July 14, 2014

Dear Health Care Provider:

In agreement with the European Medicines Agency (EMA) and the Medicines Authority we would like to inform you of two recent complaints that were received from customers relating to cracked/broken Velcade 3.5 mg vials.

One complaint was received from Germany while another was received from the USA. Upon further inspection during our internal secondary packaging process, prior to release of product to the market, four additional broken/cracked vials were detected.

While no cracked vials have been identified in Malta so far, the purpose of this letter is to provide information on the potential risk to the patients and personnel handling of cracked/broken Velcade during dispensing and preparation of the product. We appreciate your assistance and advise you to follow the instructions described below:

In Summary

Given the potential risk to patient, the Company recommends that you take the following actions when dispensing/preparing Velcade injection:

- **Thoroughly inspect the vial for any crack or other damages**
- **If you discover a broken/compromised vial, do not use it for patient administration**
- **Always wear protective gloves/ eye protection/ face protection and personal protective equipment**
- **If swallowed accidentally, immediately call a poison center or a physician, as this may potentially result in a fatal outcome**

In case of skin accidental exposure, take off contaminated clothing and shoes immediately and wash off with soap and water. In case of eyes accidental exposure, rinse them with water for 15 minutes. In either case, call a physician immediately.

Further information on this concern:

A detailed investigation covering the entire supply chain has been performed. No abnormalities or malfunctioning was observed which could result into cracked or broken vials. No systemic root cause has been identified which could explain the found cracks. As well, a review of the Company's adverse event surveillance system did not reveal any previous case of cracked/broken vials and did not indicate any evidence of changes in the safety profile of Velcade as a result of these cracked/broken vial incidents.

Velcade (bortezomib) is indicated for the treatment of adults affected by multiple myeloma as single agent or in combination with other chemotherapeutic regimens.

Velcade exists as 1 mg and 3.5 mg powder for solution for injection; upon reconstitution, 1 mg vial is administered intravenously while 3.5 mg vial can be administered both intravenously and subcutaneously.

In addition healthcare professionals are reminded of the following;

Failure of sterility:

A cracked vial may affect the integrity of the vial leading to loss of sterility. Infusion of the non-sterile injection can lead to an increased chance of potential infections, which could be life threatening.

Glass particulate in the vial:

Cracked or broken Velcade vials may also result in glass particulates in the vial that could potentially lead to the occurrence of thromboembolic events, which could be life threatening.

Accidental exposure:

A broken vial can easily be detected and discarded. Broken vials may lead to accidental exposure of the drug to personnel handling the vials. Bortezomib is a cytotoxic agent. This accidental exposure may result in injuries which could be life threatening.

In the event of discovering damaged/compromised vial, please contact AM Mangion Ltd Responsible Person, Mr. Joseph Giglio on +356 23976000. You may be asked to return the damaged vial to AM Mangion Ltd and you will receive credit through your wholeseller.

Call for reporting

Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point

If you have any questions please do not hesitate to contact the Senior Regulatory Affairs Associate in Malta.

Ms. Maria Cuschieri
Tel: +356 2397 6000
Or on pv@ammangion.com.mt

We appreciate your assistance in this matter and apologize for any inconvenience.

Sincerely,

Katerina Papathoma
Medical Affairs Director
Janssen – Cilag Pharmaceutical S.A.C.I