PUBLIC SUMMARY DOCUMENT
Product: BORTEZOMIB, powder for injection, 1 mg (solvent required), Velcade®
Sponsor: Janssen-Cilag Pty Ltd
Date of PBAC Consideration: July 2011

1. Purpose of Application

The re-submission requested listing of a new strength as an Authority required listing for treatment of a patient with newly diagnosed symptomatic multiple myeloma (MM) who has severe acute renal failure who meets certain criteria.

2. Background

At the March 2011 meeting, the PBAC deferred a submission requesting listing of a new strength of bortezomib as an Authority required listing for the first-line treatment of multiple myeloma in patients newly diagnosed who have severe renal failure or in patients treated with thalidomide who have a resultant GFR drop to less than or equal to 30 mL/minute to enable discussion with clinicians and the sponsor regarding eligibility criteria for first-line use in a patient with acute renal failure whose GFR is falling and where a renal physician would consider the patient at risk of requiring dialysis, so that those with the greatest clinical need will have access to PBS-subsidised bortezomib.

A Public Summary Document (PSD) from the March 2011 PBAC meeting is available at: http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-bortezomib-march11

3. Registration Status

Bortezomib powder for injection 1 mg was TGA registered on 1 June 2009. The approved indications are:

- Treatment, in combination with melphalan and prednisone, of patients with previously untreated multiple myeloma, who are not suitable for high dose chemotherapy;
- Treatment of multiple myeloma patients who have received at least one prior therapy, and who have progressive disease.

4. Listing Requested and PBAC's View

Authority required

Initial PBS-subsidised treatment, in combination with a corticosteroid or in combination with a corticosteroid and melphalan or cyclophosphamide, of a patient with newly diagnosed symptomatic multiple myeloma who has severe acute renal failure. Patients must require dialysis or be at high risk of requiring dialysis in the opinion of a nephrologist.

Note

Patients who have initiated treatment with thalidomide within the last month do not have to experience failure after a trial of at least 4 weeks of thalidomide or to have failed to achieve at least a minimal response after at least 8 weeks of thalidomide treatment.

The authority application must be made in writing and must include:

(1) a completed authority prescription form; and
(2) a completed Multiple Myeloma Authority Application – Supporting Information Form, which includes details of the histological diagnosis of multiple myeloma, the name of the nephrologist who has reviewed the patient and the date of review, and a

copy of the current pathology reports reporting Glomerular Filtration Rate from an Approved Pathology Authority; and

(3) a signed patient acknowledgement.

Maximum quantity: 12
Repeats: 7

Authority required
Continuing PBS-subsidised treatment in combination with a corticosteroid or in combination with a corticosteroid and melphalan or cyclophosphamide, of a patient with newly diagnosed symptomatic multiple myeloma who has severe acute renal failure and who has received an initial authority prescription for bortezomib and who, at the time of application has demonstrated at least a partial response at the completion of cycle 4.

Maximum quantity: 12
Repeats: 4

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Multiple myeloma is a cancer of plasma cells. It is a progressive haematological disease, which is incurable. Common clinical manifestations include hypercalcaemia, anaemia, renal damage, increased susceptibility to bacterial infection and impaired production of normal immunoglobulin. Diffuse osteoporosis, usually in the pelvis, spine, ribs and skull is also usually characteristic of MM.

Bortezomib is proposed as an alternative to thalidomide as a first-line treatment for MM in patients with renal failure or for patients who develop renal failure whilst being treated with thalidomide.

6. Clinical Trials

No new clinical data were presented in the re-submission.

7. Summary of Submission

The re-submission presented a revised estimate of the proportion of newly diagnosed multiple myeloma patients with renal failure severe enough to require dialysis at the time of diagnosis, of 10% (compared with more than 15% in the previous submission) where renal impairment was defined as a glomerular filtration rate (GFR) of 30 mL/minute or less.

8. Economic Analysis

The re-submission did not contain an economic analysis.

9. Estimated PBS Usage and Financial Implications

The submission presented a revised estimate of usage and financial implications, based upon the model used in the March 2011 submission, assuming 10% of patients with newly diagnosed multiple myeloma would have severe renal impairment, and be eligible for treatment under the revised restriction.

The likely number of patients per year was estimated in the re-submission to be less than 10,000 in year 5 (fewer compared with the previous submission), at a net cost per year to the PBS/RPBS (excluding co-payments) of less than $10 million in year 5 (lower compared with the previous submission).

For PBAC's view, see Recommendation and Reasons.

10. Recommendation and Reasons

The PBAC recommended the listing of bortezomib for initial treatment of multiple myeloma in newly diagnosed patients with symptomatic multiple myeloma who have severe acute renal failure on the basis of acceptable cost-effectiveness in patients with a high clinical need and in whom the currently available treatment is often inadequate. Patients must require dialysis or be at high risk of requiring dialysis in the opinion of a nephrologist.

The PBAC noted that the submission's claim that 10% of newly diagnosed patients would qualify to receive treatment with bortezomib under the restriction agreed with clinician advice. The PBAC considered the re-submission's estimate of eligible patients to be an overestimate and noted that according to the literature, an estimate of 2% would be more reasonable. However, the PBAC was advised that for every patient on dialysis, there would be 2-3 more patients at risk. The PBAC recommended that the Department enter into a risk share arrangement with the sponsor.

The PBAC also recommended that the DUSC should provide a report on prescribing of bortezomib as first line therapy 12 months after listing.

The PBAC noted the consumer comments received in its consideration of bortezomib.

The PBAC recommended that bortezomib is not suitable for inclusion in the PBS medicines for prescribing by nurse practitioners.

Recommendation:

BORTEZOMIB, powder for injection 1 mg (solvent required)

Restriction:	Note Any queries concerning the arrangements to prescribe bortezomib may be directed to Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms) is available on the Medicare Australia website at www.medicareaustralia.gov.au. Applications for authority to prescribe bortezomib should be forwarded to: Medicare Australia Prior Written Approval of Specialised Drugs Reply Paid 9826

GPO Box 9826
HOBART TAS 7001

Special Pricing Arrangements apply.

Authority required
Initial PBS-subsidised treatment, in combination with a corticosteroid and/or cyclophosphamide, of a patient with newly diagnosed symptomatic multiple myeloma who has severe acute renal failure. Patients must require dialysis or be at high risk of requiring dialysis in the opinion of a nephrologist.

Note
Patients who have initiated treatment with thalidomide within the last month do not have to experience failure after a trial of at least 4 weeks of thalidomide or to have failed to achieve at least a minimal response after at least 8 weeks of thalidomide treatment.

The authority application must be made in writing and must include:
(1) a completed authority prescription form; and
(2) a completed Multiple Myeloma Authority Application – Supporting Information Form, which includes details of the histological diagnosis of multiple myeloma, the name of the nephrologist who has reviewed the patient and the date of review, and a copy of the current pathology reports reporting Glomerular Filtration Rate from an Approved Pathology Authority; and
(3) a signed patient acknowledgement.

To enable confirmation by Medicare Australia, current diagnostic reports of at least one of the following are required:
(a) the level of serum monoclonal protein; or
(b) Bence-Jones proteinuria — the results of 24-hour urinary light chain M protein excretion; or
(c) the serum level of free kappa and lambda light chains.

No applications for increased maximum quantities and/or repeats will be authorised.

Maximum quantity	12
No. of Repeats	7

Authority required
Continuing PBS-subsidised treatment in combination with a corticosteroid and/or cyclophosphamide, of a patient with newly diagnosed symptomatic multiple myeloma who has severe acute renal failure and who has received an initial authority prescription for bortezomib and who, at the time of application has demonstrated at least a partial response at the completion of cycle 4.

Authority applications for continuing treatment may be made by telephone to Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Continuing PBS-subsidised supply will not be approved if there is a gap of more than 6 months between the initial application and this application.

Further applications for continuing PBS-subsidised bortezomib will not be approved after this application.

No applications for increased maximum quantities and/or repeats will be authorised.

Maximum quantity	12
No. of Repeats	4

11. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

12. Sponsor's Comment

Patients with newly diagnosed symptomatic multiple myeloma who have severe acute renal failure are a subset of newly diagnosed symptomatic multiple myeloma patients who are not suitable for high dose chemotherapy as a result of their renal failure. At its July 2009 meeting, the PBAC recommended the listing of bortezomib for the treatment of patients with newly diagnosed symptomatic multiple myeloma who are not eligible for high dose chemotherapy, however, the listing was not actioned by Janssen. For further details, refer to the Public Summary Document at: http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-Bortezomib-jul09. Janssen has now decided to proceed with the listing.