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Direct Healthcare Professional Communication

18 August 2017

Subject: Dacogen 50 mg, powder for concentrate for solution for infusion – Change in the recommendations for diluting reconstituted Dacogen solution

Information to Healthcare Professional,

Janssen-Cilag International N.V. in agreement with the European Medicines Agency (EMA) and the National Malta Medicines Authority would like to inform you of the following:

Summary

- **The reconstituted solution of Dacogen (decitabine) must now be diluted to a final concentration in the range 0.15 to 1.0 mg/ml to comply with the European Pharmacopoeia.**
- **The change slightly narrows the permitted range of the final concentration.**
- **This updated concentration range of Dacogen diluted solution is effective immediately and will be reflected in the package leaflet supplied with Dacogen vials by 23rd August 2017.**

Background on the change

This modification to Dacogen's permitted range of final concentration results from an update of the European Pharmacopoeia (Ph.Eur) Chapter 5.1.10. The revised Ph.Eur chapter reduces the threshold pyrogenic dose of endotoxins per hour for parenteral formulations administered per square meter of body surface area.

Taking into account the potential endotoxin contribution from Dacogen and the reconstitution and infusion fluids, Janssen has narrowed the concentration range of the final product for administration to comply with this recent Ph.Eur revision. Dacogen's quality and safety profile remain unchanged.

The summary of product characteristics (SmPC) and the package leaflet for Dacogen will be updated to reflect the new information. The full instructions for Dacogen reconstitution and dilution are provided in the attachment.

The full reconstitution procedure for Dacogen is now as follows:

The powder should be aseptically reconstituted with 10 ml of water for injections. Upon reconstitution, each ml contains approximately 5 mg of decitabine at pH 6.7 to 7.3. Within 15 minutes of reconstitution, the solution must be further diluted with cold infusion fluids [sodium chloride 9 mg/ml (0.9%) solution for injection or 5% glucose solution for injection] to a final concentration of 0.15 to 1.0 mg/ml.

If you have any questions or need further information, please contact Ms Gaby Ganado on +356 23976000 or gganado@ITS.jnj.com.

Reporting suspected adverse reactions after authorisation 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 ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal.

Yours sincerely,

Nigel Cauchi

Responsible Person

AM Mangion Ltd.

New instructions for Dacogen preparation approved by the EMA:

SmPC Section 6.6 - Special precautions for disposal and other handling

Recommendations for safe handling

Skin contact with the solution should be avoided and protective gloves must be worn. Standard procedures for dealing with cytotoxic medicinal products should be adopted.

Reconstitution procedure

The powder should be aseptically reconstituted with 10 ml of water for injections. Upon reconstitution, each ml contains approximately 5 mg of decitabine at pH 6.7 to 7.3. Within 15 minutes of reconstitution, the solution must be further diluted with cold infusion fluids (sodium chloride 9 mg/ml [0.9%] solution for injection or 5% glucose solution for injection) to a final concentration of **0.15** to 1.0 mg/ml. For the shelf-life and the precaution for storage after reconstitution, see section 6.3.

Dacogen should not be infused through the same intravenous access/line with other medicinal products.

Disposal

This medicinal product is for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

PIL – Information for medical or healthcare professionals

1. RECONSTITUTION

Skin contact with the solution should be avoided and protective gloves must be worn. Standard procedures for dealing with cytotoxic medicinal products should be adopted.

The powder should be aseptically reconstituted with 10 ml of water for injections. Upon reconstitution, each ml contains approximately 5 mg of decitabine at pH 6.7 to 7.3. Within 15 minutes of reconstitution, the solution must be further diluted with cold (2°C - 8°C) infusion fluids (sodium chloride 9 mg/ml [0.9%] solution for injection or 5% glucose solution for injection) to a final concentration of **0.15** to 1.0 mg/ml. For the shelf life and the precautions for storage after reconstitution, see section 5 of the leaflet.

2. ADMINISTRATION

Infuse the reconstituted solution intravenously over 1 hour.

3. DISPOSAL

A vial is for single use only and any remaining solution must be discarded.

Any unused product or waste material should be disposed of in accordance with local requirements.