Important information regarding
RECONSTITUTION, DOSING
AND ADMINISTRATION
of VELCADE® (bortezomib) 3.5 mg vial for
Subcutaneous (SC) and Intravenous (IV) use

VELCADE®
(bortezomib)

Prescribing Information can be found within this document.
**CORRECT RECONSTITUTION FOR SC AND IV ADMINISTRATION**

VELCADE® (bortezomib) 3.5 mg powder for solution for injection is available for intravenous (IV) or subcutaneous (SC) administration.

**Subcutaneous or Intravenous use only.**

**Do not give by other routes.**

**Intrathecal administration has resulted in death.**

VELCADE® must be reconstituted by a Health Care Professional. Aseptic technique must be strictly observed throughout the handling of VELCADE® since no preservative is present.

**Avoiding the potential risk of administration errors**

In order to avoid dosing errors, caution is required when preparing VELCADE® as the volume required for reconstitution for the SC route is lower (1.4 ml) than that used for IV route (3.5 ml) giving a higher concentration of diluted drug (details are shown in tables 1 and 2).

As the drug concentration after reconstitution differs between the SC and IV preparations, special care is required when calculating the volume of reconstituted drug, which will be delivered to the patient according to the prescribed dose. Please see pages 8-10 for examples of dosing for the different routes.
SUBCUTANEOUS ROUTE OF ADMINISTRATION

Preparation of the 3.5 mg vial

Each 3.5 mg vial of VELCADE® must be reconstituted with 1.4 ml sterile sodium chloride 9 mg/ml (0.9 %) solution for injection – dissolution of the lyophilised powder is completed in less than 2 minutes.

Reconstitute the powder with 1.4 ml sodium chloride: inject the sodium chloride solution into the vial containing the lyophilised VELCADE®.

Reconstitution volume is less than that used for IV giving a more concentrated drug solution for injection.

The reconstituted solution should be clear and colourless.

The reconstituted solution must be inspected visually for particulate matter and discolouration prior to administration. If any discolouration or particulate matter is observed, the reconstituted solution must be discarded.

**The final concentration is 2.5 mg/ml.**

PLEASE NOTE: The final drug concentration, when reconstituted for SC administration (2.5 mg/ml), is 2.5 times higher than that for the IV route (1 mg/ml) and therefore the volume required is lower when the SC route of administration is used.

Once dissolved, withdraw the appropriate amount of the reconstituted drug solution: according to calculated dose based upon the patient’s Body Surface Area (BSA).

**To avoid administration errors, syringes for SC and IV use should be labelled differently.***

* Labels will not be supplied with the product by Janssen.

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**Table 1: Reconstitution of 3.5 mg VELCADE® solution for SC injection**

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Pack size</th>
<th>Reconstitution volume</th>
<th>Final concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous use only</td>
<td>3.5 mg</td>
<td>1.4 ml</td>
<td>2.5 mg/ml</td>
</tr>
</tbody>
</table>

**Visual representation of IV and SC injections following reconstitution**

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INTRAVENOUS ROUTE OF ADMINISTRATION

Preparation of the 3.5 mg vial

Each 3.5 mg vial of VELCADE® must be reconstituted with 3.5 ml sterile sodium chloride 9 mg/ml (0.9%) solution for injection – dissolution of the lyophilised powder is completed in less than 2 minutes.

Reconstitute the powder with 3.5 ml sodium chloride: inject the sodium chloride solution into the vial containing the lyophilised VELCADE®.

Table 2: Reconstitution of 3.5 mg VELCADE® solution for IV injection

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Pack size</th>
<th>Reconstitution volume</th>
<th>Final concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous use</td>
<td>3.5 mg</td>
<td>3.5 ml</td>
<td>1.0 mg/ml</td>
</tr>
</tbody>
</table>

The reconstituted solution should be clear and colourless.

The reconstituted solution must be inspected visually for particulate matter and discolouration prior to administration. If any discolouration or particulate matter is observed, the reconstituted solution must be discarded.

The final concentration is 1.0 mg/ml.

Once dissolved, withdraw the appropriate amount of the reconstituted drug solution: according to calculated dose based upon the patient's Body Surface Area (BSA).

To avoid administration errors, syringes for SC and IV use should be labelled differently.*

* Labels will not be supplied with the product by Janssen.
DOsing EXAMPLEs FOR SC & IV ADMINISTRATION

Calculate the BSA using the Dosing Calculator. Additional examples are provided with the Dosing Calculator.

**BSA: 1.7 m², Dose: 1.3 mg/m²**

**Intravenous**
- Sample patient (1.7 m²)
- Vial size: 3.5 mg lyophilisate
- Diluent volume: 3.5 ml saline
- Final concentration: 1 mg/ml
- Dose: 1.3 mg/m²
- Total dose for patient: 2.21 mg
- Total volume*: 2.2 ml (3-5 seconds push)
- Injected SC

**Subcutaneous**
- Sample patient (1.7 m²)
- Vial size: 3.5 mg lyophilisate
- Diluent volume: 1.4 ml saline
- Final concentration: 2.5 mg/ml
- Dose: 1.3 mg/m²
- Total dose for patient: 2.21 mg
- Total volume*: 0.9 ml (3-5 seconds push)
- Injected SC

*Total volume rounded

**NOTE:** If the calculated IV volume is used with the SC concentration, the patient will be overdosed.

**NOTE:** If the calculated SC volume is used with the IV concentration the patient will be underdosed.

**BSA: 1.95 m², Dose: 1.3 mg/m²**

**Intravenous**
- Sample patient (1.95 m²)
- Vial size: 3.5 mg lyophilisate
- Diluent volume: 3.5 ml saline
- Final concentration: 1 mg/ml
- Dose: 1.3 mg/m²
- Total dose for patient*: 2.54 mg
- Total volume*: 2.5 ml
- Injected IV (3-5 seconds push)

**Subcutaneous**
- Sample patient (1.95 m²)
- Vial size: 3.5 mg lyophilisate
- Diluent volume: 1.4 ml saline
- Final concentration: 2.5 mg/ml
- Dose: 1.3 mg/m²
- Total dose for patient*: 2.54 mg
- Total volume*: 1 ml
- Injected SC

*Total volume rounded

**NOTE:** If the calculated IV volume is used with the SC concentration, the patient will be overdosed.

**NOTE:** If the calculated SC volume is used with the IV concentration the patient will be underdosed.
BSA: 1.6 m², Dose: 1.0 mg/m²

**Intravenous**
Sample patient (1.6 m²)

- **Vial size:** 3.5 mg lyophilisate
- **Diluent volume:** 3.5 ml saline
- **Final concentration** 1 mg/ml
- **Dose:** 1.0 mg/m²
- **Total dose for patient:** 1.6 mg
- **Total volume* applied to the patient:** 1.6 ml
- **Injected IV** (3-5 seconds push)

**Subcutaneous**
Sample patient (1.6 m²)

- **Vial size:** 3.5 mg lyophilisate
- **Diluent volume:** 1.4 ml saline
- **Final concentration** 2.5 mg/ml
- **Dose:** 1.0 mg/m²
- **Total dose for patient:** 1.6 mg
- **Total volume* applied to the patient:** 0.64 ml
- **Injected SC**

*Total volume rounded

**NOTE:** If the calculated IV volume is used with the SC concentration, the patient will be overdosed.

**NOTE:** If the calculated SC volume is used with the IV concentration the patient will be underdosed.

**GENERAL INFORMATION**

**General Precautions**
VELCADE® is a cytotoxic agent. Therefore, caution should be applied when handling and preparing VELCADE®. The use of gloves and other protective clothing to prevent skin contact is recommended.

Please report any adverse event experienced with the administration of VELCADE® immediately.

Subcutaneous or Intravenous use only. Do not give by other routes. Intrathecal administration has resulted in death.

**Shelf life**
3 Years.

**Reconstituted solution**
VELCADE® is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

The reconstituted product is preservative free and should be used immediately after preparation. However, the chemical and physical in-use stability of the reconstituted solution has been demonstrated for 8 hours at 25°C stored in the original vial and / or syringe, with a total storage time for the reconstituted medicinal product not exceeding 8 hours prior to administration. It is not necessary to protect the reconstituted medicinal product from light.
CORRECT ADMINISTRATION FOR SC & IV VELCADE®

How to administer VELCADE® SC?

Confirm the dose in the syringe prior to use (check that the syringe is marked as SC administration).

Inject the solution subcutaneously, at a 45-90 °angle.

The reconstituted solution should be administered subcutaneously in the thighs or abdomen and injection sites should be rotated for successive injections.

- Injections at the same site should be avoided
- Alternate between
  - right and left abdomen (upper or lower quadrant)
  - right and left thigh (proximal and distal sites)

Consider antiviral prophylaxis.

How to administer VELCADE® IV?

Confirm the dose in the syringe prior to use (check that the syringe is marked for IV administration).

Inject the solution as a 3-5 second bolus intravenous injection through a peripheral or central intravenous catheter into a vein.

Flush the peripheral or intravenous catheter with sterile 9 mg/ml (0.9 %) sodium chloride solution.

Consider antiviral prophylaxis.

Please report any adverse event experienced with the administration of VELCADE® IV or SC immediately.

All the information within this booklet is referenced from the Velcade Summary of Product Characteristics (SmPC).