July 01, 2020

Direct Healthcare Professional Communication

HERCEPTIN (trastuzumab): HERCEPTIN SOLVENT VIALS /20 ML co-packaged with Herceptin 440 mg – Recommended use of filter during infusion

Dear Healthcare professional,

F. Hoffmann-La Roche S.A. (Roche) would like to inform you of the following:

Summary

During a recent inspection of approximately 1000 retained samples of HERCEPTIN SOLVENT VIALS /20 ML which are co-packaged with Herceptin 440 mg, Roche observed shiny flake-like shaped particles in 7 solvent vials. A total of 6 batches of HERCEPTIN SOLVENT VIALS /20 ML are impacted while Herceptin 440 mg vials are not impacted. The size of the particles ranges from 160 µm to 1.3 mm. This size range includes particulates which may not be visible to the naked eye since they are below 200 µm. Furthermore, such small particles would likely pass through the needle when the product is being prepared or during administration.

If particles reach the circulation following intravenous infusion, there could be a risk of foreign particle embolism and of direct injury to the intimal lining of the blood vasculature and loss of integrity of the vascular wall.

The following batch of solvent vial potentially impacted sent to your country: B3128.

Herceptin 440 mg batch N3928B03 was co-packaged with solvent vial Batch B3128.

Note: The Herceptin 440 mg vial itself co-packaged with the above-mentioned solvent batches is NOT impacted.

Recommendations for risk minimisation

The presence of glass particulate matter in few batches of HERCEPTIN SOLVENT VIALS may potentially present a safety concern. In such case, clinical complications may include events occurring around parenteral administration, for example, as a result of mechanical pulmonary artery obstruction and local injection site reaction in case of larger particulate matter. Intravenous infusion of particles larger than the internal diameter of capillaries may increase the risk of foreign particle embolism.

The MAH recommends continuous Herceptin treatment, as if therapy is delayed, this will put the patients at risk due to lack of efficacy potentially leading to disease progression and ultimately death.

The following risk mitigation measures are suggested to prevent treatment delay:

Instructions to healthcare professionals (HCPs):

1. Check the batch number of the solvent vial co-packaged with your Herceptin 440 mg
2. If your solvent vial shows one of the batch numbers mentioned above, please inspect the vial for visible particles.
3. If you detect visible particles, discard the vial.
4. If no particles are visible in your solvent vial, follow these steps:
    a. , Reconstitute the Herceptin 440 mg vial using the co-packaged solvent vial and add the required amount of reconstituted Herceptin to the infusion bag as usual,
    b. At the time of administration, use a 0.2 micron in-line or add on filter made of polyethersulfone (PES) for the infusion.
5. Alternatively,
    a. if the solvent vial had to be discarded (as mentioned above) reconstitute Herceptin 440mg with commercially available sterile water for injection.
    --OR--
    b. if no filter is available for use during infusion, discard the co-packaged solvent vial and reconstitute Herceptin 440 mg with commercially available sterile water for injection and proceed with addition to infusion bag as usual.
6. Note that in case Herceptin is reconstituted with sterile water for injection, only one dose per Herceptin vial should be used. The reconstituted solution should be used immediately. Any unused portion must be discarded.

For markets where Herceptin 440mg is not available the use of the Herceptin 150mg single dose vials, as an alternative may be considered, if approved in the affected country and if global supply permits. For markets where Herceptin 150mg single dose vials is not available, quality-assured biosimilars if available and approved, as an alternative option may be considered in order not to put the patient at risk of lack of efficacy.

- The MAH recommends the use of an in-line or add-on filter during the infusion as described above to avoid the risk of glass particles entering into blood circulation.

Background on the safety concern

Herceptin® is a recombinant, humanized, anti-p185HER2 monoclonal antibody that binds specifically and with high affinity to the extracellular
domain (ECD) of the human epidermal growth factor receptor 2 (HER2), indicated for the treatment of breast cancer (IV / SC) and advanced gastric cancer (IV only).

Quarterly trending analysis performed as a routine PV activity for Herceptin showed no increase in clinically relevant adverse reactions related to the increased risk as described since the end of December 2019; compared to previous periods.

Overall the risk of occurrence of clinically relevant adverse reactions is deemed low, as larger visible particles would be identified during the visual inspection of the vials, while smaller non-visible particles, which could potentially cause clinically relevant risk, with the administration of impacted product can be prevented with the use of an inline filter during the infusion as described above.

Call for reporting

Healthcare professionals should report any adverse events suspected to be associated with the use of Herceptin® according to national reporting requirements. Also, Healthcare professionals should report any adverse events suspected to be associated with the use of Herceptin® (trastuzumab) at: cac.farmacovigilancia@roche.com

Company contact point

Should you have any questions about the information in this letter or the safe and effective use of HERCEPTIN, please feel free to contact us at: cac.medical_info@roche.com

Yours sincerely,

Local Safety Responsible
Roche Servicios S.A.

Medical Director
Roche Servicios S.A.