PUBLIC SUMMARY DOCUMENT

Product: Bortezomib, powder for injection, 3.5 mg, Velcade®

Sponsor: Janssen-Cilag Pty Ltd

Date of PBAC Consideration: July 2007

1. Purpose of Application

The submission requested an authority required PBS listing for initial and continuing treatment of multiple myeloma patients who have failed specified other therapy, have undergone or are ineligible for a primary stem cell transplant and who meet certain criteria.

2. Background

At the March 2006 meeting, the PBAC rejected a submission for an authority required listing for patients with multiple myeloma (MM) who met certain criteria because of uncertain clinical benefit over the mix of comparators and uncertain, but unacceptable cost effectiveness. *(See also Public Summary for March 2006).*

At the November 2006 meeting, the PBAC again rejected a submission for an authority required listing. Uncertain and unacceptable cost effectiveness was the primary reason for rejection. *(See also Public Summary for November 2006).*

At its March 2007 meeting, the PBAC considered expert advice that allogeneic stem cell transplant (SCT) was an appropriate third line treatment for a limited number of younger patients. However, the PBAC noted variations in clinical practice on the use of bortezomib and mini-alloSCT and concluded that there was divergent clinical opinion on this matter. Thus, the extent of substitution remained unresolved. The PBAC agreed the application be deferred to allow the sponsor to present a revised version of the modelled economic evaluation. *(N.B. There is no Public Summary for the March 2007 consideration).*

3. Registration Status

Bortezomib was registered by the TGA on 8 February 2006 for the 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

The PBAC made a number of recommendations for the restriction wording, including:

- that eligibility for continuing criteria be determined at the end of cycle 4 and cycle 8;
- that the eligibility criteria for partial response should be:
  - if serum or urinary M protein are measurable (secretory multiple myeloma) by a ≥ 50% reduction in the level of serum M protein (monoclonal protein), or a ≥ 90% reduction in 24 hour urinary light chain M-protein excretion or < 200 mg per 24 hours;
  - in patients in whom serum and urine M-protein levels are unmeasurable (non-secretory/oligosecretory multiple myeloma) by the difference between involved and uninvolved free light chain (FLC) levels with ≥ 50% reduction;
  - in patients in whom serum and urine M-protein levels and FLC levels are unmeasurable, by ≥ 50% reduction in plasma sells, provided baseline measurement

was ≥ 30%, or normalisation of corrected serum calcium to ≤ 2.65 mmol/L, or no increase in the size or number of lytic bone lesions (development of compression fracture does not exclude a response), or ≥ 50% reduction in the size of soft tissue plasmacytomas, or stabilisation or improvement in serum creatinine clearance;

- that no more than 11 cycles of treatment be authorised;
- where a confirmed complete response is achieved, no more than two additional cycles are administered beyond a confirmation; and
- that physicians be required to nominate the eligibility criterion for determining response in individual patients at the time of seeking approval for initial treatment.

5. Clinical Place for the Proposed Therapy

Multiple myeloma (MM) is currently incurable. In Australia, more than 1,400 new cases are diagnosed annually. After initial treatments fail, effective treatment options are limited and resistance to conventional chemotherapy develops.

Bortezomib will be used in patients who have a good performance status following failure of the standard first and second line agents.

Current third-line therapies include IV chemotherapy and high dose therapy/autologous stem cell transplant and mini - allogeneic transplant.

6. Comparator

There was no change to the comparator nominated previously.

7. Clinical Trials

There is no change to the information reported in the November 2006 Public Summary Document.

8. Results of Trials

There is no change to the information reported in the November 2006 Public Summary Document.

9. Clinical Claim

There is no change to the information reported in the November 2006 Public Summary Document.

10. Economic Analysis

The re-submission presented revised cost-effectiveness analyses. Revised results were obtained by:

i) Varying the cost-offsets for mini-alloSCT by modelling different substitution rates.;
ii) Varying the duration of comparative treatment benefit (measured as survival); and varying the time to death (or time horizon) of the model.
iii) Updated financial estimates on the PBS were also provided.

See Recommendation and Reasons for PBAC's views.

11. Estimated PBS Usage and Financial Implications

The re-submission estimated the net cost associated with a PBS listing for bortezomib to be less than $10 million per year in each of the first four years of PBS subsidy.

12. Recommendation and Reasons

The PBAC recommended the listing of bortezomib on the PBS for the treatment of multiple myeloma for patients who meet certain criteria on the basis of acceptable cost-effectiveness when compared to a mixture of salvage treatments and where the extent of substitution from mini-allogeneic transplants is zero. The PBAC noted the incremental cost effectiveness ratios per quality adjusted life year varied based on plausible assumptions about survival and extrapolation of treatment benefit all fell within the range $45,000 to $75,000. The PBAC noted that the sponsor proposed a special supply arrangement for bortezomib.

The data included in the submission provided greater certainty around the cost-effectiveness ratios than previously. The PBAC acknowledged that the place of mini-allogeneic transplants in clinical practice varied across Australia. Given the uncertainty on this point, the PBAC used the sensitivity analysis that assumed the cost offset from mini-allogeneic transplant was zero.

Recommendation

BORTEZOMIB, powder for injection, 3.5 mg

Restriction: **Please see www.pbs.gov.au for the finalised restriction.**

13. 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.

14. Sponsor's Comment

Janssen-Cilag welcomes this decision by the PBAC to provide access to a new treatment option for Australian multiple myeloma patients who have failed standard 1st and 2nd line treatments. Janssen-Cilag is committed to ongoing interaction with the Pharmaceutical Evaluation Branch and clinicians to ensure the restriction provides access to bortezomib for patients for whom the PBAC has considered it is cost effective.