PUBLIC SUMMARY DOCUMENT
Product: Bevacizumab, solution for I.V. infusion, 100 mg in 4 mL, 400 mg in 16 mL, Avastin®
Sponsor: Roche Products Pty Ltd
Date of PBAC Consideration: July 2008

1. Purpose of Application
The submission sought a Section 100 (Special Authority Program) listing for the treatment of metastatic colorectal cancer in patients previously untreated.

2. Background
At the March 2008 meeting, the PBAC rejected a submission for a section 100 listing for bevacizumab for the treatment of patients with previously untreated colorectal cancer, and for patients with disease progression following first-line treatment which includes bevacizumab, on the grounds of an unacceptably high cost effectiveness ratio in first line setting only and an unacceptably high and uncertain cost-effectiveness ratio in combined first and second line use, and noting the high overall cost to Government should listing proceed.
(See PBAC Public Summary Document - March 2008)

3. Registration Status
Bevacizumab was registered by the TGA on 2 February 2005 for use in combination with fluorouracil, folinic acid and irinotecan or fluorouracil and folinic acid, for the treatment of patients with metastatic colorectal cancer.

4. Listing Requested and PBAC's View
SPECIAL AUTHORITY PROGRAM
Section 100 Authority Required
Initial treatment of metastatic colorectal cancer in previously untreated patients with a WHO performance status of 0 or 1 in combination with chemotherapy.
Note: Not for use as monotherapy.

Section 100 Authority Required
Continuing PBS-subsidised treatment with bevacizumab plus chemotherapy in a patient with metastatic colorectal cancer who has previously been issued with an authority prescription for bevacizumab and who does not have progressive disease.
Note: Not for use as monotherapy.

Section 100 Authority Required
Initial PBS-subsidised treatment of metastatic colorectal cancer in a patient with a WHO performance status of 0 or 1 in combination with chemotherapy:
(1) who had received treatment with bevacizumab prior to the DATE OF PBS LISTING
(2) who does not have progressive disease.
Note: Not for use as monotherapy.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy
Bevacizumab would provide additional treatment for patients with previously untreated metastatic colorectal cancer.

6. Comparator
Reported in the March 2008 PBAC Public Summary Document.

7. Clinical Trials
Reported in the March 2008 PBAC Public Summary Document.

8. Results of Trials
Reported in the March 2008 PBAC Public Summary Document.

9. Clinical Claim
Reported in the March 2008 PBAC Public Summary Document.

10. Economic Analysis
The submission addressed the main matters of concern to the PBAC at the March 2008 meeting by restricting use to the first line setting and by providing an updated stepped cost-effectiveness analysis of bevacizumab.

The submission stated that no changes had been made to the structure of the economic model, compared with the March 2008 submission.

The modelled economic evaluation estimated the ICER to be in the range of $45,000 - $75,000 per quality adjusted life year (QALY) gained assuming either section 100 or section 85 listing.

For PBAC's view, see Recommendation and Reasons.

11. Estimated PBS Usage and Financial Implications
The submission estimated the total number of patients associated with first-line use to be between 10,000 – 50,000.

The total cost to PBS was estimated to be more than $100 million (using either section 100 or section 85 prices) over 5 years.

12. Recommendation and Reasons
The PBAC noted the following changes to the economic model considered at the March 2008 meeting: a price decrease, use in the first-line setting alone, the costs of urinalysis and of treating adverse events reimbursed by the sponsor, no use beyond progression in the first line setting, a 5 year time horizon, a different utility value associated with progressive disease of 0.6, removal of drug wastage from the calculations, adjustment factors to calibrate the model against the trial results. These changes to the model variable resulted in a new base case incremental cost effectiveness ratio per quality adjusted life year calculated in the range of $45,000 - $75,000 (using either section 100 or section 85 prices).

The PBAC considered that the addition of bevacizumab to first line chemotherapy in metastatic colorectal cancer results in clinically meaningful improvements in survival. The economic model is robust and although the cost effectiveness ratios are high and depend upon whether supply is through section 100 or section 85, the only uncertainty in these estimates arises from the lack of clarity as to whether the 2008-09 Chemotherapy Budget Measure

which is aimed at eliminating drug wastage, will apply to all bevacizumab dispensed. If the March 2008 pre-sub-committee response estimates of wastage are used, the ICER will increase, the cost dependent upon whether listing is enacted through section 100 or section 85, respectively.

The PBAC considered that a section 85 listing was more appropriate for bevacizumab, noting that with a section 85 listing, bevacizumab would also be eligible for inclusion in section 100 CPAP. A section 100 listing would take longer to implement due to difficulties in setting up a new program to administer bevacizumab (as it is not eligible for inclusion in the Highly Specialised Drugs Program).

Taking these factors into account, PBAC considered that the true base case ICER would fall in the range of $45,000 – $75,000 (assuming all drug is supplied through section 100 CPAP and all wastage is eliminated) and in the range of $75,000 - $105,000 (assuming all drug is supplied though section 85 and that wastage is not eliminated).

The Committee recommended that the PBS restriction for bevacizumab limit treatment to use in combination with first line chemotherapy alone. Subsidy should cease upon progressive disease or upon any change to first-line chemotherapy. No provision should be made to grandfather patients receiving bevacizumab currently, as any grandfathering would be associated with an unacceptable risk of use outside the recommended conditions of PBS-subsidy.

The PBAC recommended that a risk share arrangement be developed.

Finally, the Committee requested that the Government be advised that the total cost of subsidising bevacizumab for first line use in metastatic colorectal cancer is very high at an estimated cost of greater than $100 million over 5 years.

Recommendation

Authority required
Initial PBS-subsidised treatment, in combination with first-line chemotherapy, of a patient with previously untreated metastatic colorectal cancer with a WHO performance status of 0 or 1.
NOTE: Not for use as monotherapy.

Authority Required
Continuing PBS-subsidised treatment, in combination with first-line chemotherapy, of a patient with metastatic colorectal cancer who has previously been issued with an authority prescription for bevacizumab and who does not have progressive disease and who remains on first line chemotherapy.

NOTE: Not for use as monotherapy.

Maximum quantity: 1 (both strengths)
Repeats: Nil (both strengths)

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

Roche is very pleased with the decision of the PBAC and will work in collaboration with the Government to ensure that eligible patients with metastatic colorectal cancer have access to bevacizumab in a timely manner.