7th September 2017

Direct Healthcare Professional Communication

DACOGEN® (decitabine) 50 mg, powder for concentrate for solution for infusion – Change in the recommendations for diluting reconstituted Dacogen solution

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and Health Products Regulatory Authority (HPRA), Janssen-Cilag Limited would like to inform you of:

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 March 2018.

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.

Further information

The summary of product characteristics (SmPC) and the package leaflet for Dacogen will be updated to reflect the new information. The new instructions for Dacogen reconstitution and dilution are provided in the attachment (page 3).
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.


Call for reporting

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system.

Suspected adverse reactions should be reported to the Health Products Regulatory Authority, using a Yellow Card obtained either from the HPRA, or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling (01) 676 4971.

When reporting, please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates and product brand name.

Suspected adverse reactions should also be reported to Janssen on tel: 0044 (0)1494 567447, fax: 0044 (0)1494 567799 or by email at dsafety@its.jnj.com

Company contact points

If you have further questions or require additional information, please contact:
Janssen-Cilag Ltd. Medical Information Department:
Email: medinfo@its.jnj.com
Telephone: +353 1 800 709 122

Yours faithfully,

Dr Bríd Seoighe  
Head of Medical Affairs  
Janssen Ireland
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 0.1-0.15 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 0.1-0.15 mg/ml. For the shelf life and the precaution 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.