Roche Products (Ireland) Limited
3004 Lake Drive
Citywest Business Park
Naas Road
Dublin 24

FALSIFIED PRODUCTS LABELLED AS HERCEPTIN® (trastuzumab)

Vial containing 150mg powder for concentrate for solution for infusion

Batch numbers:

H4105B01, H4136B02, H4196B01, H4143B01, H4150B01, H4152B04, H4171B01, H4168B02, H4169B01, H4179B02, H4180B01, H4184B01, H4185B02, H4194B01, H4195B01, H4261B01, H4263B02, H4271B01, H4279B01, H4284B04, H4293B01, H4303B01, H4301B09, H4311B07, H4319B02, H4324B03, H4329B01, N1001B01, N1002B02, N1002B03, N1010B02

07 May 2014

Dear Healthcare Professional,

Roche Products (Ireland) Limited (hereafter referred to as Roche) in agreement with the Irish Medicines Board (IMB) and the European Medicines Agency (EMA) would like to inform you of the following:

Summary

- Falsified products originally labelled as Italian Herceptin 150 mg vials have been found in UK wholesale dealers for onward distribution outside of the UK and in Finland, Germany, Austria and Sweden. The original Italian label and outer package may have been replaced by labels and packaging in the local language.
- The suspect vials and original outer packaging feature genuine Roche batch numbers but numbers on the vials and outer packaging may not match. In addition, some vials may contain liquid rather than powder, or closures may show physical signs of tampering.
- The falsified products must not be used; they can be considered neither safe nor effective.
- If you have any product in your possession that you suspect may be falsified, or whose authenticity you cannot confirm, or if you suspect a patient may have received falsified drug, you should immediately contact the IMB
- Although only a small number of vials are thought to be affected, the IMB, is recalling vials labelled in Italy and distributed outside Italy, featuring the batch numbers listed
- It is not expected that this will result in a shortage of the medicine for patients.

Background information

Roche has recently been informed that confirmed falsified products, labelled as Herceptin 150 mg/vial (trastuzumab), were found in Germany. Further suspect vials have been identified in the UK (for onward distribution in other countries), Finland, Austria and Sweden. The falsified products use the same batch numbers as the genuine Roche Herceptin batches. According to current information, a German parallel importer bought the suspect products from two wholesalers in the UK, with Italian wholesalers as origin. In Italy, Roche supplies the product only to hospital pharmacies, in accordance with local legislation. The Italian wholesalers were not supplied by Roche Italy.

Chemical analysis confirmed that at least one of the falsified products does NOT contain trastuzumab (lyophilisate), the active ingredient of Herceptin, but the cephalosporin antibiotic **ceftriaxone** (lyophilisate).

Other vials contain a **liquid** instead of the white to pale yellow lyophilised powder and evidence of **tampering** was observed (see examples below). The composition of this liquid has not yet been characterised in all cases, but may contain diluted trastuzumab.
For all falsified products it has to be assumed that they are **not sterile**, even if they seem to be intact.

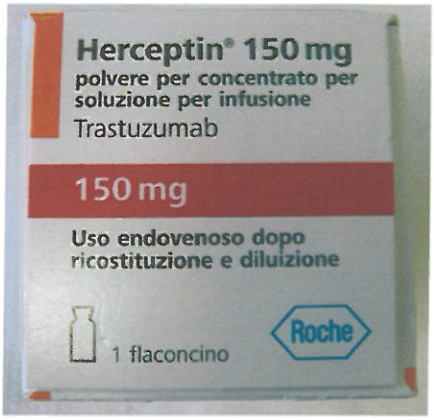
The falsified products must not be used; they can be considered neither safe nor effective.

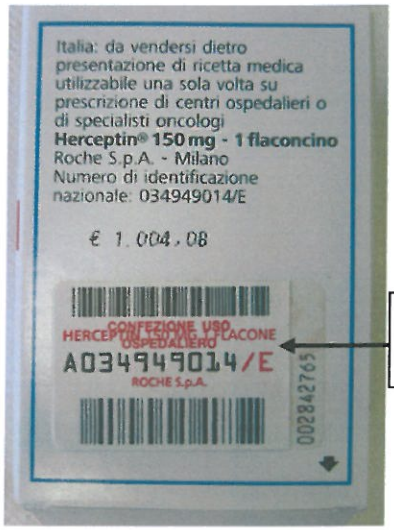
Visual Inspection

The falsified product may or may not look similar to authentic Herceptin.
The falsified products identified to date have been differentiated from genuine Herceptin based on some combination of the following features:

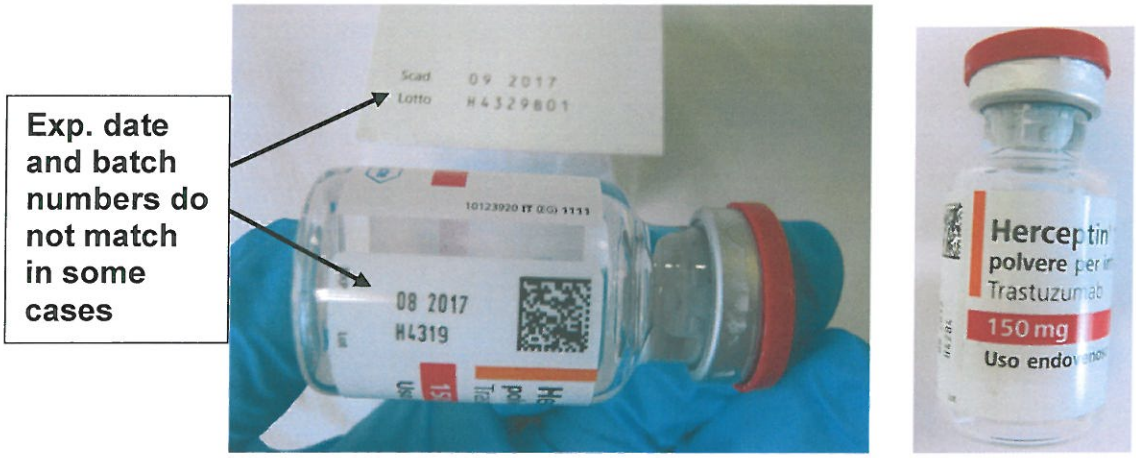
- Vial labels and carton labels printed in Italian. (Distributors may have subsequently relabelled and repackaged in the local language.)
- Batch numbers listed above
- Batch numbers and expiry date on the vial in some cases do not match those on the carton
- Presence of the "bollini-sticker" (see below) which is specific for material shipped to Italy.
- Signs that the cap was manipulated (cap not seated properly or indented).
- Liquid is present in the vial (Herceptin 150 mg powder for concentrate for solution for infusion is a white to pale yellow lyophilised powder).
- The stopper has already been punctured.

Samples of Falsified Carton:





Samples of Falsified Vials:



Possible risks for patients

- The falsified products cannot be considered effective. The treatment of the patient for HER2-positive breast or gastric cancer may be seriously impacted or delayed (e.g. if one full cycle of effective treatment is missed).
- If ceftriaxone is administered instead of trastuzumab the patient may experience the adverse effects associated with the antibiotic, as listed in the respective product information.
- Lack of sterility may lead to infection, with a risk of severe disease in immunocompromised cancer patients.
- Other adverse effects may be possible from a liquid of unknown composition.

Required Actions

If you have any product in your possession that you suspect may be falsified, or whose authenticity you cannot confirm, or if you suspect a patient may have received falsified drug, you should immediately contact the IMB. In addition, you should contact Roche's Product Quality Assurance Department at Roche Products Limited by e-mailing global.welwyn_complaints@roche.com. Please retain the suspected falsified product for further investigations.

If you are aware of a patient experiencing any adverse effects that you think may be related to Herceptin or to the use of ceftriaxone or that are different from those commonly associated with Herceptin, including lack of effect, please immediately call Roche's Drug Surveillance Centre at (01) 4690700 (please see below for alternative contact details). Alternatively, suspected adverse reactions should be reported to the Irish Medicines Board (IMB) using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie. Adverse reactions can also be reported to the IMB by calling (01) 6764971.

Roche is cooperating with the appropriate Health Authorities and law enforcement agencies to aid their investigations, to determine the source of the falsified drug, and prevent its further distribution. However, the company has no official power to intervene directly and will not assume liability for damage claims related to falsified products. We have implemented technical anti-falsifying measures relating to the design, packaging and labelling of our products, along with working with authorities on a system to track and trace products from distribution to dispensary.

We strongly recommend purchasing Herceptin exclusively through trusted sources for use in approved indications.

Yours sincerely,

Dr. Maria Luz Amador
Medical Director

For additional information, please see the following:

WHO's International Medical Products Anti-Counterfeiting Taskforce (IMPACT)
Via internet reporting: http://www.who.int/impact/en/

Roche Complaint Management: global.welwyn_complaints@roche.com

Roche Drug Surveillance Centre: Phone (01) 4690700, fax (01) 4690793 or email (ireland.drug_surveillance_centre@roche.com).