Important Safety Information

Reconstitution, Dosing and Administration of Bortada (BORTEZOMIB) 3.5 mg (Powder / Solution) Vial for Subcutaneous (SC) and Intravenous (IV) use

Correct Reconstitution

Objectives: The educational material is essential to ensure the safe and effective use of the product and appropriate management of the important selected risks. Read carefully before prescribing/ dispensing/administering the product.

Bortezomib is available in the following presentation forms for intravenous or subcutaneous administration:

- 3.5 mg powder for solution for injection
- 2.5 mg/ml solution for injection (3.5mg total content)

Subcutaneous or Intravenous use only

Do not give by other routes

Intrathecal administration has resulted in death

Where required, each vial of Bortezomib must be carefully reconstituted by a Health Care Professional using a syringe of the appropriate size, without removing the vial stopper. Aseptic technique must be strictly observed throughout the preparation because no preservative is present.

Please note that no reconstitution is required for Bortezomib 2.5mg/ml solution for injection vials when used for subcutaneous use only.

Avoiding the Potential Risk of Administration Errors

In order to avoid dosing errors, caution is required when preparing Bortezomib injection 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 reconstitution differs between the SC and IV preparations, special care is required when calculating the volume of reconstituted drug, which will be administered to the patient according to the prescribed dose.

Some examples of dosing for the different routes are given below.

Subcutaneous Route of Administration

Preparation of the 3.5 mg vial

*For **Bortezomib 3.5mg Powder for Solution for Injection**:*

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

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

*For **Bortezomib 2.5mg/ml Solution for Injection**:*

No reconstitution necessary.

Table 1: Reconstitution of Bortezomib solution for SC injection

Route of administration	Pack size	Reconstitution volume	Final concentration
Subcutaneous use only	3.5 mg **Powder**	**1.4 ml**	**2.5 mg/ml**
Subcutaneous use only	2.5mg/ml **Solution**	**n/a**	**2.5 mg/ml**

⇩ ⇧

Reconstitution volume is less than for IV, giving a more concentrated drug solution for injection

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

The final concentration for SC use is 2.5 mg/ml

The final drug concentration, when prepared 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.

For use, withdraw the appropriate amount of the drug solution: according to the 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

Intravenous Route of Administration

Preparation of the 3.5 mg vial

*For **Bortezomib 3.5mg Powder for Solution for Injection**:*

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

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

*For **Bortezomib 2.5mg/ml Solution for Injection**:*

Each 2.5mg/ml vial of Bortezomib must be reconstituted with 2.1 ml sterile sodium chloride 9 mg/ml (0.9%) solution for injection.

Reconstitute the solution with 2.1 ml sodium chloride: inject the sodium chloride solution into the vial containing the 2.5mg/ml Bortezomib solution.

Table 2: Reconstitution of Bortezomib solution for IV injection

Route of administration	Pack size	Reconstitution volume	Final concentration
Intravenous use only	3.5 mg **Powder**	**3.5 ml**	**1.0 mg/ml**
Intravenous use only	2.5mg/ml **Solution**	**2.1 ml**	**1.0 mg/ml**

⇩ ⇧

Reconstitution volume is more than 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 for IV use 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

Dosing Examples for SC & IV Administration

Calculate the Body Surface Area (BSA) 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)
3.5 mg Powder for Solution for Injection **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 3.5 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** 2.1 ml	***3.5 mg Powder for Solution for Injection*** **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 1.4 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** n/a
Final concentration **1 mg/ml**	**Final 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

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

Intravenous Sample patient (1.95 m^2)	**Subcutaneous** Sample patient (1.95 m^2)
3.5 mg Powder for Solution for Injection **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 3.5 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** 2.1 ml	***3.5 mg Powder for Solution for Injection*** **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 1.4 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** n/a
Final concentration **1 mg/ml**	**Final 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

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

Intravenous Sample patient (1.6 m^2)	**Subcutaneous** Sample patient (1.6 m^2)
3.5 mg Powder for Solution for Injection **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 3.5 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** 2.1 ml	***3.5 mg Powder for Solution for Injection*** **Vial size:** 3.5 mg (as lyophilisate) **Diluent volume:** 1.4 ml saline ***2.5 mg/ml Solution for Injection*** **Vial size:** 3.5 mg (as 2.5 mg/ml solution) **Diluent volume:** n/a
Final concentration **1 mg/ml**	**Final 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

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 about Bortezomib

General Precautions

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

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

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

Reconstituted/Final solution

Bortezomib is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

The reconstituted/final product is preservative free and should be used immediately after preparation. It is not necessary to protect the reconstituted medicinal product from light.

Correct Administration for SC & IV Bortezomib

How to administer Bortezomib 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.

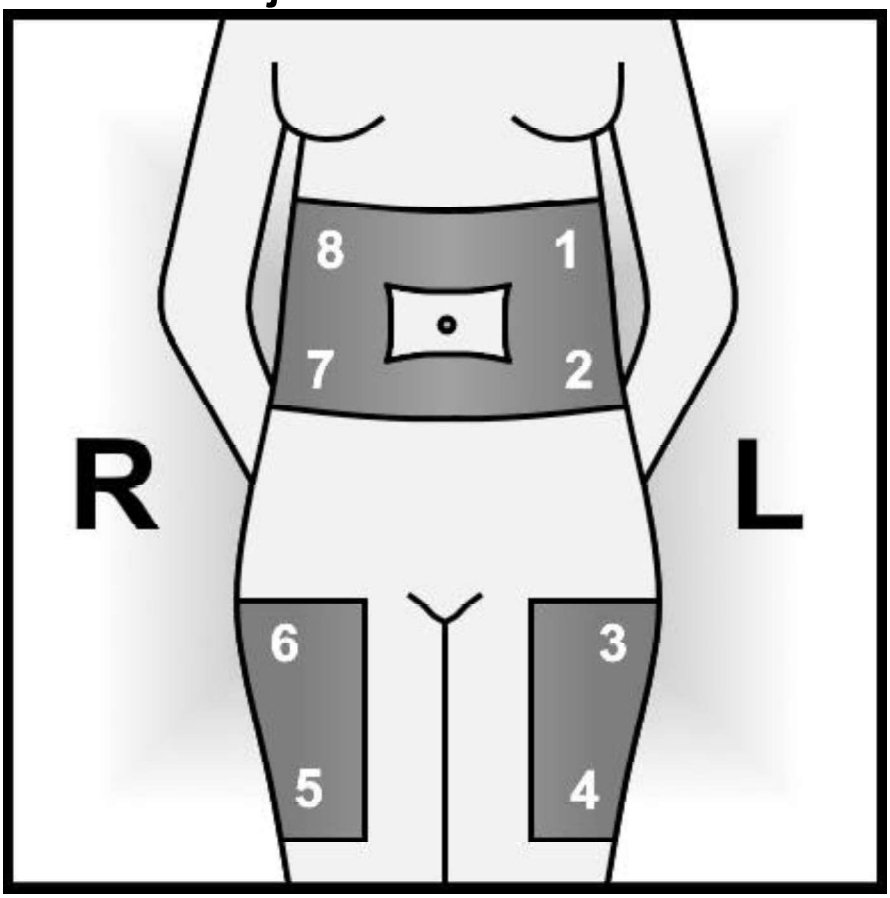
The reconstituted/final solution should be administered subcutaneously in the thighs or abdomen and injection sites should be rotated for successive injections.

- **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.

Injection site rotation



How to Administer Bortezomib 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. The use of IV hydration and an antiemetic medication as concomitant therapy prior to administration of IV Bortezomib is recommended.

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

Consider antiviral prophylaxis.

Please immediately report any adverse event experienced with the administration of Bortezomib

Reporting of suspected adverse reactions

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.

By reporting side effects you can help provide more information on the safety of this medicine.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your <doctor, health care provider, or pharmacist.
The National Pharmacovigilance Centre (NPC):
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa (Website: https://ade.sfda.gov.sa)
STADA QPPV : Alhanouf Alsunaytan
alhanouf.alsunaytan@stada.com
STADA OFFICE CO | Al-Batha District P.O. Box 708 |
Riyadh 11421 | Saudi Arabia

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