Risk Management Plan

Reconstitution, Dosing and Administration Booklet

Bortezomib SPC®

"BORTEZOMIB 3.5 mg powder for solution for injection"

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Reconstitution, Dosing and Administration Booklet

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

* Prescribing Information can be found within this document

Correct Reconstitution for SC and IV Administration

Bortezomib SPC 3.5 mg powder for solution for injection is available for intravenous or subcutaneous administration.

- Subcutaneous or Intravenous use only.
- Do not give by other routes.
- Intrathecal administration has resulted in death.
- Bortezomib SPC must be reconstituted by a Health Care Professional.
- Aseptic technique must be strictly observed throughout the handling of Bortezomib SPC since no preservative is present.

Avoiding the Potential Risk of Administration Errors

- In order to avoid dosing errors, caution is required when preparing Bortezomib SPC 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 5-6 for examples of dosing for the different routes.

Subcutaneous Route of Administration

Preparation of the 3.5 mg vial:

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

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

Table 1	**Reconstitution of Bortezomib SPC 3.5mg 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 colorless.
- The reconstituted solution must be inspected visually for particulate matter and discoloration prior to administration. If any discoloration 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.

Intravenous Route of Administration

Preparation of the 3.5 mg vial:

1. Each 3.5 mg vial of Bortezomib SPC must be reconstituted with 3.5 ml sterile sodium chloride 9 mg/ml (0.9 %) solution for injection – dissolution of the lyophilized powder is completed in less than 2 minutes.
2. Reconstitute the powder with 3.5 ml sodium chloride: inject the sodium chloride solution into the vial containing the lyophilized Bortezomib SPC.

Table 2	**Reconstitution of Bortezomib SPC 3.5mg solution for IV injection**		
Route of administration	Pack size	Reconstitution volume	Final concentration
Intravenous use only	**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.

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

* 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.

Intravenous Sample patient (1.7 m^2)	**Subcutaneous Sample patient (1.7 m^2)**
Vial size: 3.5 mg lyophilisate Diluent volume: 3.5 ml saline	Vial size: 3.5 mg lyophilisate Diluent volume: 1.4 ml saline
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

BSA: 1.95 m², Dose: 1.3 mg/m²

* 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.

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

BSA: 1.6 m², Dose: 1.0 mg/m²

* 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

Intravenous Sample patient (1.6 m²)	**Subcutaneous Sample patient (1.6 m²)**
Vial size: 3.5 mg lyophilizate Diluent volume: 3.5 ml saline	Vial size: 3.5 mg lyophilizate Diluent volume: 1.4 ml saline
Final concentration 1 mg/ml	Final concentration 2.5 mg/ml
Dose: 1.0 mg/m² Total dose for patient: 1.6 mg	Dose: 1.0 mg/m² 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

General Information

General Precautions:

- Bortezomib SPC is a cytotoxic agent. Therefore, caution should be applied when handling and preparing Bortezomib SPC. 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 SPC immediately.
- Subcutaneous or Intravenous use only. Do not give by other routes. Intrathecal administration has resulted in death.

Shelf life

2 Years.

Reconstituted Solution:

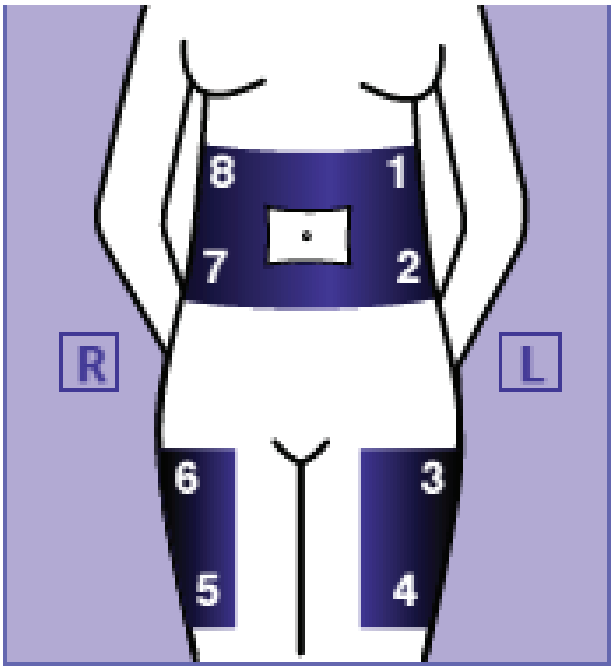
- Bortezomib SPC is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
- The reconstituted product is preservative free and should be used immediately after preparation. However, the chemical and physical in-use stability of 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 Bortezomib SPC®

How to administer Bortezomib SPC SC?

1. Confirm the dose in the syringe prior to use (check that the syringe is marked as SC administration).
2. Inject the solution subcutaneously, at a 45-90 °angle.
3. The reconstituted solution should be administered subcutaneously in the thighs or abdomen and injection sites should be rotated for successive injections.
4. Injections at the same site should be avoided
5. Alternate between
    - o Right and left abdomen (upper or lower quadrant)
    - o Right and left thigh (proximal and distal sites)

Figure1. Injection site rotation



Consider antiviral prophylaxis.

How to administer Bortezomib SPC IV?

[for bortezomib as mannitol boronic ester]

1. Confirm the dose in the syringe prior to use (check that the syringe is marked for IV administration).
2. 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 SPC is recommended.
3. Flush the peripheral or intravenous catheter with sterile 9 mg/ml (0.9 %) sodium chloride solution.
4. Consider antiviral prophylaxis.

- Please report any adverse event experienced with the administration of Bortezomib SPC IV or SC immediately.
- Please report any adverse event experienced with the administration of Bortezomib SPC IV or SC immediately.
- All the information within this booklet is referenced from the Bortezomib SPC SmPC (Reference safety information).

Information for Adverse Drug Reaction reporting:

The National Pharmacovigilance Centre (NPC)

Saudi Food and Drug Authority (SFDA)
SFDA call center: 19999
Toll free phone: 800 24 90000
Fax: +966-11- 205 7662
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/

Sudair Pharma Company (SPC)

Pharmacovigilance and Drug Safety Department
Toll phone: + 966 11 466 8193 **Ext.** 107
Fax: + (966) 11 466 8195
Mob: +(966) 56 738 6869
Email: Pharmacovigilance@SudairPharma.com
Website: www.sudairpharma.com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