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Important Safety Information for Healthcare Professionals

Dilution, Dosing and Administration of Veltero (Bortezomib) 3.5 mg Powder for Injection

This document is approved by the Executive Directorate of Pharmacovigilance at SFDA

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Dilution, Dosing and Administration of

Veltero (Bortezomib) 3.5 mg Powder for Injection

Objectives: The educational material is essential to ensure the safe and effective use of the product and appropriate management of the Medication error.

Read carefully before prescribing/dispensing/administering the product.

Correct dilution for SC and IV Administration

Veltero (Bortezomib) 3.5 mg powder for injection is available for intravenous or subcutaneous administration.

- **Veltero (Bortezomib) 3.5 mg powder for injection is for subcutaneous or intravenous use only.**
- **Do not give by other routes.**
- **Intrathecal administration has resulted in death.**
- **For Subcutaneous injection and Intravenous injection dilution is necessary.**

Veltero (Bortezomib) must be diluted by a Healthcare Professional before being administered intravenously. Each vial of Veltero (Bortezomib) for Injection 3.5 mg for intravenous injection must be carefully diluted by using a syringe of the appropriate size, without removing the vial stopper. Aseptic technique must be strictly observed throughout the handling of Veltero (Bortezomib) since no preservative is present.

Avoiding the potential risk of administration errors

- In order to avoid dosing errors, caution is required when preparing Bortezomib as the volume required for reconstitution for the SC route (where required) is lower than that used for IV use giving a higher concentration of diluted drug.
- As the drug concentration after dilution differs between the SC and IV preparations, special care is required when calculating the volume of diluted drug, which will be delivered to the patient according to the prescribed dose. Please see below pages for examples of dosing for the different routes.

SUBCUTANEOUS ROUTE OF ADMINISTRATION

PREPARATION FOR SUBCUTANEOUS INJECTION

ASEPTIC TECHNIQUE MUST BE STRICTLY OBSERVED THROUGHOUT HANDLING OF BORTEZOMIB SINCE NO PRESERVATIVE IS PRESENT.

Preparation of the 3.5 mg vial: add 1.4 ml of sterile sodium chloride 9 mg/ml (0.9%) solution for injection to the vial containing Bortezomib powder for injection. dissolution of the lyophilized powder is completed in less than 2 minutes.

Table 1: Dilution of Veltero (Bortezomib) solution for SC injection			
Route of administration	**Pack size**	**Dilution volume**	**Final concentration**
Subcutaneous Use only	3.5 mg Powder for Injection	1.4 ml	2.5 mg/mL

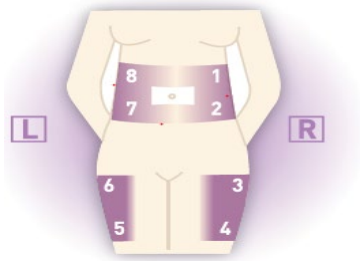
- Before administration, visually inspect the solution for particulate matter and discolouration.
- If any discolouration or particulate matter is observed, the solution should be discarded.
- Be sure that the final concentration is being given for the subcutaneous route of administration (2.5 mg/ml).

ADMINISTRATION

1. Withdraw the appropriate amount of the solution according to calculated dose based upon the patient's Body Surface Area (BSA).
2. Confirm the dose and concentration in the syringe prior to use (check that the syringe is marked as subcutaneous administration).
3. Inject the solution subcutaneously, under a 45-90° angle.
4. The solution is administered subcutaneously through the thighs (right or left) or abdomen (right or left).
5. Remind the patient to take the antiviral prophylaxis.

Alternate between (illustrations of the body sites to be injected)

- Right and left abdomen (upper or lower quadrant)
- Right and left thigh (proximal and distal sites)



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

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INTRAVENOUS ROUTE OF ADMINISTRATION

PREPARATION FOR INTRAVENOUS INJECTION

ASEPTIC TECHNIQUE MUST BE STRICTLY OBSERVED THROUGHOUT HANDLING OF VELTERO (BORTEZOMIB) SINCE NO PRESERVATIVE IS PRESENT.

- Preparation of the 3.5 mg vial: add 3.5 ml of sterile sodium chloride 9 mg/ml (0.9%) solution for injection to the vial containing Veltero (Bortezomib) powder for injection. dissolution of the lyophilized powder is completed in less than 2 minutes.

Table 1: Dilution of Veltero (Bortezomib) solution for IV injection

Route of administration	Pack size	Dilution volume	Final concentration
Intravenous use only	3.5mg Powder for Injection	3.5 ml	1.0 mg/ml

The concentration of the resulting solution will be 1 mg/ml

- The diluted solution will be clear and colourless
- Before administration, visually inspect the solution for particulate matter and discolouration.
- If any discolouration or particulate matter is observed, the solution should be discarded.
- Be sure that the final concentration is being given for the intravenous route of administration (1mg/ml).

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ADMINISTRATION

1. Once diluted, withdraw the appropriate amount of the diluted solution according to calculated dose based upon the patient's Body Surface Area.
2. Confirm the dose and concentration in the syringe prior to use (check that the syringe is marked as intravenous administration).
3. Inject the solution as 3-5 second bolus intravenous injection through a peripheral or central intravenous catheter into a vein.
4. Flush the peripheral or intravenous catheter with sterile, 9 mg/ml (0.9%) sodium chloride solution.
5. Remind the patient to take the antiviral prophylaxis.

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

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DOSING EXAMPLES FOR SC & IV ADMINISTRATION

Calculate the Body surface Area (BSA) based using the slide rule. Additional examples are provided with the dosing slide rule.

BSA: 1.7 m^2, Dose: 1.3 mg/m^2

Intravenous Sample Patient (1.7 m^2)	Subcutaneous Sample Patient (1.7 m^2)
Vial Size: 3.5 mg/1.4 ml Diluent Volume: 2.1 ml Saline	Vial Size: 3.5 mg/1.4 ml Diluent Volume: no dilution required
Final concentration 1 mg/ml	concentration 2.5 mg/ml
Dose: 1.3 mg/m^2 Total dose for patient: 2.21 mg	Dose: 1.3 mg/m^2 Total dose for patient: 2.21 mg
Total Volume* applied to the patient: 2.2 ml	Total Volume* applied to the patient: 0.9 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	

BSA: 1.9 m^2, Dose: 1.3 mg/m^2

Intravenous Sample Patient (1.95 m^2)	Subcutaneous Sample Patient (1.95 m^2)
Vial Size: 3.5 mg/1.4 ml Diluent Volume: 2.1 ml Saline	Vial Size: 3.5 mg/1.4 ml Diluent Volume: no dilution required
Final concentration 1 mg/ml	concentration 2.5 mg/ml
Dose: 1.3 mg/m^2 Total dose for patient: 2.54 mg	Dose: 1.3 mg/m^2 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 under dosed.	If the calculated SC volume is used with the IV concentration, the patient will be under dosed.

BSA: 1.6 m^2, Dose: 1.0 mg/m^2

Intravenous Sample Patient (1.6 m^2)	Subcutaneous Sample Patient (1.6 m^2)
Vial Size: 3.5 mg/1.4 ml Diluent Volume: 2.1 ml Saline	Vial Size: 3.5 mg/1.4 ml Diluent Volume: no dilution required
Final concentration 1 mg/ml	concentration 2.5 mg/ml
Dose: 1.0 mg/m^2 Total dose for patient: 1.6 mg	Dose: 1.0 mg/m^2 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 under dosed.

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GENERAL PRECAUTIONS

Note: Bortezomib is a cytotoxic agent. Therefore, caution should be used during handling and preparation. Use of gloves and other protective clothing to prevent skin contact is recommended.

Bortezomib as monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone is indicated for the treatment of adult patients with progressive multiple myeloma who have received at least 1 prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation.

Bortezomib in combination with melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.

Bortezomib in combination with dexamethasone, or with dexamethasone and thalidomide, is indicated for the induction treatment of adult patients with previously untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.

Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.

Special precautions for storage

- The product is preservative free and should be used immediately after withdrawal of the appropriate amount of solution. However, the chemical and physical in-use stability has been demonstrated for 8 hours at 25° C stored in the original vial and/or a polypropylene syringe.
- The total storage time for the medicinal product should not exceed 8 hours prior to administration.
- If the solution is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.
- During preparation for administration and during administration itself it is not necessary to protect the medicinal product from light.

Shelf life

Unopened vial: 24 months

In-use stability

- The diluted solution is preservative free and should be used immediately after preparation. However, the chemical and physical in-use stability has been demonstrated for 8 hours at 25° C stored in the original vial and/or a polypropylene syringe.
- The total storage time for the medicinal product should not exceed 8 hours prior to administration.
- If the solution is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.
- It is not necessary to protect the diluted medicinal product from light.

Disposal

A vial for single use only and the remaining solution must be discarded. Any unused product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.

Please refer to Summary of Product Characteristics (SPC) for further information

Reporting of side effects

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 Pharmacovigilance Centre
Saudi Food and Drug Authority
Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

Saudi Amarox contact details:
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