Important information regarding

RECONSTITUTION, DOSING AND ADMINISTRATION

of VELCADE® (bortezomib) 3.5 mg vial for Subcutaneous (SC) and Intravenous (IV) use

VELCADE®
(bortezomib)

VELCADE®
(bortezomib)

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

CORRECT RECONSTITUTION FOR SC AND IV ADMINISTRATION

VELCADE® (bortezomib) 3.5 mg powder for solution for injection is available for intravenous or subcutaneous administration, VELCADE® 1 mg powder for solution for injection is available for intravenous administration only.

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.

Each vial of VELCADE® must be carefully reconstituted by using a 1 ml syringe (VELCADE® 1mg) or by using a syringe of the appropriate size (VELCADE® 3.5mg). without removing the vial stopper.

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 use (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.

VELCADE® (bortezomib)

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

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®.

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

Route of administration	Pack size	Reconstitution volume	Final concentration
Subcutaneous use only	3.5 mg	1.4 ml	2.5 mg/ml

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.

VELCADE® (bortezomib)

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

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

Route of administration	Pack size	Reconstitution volume	Final concentration
Intravenous use	3.5 mg	3.5 ml	1.0 mg/ml

Reconstitution volume is more than that used for SC giving a less 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 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.

VELCADE®
(bortezomib)

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

DOSING EXAMPLES FOR SC & IV ADMINISTRATION

Calculate the BSA using the slide rule. Additional examples are provided with the dosing slide rule.

BSA: 1.7 m², Dose: 1.3 mg/m²

Intravenous Sample patient (1.7 m²)	Subcutaneous Sample patient (1.7 m²)
Vial size: 3.5 mg lyophilisate	**Vial size:** 3.5 mg lyophilisate
Diluent volume: 3.5 ml saline	**Diluent volume:** 1.4 ml saline
Final concentration 1 mg/ml	**Final concentration 2.5 mg/ml**
Dose: 1.3 mg/m²	**Dose:** 1.3 mg/m²
Total dose for patient: **2.21 mg**	**Total dose for patient:** 2.21 mg
Total volume* applied to the patient: 2.2 ml	**Total volume* applied to the patient:** **0.9ml**
Injected IV (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.

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

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

VELCADE®
(bortezomib)

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

BSA: 1.6 m², Dose: 1.0 mg/m²

Intravenous Sample patient (1.6 m²)	Subcutaneous Sample patient (1.6 m²)
Vial size: 3.5 mg lyophilisate	**Vial size:** 3.5 mg lyophilisate
Diluent volume: 3.5 ml saline	**Diluent volume:** 1.4 ml saline
Final concentration 1 mg/ml	**Final concentration 2.5 mg/ml**
Dose: 1.0 mg/m²	**Dose:** 1.0 mg/m²
Total dose for patient: 1.6 mg	**Total dose for patient: 1.6 mg**
Total volume* applied to the patient: 1.6 ml	**Total volume* applied to the patient: 0.64 ml**
Injected IV (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.

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).

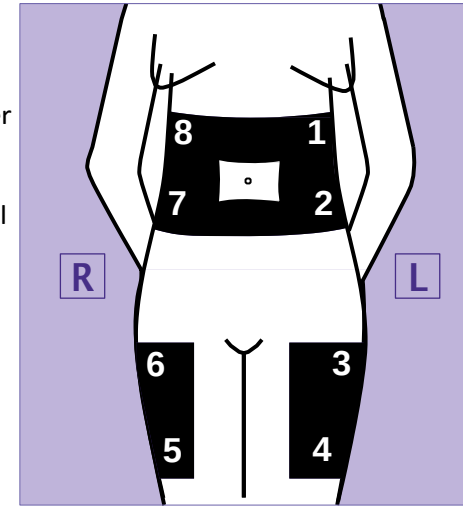
Inject the solution subcutaneously, at a 45-90 °angle.

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)

Remind the patient to take the antiviral prophylaxis.

Figure1. Injection site rotation



Inject the solution as a 3-5 second bolus intravenous injection through a peripheral or central intravenous catheter into a vein. The use of IV hydration and an antiemetic medication as concomitant therapy prior to administration of IV VELCADE® is recommended. Remind the patient to take the antiviral prophylaxis.

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

Please report any adverse event experienced with the administration of VELCADE® immediately. If you have further questions or require additional information, please contact Pharmacovigilance Department (AM Mangion Ltd.) on +356 2397 6000 or pv@ammangion.com

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system. 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 ADR Reporting Website:
www.medicines authority.gov.mt/adrportal

VELCADE

(bortezomib)

Please refer to Summary of Product Characteristics (SmPC) for further instructions