

7<sup>th</sup> September 2017

**Direct Healthcare Professional Communication**

**DACOGEN<sup>®</sup> (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 the Medicines and Healthcare products Regulatory Agency (MHRA), 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.

The Dacogen Summary of Product Characteristics is available from <http://www.medicines.org.uk/emc/>

### ***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 MHRA through the Yellow Card Scheme: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD" (no other address details necessary)
- by emailing [yellowcard@mhra.gov.uk](mailto:yellowcard@mhra.gov.uk)
- at the back of the British National Formulary (BNF)
- by telephoning the MHRA Yellow Card free phone reporting line: 0800-731-6789
- or by electronic download through the Yellow Card section of the MHRA website

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

Suspected adverse reactions should also be reported to Janssen-Cilag Limited on tel: 01494 567447, fax: 01494 567799 or by email at [dsafety@its.jnj.com](mailto:dsafety@its.jnj.com)

### ***Company contact points***

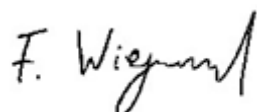
If you have further questions or require additional information, please contact:

Janssen-Cilag Ltd. Medical Information Department:

Email: [medinfo@its.jnj.com](mailto:medinfo@its.jnj.com)

Telephone: 0800 731 8450 or 01494 567 444

Yours faithfully,



Dr Frank Wiegand  
Medical Director UK & Ireland  
Janssen-Cilag 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 ~~0.1~~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 ~~0.1~~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.