capecitabine for patients with advanced or metastatic disease with progression following prior therapy, which must have included anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting.

- in combination with trastuzumab for patients with hormone receptor-negative metastatic disease that has progressed on prior trastuzumab therapy(ies) in combination with chemotherapy.

- in combination with an aromatase inhibitor for postmenopausal women with hormone receptor positive metastatic disease, not currently intended for chemotherapy.

Following the granting of the initial marketing authorization, study EGF114299 was conducted to fulfill a post-approval commitment to evaluate the efficacy and safety of Tyverb in combination with an aromatase inhibitor in postmenopausal women who had hormone receptor-positive/ HER2-positive metastatic breast cancer which had progressed after prior trastuzumab-containing chemotherapy regimen and who had previously received endocrine therapy. Results were reflected in SmPC section 5.1 Pharmacodynamic Properties. The indication statement was also amended at that time, to remove the statement that no data are available on relative efficacy versus trastuzumab-based combination therapy in such a population.

Programming errors were identified in study EGF114299 primarily affecting the comparison between lapatinib + aromatase inhibitor and trastuzumab + aromatase inhibitor, erroneously suggesting a

relative benefit of lapatinib over trastuzumab. In order to address this and in agreement with EMA, the results of study EGF114299 have been removed from section 5.1 of the SmPC and the statement relating to lack of availability of comparative efficacy data has been reinstated in the Indication. An assessment of the corrected data is ongoing at this time.

For patients who have previously progressed on trastuzumab who are receiving lapatinib in combination with an aromatase inhibitor currently, an evaluation of benefit-risk and a decision on continuation of therapy should be made on a case-by-case basis.

There are no additional safety concerns related to use of lapatinib-based regimens.

Call for reporting

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system and company contact points.

Company contact points

Asteria Ltd, located at apt. 24, 28, T. Mets Str., Yerevan, phone: +374 105 19 070, e-mail: drugsafety.cis@novartis.com.

You may also to contact to Scientific Centre of Drug and Medical technology Expertise CJSC via following contacts: address: 49/4 Komitas av., 0051 Yerevan, Armenia, phone: +37410231682 (ext: 123), Hot line for ADR reporting: + 37410200505/ email: vigilance@pharm.am