

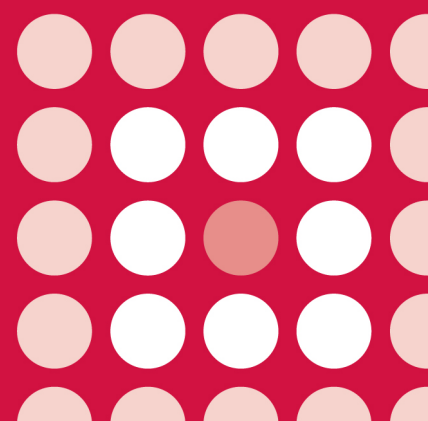


AWMSG SECRETARIAT ASSESSMENT REPORT

Bortezomib (Velcade®)
3.5 mg powder for solution for injection

Reference number: 1807

LIMITED SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics & Medicines Evaluation, Bangor University.

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AWMSG Secretariat Assessment Report
Bortezomib (Velcade®) 3.5 mg powder for solution for injection

This assessment report is based on evidence from a limited submission by Janssen-Cilag Ltd on 8 May 2014¹.

1.0 PRODUCT AND APPRAISAL DETAILS

Licensed indication under consideration	Bortezomib (Velcade®) 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 ² .
Dosing	<p>Bortezomib (Velcade®) 3.5 mg powder for solution for intravenous (IV) or subcutaneous (SC) injection is administered at a recommended dose of 1.3 mg/m² body surface area twice a week for two weeks on days 1, 4, 8 and 11 in a 21-day treatment cycle. At least 72 hours should elapse between consecutive doses.</p> <p>Dexamethasone is administered orally at a dose of 20 mg on days 1, 2, 4, 5, 8, 9, 11 and 12 of the 21-day treatment cycle. Patients achieving a response or a stable disease after four cycles of this combination therapy can continue to receive the same combination for a maximum of four additional cycles.</p> <p>Refer to the Summary of Product Characteristics (SPC) for further dosing information².</p>
Marketing authorisation date	18 December 2013 ³ (licensed for the treatment of patients with multiple myeloma who have received at least two prior therapies and have demonstrated disease progression on the last therapy on 26 April 2004) ^{2,4} .
Comparators	The comparator included in the company submission was bortezomib (Velcade®) monotherapy.
Limited submission details	<p>Bortezomib (Velcade®) for the above indication met the following criteria for eligibility for a limited submission:</p> <ul style="list-style-type: none"> • A minor licence extension. • Anticipated usage in NHS Wales is considered to be of minimal budgetary impact. • Estimated small difference in cost compared to comparator.

2.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

The All Wales Medicines Strategy Group (AWMSG) appraises a medicine within the whole of its licensed indication. However, the applicant company has requested that AWMSG considers bortezomib in combination with dexamethasone for the indication under consideration only and has not provided information in the submission for the use of bortezomib in combination with pegylated liposomal doxorubicin.

2.1 Matched pair analysis

In order to provide evidence in support of the use of bortezomib in combination with dexamethasone in relapsed or refractory multiple myeloma, the applicant company performed a matched pair analysis in which the outcomes of subjects treated with bortezomib in combination with dexamethasone from study MMY-2045 were compared to the outcomes of a systematically matched control group of subjects from the bortezomib monotherapy groups of the M34101-039 study¹.

The applicant company performed a sensitivity analysis using eight variables that were identified from a literature review as being related to clinical outcome in the matching algorithm: age, Eastern Cooperative Oncology Group (ECOG) score, myeloma type, percentage of plasma cells, prior dexamethasone, haemoglobin, creatinine clearance and albumin. Using this matching algorithm, 127 pairs were identified accounting for approximately 90% of patients participating in study MMY-2045^{1,5}.

The odds ratio of achieving a response for bortezomib in combination with dexamethasone versus bortezomib monotherapy was 3.769 (95% confidence interval [CI]: 2.045-6.947; $p < 0.001$). The addition of dexamethasone to bortezomib improved progression free survival (hazard ratio [HR]: 0.511; 95% CI: 0.309-0.845; $p = 0.008$) and time to progression (HR: 0.385; 95% CI: 0.212-0.698; $p = 0.001$) when compared to bortezomib monotherapy^{1,5}.

At the time of licensing, the Committee for Medicinal Products for Human Use (CHMP) confirmed that the adverse events observed with the combination treatment regimen was consistent with the known safety profile of each medicine administered in monotherapy⁵.

2.2 Points to note

- The company submission does not include any evidence for the use of bortezomib in combination with pegylated liposomal doxorubicin for the indication under consideration.
- In October 2007, the National Institute for Health and Care Excellence (NICE) recommended the use of bortezomib monotherapy as an option for the treatment of progressive multiple myeloma in patients who are at first-relapse having received one prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation⁶.
- In their submission, the applicant company highlighted that bortezomib in combination with dexamethasone is already used as standard clinical practice in Wales¹; this was confirmed by clinical expert opinion sought by AWTTTC.
- No direct comparison has been submitted between bortezomib monotherapy and bortezomib in combination with dexamethasone for this indication. However, supportive evidence was provided in a matched pair analysis based on appropriate covariate selection⁵.
- The overall survival (OS) data was not yet mature and the median OS had not been reached in either treatment arm^{1,5}.

3.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

3.1 Budget impact evidence

The company anticipates that all patients eligible for bortezomib monotherapy will be treated with bortezomib in combination with dexamethasone¹. The company-estimated number of eligible patients is based on UK prevalence data and the NICE costing template for bortezomib monotherapy^{6,7}. It is estimated that 38% of patients diagnosed with multiple myeloma each year in Wales will be at first-relapse following one prior

treatment and that 67% of these patients will be eligible for treatment with bortezomib monotherapy, and therefore bortezomib in combination with dexamethasone^{1,7}.

The budget impact figures provided by the company are based on the approved Department of Health Patient Access Scheme, where the manufacturer rebates the full cost of bortezomib for people who have less than a partial response after a maximum of four treatment cycles according to the Velcade[®] Response Scheme. The company assumes that 52% of patients respond to treatment after four cycles and that the remaining 48% do not respond, which is reflected in the budget impact estimates provided in Table 1^{1,7}.

Table 1. Incremental budget impact when using bortezomib in combination with dexamethasone instead of bortezomib monotherapy¹.

	Year 1	Year 2	Year 3	Year 4	Year 5
Total number of patients eligible for bortezomib in combination with dexamethasone	167	168	169	169	169
Budget impact with bortezomib in combination with dexamethasone	£2,132,220	£2,132,258	£2,156,731	£2,156,731	£2,156,731
Budget impact with bortezomib monotherapy	£2,122,466	£2,122,466	£2,146,862	£2,146,862	£2,146,862
Incremental budget impact	£9,754	£9,792	£9,869	£9,869	£9,869
*Costs are based on British National Formulary (BNF) list prices as of 20 June 2014 ⁸ ; figures are based on medicine acquisition costs only.					

3.1.1 AWTC critique

- The UK sources used for estimating prevalence, incidence and the proportion of patients eligible to receive treatment for the indication under consideration seems reasonable, although it is recognised that they do not specifically relate to Welsh data.
- As bortezomib in combination with dexamethasone is already considered standard clinical practice and is used in Wales, the applicant company expects the budgetary impact to be smaller than estimated¹.

3.2 Comparative unit costs

Table 2 provides an example of the comparative acquisition costs for bortezomib in combination with dexamethasone and bortezomib monotherapy. Bortezomib is individually dosed according to patient surface area (1.3 mg/m²); therefore, Table 2 is based on the cost of one 3.5 mg vial per dose of bortezomib.

Table 2. Example of acquisition costs for bortezomib in combination with dexamethasone and comparator for the treatment of progressive multiple myeloma in adult patients.

Product	Example regimen*	Cost per year†
bortezomib (Velcade®) 3.5 mg powder for solution for IV or SC injection	<u>Adult patients (male and female ≥ 18 years of age):</u> 1.3 mg/m ² twice weekly on days 1, 4, 8 and 11 of each 21-day cycle	£24,396 for eight cycles
bortezomib (Velcade®) 3.5 mg powder for solution for IV or SC injection in combination with dexamethasone 2 mg tablets	<u>Adult patients (male and female ≥ 18 years of age):</u> 1.3 mg/m ² twice weekly on days 1, 4, 8 and 11 plus dexamethasone 20 mg daily on days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle	£24,473 for eight cycles
*Based on SPC dosing instructions ² †Costs are based on BNF list prices as of 20 June 2014 ³ .		

4.0 ADDITIONAL INFORMATION

4.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, bortezomib (Velcade®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company do not anticipate that bortezomib (Velcade®) will be supplied by a home healthcare provider.

4.2 AWMSG review

This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

4.3 Evidence search

Date of evidence search: 9 June 2014

Date range of evidence search: No date limits were applied to database searches.

REFERENCES

- 1 Janssen-Cilag Ltd. Form C: Limited appraisal submission. Bortezomib (Velcade®). 2014.
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