Induction regimes prior to transplant:

Dosing and duration of treatment

VELCADE 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.

Posology for previously untreated multiple myeloma patients eligible for haematopoietic stem cell transplantation

Velcade in combination therapy with dexamethasone

VELCADE 3.5 mg powder for solution for injection is administered via intravenous or subcutaneous injection at the recommended dose of 1.3 mg/m^2 body surface area twice weekly for two weeks on days 1, 4, 8, and 11, followed by a 10-day rest period on days 12-21.

This 3-week period is considered a treatment cycle. Four VELCADE treatment cycles are administered. At least 72 hours should elapse between consecutive doses of VELCADE.

Dexamethasone is administered orally at 40 mg on days 1, 2, 3, 4 and days 8, 9, 10, 11 of the VELCADE treatment cycle (VELCADE® EU SmPC).

Vc+ Dx*	**Cycles 1 to 4****			
	Week	**1**	**2**	**3**
	Vc (1.3 mg/m^2)	Day 1, 4	Day 8, 11	Rest Period
	Dx 40 mg*	Day 1, 2, 3, 4	Day 8, 9, 10, 11	-

Vc=VELCADE; Dx=dexamethasone

*Dexamethasone is administered orally at 40 mg on days 1, 2, 3, 4 and 8, 9, 10, 11 of the VELCADE® treatment cycles.

****Up to 4 cycles**

Velcade in combination therapy with dexamethasone and thalidomide

VELCADE 3.5 mg powder for solution for injection is administered via intravenous or subcutaneous injection at the recommended dose of 1.3 mg/m^2 body surface area twice weekly for two weeks on days 1, 4, 8, and 11, followed by a 17-day rest period on days 12-28.

This 4-week period is considered a treatment cycle. Four VELCADE treatment cycles are administered. It is recommended that patients with at least partial response receive 2 additional cycles. At least 72 hours should elapse between consecutive doses of VELCADE.

Dexamethasone is administered orally at 40 mg on days 1, 2, 3, 4 and days 8, 9, 10, 11 of the VELCADE treatment cycles.

Thalidomide is administered orally at 50 mg daily on days 1-14 and **if tolerated the dose is increased to 100 mg on days 15-28, and thereafter may be further increased to 200 mg daily** (VELCADE® EU SmPC).

Vc+Dx*+T**	**Cycle 1**			
Week	**1**	**2**	**3**	**4**
Vc (1.3 mg/m^2)	Day 1, 4	Day 8, 11	Rest Period	Rest Period
T 50 mg	Daily	Daily	-	-
T 100 mg**	-	-	Daily	Daily
Dx 40 mg	Day 1, 2, 3, 4	Day 8, 9, 10, 11	-	-
Cycles 2 to 4* **				
Vc (1.3 mg/m^2)	Day 1, 4	Day 8, 11	Rest Period	Rest Period
T 200 mg**	Daily	Daily	Daily	Daily
Dx 40 mg	Day 1, 2, 3, 4	Day 8, 9, 10, 11	-	-

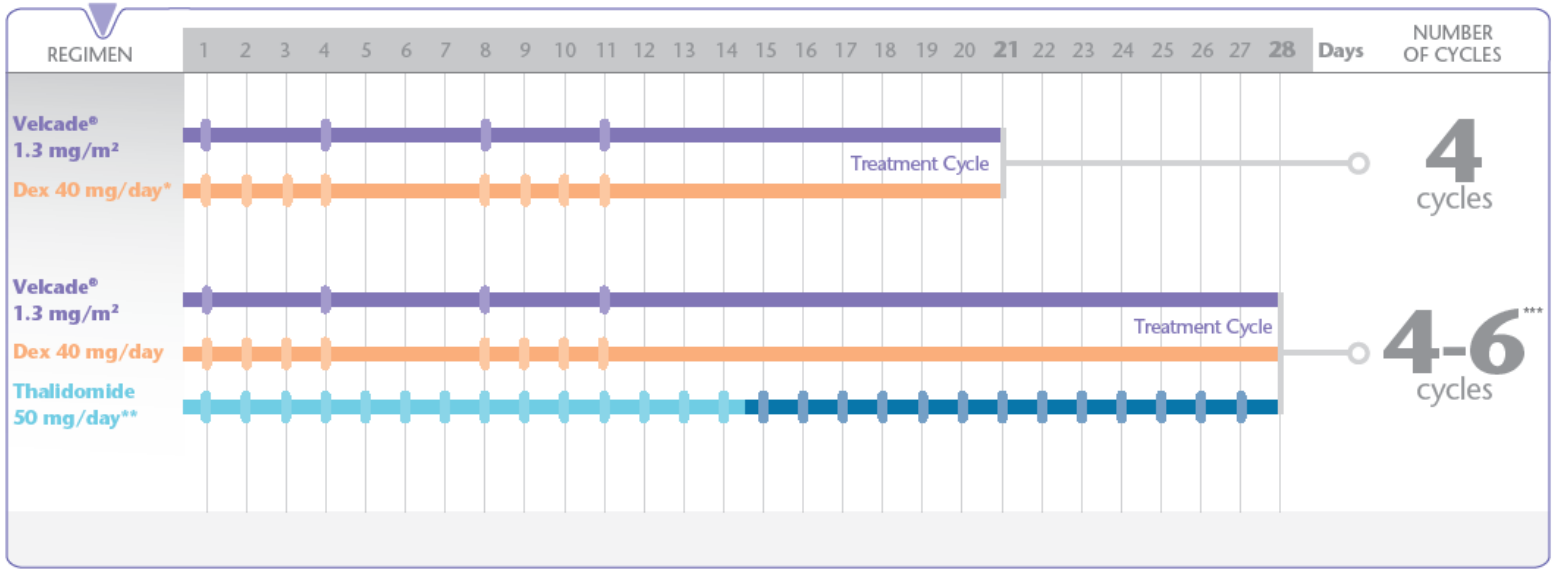
Vc=VELCADE; Dx=dexamethasone; T=thalidomide

*Dexamethasone is administered orally at 40 mg on days 1, 2, 3, 4 and 8, 9, 10, 11 of the VELCADE® treatment cycles.

****Thalidomide dose is increased to 100 mg from week 3 of Cycle 1 only if 50 mg is tolerated and to 200 mg from cycle 2 onwards if 100 mg is tolerated.**

*****Up to 6 cycles may be given to patients who achieve at least a partial response after 4 cycles**

Important Note: Patients receiving VELCADE® in combination with Thalidomide should adhere to the pregnancy prevention programme of Thalidomide. Refer to the SMPC of Thalidomide for additional information.



*Dexamethasone is administered orally at 40 mg on days 1, 2, 3, 4 and 8, 9, 10, 11 of the VELCADE® treatment cycles.

**Thalidomide dose is increased to 100 mg from week 3 of cycle 1 only if 50 mg is tolerated and to 200 mg from cycle 2 onwards if 100 mg is tolerated.

Patients receiving VELCADE® in combination with Thalidomide should adhere to the pregnancy prevention programme of Thalidomide. Refer to the SMPC of Thalidomide for additional information.

***Up to 6 cycles may be given to patients who achieve at least a partial response after 4 cycles.

Dosage adjustments for transplant eligible patients

For VELCADE dosage adjustments for neuropathy refer to the table below.
In addition, when VELCADE is given in combination with other chemotherapeutic medicinal products, appropriate dose reductions for these products should be considered in the event of toxicities according to the recommendations in the Summary of Product Characteristics.

Table 1: Recommended posology modifications for bortezomib-related neuropathy*

Severity of neuropathy	Posology modification
Grade 1 (asymptomatic; loss of deep tendon reflexes or paresthesia) with no pain or loss of function	None
Grade 1 with pain or Grade 2 (moderate symptoms; limiting instrumental Activities of Daily Living (ADL)**)	Reduce VELCADE to 1.0 mg/m^2 or Change VELCADE treatment schedule to 1.3 mg/m^2 once per week
Grade 2 with pain or Grade 3 (severe symptoms; limiting self-care ADL***)	Withhold VELCADE treatment until symptoms of toxicity have resolved. When toxicity resolves re-initiate VELCADE treatment and reduce dose to 0.7 mg/m^2 once per week.
Grade 4 (life-threatening consequences; urgent intervention indicated) and/or severe autonomic neuropathy	Discontinue VELCADE

* Based on posology modifications in Phase II and III multiple myeloma studies and post-marketing experience. Grading based on NCI Common Toxicity Criteria CTCAE v 4.0.
** *Instrumental ADL*: refers to preparing meals, shopping for groceries or clothes, using telephone, managing money, etc;
*** *Self care ADL*: refers to bathing, dressing and undressing, feeding self, using the toilet, taking medicinal products, and not bedridden.

Any suspected adverse drug reactions can be reported to:

Medicines Authority Post-Licensing Directorate, 203 Level 3, Rue D'Argens, Gzira GZR1368, Malta, or at http://medicinesauthority.gov.mt/adrportal

For more information contact:

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